Supporting Information

Towards the synthesis of Calotropin and related Cardenolides from 3-Epiandrosterone: A-ring related modifications

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Contents

1. General remarks

NMR spectra were recorded on a *Bruker* Avance 300, *Bruker* Avance 400, *Bruker* Avance 500 DRX 500 or *Bruker* Avance 600 spectrometer as solutions at room temperature. Chemical shifts δ are expressed in parts per million (ppm) and referenced to the residual solvent peak of chloroform (^{1}H: δ = 7.26 ppm; ^{13}C: δ = 77.2 ppm). All coupling constants (*J*) are absolute values and are expressed in Hertz (Hz). The description of signals includes: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, dd = doublet of doublets and ddd = double doublet of doublets and so forth. The spectra were analyzed according to first order. The assignments of the signal structure in ^{1}H NMR were made by the interpretation of the multiplicity and chemical shifts including the usage of calculation based on increments as well as 2D-experiments such as COSY (correlation spectroscopy), HSQC (Heteronuclear single-quantum correlation spectroscopy), HMBC (Heteronuclear multiple-bond correlation spectroscopy) and NOESY (Nuclear Overhauser effect spectroscopy). In addition to these methods, the assignments for ^{13}C NMR were based on the evaluation by DEPT 90- and DEPT 135-spectra (DEPT = distortionless enhancement by polarization transfer) and are described as follows: + = primary or tertiary C-atom (positive DEPT-signal), – = secondary C-atom (negative signal) and C_q = quaternary C-atom (no signal). Since the O*H* at C-3 of the steroidal framework is not always visible in the ^{1}H NMR spectrum, the sum of H-atoms does not add up to the number of H atoms in the sum formula.

IR spectra were recorded on a FT-IR *Bruker* IFS 88 spectrometer. The compounds were measured either between KBr plates or as pure substances by ATR technique (ATR = attenuated total reflection). The position of the absorption band is given in wave numbers $\tilde{\nu}$ in cm^{-1}. The intensities of the bands were characterized as follows:
vs = very strong (0–20% T), s = strong (21–40% T), m = medium (41–60% T), w = weak (61–80% T), vw = very weak (81–100% T), br = broad.

Mass spectra were measured by EI-MS (electron impact mass spectrometry) and FAB-MS (fast atom bombardment mass spectrometry) and were recorded on a *Finnigan MAT 95*. The peaks are given as mass-to-charge-ratio (*m*/*z*). For the EI-MS spectra, the molecule peak is given as $[M]^{\bullet+}$ and characteristic fragment peaks are given as $[M - \text{fragment}]^+$ or $[\text{fragment}]^+$; for the FAB-MS spectra, the molecule peak is given as $[M]^+$, $[M+H]^+$ or $[M-H]^+$. The signal intensities are given in percent, relatively to the intensity of the base signal (100%). For the high resolution mass, the following abbreviations were used: calc.: calculated data; found: measured data.

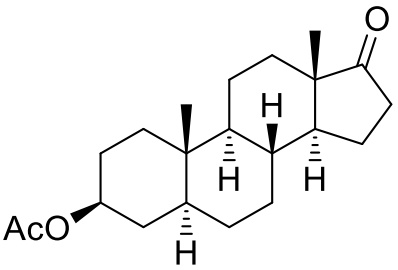
Analytical thin layer chromatography (TLC) was carried out on Merck silica gel coated aluminum plates (silica gel 60, F_{254}), detected under UV-light at 254 nm or stained with "Seebach staining solution" (mixture of molybdato phosphoric acid, cerium(IV)-sulfate tetrahydrate, sulfuric acid and water). Solvent mixtures are understood as volume/volume. Solvents, reagents and chemicals were purchased from *Sigma-Aldrich*, *abcr*, *Thermo Fisher Scientific*, *TCI*, *ChemPur* and *Acros Organics*. All solvents, reagents and chemicals were used as purchased unless stated otherwise.

Air- or moisture-sensitive reactions were carried out under argon atmosphere in oven-dried and previously evacuated glass ware. Liquids were transferred with plastic syringes and steel cannula. Reaction control was performed by thin layer chromatography. If not stated otherwise, crude products were purified by flash chromatography by the procedure of Still.[1] Silica gel 60 (0.040 × 0.063 mm, Geduran®, Merck) was used as stationary phase and as mobile phase, solvents of *p.a.* quality were used.

2. Experimental procedures and analytical data

2.1 Experimental procedures for the synthesis of 3*β*-acetoxy-5*α*-androstane-2*β*-ol derivatives using the first generation approach (Scheme 3)

3*β*-Acetoxy-5*α*-androstane-17-on (**SI-01**)[2]

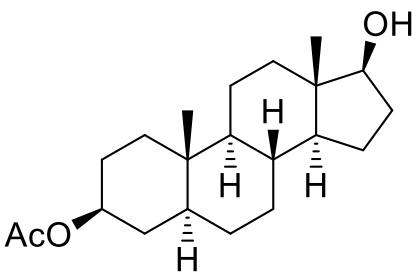


Under argon atmosphere, e*pi*-androsterone (**12**) (662 mg, 2.28 mmol, 1.00 equiv) was dissolved in acetic anhydride (2.0 mL) and pyridine (0.37 mL, 4.56 mmol, 2.00 equiv). The suspension was stirred overnight at r.t. while the suspension cleared off. The mixture was carefully poured into a saturated aqueous solution of $NaHCO_3$ (50 mL), ethyl acetate (50 mL) was added and the mixture was stirred for 30 minutes. The phases were separated and the aqueous phase was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na_2SO_4 and after filtration the solvent was evaporated. The residue was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) to afford the title compound **SI-01** (745 mg, 2.24 mmol, 98%) as a colorless solid.

R_f = 0.35 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.67 (dddd, ^3J = 11.0, 11.0, 4.9, 4.9 Hz, 1H, C*H*OAc), 2.41 (dd, ^2J = 19.3 Hz, ^3J = 8.8 Hz, 1H, 16-CH_2^a), 2.05 (dd, ^2J = 19.3 Hz, ^3J = 8.8 Hz, 1H, 16-CH_2^b), 2.00 (s, 3H, COCH_3), 1.96–1.91 (m, 1H, CH_2), 1.82 – 1.66 (m, 4H, 3 different CH_2), 1.66–1.59 (m, 2H, CH_2), 1.57–1.47 (m, 3H, 2 different CH_2 + 8-C*H*), 1.41–1.19 (m, 7H, 4 different CH_2, C*H* + 5-C*H*), 1.06–0.91 (m, 2H, CH_2) 0.84 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 0.72 (td, ^3J = 11.4, 4.1 Hz, 1H, C*H*). – **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 221.3 (17-C_qO), 170.8 (C_qOAc), 73.6 (+, 3-*C*HOAc), 54.4 (+, *C*H), 51.5 (+, *C*H), 47.9 (13-C_q), 44.8 (+, 5-*C*H), 36.8 (–, *C*H_2), 36.0 (–, 16-*C*H_2), 35.8 (10-C_q), 35.2 (+, 8-*C*H), 34.1 (–, *C*H_2), 31.7 (–, *C*H_2), 30.9 (–, *C*H_2), 28.4 (–, *C*H_2), 27.5 (–, *C*H_2), 21.9 (–, *C*H_2), 21.6 (+, CO*C*H_3), 20.6 (–, *C*H_2), 13.9 (+, 18-*C*H_3), 12.3 (+, 19-*C*H_3). – **IR (ATR)**: $\tilde{\nu}$ = 2920 (w), 2840 (vw), 1723 (m), 1450 (vw), 1366 (w), 1233 (m), 1130 (vw), 1060 (w), 965 (vw) cm^{-1}. – **MS** (EI, 70 eV, 110 °C): m/z (%) = 332 (55) $[M]^{\bullet+}$, 272 (100) $[M–AcO]^+$, 257 (28), 218 (40), 201 (29), 107 (23). – **HRMS** ($C_{21}H_{32}O_3$): calc.: 332.2346; found: 332.2345.

The analytical and spectroscopical data match those reported in the literature.[2]

3*β*-Acetoxy-5*α*-androstane-17*β*-ol (**SI-02**)[3]



Under argon atmosphere, 3*β*-acetoxy-5*α*-androstane-17-on (**SI-01**) (6.84 g, 20.6 mmol, 1.00 equiv) was dissolved in absolute methanol (150 mL) and at –20 °C sodium borohydride (856 mg, 22.6 mmol, 1.10 equiv) was added portionwise. The reaction was allowed to warm to 0 °C and was stirred for 3 h. Afterwards concentrated acetic acid (ca. 15 mL) was added to adjust the pH value to 5 and the

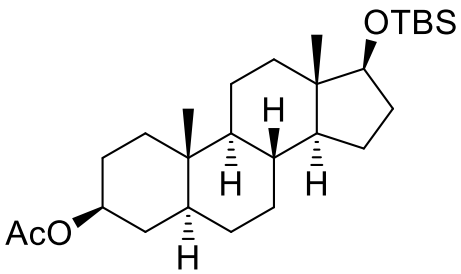
solution was concentrated. Water (250 mL) was added and the precipitate was filtered off. The residue was washed with water (200 mL) and dried *in vacuo*. Filtration over a pad of silica gel (cyclohexane/ethyl acetate, 1:1) afforded the title compound **SI-02** as colorless solid (6.74 g, 20.1 mmol, 98%).

R_f = 0.26 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (300 MHz, $CDCl_3$): δ = 4.68 (dddd, ^3J = 10.9, 10.9, 4.9, 4.9 Hz, 1H, 3-C*H*OAc), 3.62 (dd, ^3J = 8.5, 8.5 Hz, 1H, 17-C*H*OH), 2.13–2.03 (m, 1H, CH_2), 2.02 (s, 3H, COCH_3), 1.86–1.73 (m, 3H, 3 different CH_2), 1.74–1.66 (m, 1H, CH_2), 1.66–1.49 (m, 4H, 4 different CH_2), 1.49–1.32 (m, 3H, 2 different CH_2 + 8-C*H*), 1.31–1.17 (m, 5H, 3 different CH_2 + 5-C*H*), 1.11–0.85 (m, 4H, 3 different CH_2 + 14-C*H*), 0.83 (s, 3H, 19-CH_3), 0.72 (s, 3H, 18-CH_3), 0.64 (ddd, *J* = 12.1, 10.4, 4.2 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.8 (C_qO), 82.0 (+, 17-*C*HOH), 73.8 (+, 3-*C*HOAc), 54.5 (+, 9-*C*H), 51.1 (+, 14-*C*H), 44.9 (+, 5-*C*H), 43.1 (13-C_q), 36.9 (–, *C*H_2), 36.8 (–, *C*H_2), 35.7 (10-C_q), 35.7 (+, 8-*C*H), 34.1 (–, *C*H_2), 31.7 (–, *C*H_2), 30.7 (–, *C*H_2), 28.6 (–, *C*H_2), 27.6 (–, *C*H_2), 23.5 (–, *C*H_2), 21.6 (+, CO*C*H_3), 20.9 (–, *C*H_2), 12.4 (+, 19-*C*H_3), 11.3 (+, 18-*C*H_3) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 3566 (br), 2926 (w), 2846 (w), 1728 (m), 1439 (vw), 1360 (vw), 1235 (m), 1132 (w), 1066 (w), 1052 (w), 1019 (w), 608 (vw), 447 (vw) cm^{-1}. – **MS** (EI, 70 eV, 80 °C): *m/z* (%) = 334 (15) $[M]^{\bullet+}$, 274 (100) $[M–OAc]^+$, 259 (18), 230 (17), 215 (43), 147 (18), 107 (16), 93 (14), 69 (13). – **HRMS** (EI, $C_{21}H_{34}O_3$): calc.: 334.2502; found: 334.2502.

The analytical and spectroscopical data match those reported in the literature.[3]

2.1.1 TBS/Ac-protected hydroxyl group at C-17

3*β*-Acetoxy-17*β*-[[(*tert*-butyl)dimethylsilyl]oxy]-5*α*-androstane (**SI-03-TBS**)[3]



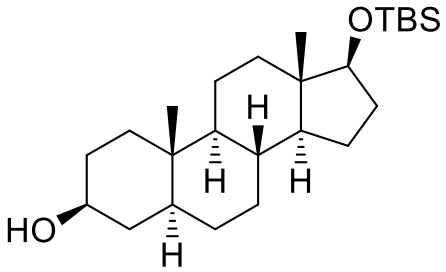
Under argon atmosphere, 3*β*-acetoxy-5*α*-androstane-17*β*-ol (**SI-02**) (3.56 g, 10.7 mmol, 1.00 equiv) was dissolved in absolute DMF (12 mL). Imidazole (1.11 g, 16.3 mmol, 1.52 equiv) and *tert*-butyldimethylsilyl chloride (1.64 g, 10.8 mmol, 1.01 equiv) were added. The reaction was stirred overnight at r.t. and then quenched with water (100 mL). The aqueous phase was extracted with diethyl ether (3 × 40 mL). The combined organic phases were washed with water (30 mL) und brine (30 mL) and dried over Na_2SO_4. After filtration the solvent was removed under reduced pressure to give the crude product which was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 10:1) to afford the title compound **SI-03-TBS** as colorless solid (3.85 g, 8.58 mmol, 80%).

R_f = 0.70 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$: δ = 4.68 (dddd, ^3J = 11.4, 11.4, 4.9, 4.9 Hz, 1H, 3-C*H*OAc), 3.53 (dd, ^3J = 8.8, 7.8 Hz, 1H, 17-C*H*OTBS), 2.02 (s, 3H, COCH_3), 1.91–1.76 (m, 2H, 2 different CH_2), 1.76–1.68 (m, 2H, 2 different CH_2), 1.68–1.56 (m, 2H, 2 different CH_2), 1.57–1.49 (m, 4H, 3 different CH_2), 1.46–1.39 (m, 1H, CH_2), 1.39–1.30 (m, 2H, CH_2 + 8-C*H*), 1.30–1.10 (m, 4H, 3 different CH_2 + 5-C*H*), 0.98–0.92 (m, 2H, 2 different CH_2), 0.91–0.83 (m, 2H, CH_2 + 14-C*H*), 0.87 (s, 9H, $SiC_q(CH_3)_3$), 0.82 (s, 3H, 19-CH_3), 0.68

(s, 3H, 18-CH_3), 0.62 (ddd, ^3J = 12.3, 10.4, 4.1 Hz, 1H, 9-CH), 0.00 (s, 3H, SiCH_3), -0.01 (s, 3H, SiCH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.8 (C_qO), 82.0 (+, 3-CHOAc), 73.9 (+, 17-CHOTBS), 54.7 (+, 9-CH), 50.8 (+, 14-CH), 44.9 (+, 5-CH), 43.5 (13-C_q), 37.3 (–, CH$_2$), 37.0 (–, CH$_2$), 35.7 (10-C_q), 35.7 (+, 8-CH), 34.2 (–, CH$_2$), 31.8 (–, CH$_2$), 31.1 (–, CH$_2$), 28.7 (–, CH$_2$), 27.6 (–, CH$_2$), 26.0 (+, 3 × C_q(CH$_3$)), 23.7 (–, CH$_2$), 21.6 (+, COCH$_3$), 21.0 (–, CH$_2$), 18.3 (SiC_q), 12.4 (+, 19-CH$_3$), 11.6 (+, 18-CH$_3$), –4.7 (+, SiCH$_3$), –4.3 (+, SiCH$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2929 (w), 2847 (w), 1737 (m), 1362 (w), 1239 (w), 1093 (w), 1032 (w), 881 (w), 833 (w), 773 (w), 667 (w) cm^{-1}. – **MS** (EI, 70 eV, 120 °C): *m/z* (%) = 448 (3) [M]$^{\bullet+}$, 391 (100) [M–^{t}Bu]$^{\bullet+}$, 315 (24), 255 (25), 181 (26), 131 (32), 75 (32), 69 (56). – **HRMS** (EI, $C_{27}H_{48}O_3Si$): calc.: 448.3368; found: 448.3367.

The analytical and spectroscopical data match those reported in the literature.[3]

17β-[(*tert*-Butyldimethylsilyl)oxy]-5α-androstane-3β-ol (**SI-04-TBS**)[3]

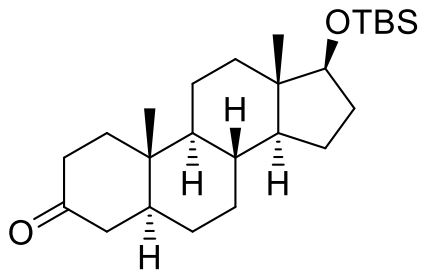


3β-Acetoxy-17β-[(*tert*-butyldimethylsilyl)oxy]-5α-androstane (**SI-03-TBS**) (3.72 g, 8.30 mmol, 1.00 equiv) was dissolved in methanol (23 mL) and KOH in methanol (w/w = 10%, 19 mL) was added. The reaction was refluxed for 5 h and cooled to r.t. Water (100 mL) was added and a colorless precipitate was formed which was filtered and washed as long with water (ca. 200 mL) as the filtrate showed neutral pH value. The product was dried *in vacuo* and the title compound **SI-04-TBS** was obtained as colorless solid (3.33 g, 8.19 mmol, 99%).

***R**$_f$* = 0.25 (*c*Hex/EtOAc, 10:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.59 (dddd, ^3J = 10.4, 10.4, 5.1, 5.1 Hz, 1H, 3-CHOH), 3.53 (dd, ^3J = 8.7, 7.8 Hz, 1H, 17-CHOTBS), 1.92–1.83 (m, 1H, CH_2), 1.83–1.79 (m, 1H, CH_2), 1.79–1.75 (m, 1H, CH_2), 1.73 (dd, J = 4.1, 2.7 Hz, 1H, CH_2), 1.71–1.68 (m, 1H, CH_2), 1.66–1.62 (m, 1H, CH_2), 1.60–1.47 (m, 3H, different CH_2), 1.46–1.36 (m, 2H, CH_2), 1.33 (dd, J = 10.8, 4.1 Hz, 1H, CH), 1.30–1.15 (m, 5H, different CH_2 + CH), 1.15–1.01 (m, 1H, CH), 0.98 (t, J = 3.5 Hz, 1H, CH_2), 0.95 (t, J = 3.2 Hz, 1H, CH_2), 0.93–0.89 (m, 1H, 14-CH), 0.87 (s, 9H, SiC(CH_3)$_3$), 0.80 (s, 3H, 19-CH_3), 0.68 (s, 3H, 18-CH_3), 0.60 (ddd, ^3J = 12.3, 10.4, 4.1 Hz, 1H, 9-CH), 0.00 (s, 3H, SiCH_3), –0.01 (s, 3H, SiCH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 82.0 (+, 3-CHOH), 71.3 (+, 17-CHOTBS), 54.8 (+, 9-CH), 50.9 (+, 14-CH), 45.1 (+, 5-CH), 43.5 (13-C_q), 38.3 (–, CH$_2$), 37.4 (–, CH$_2$), 37.2 (–, CH$_2$), 35.8 (+, 8-CH), 35.7 (10-C_q), 31.9 (–, CH$_2$), 31.6 (–, CH$_2$), 31.1 (–, CH$_2$), 28.8 (–, CH$_2$), 26.0 (+, 3 × C(CH$_3$)), 23.7 (–, CH$_2$), 21.1 (–, CH$_2$), 18.3 (SiC_q), 12.5 (+, 19-CH$_3$), 11.6 (+, 18-CH$_3$), –4.3 (+, SiCH$_3$), –4.7 (+, SiCH$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3500–3100 (br), 2926 (w), 2852 (w), 1648 (vw), 1470 (w), 1360 (w), 1248 (m), 1134 (w), 1093 (m), 1076 (m), 895 (w), 879 (w), 832 (m), 772 (m), 667 (w) cm^{-1}. – **MS** (EI, 70 eV, 100 °C): *m/z* (%) = 407 (3) [M]$^{\bullet+}$, 349 (100) [M–^{t}Bu]$^+$, 273 (43), 255 (11). – **HRMS** (EI, $C_{25}H_{46}O_2Si$): calc.: 406.3262; found: 406.3263.

The analytical and spectroscopical data match those reported in the literature.[3]

17*β*-[(*tert*-Butyldimethylsilyl]oxy]-5*α*-androstane-3-on (**17-TBS**)[3-4]

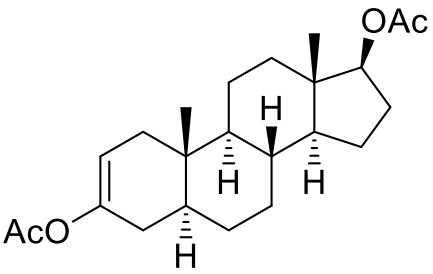


Under argon atmosphere, 17*β*-[(*tert*-butyldimethylsilyl)oxy]-5*α*-androstane-3*β*-ol (**SI-04-TBS**) (3.29 g, 8.31 mmol, 1.00 equiv), NMO (1.95 g, 16.6 mmol, 2.00 equiv) and 4 Å molecular sieves (ca. 2.0 g) were dissolved in absolute dichloromethane (55 mL). At 0 °C, TPAP (292 mg, 831 µmol, 0.10 equiv) was added and the reaction mixture was allowed to warm to r.t. overnight. After filtration over Celite® (dichloromethane as eluent) the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to afford the title compound **17-TBS** as colorless solid (3.06 g, 7.56 mmol, 91%).

***R*$_f$** = 0.48 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.54 (dd, ^3J = 8.3, 8.3 Hz, 1H, 17-C*H*OTBS), 2.45–2.19 (m, 3H, 4-CH_2^a + CH_2), 2.07 (ddd, ^2J = 15.0 Hz, ^3J = 3.9, 2.3 Hz, 1H, 4-CH_2^b), 2.01 (ddd, ^2J = 13.2 Hz, ^3J = 6.5, 2.3 Hz, 1H, CH_2), 1.93–1.80 (m, 1H, CH_2), 1.79–1.64 (m, 2H, 2 different CH_2), 1.60–1.17 (m, 10H, 5 different CH_2 + 5-C*H* + 8-C*H*), 1.02–0.81 (m, 3H, 2 different CH_2 + 14-C*H*), 1.02 (s, 3H, 19-CH_3), 0.87 (s, 9H, Si(CH_3)$_3$), 0.75–0.66 (m, 1H, 9-C*H*), 0.71 (s, 3H, 18-CH_3), 0.00 (s, 3H, SiCH_3), –0.01 (s, 3H, SiCH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 212.2 (3-C_qO), 81.9 (+, 17-*C*HOTBS), 54.3 (+, 9-*C*H), 50.7 (+, 14-*C*H), 47.0 (+, 5-*C*H), 44.9 (–, 4-*C*H$_2$), 43.5 (13-C_q), 38.8 (–, *C*H$_2$), 38.3 (–, *C*H$_2$), 37.2 (–, *C*H$_2$), 35.9 (10-C_q), 35.7 (+, 8-*C*H), 31.5 (–, *C*H$_2$), 31.1 (–, *C*H$_2$), 29.0 (–, *C*H$_2$), 26.0 (+, 3 × C(*C*H$_3$)), 23.7 (–, *C*H$_2$), 21.3 (–, *C*H$_2$), 18.3 (SiC_q), 11.7 (+, *C*H$_3$), 11.6 (+, *C*H$_3$), –4.3 (+, Si*C*H$_3$), –4.7 (+, Si*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2928 (m), 2853 (m), 1712 (m), 1471 (w), 1249 (m), 1140 (w), 1108 (m), 1084 (m), 910 (w), 890 (m), 869 (m), 831 (m), 772 (m), 667 (w) cm^{-1}. – **MS** (EI, 70 eV, 100 °C): *m/z* (%) = 404 (5) [M]$^{\bullet+}$, 347 (100) [M–^{t}Bu]$^+$, 271 (37), 161 (11). – **HRMS** (EI, $C_{25}H_{44}O_2Si$): calc.: 404.3105; found: 404.3107.

The analytical and spectroscopical data match those reported in the literature.[3-4]

3,17*β*-Diacetoxy-5*α*-androst-2-ene (**16-Ac**)[4]



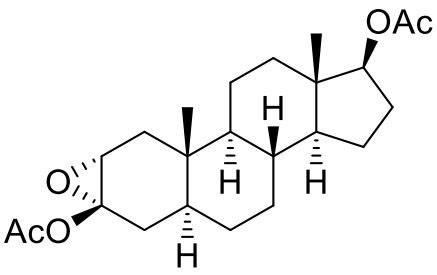
Under argon atmosphere, 17*β*-[(*tert*-butyldimethylsilyl)oxy]-5*α*-androstane-3-on (**17-TBS**) (1.83 g, 4.52 mmol, 1.00 equiv) was dissolved in ethyl acetate (55 mL). Acetic anhydride (2.1 mL, 1.31 g, 22.6 mmol, 5.00 equiv) and aqueous perchloric acid (w/w = 70%, 39 µL, 452 µmol, 0.10 equiv) were added dropwise. The reaction was stirred for 3 h at r.t. (TLC control) and then quenched with saturated aqueous $NaHCO_3$ solution (150 mL). The resulting mixture was as long stirred as the gas evolution stopped. After phase separation, the aqueous phase was extracted with ethyl acetate (2 × 200 mL) and the combined organic phases were washed with brine (120 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. The crude

product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to afford the title compound **16-Ac** as colorless solid (1.40 g, 3.14 mmol, 69%).

R_f = 0.39 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 5.25 (d, ^3J = 5.2 Hz, 1H, 2-C*H*), 4.58 (t, ^3J = 8 Hz, 1H, 17-C*H*OAc), 2.20–2.10 (m, 1H, CH_2), 2.10 (s, 3H, COCH_3), 2.06–2.00 (m, 1H, CH_2), 2.03 (s, 3H, COCH_3) 2.00–1.90 (m, 2H, CH_2), 1.87 – 1.78 (m, 1H, CH_2), 1.73 (dt, *J* = 12.5, 3.4 Hz, 1H, 12-CH_2), 1.67 (dq, *J* = 13.9, 3.8 Hz, 1H, CH_2), 1.65–1.55 (m, 1H, CH_2), 1.55–1.41 (m, 4H, 3 different CH_2 + 5-C*H*), 1.40–1.19 (m, 4H, 4 different CH_2 + 8-C*H*,), 1.15 (td, ^3J = 12.9, 4.3 Hz, 1H, CH_2), 1.01 (ddd, *J* = 12.3, 10.9, 7.1 Hz, 1H, 14-C*H*), 0.92–0.85 (m, 1H, CH_2), 0.83 (s, 3H, 19-CH_3), 0.79 (s, 3H, 18-CH_3), 0.72 (ddd, *J* = 12.2, 10.5, 4.3 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (151 MHz, $CDCl_3$): δ = 171.3 (C_qO), 169.7 (C_qO), 147.1 (=C_qOAc), 112.7 (+, 2-*C*H), 83.0 (+, 17-*C*HOAc), 53.7 (+, 9-*C*H), 50.8 (+, 14-*C*H), 42.7 (13-C_q), 41.9 (+, 5-*C*H), 38.4 (–, *C*H$_2$), 37.0 (–, *C*H$_2$), 35.5 (+, 8-*C*H), 34.8 (10-C_q), 31.5 (–, *C*H$_2$), 31.3 (–, *C*H$_2$), 28.4 (–, *C*H$_2$), 27.7 (–, *C*H$_2$), 23.7 (–, *C*H$_2$), 21.3 (+, O*C*H$_3$), 21.2 (+, O*C*H$_3$), 20.8 (–, *C*H$_2$), 12.2 (+, 19-*C*H$_3$), 11.9 (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2914 (w), 2851 (w), 1729 (m), 1445 (v), 1364 (w), 1220 (m), 1152 (w), 1102 (w), 1043 (m), 917 (w), 841 (w), 604 (w), 508 (w), 417 (w) cm^{-1}. – **MS** (EI, 70 eV, 90 °C): *m/z* (%) = 374 (10) [M]$^{\bullet+}$, 332 (100), 262 (23), 202 (31), 181 (39), 131 (42), 71 (13), 69 (76). – **HRMS** (EI, $C_{23}H_{34}O_4$): calc.: 374.2452; found: 374.2452.

The analytical and spectroscopical data match those reported in the literature.[4]

3*β*,17*β*-Diacetoxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Ac**)[5]



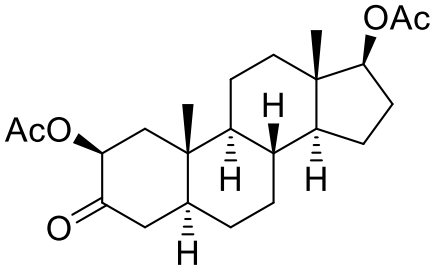
Under argon atmosphere, 3,17*β*-diacetoxy-5*α*-androst-2-ene (**16-Ac**) (1.38 g, 3.69 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (25 mL) and *meta*-chloroperoxybenzoic acid (w/w = 70%, 1.09 g, 6.32 mmol, 1.20 equiv) was added portionwise. The reaction was stirred overnight at r.t. and diluted with diethyl ether (100 mL). The organic phase was consecutively washed with $NaHCO_3$ solution (3 × 50 mL) and brine (50 mL). The combined organic phases were dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to afford the title compound **18-Ac** as colorless solid (1.00 g, 2.56 mmol, 70%).

R_f = 0.40 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (600 MHz, $CDCl_3$): δ = 4.57 (dd, ^3J = 8.5 Hz, 1H, 17-C*H*OAc), 3.32 (d, *J* = 5.6 Hz, 1H, 2-C*H*O), 2.19–2.11 (m, 1H, CH_2), 2.11–2.05 (m, 1H, CH_2), 2.05 (s, 3H, COCH_3), 2.03 (s, 3H, COCH_3), 2.03–1.99 (m, 1H, CH_2), 1.92 (dd, *J* = 14.1, 11.9 Hz, 1H, CH_2), 1.72 (dt, *J* = 12.7, 3.5 Hz, 1H, CH_2), 1.67–1.55 (m, 2H, 2 different CH_2), 1.53–1.41 (m, 2H, 2 different CH_2), 1.41–1.19 (m, 7H, 5 different CH_2 + 5-C*H* + 8-C*H*), 1.13 (dt, *J* = 12.9, 4.3 Hz, 1H, CH_2), 1.02–0.97 (m, 1H, 14-C*H*), 0.96 (s, 3H, 19-CH_3), 0.88–0.78 (m, 1H, CH_2), 0.77 (s, 3H, 18-CH_3), 0.63 (ddd, *J* = 15.0, 11.1, 4.3 Hz, 1H, 9-C*H*) ppm. –

^{13}C NMR (151 MHz, $CDCl_3$): δ = 171.3 (C_qO), 169.6 (C_qO), 83.2 (3-C_qOAc), 82.9 (+, 17-*C*HOAc), 58.5 (+, 2-*C*HO), 53.5 (+, 9-*C*H), 50.7 (+, 14-*C*H), 42.6 (13-C_q), 38.9 (–, *C*H$_2$), 38.9 (–, 5-*C*H), 37.0 (–, *C*H$_2$), 35.4 (+, 8-*C*H), 34.6 (10-C_q), 31.2 (–, *C*H$_2$), 30.9 (–, 4-*C*H$_2$), 28.1 (–, *C*H$_2$), 27.6 (–, *C*H$_2$), 23.6 (–, *C*H$_2$), 21.3 (+, CO*C*H$_3$), 21.3 (+, CO*C*H$_3$), 20.7 (–, *C*H$_2$), 13.0 (+, 19-*C*H$_3$), 12.2 (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2919 (w), 2847 (vw), 1748 (m), 1727 (m), 1373 (w), 1251 (m), 1220 (m), 1171 (w), 1047 (m), 821 (w), 693 (w), 467 (w) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 390 (3) [M]$^{\bullet+}$, 348 (72), 347 (45), 331 (14) [M–OAc]$^+$, 288 (19), 262 (13), 202 (18), 181 (49), 131 (58), 119 (17), 100 (23), 81 (14), 69 (100). – **HRMS** (EI, $C_{23}H_{34}O_5$): calc.: 390.2401; found: 390.2399.

The analytical and spectroscopical data match those reported in the literature.[5]

2*β*,17*β*-Diacetoxy-5*α*-androstane-3-on (**19-Ac**)[5]

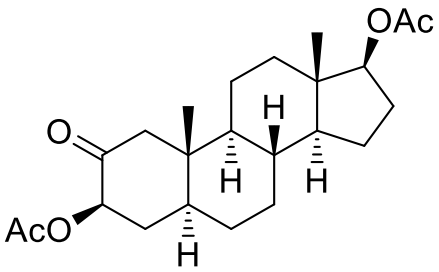


3*β*,17*β*-Diacetoxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Ac**) (1.00 g, 2.56 mmol, 1.00 equiv) was dissolved in a mixture of toluene and pyridine (10:1, 50 mL) and refluxed for 24 h. The solvent was removed and the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to afford the title compound **19-Ac** as colorless solid (860 mg, 2.20 mmol, 86%).

***R*$_f$** = 0.41 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 5.37 (dd, ^3J = 10.2, 7.1 Hz, 1H, 2-C*H*OAc), 4.60 (dd, ^3J = 9.2, 7.8 Hz, 1H, 17-C*H*OAc), 2.40 (dd, J = 17.8, 6.2 Hz, 1H, 4*α*-C*H*$_2$), 2.24 (dd, ^2J = 17.8 Hz, ^3J = 12.1 Hz, 1H, 4*β*-C*H*$_2$), 2.19–2.13 (m, 2H, 2 different C*H*$_2$), 2.13 (s, 3H, COC*H*$_3$), 2.03 (s, 3H, COC*H*$_3$), 2.02–1.96 (m, 1H, 5-C*H*), 1.80–1.67 (m, 3H, 3 different C*H*$_2$), 1.67–1.57 (m, 1H, C*H*$_2$), 1.57–1.44 (m, 3H, 3 different C*H*$_2$), 1.42–1.11 (m, 5H, 4 different C*H*$_2$ + 8-C*H*), 1.04 (ddd, J = 12.7, 10.9, 7.2 Hz, 1H, 14-C*H*), 0.99–0.86 (m, 2H, C*H*$_2$ + 9-C*H*), 0.85 (s, 3H, C*H*$_3$), 0.79 (s, 3H, C*H*$_3$) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 204.1 (3-C_qO), 171.3 (C_qO), 170.1 (C_qO), 87.3 (+, 2-*C*HOAc), 74.5 (+, 17-*C*HOAc), 54.8 (+, 9-*C*H), 50.6 (+, 14-*C*H), 45.0 (13-C_q), 43.7 (–, *C*H$_2$), 42.3 (–, 4-*C*H$_2$), 41.9 (+, 5-*C*H), 37.0 (–, *C*H$_2$), 36.3 (10-C_q), 35.2 (+, 8-*C*H), 31.0 (–, *C*H$_2$), 28.3 (–, *C*H$_2$), 27.7 (–, *C*H$_2$), 23.6 (–, *C*H$_2$), 21.3 (+, CO*C*H$_3$), 21.2 (–, *C*H$_2$), 21.0 (+, CO*C*H$_3$), 14.5 (+, 19-*C*H$_3$), 12.2 (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2921 (w), 2877 (w), 1729 (m), 1446 (w), 1371 (w), 1245 (m), 1044 (w), 1029 (w), 915 (vw), 613 (vw), 460 (vw) cm^{-1}. – **MS** (EI, 70 eV, 120 °C): *m/z* (%) = 390 (20) [M]$^{\bullet+}$, 348 (100), 330 (69) [M–HOAc]$^+$, 288 (38), 270 (19), 215 (20), 147 (17), 107 (19), 93 (22), 81 (21), 79 (14). – **HRMS** (EI, $C_{23}H_{34}O_5$): calc.: 390.2401; found: 390.2402.

The analytical and spectroscopical data match those reported in the literature.[5]

3*β*,17*β*-Diacetoxy-5*α*-androstane-2-on (**20-Ac**)

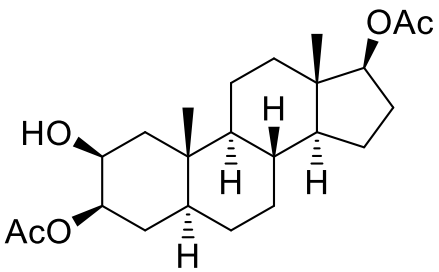


Under argon atmosphere, 2*β*,17*β*-diacetoxy-5*α*-androstane-3-on (**19-Ac**) (102 mg, 260 µmol, 1.00 equiv) was dissolved in isopropanol (11 mL) and a solution of potassium carbonate (184 mg, 1.33 mmol, 5.12 equiv) in water (1.0 mL) was added. The reaction was stirred for 24 h at r.t. and was then diluted with water (20 mL). The aqueous phase was extracted with dichloromethane (3 × 10 mL) and the combined organic phases were washed with aqueous 1 M HCl solution (2 × 10 mL) and brine (50 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. After flash column chromatography on silica gel (cyclohexane/ethyl acetate, 6:1) the title compound **20-Ac** was obtained as colorless solid (57 mg, 150 µmol, 58%).

***R**_f* = 0.30 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.20 (dd, ^3J = 11.5, 7.5 Hz, 1H, 3-C*H*OAc), 4.59 (dd, ^3J = 9.2, 7.7 Hz, 1H, 17-C*H*OAc), 2.49 (d, ^2J = 13.0 Hz, 1H, 1-CH_2^a), 2.22–2.15 (m, 1H, CH_2), 2.15 (s, 3H, COCH_3), 2.09 (d, ^2J = 13.3 Hz, 1H, 1-CH_2^b), 2.03 (s, 3H, COCH_3), 2.00 (dd, ^3J = 9.9, 2.5 Hz, 1H, CH_2), 1.82–1.70 (m, 4H, 3 different CH_2 + 5-C*H*), 1.69–1.59 (m, 1H, CH_2), 1.55–1.40 (m, 3H, 3 different CH_2), 1.37–1.23 (m, 4H, 3 different CH_2 + 8-C*H*), 1.16 (td, *J* = 12.7, 4.2 Hz, 1H, CH_2), 1.10–0.90 (m, 3H, CH_2 + 9-C*H* + 14-C*H*), 0.77 (s, 6H, 18-CH_3 + 19-CH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 204.5 (2-C_qO), 171.3 (C_qO), 170.2 (C_qO), 82.7 (+, 3-*C*HOAc), 75.2 (+, 17-*C*HOAc), 53.8 (+, 9-*C*H), 52.5 (–, 1-*C*H_2), 50.6 (+, 14-*C*H), 44.3 (+, 5-*C*H), 42.7 (13-C_q), 41.5 (10-C_q), 36.8 (–, *C*H_2), 35.1 (–, *C*H_2), 34.7 (+, 8-*C*H), 31.2 (–, *C*H_2), 27.7 (–, *C*H_2), 27.6 (–, *C*H_2), 23.7 (–, *C*H_2), 21.3 (+, CO*C*H_3), 20.9 (–, *C*H_2), 20.9 (+, CO*C*H_3), 12.6 (+, *C*H_3), 12.2 (+, *C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2922 (w), 2846 (w), 1749 (m), 1725 (m), 1371 (w), 1226 (m), 1091 (w), 1042 (m), 891 (w), 484 (w) cm^{-1}. – **MS** (EI, 70 eV, 140 °C): *m/z* (%) = 390 (31) $[M]^{\bullet+}$, 348 (64), 330 (100) $[M–AcOH]^+$, 288 (53), 270 (57), 261 (40), 201 (22), 149 (13), 121 (18), 107 (22), 93 (21), 81 (17), 69 (13). – **HRMS** (EI, $C_{23}H_{34}O_5$): calc.: 390.2401; found: 390.2399.

Although literature known, no complete analytical data set for comparison has been published.[6]

3*β*,17*β*-Diacetoxy-5*α*-androstane-2*β*-ol (**14-Ac**)



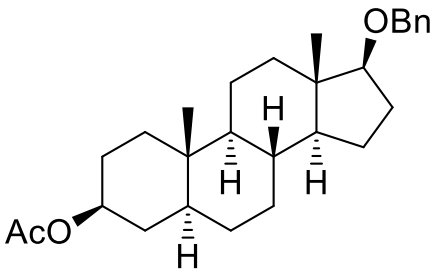
Under argon atmosphere, 3*β*,17*β*-diacetoxy-5*α*-androstane-2-on (**20-Ac**) (545 mg, 1.40 mmol, 1.00 equiv) was dissolved in absolute methanol (40 mL). At –10 °C sodium borohydride (106 mg, 2.79 mmol, 2.00 equiv) was added slowly and the reaction was stirred for 3 h. The mixture was allowed to warm to r.t. and was quenched with water (50 mL). After the addition of dichloro-methane, the aqueous layer was extracted with dichloromethane (3 × 70 mL). The combined organic phases were washed with aqueous 2 M HCl solution (60 mL) and brine (60 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under

reduced pressure. After flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) the title compound **14-Ac** was obtained as colorless solid (419 mg, 1.07 mmol, 76%).

R_f = 0.36 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.77 (ddd, *J* = 11.8, 4.8, 3.3 Hz, 1H, 3-C*H*OAc), 4.57 (dd, *J* = 9.2, 7.7 Hz, 1H, 17-C*H*OAc), 4.09 (d, *J* = 3.3 Hz, 1H, 2-C*H*OH), 2.20–2.10 (m, 1H, 4-CH_2^a), 2.08 (s, 3H, COCH_3), 2.07–2.04 (m, 1H, 1-CH_2^a), 2.03 (s, 3H, COCH_3), 1.94–1.85 (m, 1H, 2-CHO*H*), 1.83–1.59 (m, 4H, 4 different CH_2), 1.53–1.41 (m, 5H, 4 different CH_2 + 8-C*H*), 1.34–1.09 (m, 6H, 4 different CH_2 + 1-CH_2^b + 5-C*H*), 1.06–0.97 (m, 1H, 14-C*H*), 1.04 (s, 3H, 19-CH_3), 0.94–0.81 (m, 1H, CH_2), 0.77 (s, 3H, 18-CH_3), 0.62 (ddd, *J* = 12.3, 10.4, 4.0 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$) δ = 171.4 (C_qO), 170.2 (C_qO), 83.0 (+, 3-*C*HOAc), 75.7 (+, 17-*C*HOAc), 68.8 (+, 2-*C*HOH), 55.3 (+, 14-*C*H), 50.8 (+, 9-*C*H), 45.6 (+, 5-*C*H), 43.1 (13-C_q), 42.8 (–, 1-*C*H_2), 37.1 (–, *C*H_2), 35.6 (10-C_q), 34.8 (+, 8-*C*H), 31.6 (–, *C*H_2), 28.7 (–, *C*H_2), 28.1 (–, *C*H_2), 27.7 (–, *C*H_2), 23.6 (–, *C*H_2), 21.5 (+, CO*C*H_3), 21.3 (+, CO*C*H_3), 20.9 (–, *C*H_2), 14.7 (+, 19-*C*H_3), 12.3 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3483 (w), 2914 (m), 1729 (m), 1714 (m), 1450, (w), 1358 (m), 1245 (s), 1139 (w), 1077 (w), 1024 (s), 973 (m), 941 (w), 923 (w), 884 (w), 853 (w) cm^{-1}. – **MS** (EI, 70 eV, 90 °C): *m/z* (%) = 390 (100) $[M–HOAc]^+$, 314 (24). 306 (20). – **HRMS** (EI, $C_{21}H_{32}O_3$, $[M–HOAc]^+$): calc.: 332.2351; found: 332.2353.

2.1.2 Benzyl-protected hydroxyl group at C-17

3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane (**SI-03-Bn**)

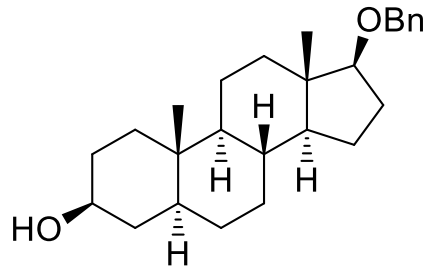


Under argon atmosphere, 3*β*-acetoxy-5*α*-androstane-17*β*-ol (**SI-02**) (7.25 g, 21.7 mmol, 1.00 equiv) was dissolved in absolute 1,4-dioxane (80 mL). At 0 °C, benzyl 2,2,2-trichloroacetimidate (4.6 mL, 6.30 g, 25.0 mmol, 1.15 equiv) and trifluoromethanesulfonic acid (0.20 mL) were added and the reaction mixture was stirred overnight. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (200 mL) and dichloromethane (200 mL) was added. After phase separation, the aqueous phase was extracted with dichloromethane (2 × 200 mL) and the combined organic phases were washed with brine. Then the organic phase was dried over Na_2SO_4 and after filtration, the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 20:1→10:1) to obtain the title compound **SI-03-Bn** as colorless powder (7.49 g, 17.6 mmol, 82%).

$\boldsymbol{R_f}$ = 0.57 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.37–7.31 (m, 4H, 4×CH_{Ar}), 7.29–7.23 (m, 1H, CH_{Ar}), 4.76–4.64 (m, 1H, 3-C*H*OAc), 4.55 (s, 2H, OCH_2Ph), 3.41 (t, *J* = 8.4 Hz, 1H, 17-C*H*OBn), 2.03 (s, 3H, COCH_3), 1.99–1.89 (m, 2H, 2 different CH_2), 1.86–1.78 (m, 1H, CH_2), 1.74 (d, *J* = 13.5 Hz, 1H, CH_2), 1.69–1.22 (m, 12H, 7 different CH_2 + 8-C*H*), 1.22–1.08 (m, 2H, CH_2 + 5-C*H*), 1.06–0.90 (m, 2H, CH_2 + 14-C*H*), 0.84 (s, 6H, 2 × CH_3), 0.83–0.76 (m, 1H, CH_2), 0.64 (tt, *J* = 12.1, 9.9, 3.7 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.4 (C_qO), 139.1 (1'-$C_{q,Ph}$), 128.0 (+, 3',5'-*C*H$_{Ar}$), 127.0 (+, 2',6'-*C*H$_{Ar}$), 127.0 (+, 4'-*C*H$_{Ar}$), 88.1 (+, 17-*C*HOBn), 73.4 (+, 3-*C*HOAc), 71.4 (–, O*C*H$_2$Ph), 54.1 (+, 9-*C*H), 50.9 (+, 14-*C*H), 44.5 (+, 5-*C*H), 42.9 (13-C_q), 37.7 (–, *C*H$_2$), 36.6 (–, *C*H$_2$), 35.3 (+, 8-*C*H), 35.1 (10-C_q), 33.8 (–, *C*H$_2$), 31.3 (–, *C*H$_2$), 28.2 (–, *C*H$_2$), 27.7 (–, *C*H$_2$), 27.2 (–, *C*H$_2$), 23.2 (–, *C*H$_2$), 21.2 (+, CO*C*H$_3$), 20.6 (–,11-*C*H$_2$), 12.0 (+, *C*H$_3$), 11.7 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2926 (m), 2844 (m), 1724 (m), 1381 (w), 1366 (w), 1252 (s), 1142 (m), 1089 (m), 1072 (m), 1024 (m), 914 (w), 898 (w), 827 (w), 754 (m), 733 (w), 698 (m), 638 (w), 609 (w), 542 (w), 519 (vw) cm^{-1}. – **MS** (EI, 70 eV, 100°C): *m/z* (%) = 424 (10) [M]$^{\bullet+}$, 333 (9) [M–Bn]$^+$ (9), 273 (8) [M–Bn–HOAc]$^+$, 180 (100). – **HRMS** (EI, $C_{28}H_{40}O_3$): calc.: 424.2977; found: 424.2977.

Although literature known, no complete analytical data set for comparison has been published.[7]

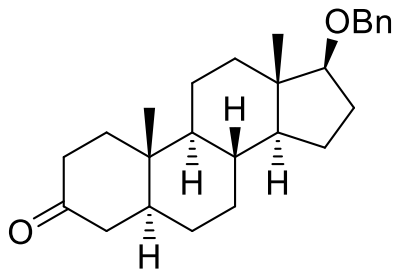
17*β*-Benzyloxy-5*α*-androstane-3*β*-ol (**SI-04-Bn**)



3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane (**SI-03-Bn**) (6.74 g, 15.9 mmol, 1.00 equiv) was dissolved in methanol (100 mL), KOH in methanol (w/w = 10%, 100 mL) was added and the mixture was refluxed for 5 h. After cooling to r.t., water (300 mL) was added. The colorless precipitate was filtered and washed as long with water (ca. 300 mL) till the filtrate shows a neutral pH value. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 4:1) to obtain the title compound **SI-04-Bn** as colorless powder (5.40 g, 14.1 mmol, 89%).

***R*$_f$** = 0.29 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.26 (d, *J* = 4.4 Hz, 4H, 4×C*H*$_{Ar}$), 7.21–7.16 (m, 1H, C*H*$_{Ar}$), 4.47 (s, 2H, OC*H*$_2$Ph), 3.51 (tt, *J* = 10.6, 4.8 Hz, 1H, 3-C*H*OH), 3.33 (dd, ^3J = 8.4 Hz, 1H, 17-C*H*OBn), 1.98–1.81 (m, 2H, 2 different C*H*$_2$), 1.78–1.69 (m, 1H, C*H*$_2$), 1.64 (dt, *J* = 13.5, 3.8 Hz, 1H, C*H*$_2$), 1.61–1.56 (m, 1H, C*H*$_2$), 1.54–1.41 (m, 4H, 4 different C*H*$_2$), 1.40–1.11 (m, 7H, 5 different C*H*$_2$ + 8-C*H*), 1.10–0.96 (m, 2H, C*H*$_2$ + 5-C*H*), 0.93–0.81 (m, 2H, C*H*$_2$ + 14-C*H*), 0.80–0.69 (m, 1H, C*H*$_2$), 0.75 (s, 3H, C*H*$_3$), 0.74 (s, 3H, C*H*$_3$), 0.62–0.47 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 139.2 (1′-*C*$_q$), 128.0 (+, 3′,5′-*C*H$_{Ar}$), 127.1 (+, 2′,6′-*C*H$_{Ar}$), 127.0 (+, 4′-*C*H$_{Ar}$), 88.2 (+, 17-*C*HOBn), 71.4 (–, O*C*H$_2$Ph), 71.1 (+, 3-*C*HOH), 54.3 (+, 9-*C*H), 51.1 (+, 14-*C*H), 44.7 (+, 5-*C*H), 43.0 (13-*C*$_q$), 38.0 (–, *C*H$_2$), 37.8 (–, *C*H$_2$), 36.9 (–, *C*H$_2$), 35.4 (10-*C*$_q$), 35.2 (+, 8-*C*H), 31.5 (–, *C*H$_2$), 31.3 (–, *C*H$_2$), 28.4 (–, *C*H$_2$), 27.8 (–, *C*H$_2$), 23.2 (–, *C*H$_2$), 20.8 (–, *C*H$_2$), 12.2 (+, *C*H$_3$), 11.7 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3278 (br), 2922 (w), 2854 (w), 1652 (vw), 1496 (vw), 1444 (w), 1398 (vw), 1373 (vw), 1346 (w), 1210 (vw), 1135 (w), 1120 (w), 1102 (w), 1077 (w), 1037 (w), 964 (vw), 937 (vw), 907 (vw), 889 (vw), 741 (vw), 741 (w), 695 (w), 648 (w), 613 (w) cm^{-1}. – **MS** (EI, 70 eV, 120°C): *m/z* (%) = 382 (77) $[M]^{\bullet+}$, 291 (100) $[M - Bn]^+$, 273 (42). – **HRMS** (EI, $C_{26}H_{38}O_2$): calc.: 382.2866; found: 382.2867.

17*β*-Benzyloxy-5*α*-androstane-3-on (**17-Bn**)

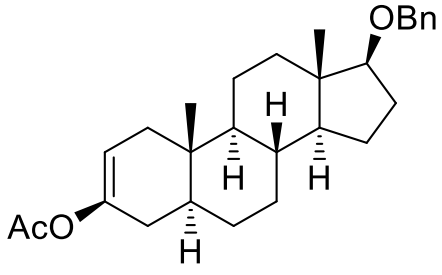


Under argon atmosphere, 17*β*-benzyloxy-5*α*-androstane-3*β*-ol (**SI-03-Bn**) (5.51 g, 14.4 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (100 mL) and Dess-Martin periodinane (7.94 g, 18.7 mmol, 1.30 equiv) was added portionwise at 0 °C. After 15 minutes, the reaction was warmed to r.t. and stirred for 3 h. After addition of further dichloromethane (100 mL), the organic phase was washed with a mixture of saturated aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution (3:1, 120 mL). The organic phase was washed with brine (50 mL) and dried over Na_2SO_4. After filtration, the solvent was removed. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to obtain the title compound **17-Bn** as colorless solid (4.88 g, 12.8 mmol, 89%).

R_f = 0.50 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR (**400 MHz, $CDCl_3$): δ = 7.34–7.31 (m, 4H, CH_{Ar}), 7.29–7.22 (m, 1H, CH_{Ar}), 4.54 (s, 2H, OCH_2Ph), 3.41 (dd, ^3J = 8.9, 7.8 Hz, 1H, C*H*OBn), 2.47–2.18 (m, 3H, 3 different CH_2), 2.09–1.90 (m, 4H, 4 different CH_2), 1.70 (dd, J = 13.1, 3.5 Hz, 1H, CH_2), 1.66–1.25 (m, 10H, 6 different CH_2 + 5-C*H* + 8-C*H*), 1.15 (td, ^2J = 12.8 Hz, ^3J = 4.3 Hz, 1H, CH_2), 1.02 (s, 3H, CH_3), 0.99–0.89 (m, 2H, CH_2 + 14-C*H*), 0.85 (s, 3H, CH_3), 0.72 (ddd, J = 12.3, 10.4, 4.1 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 211.8 (*C*$_q$O), 139.1 (1'-*C*$_q$), 128.1 (+, 3',5'-*C*H$_{Ar}$), 127.1 (+, 2',4',6'-*C*H$_{Ar}$), 88.1 (+, 17-*C*HOBn), 71.4 (–, O*C*H$_2$Ph), 53.8 (+, 9-*C*H), 50.9 (+, 14-*C*H), 46.6 (+, 5-*C*H), 44.5 (–, *C*H$_2$), 43.0 (13-*C*$_q$), 38.4 (–, *C*H$_2$), 38.0 (–, *C*H$_2$), 37.7 (–, *C*H$_2$), 35.6 (10-*C*$_q$), 35.1 (+, 8-*C*H), 31.1 (–, *C*H$_2$), 28.7 (–, *C*H$_2$), 27.8 (–, *C*H$_2$), 23.3 (–, *C*H$_2$), 21.0 (–, *C*H$_2$), 11.7 (+, *C*H$_3$), 11.3 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2931 (w), 2851 (w), 1704 (m), 1494 (vw), 1450 (w), 1415 (vw), 1386 (vw), 1357 (w), 1300 (vw), 1255 (vw), 1214 (vw), 1171 (vw), 1140 (w), 1111 (w), 1089 (w), 1027 (w), 1002 (vw), 956 (vw), 876 (vw), 730 (m), 693 (w), 530 (vw), 515 (vw) cm^{-1}. – **MS** (EI, 70 eV, 120 °C): *m/z* (%) = 380 (54) [M]$^{\bullet+}$, 289 (100) [M–Bn]$^+$, 271 (51). – **HRMS** (EI, $C_{26}H_{36}O_2$): calc.: 380.2711; found: 380.2710.

Although literature known, no complete analytical data set for comparison has been published.[8]

3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androst-2-ene (**16-Bn**)

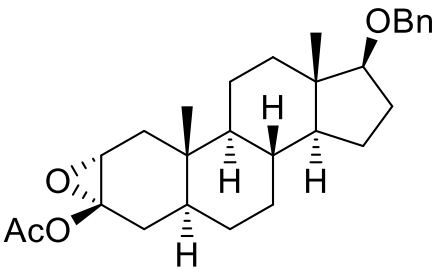


Under argon atmosphere, 17*β*-benzyloxy-5*α*-androstane-3-on (**17-Bn**) (4.37 g, 10.4 mmol, 1.00 equiv) was dissolved in ethyl acetate (60 mL). After addition of acetic anhydride (5.4 mL, 5.86 g, 57.4 mmol, 5.00 equiv) and perchloric acid (w/w = 70%, 89 µL, 1.04 mmol, 0.10 equiv) the reaction mixture was stirred for 3 h at r.t. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (150 ml) and stirred until CO_2 evolution stopped. The aqueous layer was extracted with ethyl acetate (2 × 200 mL) and the combined organic phases were washed with

brine (120 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to give the title compound **16-Bn** as colorless solid (3.74 g, 8.85 mmol, 77%).

R_f = 0.56 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 4H, 4×CH_{Ar}), 7.30–7.25 (m, 1H, CH_{Ar}), 5.27 (d, ^3J = 6.0 Hz, 1H, 2-C*H*), 4.56 (s, 2H, OCH_2Ph), 3.43 (dd, ^3J = 8.3 Hz, 1H, 17-C*H*OBn), 2.13 (s, 3H, COCH_3), 2.09–1.91 (m, 4H, 4 different CH_2), 1.89–1.79 (m, 1H, CH_2), 1.73–1.64 (m, 1H, CH_2), 1.64–1.21 (m, 9H, 4 different CH_2, 8-C*H* + 5-C*H*), 1.21–1.11 (m, 1H, CH_2), 1.02–0.85 (m, 1H, 14-C*H*), 0.86–0.79 (m, 2H, CH_2), 0.83 (s, 6H, 2 × CH_3), 0.78–0.64 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.4 (C_qO), 146.8 (3-C_q), 139.2 (1'-C_q,$_{Ar}$), 128.1 (+, 3',5'-*C*H$_{Ar}$), 127.1 (+, 2',6'-*C*H$_{Ar}$), 127.0 (+, 4'-*C*H$_{Ar}$), 112.4 (+, 2-*C*H), 88.2 (+, 17-*C*HOBn), 71.4 (–, O*C*H$_2$Ph), 53.6 (+, 9-*C*H), 50.9 (+, 14-*C*H), 42.9 (13-C_q), 41.7 (+, 5-*C*H), 38.1 (–, *C*H$_2$), 37.4 (–, *C*H$_2$), 35.2 (+, 8-*C*H), 34.5 (10-C_q), 31.2 (–, *C*H$_2$), 31.0 (–, *C*H$_2$), 28.1 (–, *C*H$_2$), 27.8 (–, *C*H$_2$), 23.3 (–, *C*H$_2$), 20.9 (+, CO*C*H$_3$), 20.7 (–, 11-*C*H$_2$), 11.7 (+, *C*H$_3$), 11.6 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2931 (w), 2907 (w), 2847 (w), 1747 (m), 1696 (w), 1444 (w), 1364 (w), 1345 (w), 1207 (m), 1157 (m), 1133 (m), 1108 (m), 1086 (m), 1027 (w), 993 (w), 944 (w), 914 (w), 852 (w), 758 (w), 697 (m), 628 (w), 607 (w), 594 (w), 540 (w), 523 (w) cm^{-1}. – **MS** (EI, 70 eV, 120 °C): *m/z* (%) = 422 (33) [M]$^{\bullet+}$, 380 (100), 289 (31). – **HRMS** (EI, $C_{28}H_{38}O_3$): calc.: 422.2815; found: 422.2817.

3*β*-Acetoxy-17*β*-benzyloxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Bn**)

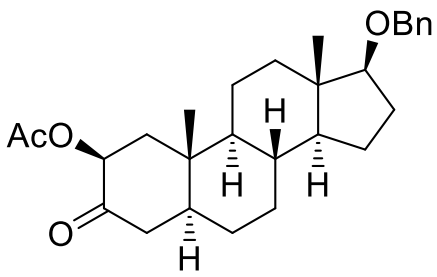


Under argon atmosphere, 3-acetoxy-17*β*-benzyloxy-5*α*-androst-2-ene (**16-Bn**) (5.03 g, 11.9 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (80 mL). At 0 °C *meta*-chloroperoxybenzoic acid (w/w = 70%, 3.52 g, 14.3 mmol, 1.20 equiv) was added slowly and the reaction mixture was allowed to warm to r.t. overnight. After adding diethyl ether (200 mL), the organic phase was washed with saturated aqueous $NaHCO_3$ solution (3 × 40 mL), dried over Na_2SO_4 and filtered. The solvent was evaporated and the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 10:1) to give the title compound **18-Bn** as colorless solid (2.46 g, 5.61 mmol, 47%).

R_f = 0.50 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33–7.32 (m, 4H, 4×CH_{Ar}), 7.30–7.22 (m, 1H, CH_{Ar}), 4.53 (s, 2H, OCH_2Ph), 3.39 (dd, *J* = 8.9, 7.8 Hz, 1H, 17-C*H*OBn), 3.32 (d, *J* = 5.2 Hz, 1H, 2-C*H*O), 2.07–1.88 (m, 5H, 5 different CH_2), 2.06 (s, 3H, COCH_3), 1.67–1.61 (m, 1H, CH_2), 1.59–1.49 (m, 2H, 2 different CH_2), 1.46–1.19 (m, 8H, 4 different CH_2 + C*H* + C*H*), 1.18–1.05 (m, 1H, CH_2), 0.97 (s, 3H, CH_3), 0.92–0.76 (m, 2H, CH_2 + C*H*), 0.81 (s, 3H, CH_3), 0.66–0.53 (m, 1H, C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.2 (C_qO), 139.1 (1'-C_q,$_{Ar}$), 128.1 (+, 3',5'-*C*H$_{Ar}$), 127.1 (+, 2',6'-*C*H$_{Ar}$), 127.0 (+, 4'-*C*H$_{Ar}$), 88.1 (+, 17-*C*HOBn), 82.9 (3-C_qO), 71.4 (–, *C*H$_2$OPh), 58.2 (+, 2-*C*HO), 53.4 (+, *C*H), 50.8 (+, *C*H), 42.8 (13-C_q), 38.6 (–, *C*H$_2$), 38.6 (+, *C*H), 37.6 (–, *C*H$_2$), 35.1 (+, *C*H), 34.3 (10-C_q), 30.9 (–,

CH_2), 30.6 (–, CH_2), 27.8 (–, CH_2), 27.7 (–, CH_2), 23.2 (–, CH_2), 21.0 (+, COCH_3), 20.6 (–, CH_2), 12.6 (+, CH_3), 11.6 (+, CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2912 (w), 1741 (w), 1443 (vw), 1367 (w), 1223 (m), 1192 (w), 1173 (w), 1153 (w), 1088 (w), 1075 (w), 1055 (w), 1027 (w), 988 (w), 947 (vw), 930 (w), 891 (vw), 850 (vw), 821 (vw), 747 (w), 700 (w), 623 (vw), 598 (vw) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 438 (22) $[M]^{\bullet+}$, 397 (15) $[M–C_2H_2O]^+$, 347 (37) $[M–Bn]^+$, 287 (22) $[M–Bn–HOAc]^+$, 269 (14) $[M–Bn–HOAc–H_2O]^+$, 91 (100). – **HRMS** (EI, $C_{28}H_{38}O_4$): calc.: = 438.2765; found: 438.2766.

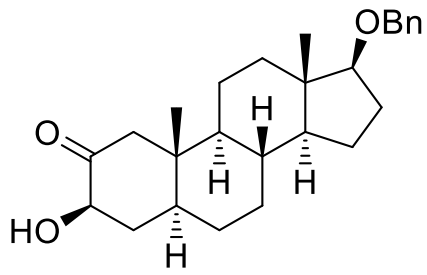
2*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-3-on (**19-Bn**)



Under argon atmosphere, 3*β*-acetoxy-17*β*-benzyloxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Bn**) (2.98 g, 6.80 mmol, 1.00 equiv) in a 10:1 mixture of absolute toluene (85 mL) and pyridine (8.5 mL) was refluxed overnight. The solvent was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 7:1) to give the title compound **19-Bn** as colorless solid (2.26 g, 5.13 mmol, 75%).

R_f = 0.52 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR (**400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 4H, 4×CH_{Ar}), 7.30–7.24 (m, 1H, CH_{Ar}), 5.38 (dd, ^3J = 10.1, 7.0 Hz, 1H, 3-C*H*OAc), 4.55 (s, 2H, OCH_2Ph), 3.44 (dd, *J* = 8.7 Hz, 1H, C*H*OBn), 2.47–2.35 (m, 1H, CH_2), 2.33–2.19 (m, 1H, CH_2), 2.18–2.10 (m, 1H, CH_2), 2.15 (s, 3H, COCH_3), 2.06–1.92 (m, 3H, 2 different CH_2 + 5-C*H*), 1.82–1.68 (m, 2H, 2 different CH_2), 1.63–1.16 (m, 9H, 5 different CH_2 + 8-CH_2), 1.03–0.76 (m, 3H, CH_2 + 9-C*H* + 14-C*H*), 0.88 (s, 3H, CH_3), 0.85 (s, 3H, CH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 206.6 (3-C_qO), 169.7 (C_qO), 139.0 (1'-C_q), 128.0 (+, 3',5'-CH_{Ar}), 127.1 (+, 4'-CH_{Ar}), 127.0 (+, 2',6'-CH_{Ar}), 88.0 (+, 17-*C*HOBn), 74.1 (+, 2-*C*HOAc), 71.4 (–, *C*H_2OPh), 54.7 (+, 9-*C*H), 50.7 (+, 14-*C*H), 43.3 (–, *C*H_2), 43.0 (13-C_q), 42.0 (–, *C*H_2), 41.6 (+, 5-*C*H), 37.6 (–, *C*H_2), 35.9 (10-C_q), 34.9 (+, 8-*C*H), 30.6 (–, *C*H_2), 28.0 (–, *C*H_2), 27.7 (–, *C*H_2), 23.1 (–, *C*H_2), 21.0 (–, *C*H_2), 20.6 (+, CO*C*H_3), 14.2 (+, *C*H_3), 11.6 (+, *C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2923 (m), 2848 (w), 1747 (m), 1729 (m), 1495 (vw), 1450 (w), 1370 (w), 1232 (m), 1093 (m), 1070 (m), 1039 (m), 1026 (m), 925 (w), 885 (w), 736 (m), 696 (m), 611 (w), 535 (vw), 457 (w) cm^{-1}. – **MS** (EI, 70 eV, 180 °C): *m/z* (%) = 438 (100) $[M]^{\bullet+}$, 380 (35) $[M–Ac]^+$, 347 (81) $[M–Bn]^+$, 287 (80) $[M–Ac–Bn]^+$. – **HRMS** (EI, $C_{28}H_{38}O_4$): calc.: = 438.2765; found: 438.2766.

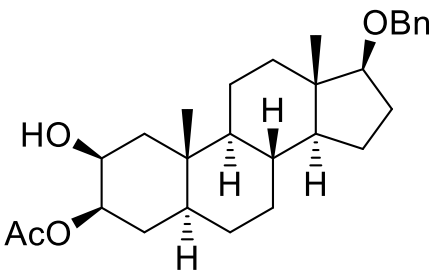
3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-2-on (**20-Bn**)



2*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-3-on (**19-Bn**) (2.25 g, 5.13 mmol, 1.00 equiv) was dissolved in isopropanol (100 mL) and potassium carbonate (3.35 g, 25.6 mmol, 5.00 equiv) in water (10 mL) was added. The reaction mixture was stirred overnight at r.t. and then quenched with water (200 mL). The aqueous phase was extracted with dichloromethane (3 × 150 mL), and the combined organic phases were washed with 1 M aqueous HCl solution (200 mL) and brine (200 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ ethyl acetate, 10:1–~~5~~:1) to obtain the title compound **20-Bn** as colorless solid (1.09 g, 2.46 mmol, 48%).

***R*$_f$** = 0.52 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.34–7.32 (m, 4H, C*H*$_{Ar}$), 7.28–7.24 (m, 1H, C*H*$_{Ar}$), 5.20 (dd, *J* = 11.6, 7.2 Hz, 1H, 3-C*H*OAc), 4.53 (s, 2H, OC*H*$_2$Ph), 3.41 (dd, *J* = 8.3 Hz, 1H, 17-C*H*OBn), 2.50 (d, ^2J = 12.9 Hz, 1H, 1-C*H*$_2^a$), 2.15 (s, 3H, COC*H*$_3$), 2.07 (d, ^2J = 12.9 Hz, 1H, 1-C*H*$_2^b$), 2.04–1.92 (m, 3H, C*H*$_2$ + 2-C*H*$_2^a$ + 16-C*H*$_2^a$), 1.80–1.66 (m, 3H, C*H*$_2$ + 2-C*H*$_2^b$ + 5-C*H*), 1.63–1.22 (m, 8H, 3 different C*H*$_2$ + 16-C*H*$_2^b$ + 8-C*H*), 1.21–1.08 (m, 1H, C*H*$_2$), 1.03–0.88 (m, 3H, C*H*$_2$ + 9-C*H* + 14-C*H*), 0.82 (s, 3H, C*H*$_3$), 0.77 (s, 3H, C*H*$_3$) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 204.2 (2-*C*$_q$O), 169.9 (*C*$_q$O$_2$Me), 139.0 (1ˈ-*C*$_{q,Ar}$), 128.1 (+, 3ˈ,5ˈ-C*H*$_{Ar}$), 127.1 (+, 4ˈ-C*H*$_{Ar}$), 127.1 (+, 2ˈ,6ˈ-C*H*$_{Ar}$), 87.9 (+, *C*HOBn), 75.9 (+, *C*HOAc), 71.4 (–, *C*H$_2$OPh), 53.7 (+, 9-*C*H), 52.2 (–, 1-*C*H$_2$), 50.8 (+, 14-*C*H), 44.0 (+, 5-*C*H), 42.9 (13-*C*$_q$), 41.2 (10-*C*$_q$), 37.4 (–, *C*H$_2$), 34.8 (–, 4-*C*H$_2$), 34.4 (+, 8-*C*H), 30.9 (–, *C*H$_2$), 27.7 (–, *C*H$_2$), 27.3 (–, 16-*C*H$_2$), 23.2 (–, *C*H$_2$), 20.8 (–, *C*H$_2$), 20.6 (+, COC*H*$_3$), 12.3 (+, *C*H$_3$), 11.6 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2922 (vw), 2847 (vw), 1748 (w), 1724 (w), 1452 (w), 1434 (vw), 1372 (vw), 1235 (w), 1193 (vw), 1101 (w), 1083 (w), 1040 (w), 1026 (w), 942 (vw), 920 (vw), 890 (vw), 738 (w), 694 (w), 635 (vw), 550 (vw), 531 (vw), 487 (vw), 474 (vw), 455 (vw) cm^{-1}. – **MS** (EI, 70 eV, 140 °C): *m/z* (%) = 438 (21) [M]$^{\bullet+}$, 347 (45) [M–Bn]$^+$, 287 (15) [M–Ac–Bn]$^+$, 91 (100). – **HRMS** (EI, $C_{28}H_{38}O_4$): calc. = 438.2765; found: 438.2764.

3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-2*β*-ol (**14-Bn**)



Under argon atmosphere, 3*β*-acetoxy-17*β*-benzyloxy-5*α*-androstane-2-on (**20-Bn**) (900 mg, 2.30 mmol, 1.00 equiv) was dissolved in absolute methanol (60 mL) and cooled to –10 °C. Sodium borohydride (174 mg, 4.61 mmol, 2.00 equiv) was added portionwise and the mixture was stirred 2 h at –10 °C (TLC control). The reaction mixture was allowed to warm to r.t. and quenched with water (50 mL). The product was extracted with dichloromethane (3 × 70 mL) and the combined organic phases were washed with aqueous 2 M HCl solution (60 mL) and brine (60 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed. The

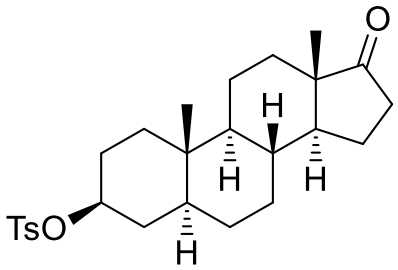
crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) to give the title compound **14-Bn** as colorless solid (739 mg, 1.68 mmol, 82%).

R_f = 0.52 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR (**400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 4H, 4×CH_{Ar}), 7.31–7.24 (m, 1H, CH_{Ar}), 4.79 (ddd, *J* = 11.8, 4.8, 3.3 Hz, 1H, 3-C*H*OAc), 4.55 (s, 2H, OCH_2Ph), 4.14–4.08 (m, 1H, 2-C*H*OH), 3.43 (dd, ^3J = 8.4 Hz, 1H, 17-C*H*OBn), 2.11 (s, 3H, COCH_3), 2.09–1.89 (m, 3H, CH_2 + 1-CH_2^a + CH_2^a), 1.80 (q, *J* = 12.2 Hz, 1H, CH_2^a), 1.72–1.62 (m, 1H, CH_2), 1.63–1.50 (m, 3H, 2 different CH_2 + CH_2^b), 1.49–1.08 (m, 9H, 4 different CH_2 + 1-CH_2^b + CH_2^b + 5-C*H* + 8-C*H*), 1.06 (s, 3H, CH_3), 1.03–0.84 (m, 2H, CH_2 + 14-C*H*), 0.84 (s, 3H, CH_3), 0.67–0.53 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 169.9 (C_qO), 139.2 (1'-C_q), 128.0 (+, 3',5'-*C*H$_{Ar}$), 127.1 (+, 2',6'-*C*H$_{Ar}$), 127.0 (+, 4'-*C*H$_{Ar}$), 88.1 (+, 17-*C*HOBn), 75.4 (+, 3-*C*HOAc), 71.4 (–, *C*H$_2$OPh), 68.5 (+, 2-*C*HOH), 55.2 (+, 9-*C*H), 50.9 (+, 14-*C*H), 45.3 (+, 5-*C*H), 43.0 (13-C_q), 42.8 (–, 1-*C*H$_2$), 37.8 (–, *C*H$_2$), 35.3 (10-C_q), 34.5 (+, 8-*C*H), 31.3 (–, *C*H$_2$), 28.4 (–, *C*H$_2$), 27.8 (–, *C*H$_2$), 27.7 (–, *C*H$_2$), 23.2 (–, *C*H$_2$), 21.2 (+, CO*C*H$_3$), 20.8 (–, *C*H$_2$), 14.4 (+, *C*H$_3$), 11.8 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3599 (vw), 2926 (w), 2842 (w), 1727 (m), 1450 (vw), 1390 (w), 1369 (w), 1322 (w), 1246 (m), 1131 (w), 1072 (m), 1032 (m), 975 (w), 940 (w), 919 (w), 852 (vw), 835 (vw), 759 (w), 740 (vw), 702 (w), 638 (w), 567 (vw), 545 (vw) cm^{-1}. – **MS** (EI, 70 eV, 160 °C): *m/z* (%) = 440 (21) [M]$^{\bullet+}$, 380 (30) [M–Ac]$^+$, 349 (49) [M–Bn]$^+$, 289 (43) [M–Ac–OBn]$^+$, 271 (35), 91 (100). – **HRMS** (EI, $C_{28}H_{40}O_4$): calc.: = 440.2921; found: 440.2923.

2.2 Experimental procedures for the synthesis of 2*β*-acetoxy-3*β*-hydroxy-5*α*-androstane-17-on and related steroids using the second generation approach (Scheme 4 and 6)

2.2.1 Synthesis of the alkenes

3*β*-[[(4-Methylphenyl)sulfonyl]oxy]-5*α*-androstane-17-on (**SI-03**)[9]



Epi-androsterone (**12**) (10.0 g, 34.4 mmol, 1.00 equiv) and *para*-toluenesulfonyl chloride (8.53 g, 44.8 mmol, 1.30 equiv) were dissolved in pyridine (50 mL) and stirred overnight at r.t.

Workup A:

The solution was concentrated, diluted with dichloromethane (500 mL) and washed with aqueous 1 M HCl solution (3 × 300 mL), saturated aqueous $NaHCO_3$ solution (300 mL) and brine (300 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was evaporated. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 2:1) to give the title compound **SI-03** as colorless crystalline solid (14.0 g, 31.4 mmol, 92%).

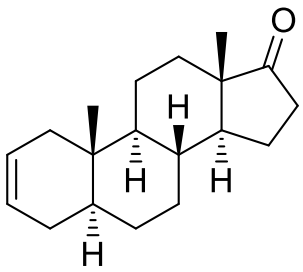
Workup B:

The reaction was poured into an aqueous $NaHCO_3$ solution (100 mL) and the precipitate was filtered off. The colorless residue was washed multiple times with H_2O and dried in vacuo to afford the product as colorless solid (11.5 g, 25.8 mmol, 95%).

R_f = 0.28 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.78 (d, J = 8.3 Hz, 2H, 2×CH_{Ar}), 7.32 (d, J = 8.3 Hz, 2H, 2×CH_{Ar}), 4.40 (tt, ^3J = 10.9, 5.2Hz, 1H, 3-C*H*OTs), 2.44 (s, 3H, $C_{Ar}CH_3$), 2.42 (dd, J = 2.4 Hz, 1H, 16-CH_2^a), 2.11–1.99 (m, 1H, 16-CH_2^b), 1.96–1.85 (m, 1H, CH_2), 1.81–1.44 (m, 10H, 8 different CH_2 + 8-C*H*), 1.34–1.17 (m, 5H, 4 different CH_2 + 14-C*H*), 1.14–1.05 (m, 1H, 5-C*H*), 0.99–0.87 (m, 2H, 2 different CH_2), 0.83 (s, 3H, 19-CH_3), 0.80 (s, 3H, 18-CH_3), 0.64 (td, J = 11.8, 3.8 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 221.3 (17-C_qO), 144.5 (C_qSO_2), 134.8 (C_q), 129.9 (+, 2×CH_{Ar}), 127.7 (+, 2×CH_{Ar}), 82.3 (+, 3-*C*H), 54.3 (+, 9-*C*H), 51.4 (+, 14-*C*H), 47.9 (13-C_q), 44.9 (+, 5-*C*H), 36.9 (–, CH_2), 35.9 (–, 16-CH_2), 35.5 (10-C_q), 35.1 (+, 8-*C*H), 34.9 (–, CH_2), 31.6 (–, CH_2), 30.8 (–, CH_2), 28.4 (–, CH_2), 28.2 (–, CH_2), 21.9 (–, CH_2), 21.8 (+, C_qCH_3), 20.6 (–, CH_2), 13.9 (+, 18-CH_3), 12.2 (+, 19-CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2933 (vw), 2854 (vw), 1735 (w), 1596 (vw), 1450 (vw), 1407 (vw), 1352 (w), 1291 (vw), 1172 (w), 1095 (vw), 1044 (vw), 1011 (vw), 926 (w), 903 (w), 867 (w), 853 (w), 813 (w), 732 (vw), 705 (vw), 667 (w), 612 (vw), 556 (w), 534 (w), 507 (vw), 381 (vw) cm^{-1}. – **MS** (EI, 70 eV, 170 °C): *m/z* (%) = 444 (23) $[M]^{\bullet+}$, 272 (100) $[M–OTs]^+$, 257 (18) $[M–OTs–CH_3]^+$, 218 (72). – **HRMS** (EI, $C_{26}H_{36}O_4S$): calc.: 444.2329; found: 444.2330.

The analytical and spectroscopical data match those reported in the literature.[9]

5*α*-Androst-2-ene-17-on (**15**)[10]



3-Tosylandrost-17-on **SI-03** (14.0 g, 31.4 mmol, 1.00 equiv), lithium carbonate (4.65 g, 62.9 mmol, 2.00 equiv) and lithium bromide (5.47 g, 62.9 mmol, 2.00 equiv) were suspended in *N*,*N*-dimethylformamide (200 mL) and refluxed for 7 h.

Workup A:

The reaction was diluted with dichloromethane (250 mL) and washed with diluted aqueous HCl solution (400 mL), water (400 mL) and brine (100 mL). The organic phase was dried over Na_2SO_4, filtered and the solvent was removed. The crude product was purified by flash column chromatography on silica gel (*n*-pentane/diethyl ether, 10:1) to give the title compound **15** (8.09 g, 29.7 mmol, 95%)* in inseparable mixture with its regioisomer (5*α*-androste-3-en-17-on).

Workup B:

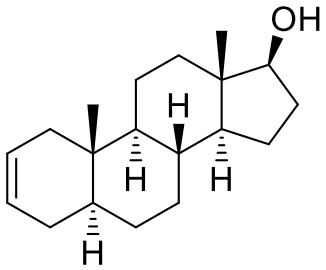
The reaction was poured into H_2O (500 mL), the formed precipitate was filtered and washed multiple times with H_2O. The obtained solid was further purified by filter column on silica gel (*n*-pentane/diethyl ether, 50:1) to give the title compound in inseparable mixture with its regioisomer (5*α*-androste-3-en-17-on) as colorless solid (7.87 g, 28.9 mmol, 92%).

***R*$_f$** = 0.45 (*n*-pent/Et_2O, 20:1). – **^{1}H NMR** (400 MHz, $CDCl_3$, major isomer)*: δ = 5.65–5.52 (m, 2H, 2-C*H* + 3-C*H*),2.43 (dd, ^2J = 19.2 Hz, ^3J = 8.8 Hz, 1H, 16-CH_2^a), 2.06 (dd, ^2J = 19.2 Hz, ^3J = 8.8 Hz, 1H, 16-CH_2^b), 1.98–1.56 (m, 8H, 8 × CH_2), 1.56–1.50 (m, 1H, 8-C*H*), 1.50–1.44 (m, 2H, 2 different CH_2), 1.42–1.32 (tt, ^3J = 13.0, 3.5 Hz, 1H, 5-C*H*), 1.29–1.16 (m, 3H, 2 different CH_2 and 14-C*H*), 1.09–0.89 (m, 2H, CH_2), 0.87 (s, 3H, 18-CH_3), 0.78 (s, 3H, 19-CH_3), 0.74 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$, major isomer)*: δ = 221.6 (17-C_qO), 125.9 (+, 2-*C*H or 3-*C*H), 125.9 (+, 3-*C*H or 2-*C*H), 54.3 (+, 9-*C*H), 51.6 (+, 14-*C*H), 47.9 (13-C_q), 41.6 (+, 5-*C*H), 39.8 (–, *C*H_2), 36.0 (–, 16-*C*H_2), 35.3 (+, 8-*C*H), 34.9 (10-C_q), 31.7 (–, *C*H_2), 30.8 (–, *C*H_2), 30.4 (–, *C*H_2), 28.6 (–, *C*H_2), 21.9 (–, *C*H_2), 20.3 (–, *C*H_2), 13.9 (+, 18-*C*H_3), 11.8 (+, 19-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3019 (vw), 2928 (w), 1736 (m), 1443 (w), 1403 (vw), 1375 (w), 1258 (vw), 1181 (vw), 1107 (vw), 1011 (w), 959 (vw), 890 (vw), 822 (vw), 773 (vw), 713 (vw), 664 (m), 641 (vw), 582 (vw), 530 (vw), 499 (vw), 427 (vw) cm^{-1}. – **MS** (EI, 70 eV, 70 °C): *m/z* (%) = 272 (100) $[M]^{\bullet+}$, 257 (17) $[M–CH_3]^+$, 218 (47). – **HRMS** (EI, $C_{19}H_{28}O$): calc.: 272.2135; found: 272.2134.

* The yield refers to the mixture of regioisomers whose ratio was determined to 10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum.

The analytical and spectroscopical data match those reported in the literature.[9]

5*α*-Androst-2-ene-17*β*-ol (**SI-06-OH**)[9]



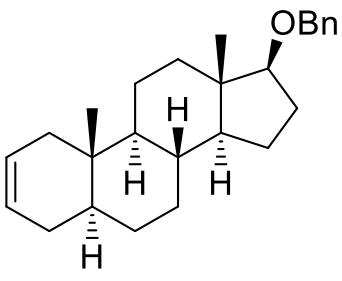
Under argon atmosphere, 5*α*-androste-2-ene-17-on (**15**) (2.44 g, 8.96 mmol, 1.00 equiv) was dissolved in absolute dichloromethane and absolute methanol (4:1, 50 mL). At –20 °C sodium borohydride (1.36 g, 35.8 mmol. 4.00 equiv) was added portionwise and the reaction was stirred for 4 h while slowly warming to r.t. The reaction was diluted with saturated aqueous $NaHCO_3$ solution (200 mL) and ethyl acetate (200 mL). After phase separation, the aqueous phase was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na_2SO_4 and filtered. The solvent was removed and the obtained crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1→1:1) to afford the title compound **SI-06-OH** as colorless solid (2.45 g, 8.92 mmol, quantitative)*.

$\boldsymbol{R_f}$ = 0.47 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (400 MHz, $CDCl_3$ + CD_3OD, major isomer)*: δ = 5.60–5.43 (m, 2H, 2-C*H* + 3-C*H*), 3.55 (t, *J* = 8.6 Hz, 1H, 17-C*H*OH), 2.04–0.73 (m, 19H, 8 different CH_2 + 5-C*H* + 8-C*H* + 14-C*H*), 0.69 (s, 3H, CH_3), 0.67 (s, 3H, CH_3), 0.67–0.57 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$+ CD_3OD, major isomer)*: δ = 125.7 (+, 2- or 3-*C*H), 125.6 (+, 2- or 3-*C*H), 81.6 (+, 17-*C*HOH), 54.0 (+, 14-*C*H), 50.8 (+, 9-*C*H), 42.6 (13-C_q), 41.3 (+, 5-*C*H), 39.6 (–, *C*H_2), 36.5 (–, *C*H_2), 35.4 (+, 8-*C*H), 34.5 (10-C_q), 31.2 (–, *C*H_2), 30.1 (–, *C*H_2), 30.1 (–, *C*H_2), 28.4 (–, *C*H_2), 23.1 (–, *C*H_2), 20.3 (–, *C*H_2), 11.5 (+, *C*H_3), 10.8 (+, *C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3272 (vw), 3017 (vw), 2912 (w), 2868 (w), 2844 (w), 1655 (vw), 1443 (vw), 1376 (vw), 1351 (vw), 1336 (vw), 1322 (vw), 1248 (vw), 1185 (vw), 1137 (vw), 1113 (vw), 1083 (w), 1058 (w), 1030 (w), 990 (vw), 958 (vw), 945 (vw), 925 (vw), 925 (vw), 871 (vw), 831 (vw), 772 (vw), 705 (vw), 664 (w), 614 (vw) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 274 (27) $[M]^{\bullet+}$, 220 (16), 184 (34), 155 (67), 98 (100). – **HRMS** ($C_{19}H_{30}O$): calc.: 274.2291; found: 274.2292.

* The yield refers to the inseparable mixture of regioisomers whose ratio was determined to 10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum.

The analytical and spectroscopical data match those reported in the literature.[9]

17*β*-Benzyloxy-5*α*-androst-2-ene (**SI-06-Bn**)



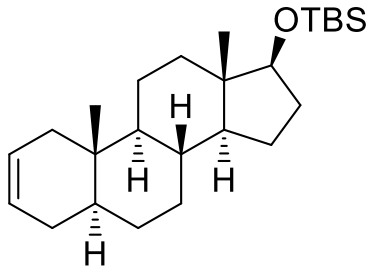
Under argon atmosphere, 5*α*-androst-2-ene-17*β*-ol (**SI-06-OH**) (2.45 g, 8.92 mmol, 1.00 equiv) was dissolved in absolute 1,4-dioxane (100 mL) and at 0 °C benzyl 2,2,2-trichloroacetimidate (1.8 mL, 2.49 g, 9.86 mmol, 1.11 equiv) and trifluoromethanesulfonic acid (0.20 mL) were added. The reaction was stirred overnight at r.t. If not all starting material was converted (TLC control), a second portion of benzyl 2,2,2-trichloracetimidate (0.30 mL, 0.408 g, 1.61 mmol, 0.18 equiv) and trifluoromethanesulfonic acid (0.05 mL) was added and the reaction was stirred for further 19 h at r.t. The reaction was stopped by adding a

saturated aqueous $NaHCO_3$ solution (200 mL). After dilution with dichloromethane (200 mL), the phases were separated and the aqueous phase was extracted with dichloromethane (2 × 200 mL). The combined organic extracts were washed with brine (200 mL) and dried over Na_2SO_4. After filtration and solvent removal, the obtained crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 20:1 → 10:1) to afford the title compound **SI-06-Bn** as pale yellow oil (2.03 g, 5.57 mmol, 62%)*.

$\boldsymbol{R_f}$ = 0.76 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR (**400 MHz, $CDCl_3$, major isomer): δ = 7.39–7.29 (m, 4H, 4×CH_{Ar}), 7.31–7.25 (m, 1H, CH_{Ar}), 5.66–5.53 (m, 2H, 2-C*H* + 3-C*H*), 4.56 (s, 2H, OCH_2Ph), 3.48–3.37 (m, 1H, 17-C*H*OH), 2.07–1.83 (m, 4H, 4 different CH_2), 1.76–1.49 (m, 6H, 6 different CH_2), 1.46–1.10 (m, 7H, 4 different CH_2 + 5-C*H* + 8-C*H*), 0.99–0.87 (m, 2H, CH_2 + 14-C*H*), 0.85 (s, 3H, CH_3), 0.78 (s, 3H, CH_3), 0.73–0.68 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$, major isomer): δ = 140.3 (C_q), 129.1 (+, 2×CH_{Ar}), 128.2 (+, 2×CH_{Ar}), 128.1 (+, CH_{Ar}), 126.8 (+, 2- or 3-*C*H), 126.7 (+, 2- or 3-*C*H), 89.3 (+, 17-*C*HOBn), 72.5 (–, OCH_2Ph), 55.2 (+, 9-*C*H), 52.2 (+, 14-*C*H), 44.0 (13-C_q), 42.4 (+, 5-*C*H), 40.7 (–, CH_2), 39.0 (–, CH_2), 36.4 (+, 8-*C*H), 35.6 (10-C_q), 32.3 (–, CH_2), 31.2 (–, CH_2), 29.6 (–, CH_2), 28.9 (–, CH_2), 24.3 (–, CH_2), 21.5 (–, CH_2), 12.8 (+, CH_3), 12.6 (+, CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3021 (vw), 2909 (m), 2846 (w), 1720 (vw), 1494 (w), 1452 (w), 1377 (w), 1352 (w), 1203 (vw), 1092 (m), 1072 (m), 1028 (w), 831 (vw), 733 (m), 696 (m), 665 (m), 635 (w) cm^{-1}. – **MS** (EI, 70 eV, 60 °C): *m/z* (%) = 364 (1) $[M]^{\bullet+}$, 273 (2) $[M–CH_2Ph]^+$, 91 (100). – **HRMS** ($C_{26}H_{36}O$): calc.: 364.2766; found: 364.2765.

* The yield refers to the inseparable mixture of regioisomers whose ratio was determined to 10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum.

17*β*-[(*tert*-Butyldimethylsilyl)oxy]-5*α*-androst-2-ene (**SI-06-TBS**)



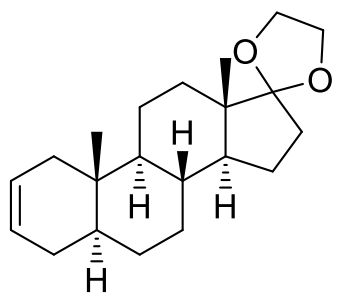
Under argon atmosphere, 5*α*-androst-2-ene-17*β*-ol (**SI-06-OH**) (180 mg, 0.656 mmol, 1.00 equiv) was dissolved in absolute *N*,*N*-dimethylformamide (5.0 mL) and imidazole (70 mg, 0.984 mmol, 1.50 equiv) and *tert*-butyldimethylsilyl chloride (109 mg, 0.656 mmol, 1.10 equiv) were added. The reaction was stirred overnight at r.t. whereby after a few minutes the formation of a precipitate was observed. The reaction was quenched with water (50 mL) and the aqueous phase was extracted with diethyl ether (3 × 50 mL). The combined organic phases were washed with water (30 mL) and brine (30 mL) and dried over Na_2SO_4. After filtration and removal of the solvent, the obtained crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 10:1) to give the title compound **SI-06-TBS** as colorless solid (168 mg, 0.432 mmol, 66%)*.

$\boldsymbol{R_f}$ = 0.91 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (400 MHz, $CDCl_3$, major isomer): δ = 5.63–5.56 (m, 2H, 2-C*H* + 3-C*H*), 3.54 (dd, ^3J = 8.3 Hz, 1H, 17-C*H*OTBS), 1.99–1.81 (m, 3H, 3 different CH_2), 1.76–1.64 (m, 4H, 4 different CH_2), 1.59–1.11 (m, 9H, 4 different CH_2 + 5-C*H* + 8-C*H*), 1.03–0.82 (m, 3H, 2 different CH_2 + 14-C*H*), 0.87 (s, 9H, SiC(CH_3)$_3$), 0.76 (s, 3H, CH_3), 0.70

(s, 3H, CH_3), 0.68–0.61 (m, 1H, 9-C*H*), 0.01 (s, 3H, SiCH_3), 0.00 (s, 3H, SiCH_3). – **^{13}C NMR** (101 MHz, $CDCl_3$, major isomer): δ = 125.8 (+, 2- or 3-*C*H), 125.7 (+, 2- or 3-*C*H), 81.7 (+, 17-*C*HOTBS), 54.2 (+, 14-*C*H), 50.5 (+, 9-*C*H), 43.0 (13-C_q), 41.4 (+, 5-*C*H), 39.7 (–, CH_2), 37.1 (–, CH_2), 35.5 (+, 8-*C*H), 34.6 (10-C_q), 31.3 (–, CH_2), 30.8 (–, CH_2), 30.2 (–, CH_2), 28.5 (–, CH_2), 25.7 (+, 3×C_q(CH_3)), 23.4 (–, CH_2), 20.4 (–, CH_2), 18.0 (SiC_q), 11.6 (+, CH_3), 11.2 (+, CH_3), –4.7 (+, SiCH_3), –5.0 (+, SiCH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3021 (w), 2927 (m), 2852 (m), 1461 (w), 1443 (w), 1359 (w), 1247 (m), 1139 (m), 1114 (m), 1090 (m), 1032 (w), 1016 (w), 939 (w), 901 (w), 877 (m), 830 (s), 774 (s), 664 (m), 619 (w), 577 (w), 469 (w) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 389 (7) $[M]^{\bullet+}$, 331 (100) $[M–{}^t\mathrm{Bu}]^{\bullet+}$, 255 (60) $[M–SiMe_2{}^t\mathrm{Bu}–H_2O]^{\bullet+}$. – **HRMS** ($C_{25}H_{44}OSi$): calc.: 388.3156; found: 388.3154.

* The yield refers to the inseparable mixture of regioisomers whose ratio was determined to 10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum.

17,17-(Ethylendioxy)-5*α*-androst-2-ene (**SI-07**)



Under argon atmosphere, 5*α*-androst-2-ene-17*β*-on (**15**) (200 mg, 0.734 mmol, 1.00 equiv) and *para*-toluenesulfonic acid monohydrate (28 mg, 0.147 mmol, 0.20 equiv) was dissolved in absolute dichloromethane (5.0 mL) followed by the addition of absolute ethylene glycol (0.82 mL, 911 mg, 14.7 mmol, 20.0 equiv) and trimethyl orthoformate (0.80 mL, 779 mg, 7.34 mmol, 10.0 equiv). The reaction was stirred overnight at r.t. before being quenched with 1 M aqueous NaOH solution (50 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic phases were washed with brine (100 mL) and then dried over Na_2SO_4. Filtration and evaporation of the solvent gave the crude product which was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 10:1) to obtain the title compound **SI-07** as colorless solid (204 mg, 0.645 mmol, 88%)*.

R_f = 0.77 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (500 MHz, $CDCl_3$, major isomer): δ = 5.66–5.48 (m, 2H, 2-C*H* + 3-C*H*), 3.98–3.81 (m, 4H, 2×OCH_2), 2.05–1.60 (m, 8H, 2 different CH_2 + 1-CH_2 + 16-CH_2 + 4-CH_2), 1.55–1.48 (m, 2H, 2 different CH_2), 1.43–1.11 (m, 8H, 5 different CH_2 + 5-C*H* + 8-C*H* + 14-C*H*), 0.95–0.87 (m, 1H, CH_2), 0.84 (s, 3H, 18-CH_3), 0.74 (s, 3H, 19-CH_3), 0.76–0.70 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$, major isomer): δ = 126.0 (+, 2- or 3-*C*H), 125.9 (+, 2- or 3-*C*H), 119.6 (17-C_qO), 65.3 (–, OCH_2), 64.7 (–, OCH_2), 54.0 (+, 9-*C*H), 50.4 (+, 14-*C*H), 46.0 (13-C_q), 41.5 (+, 5-*C*H), 39.9 (–, 1-CH_2), 35.9 (+, 8-*C*H), 34.8 (10-C_q), 34.3 (–, 16-CH_2), 31.2 (–, CH_2), 30.8 (–, CH_2), 30.4 (–, 4-CH_2), 28.7 (–, CH_2), 22.8 (–, CH_2), 20.4 (–, CH_2), 14.5 (+, 18-CH_3), 11.8 (+, 19-CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3021 (vw), 2966 (w), 2935 (w), 2881 (w), 1739 (w), 1444 (w), 1377 (w), 1343 (vw), 1303 (w), 1275 (w), 1203 (w), 1169 (w), 1112 (w), 1053 (m), 1035 (m), 1013 (w), 979 (w), 950 (w), 899 (w), 881 (w), 830 (w), 786 (w), 752 (w), 666 (m), 639 (w), 598 (vw) cm^{-1}. – **MS** (EI, 70 eV, 60 °C): *m/z* (%) = 316 (68) $[M]^{\bullet+}$, 272 (26) $[M–C_2H_4O]^{\bullet+}$, 218 (21), 99 (100). – **HRMS** ($C_{21}H_{32}O_2$): calc.: 316.2397; found: 316.2397.

* The yield refers to the inseparable mixture of regioisomers whose ratio was determined to 10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum.

2.2.2 Synthesis of the *cis*-diol derivatives in Scheme 4

All reaction protocols of this section are based on the general procedure **GP-1** described in the experimental section of the paper.

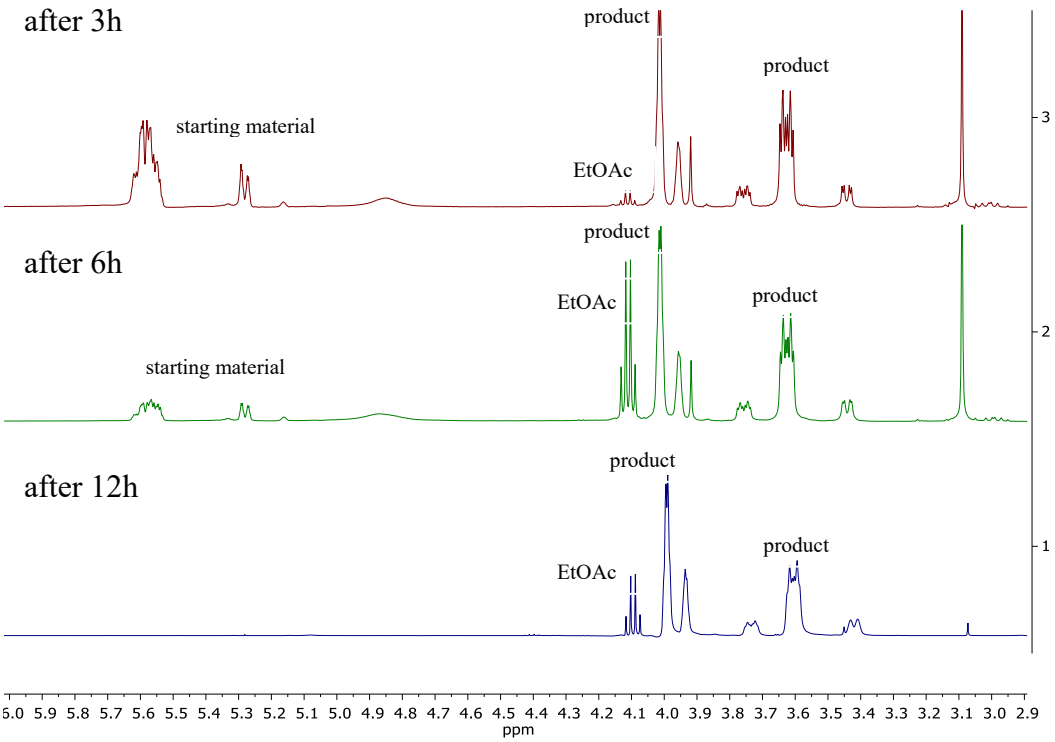
General procedure for the dihydroxylation (GP-1)

Under argon atmosphere, the androst-2-ene derivative (1.00 equiv) was dissolved in *tert*-butanol and the required commercially available AD-mix, dissolved in the same amount of water, was added. The mixture was stirred for 10 minutes at r.t. before methanesulfonamide (0.40 equiv) was added. The yellow suspension was stirred vigorously for 7 d at r.t. and was then quenched with saturated aqueous $Na_2S_2O_3$ solution. After extraction with ethyl acetate (3 ×) the combined organic phases were washed consecutively with 2 M aqueous solution of KOH, water and brine. The organic phases were dried over Na_2SO_4 and after filtration the solvent was removed. The residue was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate) to obtain the corresponding *cis*-diol as a colorless powder.

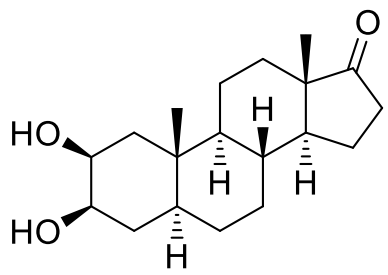
Please note that the reaction times were successfully reduced when "self-made" AD-mix was used instead of the commercially available AD-mix *α*. The following mixture was used:

$K_3Fe(CN)_6$: 2.50 equiv
K_2CO_3 : 2.50 equiv
$(DHQ)_2PHAL$: 0.010 equiv
K_2OsO_4 : 0.0090 equiv

Crude ^1H NMR spectra (500 MHz, $CDCl_3$):



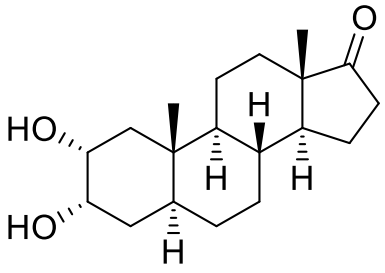
2*β*,3*β*-Dihydroxy-5*α*-androstane-17-on (**21**)



According to the general procedure for the dihydroxylation **GP-1**, 5*α*-androste-2-ene-17-on (**15**) (5.25 g, 19.3 mmol, 1.00 equiv) was dissolved in *tert*-butanol (250 mL) and AD-mix *α* (26.9 g) in water (250 mL) was added. After 10 min methanesulfonamide (733 mg, 7.71 mmol, 0.40 equiv) was added. The work up followed **GP-1**, whereby the crude product was purified by flash column chromatography on silica (EtOAc) to obtain the title compound **21** as colorless solid (3.62 g, 11.8 mmol, 61%).

R_f = 0.49 (EtOAc/MeOH, 200:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.09–3.96 (m, 1H, 2-C*H*OH), 3.64 (ddd, J = 11.0, 8.9, 4.9 Hz, 1H, 3-C*H*OH), 2.43 (ddd, ^2J = 19.0 Hz, ^3J = 8.9, 1.1 Hz, 1H, 16-CH_2^a), 2.23–2.18 (m, 1H, O*H*), 2.11–1.99 (m, 3H, 1-CH_2^a + 16-CH_2^b + O*H*), 1.96–1.87 (m, 1H, CH_2), 1.85–1.75 (m, 2H, 2 different CH_2), 1.72–1.60 (m, 2H, 2 different CH_2), 1.60–1.45 (m, 2H, CH_2 + 8-C*H*), 1.42–1.31 (m, 4H, 3 different CH_2), 1.30–1.19 (m, 2H, CH_2 + 14-C*H*), 1.18–1.10 (m, 2H, 1-CH_2^b + 5-C*H*), 1.03 (s, 3H, CH_3), 0.99–0.92 (m, 1H, CH_2), 0.85 (s, 3H, CH_3), 0.65 (ddd, J = 12.3, 10.7, 4.0 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 221.5 (17-*C*O), 72.4 (+, 3-*C*H), 70.2 (+, 2-*C*H), 55.4 (+, 9-*C*H), 51.5 (+, 14-*C*H), 48.0 (13-C_q), 45.5 (+, 5-*C*H), 43.2 (–, 1-*C*H_2), 36.0 (–, 16-*C*H_2), 35.6 (10-C_q), 34.6 (+, 8-*C*H), 32.5 (–, 4-*C*H_2), 31.7 (–, *C*H_2), 30.9 (–, *C*H_2), 28.2 (–, *C*H_2), 21.9 (–, *C*H_2), 20.7 (–, *C*H_2), 14.6 (+, 19-*C*H_3), 14.0 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3520 (ν-O-H, vw), 3395 (vw), 2920 (w), 2850 (w), 1730 (w), 1452 (vw), 1404 (w), 1291 (vw), 1250 (vw), 1193 (vw), 1130 (vw), 1087 (vw), 1046 (w), 1006 (w), 967 (w), 932 (vw), 904 (vw), 851 (vw), 821 (vw), 739 (vw), 692 (vw), 661 (vw), 626 (vw), 580 (vw), 490 (vw), 452 (vw), 415 (vw) cm^{-1}. – **MS** (EI, 120 °C, 70 eV): *m/z* (%) = 306 (100) $[M]^{\bullet+}$, 291 (5) $[M–CH_3]^+$, 288 (9), 262 (16). – **HRMS** (EI, $C_{19}H_{30}O_3$): calc.: 306.2189; found: 306.2191.

2*α*,3*α*-Dihydroxy-5*α*-androstane-17-on (**22**)



According to the general procedure for the dihydroxylation **GP-1**, 5*α*-androste-2-ene-17-on (**15**) (73 mg, 268 µmol, 1.00 equiv) was dissolved in *tert*-butanol (5.6 mL) and AD-mix *β* (525 mg) in water (6.0 mL) was added. After 10 min methanesulfonamide (13 mg, 138 µmol, 0.40 equiv) was added and the suspension was stirred for 4 d at r.t. The work up followed **GP-1**, whereby the crude product was purified by flash column chromatography on silica gel (EtOAc) to obtain the title compound **22** as colorless solid (34 mg, 110 µmol, 41%)*.

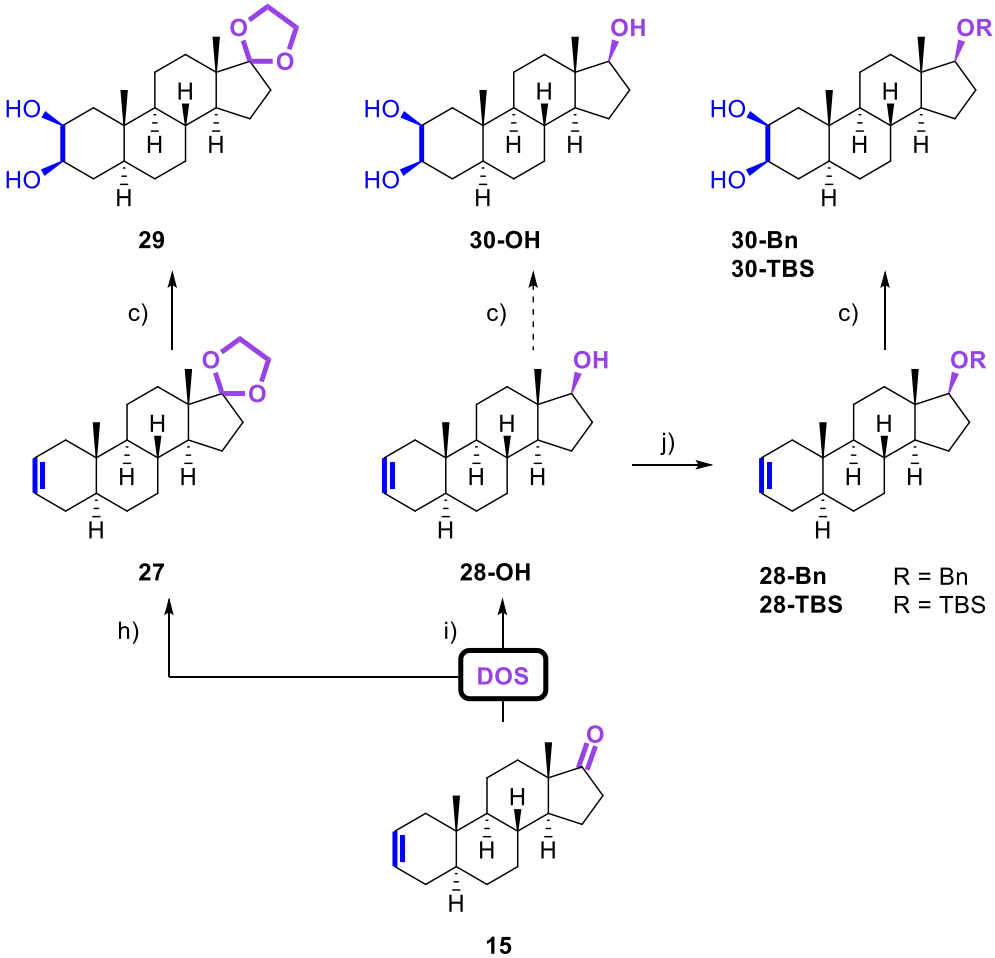
R_f = 0.38 (EtOAc/MeOH, 200:1). – **^{1}H NMR** (500 MHz, $CDCl_3$, major isomer): δ = 3.99–3.93 (m, 1H, 3-C*H*OH), 3.76 (ddd, J = 1.9, 4.6, 3.4 Hz, 1H, 2-C*H*OH), 2.43 (dd, ^2J = 19.3 Hz, ^3J = 8.6 Hz, 1H, 16-CH_2^a), 2.14–1.99 (m, 1H, 16-CH_2^b), 1.97–1.88 (m, 1H, CH_2), 1.84–1.74 (m, 1H, CH_2), 1.73–1.64 (m, 2H, CH_2), 1.61–1.13 (m, 12H, 6 different CH_2 + 5-C*H* + 8-C*H* + 14-C*H*), 1.05–0.94 (m, 1H, CH_2), 0.86–0.81 (m, 1H, 9-C*H*), 0.85 (s, 3H, CH_3), 0.82 (s, 3H,

CH_3) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$, major isomer): δ = 221.5 (17-C_qO), 69.3 (+, 2- or 3-*C*H), 69.1 (+, 3- or 2-*C*H), 54.4 (+, 9-*C*H), 51.5 (+, 14-*C*H), 47.9 (13-C_q), 41.0 (–, *C*H_2), 38.3 (+, 5-*C*H), 37.2 (10-C_q), 36.0 (–, 16-*C*H_2), 34.5 (+, 8-*C*H), 34.3 (–, *C*H_2), 31.6 (–, *C*H_2), 30.8 (–, *C*H_2), 27.5 (–, *C*H_2), 21.9 (–, *C*H_2), 20.3 (–, *C*H_2), 14.0 (+, *C*H_3), 12.6 (+, *C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3444 (vw), 2920 (w), 2854 (vw), 1718 (w), 1441 (vw), 1401 (vw), 1374 (vw), 1290 (vw), 1213 (vw), 1108 (vw), 1040 (w), 1004 (w), 976 (vw), 937 (vw), 875 (vw), 832 (vw), 730 (vw), 697 (vw), 665 (vw), 583 (vw), 526 (vw), 445 (vw), 386 (vw) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 306 (100) $[M]^{\bullet+}$, 291 (6) $[M–CH_3]^+$, 288 (19), 273 (12), 270 (15), 262 (20), 232 (15), 231 (14). – **HRMS** (EI, $C_{19}H_{30}O_3$): calc.: 306.2189; found: 306.2191.

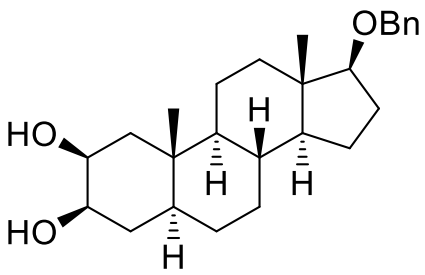
* The desired 2*α*,3*α*-diol **22** could not be completely separated from its isomers.

2.2.3 Synthesis of further *cis*-diol derivatives

In order to demonstrate the generality of the dihydroxylation and its potential in terms of the diversification of the lead structure, the keto group at C-17 was protected as ketal **SI-07** and reduced to **SI-06-OH**. For better comparison with previously presented results, the hydroxyl group was protected with a TBS and a benzyl group. The corresponding 2*β*,3*β*-*cis*-diols **SI-08-Bn** and **SI-08-TBS** were built in good yields even if the separation of the diastereomers *via* column chromatography on silica was challenging resulting in lower isolated yields. Unfortunately, the purification of **SI-08-OH** under similar conditions was not successful. Nevertheless, its formation was confirmed by ^{1}H NMR spectroscopy.



2*β*,3*β*-Dihydroxy-17*β*-benzyloxy-5*α*-androstane-17-on (**SI-08-Bn**)

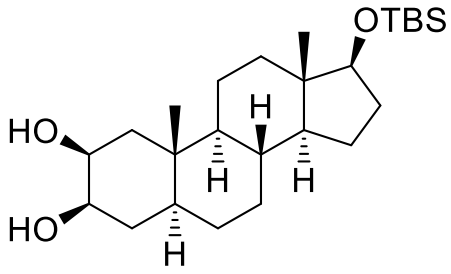


According to the general procedure for the dihydroxylation **GP-1**, 17*β*-benzyloxy-5*α*-androst-2-ene (**SI-06-Bn**) (2.20 g, 6.03 mmol, 1.00 equiv) was dissolved in *tert*-butanol (80 mL) and AD-mix *α* (8.50 g) in water (100 mL) was added. After 10 min methanesulfonamide (228 mg, 2.41 mmol, 0.40 equiv) was added. The work up followed **GP-1**, whereby the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 2:1) to obtain the title compound **SI-08-Bn** as colorless solid (756 mg, 1.90 mmol, 31%)*****.

***R*$_f$** = 0.38 (EtOAc/MeOH, 200:1). – **^{1}H NMR** (400 MHz, $CDCl_3$, major isomer): δ = 7.29–7.20 (m, 4H, 4×C*H*$_{Ar}$), 7.21–7.15 (m, 1H, C*H*$_{Ar}$), 4.46 (s, 2H, OC*H*$_2$Ph), 3.94 (d, ^3J = 3.4 Hz, 1H, 2-C*H*OH), 3.54 (ddd, ^3J = 8.8, 4.2 Hz, 1H, 3-C*H*OH), 3.32 (t, ^3J = 8.4 Hz, 1H, 17-C*H*OBn), 2.15 (s, 1H, O*H*), 2.02 (s, 1H, O*H*), 1.98 (dd, J = 14.6, 3.0 Hz, 1H, C*H*$_2$), 1.94–1.82 (m, 2H, 1-C*H*$_2^a$ + C*H*$_2$), 1.67–1.56 (m, 2H, 2 different C*H*$_2$), 1.54–1.41 (m, 3H, 4-C*H*$_2^a$ + 2 different C*H*$_2$), 1.38–1.16 (m, 6H, 4-C*H*$_2^b$ + 3 different C*H*$_2$ + 8-C*H*), 1.10–0.97 (m, 3H, 1-C*H*$_2^b$ + C*H*$_2$ + 5-C*H*), 0.94 (s, 3H, 19-C*H*$_3$), 0.90–0.78 (m, 1H, 14-C*H*), 0.78–0.71 (m, 1H, C*H*$_2$), 0.74 (s, 3H, 18-C*H*$_3$), 0.50 (ddd, ^3J = 12.3, 10.3, 4.1 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$, major isomer): δ =139.1 (*C*$_{q,Ar}$), 128.0 (+, 2 × *C*H$_{Ar}$), 127.1 (+, 2 × *C*H$_{Ar}$), 127.1 (+, *C*H$_{Ar}$), 88.2 (+, 17-*C*HOBn), 72.2 (+, 3-*C*HOH), 71.4 (–, O*C*H$_2$Ph), 70.0 (+, 2-*C*HOH), 55.2 (+, 9-*C*H), 51.0 (+, 14-*C*H), 45.2 (+, 5-*C*H), 43.0 (–, 1-*C*H$_2$), 43.0 (13-*C*$_q$), 37.9 (–, *C*H$_2$), 35.2 (10-*C*$_q$), 34.5 (+, 8-*C*H), 32.3 (–, 4-*C*H$_2$), 31.3 (–, *C*H$_2$), 28.0 (–, *C*H$_2$), 27.8 (–, *C*H$_2$), 23.2 (–, *C*H$_2$), 20.8 (–, *C*H$_2$), 14.4 (+, 19-*C*H$_3$), 11.7 (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3381 (vw), 2924 (w), 2846 (w), 1496 (vw), 1453 (w), 1398 (vw), 1377 (vw), 1348 (w), 1136 (w), 1120 (w), 1103 (m), 1089 (w), 1075 (w), 1040 (w), 970 (w), 937 (vw), 896 (vw), 852 (vw), 741 (m), 695 (w), 648 (w) 609 (w) cm^{-1}. – **MS** (EI, 70 eV, 150 °C): *m/z* (%) = 399 (41) [M]$^{\bullet+}$, 307 (34) [M–CH$_2$Ph]$^+$, 289 (14) [M–HOCH$_2$Ph]$^+$, 271 (15) [M–HOCH$_2$Ph–H$_2$O]$^+$, 91 (100). – **HRMS** (EI, $C_{26}H_{38}O_3$): calc.: 398.2819; found: 398.2819.

* The product **SI-08-Bn** could not be completely separated from its isomer (no assignment). According to ^{1}H NMR analysis, the ratio of the isomers was determined to 10:1 (**SI-08-Bn**/undesired isomer).

2*β*,3*β*-Dihydroxy-17*β*-[(*tert*-butyldimethylsilyl)oxy]-5*α*-androstane-17-on (**SI-08-TBS**)

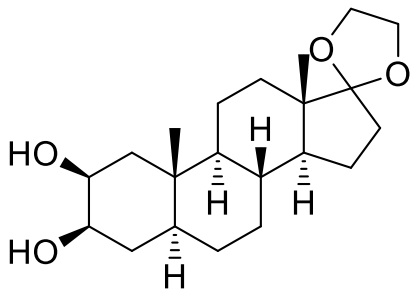


According to the general procedure for the dihyroxylation **GP-1**, 17*β*-[(*tert*-butyldimethyl-silyl)oxy]-5*α*-androst-2-ene (**SI-06-TBS**) (158 mg, 0.409 mmol, 1.00 equiv) was dissolved in *tert*-butanol (6.0 mL) and AD-mix *α* (572 mg) in water (5.0 mL) was added. After 10 min methanesulfonamide (16 mg, 0.164 mmol, 0.40 equiv) was added and the work up

followed **GP-1**, whereby the crude product was purified by flash column chromatography on silica gel (ethyl acetate → ethyl acetate/methanol, 200:1) to give the title compound **SI-08-TBS** as colorless solid (51 mg, 120 mmol, 29%).

R_f = 0.71 (EtOAc). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.05–3.97 (m, 1H, 2-C*H*OH), 3.68–3.58 (m, 1H, 3-C*H*OH), 3.52 (dd, ^3J = 8.3 Hz, 1H, 17-C*H*OTBS), 2.13 (bs, 1H, O*H*), 2.06 (dd, *J* = 14.6, 2.9 Hz, 1H, CH_2), 1.91 (d, *J* = 5.7 Hz, 1H, O*H*), 1.87–1.80 (m, 1H, CH_2), 1.74–1.60 (m, 3H, 3 different CH_2), 1.58–1.49 (m, 2H, 2 different CH_2), 1.42–1.18 (m, 7H, 5 different CH_2 + 8-C*H*), 1.15–1.06 (m, 2H, CH_2 + 5-C*H*), 1.00 (s, 3H, CH_3), 0.96–0.75 (m, 3H, 2 different CH_2 + 14-C*H*), 0.87 (s, 9H, $SiC_q(CH_3)_3$), 0.68 (s, 3H, CH_3), 0.62–0.48 (m, 1H, 9-C*H*), 0.00 (s, 3H, SiCH_3), –0.01 (s, 3H, SiCH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 81.6 (+, 17-*C*HOTBS), 72.2 (+, 3-*C*HOH), 70.0 (+, 2-*C*HOH), 55.4 (+, 9-*C*H), 50.5 (+, 14-*C*H), 45.3 (+, *C*H), 43.2 (13-C_q), 43.1 (–, *C*H_2), 37.1 (–, *C*H_2), 35.2 (10-C_q), 34.8 (+, 8-*C*H), 32.4 (–, *C*H_2), 31.4 (–, *C*H_2), 30.7 (–, *C*H_2), 28.1 (–, *C*H_2), 25.7 (+, 3 × C_q(*C*H_3)), 23.3 (–, *C*H_2), 20.8 (–, *C*H_2), 17.9 (SiC_q(*C*H_3)), 14.4 (+, *C*H_3), 11.3 (+, *C*H_3), –4.7 (+, Si*C*H_3), –5.0 (+, Si*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3348 (vw), 2927 (w), 2855 (w), 1461 (vw), 1361 (w), 1248 (w), 1189 (vw), 1136 (w), 1118 (w), 1079 (m), 1047 (w), 971 (vw), 937 (vw), 910 (vw), 884 (w), 834 (m), 831 (m), 667 (w), 464 (vw) cm^{-1}. – **MS** (EI, 70 eV, 110 °C): *m/z* (%) = 422 (3) $[M]^{\bullet+}$, 365 (100) $[M-{}^t\text{Bu}]^+$, 347 (25) $[M-{}^t\text{Bu}-H_2O]^+$, 289 $[M-\text{TBS}-H_2O]^+$ (35). – **HRMS** ($C_{25}H_{46}O_3Si$): calc.: 422.3216; found: 422.3217.

17,17-(Ethylendioxy)-2*β*,3*β*-dihydroxy-5*α*-androstane (**SI-09**)



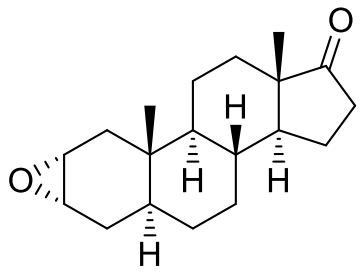
According to the general procedure for the dihydroxylation **GP-1**, 17,17-(ethylendioxy)-5*α*-androst-2-ene (**SI-07**) (90 mg, 286 µmol, 1.00 equiv) was dissolved in *tert*-butanol (6.0 mL) and AD-mix *α* (510 mg) in water (4.0 mL) was added. After 10 min methanesulfonamide (11 mg, 114 µmol, 0.40 equiv) was added and the work up followed **GP-1**, whereby the crude product was purified by flash column chromatography on silica gel (ethyl acetate → ethyl acetate/methanol, 200:1) to give the title compound **SI-09** as colorless solid (34 mg, 97.6 µmol, 34%)*.

***R*$_f$** = 0.58 (EtOAc/MeOH, 200:1). – **^{1}H NMR** (500 MHz, $CDCl_3$, major isomer): δ = 4.00 (d, J = 3.4 Hz, 1H, 2-C*H*OH), 3.95–3.80 (m, 4H, 2×OCH_2), 3.62 (dt, ^3J = 11.3, 4.4 Hz, 1H, 3-C*H*OH), 2.27 (bs, 1H, O*H*), 2.14 (bs, 1H, O*H*), 2.05 (dd, ^2J = 14.6, ^3J = 3.0 Hz, 1H, 1-CH_2^a), 1.96 (ddd, ^2J = 14.4 Hz, ^3J = 11.6, 3.0 Hz, 1H, 16-CH_2^a), 1.84–1.71 (m, 1H, 16-CH_2^b), 1.68–1.44 (m, 5H, 5 different CH_2), 1.43–1.19 (m, 8H, 5 different CH_2 + 8-C*H* + 14-C*H*), 1.13–1.06 (m, 2H, 1-CH_2^b + 5-C*H*), 0.99 (s, 3H, 19-CH_3), 0.91–0.86 (m, 1H, CH_2), 0.82 (s, 3H, 18-CH_3), 0.65–0.58 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$, major isomer): δ = 119.6 (17-C_qO), 72.4 (+, 3-*C*HOH), 70.3 (+, 2-*C*HOH), 65.3 (–, O*C*H$_2$), 64.7 (–, O*C*H$_2$), 55.1 (+, 9-*C*H), 50.4 (+, 14-*C*H), 46.1 (13-C_q), 45.4 (+, 5-*C*H), 43.3 (–, 1-*C*H$_2$), 35.4 (10-C_q), 35.2 (+, 8-*C*H), 34.3 (–, 16-*C*H$_2$), 32.6 (–, 4-*C*H$_2$), 31.3 (–, 7-*C*H$_2$), 30.8 (–, 12-*C*H$_2$), 28.3 (–, 6-*C*H$_2$), 22.7 (–, 15-*C*H$_2$), 20.8 (–, 11-*C*H$_2$), 14.7 (+, *C*H$_3$), 14.6 (+, *C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3387 (br), 2922 (w), 1453 (vw), 1375 (vw), 1306 (w), 1167 (w), 1140 (w), 1106 (w), 1073 (w), 1050 (w), 1011 (w), 969 (w), 951 (w), 897 (vw), 883 (vw), 849 (vw), 785 (vw), 693 (vw), 660 (vw), 597 (vw), 525 (vw) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 350 (65) [M]$^{\bullet+}$, 99 (100). – **HRMS** ($C_{21}H_{34}O_4$): calc.: 350.2452; found: 350.2453.

* The product **SI-09** could not be completely separated from its isomer (no assignment). According to ^{1}H NMR analysis, the ratio of the isomers was determined to 4:1 (**SI-09**/undesired isomer).

2.2.4 Synthesis of the 2*β*,3*α*-*trans*-diol 23 in Scheme 4

2*α*,3*α*-Epoxy-5*α*-androstane-17-on (**24**)[9]



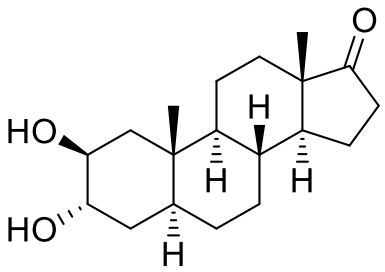
Under argon atmosphere, 5*α*-androst-2-ene-17-on (**15**) (100 mg, 0.367 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (7.5 mL) and after addition of *meta*-chloroperoxybenzoic acid (w/w = 70%, 274 mg, 1.59 mmol, 3.02 equiv), the mixture was stirred overnight at r.t. Then water was added (20 mL) and the aqueous phase was extracted with dichloromethane (3 × 15 mL). The combined organic phases were washed with diluted aqueous $Na_2S_2O_3$ solution (15 mL) and brine (20 mL). After phase separation, the organic phase was dried over Na_2SO_4, filtered and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 4:1) to afford the title compound **24** as colorless solid (80 mg, 0.276 mmol, 75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.15 (d, J = 3.7 Hz, 1H, 3β-C*H*), 3.13–3.08 (m, 1H, 2β-C*H*), 2.42 (dd, ^2J = 19.2 Hz, ^3J = 8.9 Hz, 1H, 16-CH_2^a), 2.11–1.99 (m, 1H, 16-CH_2^b), 1.96–1.69 (m, 5H, different CH_2), 1.67–1.37 (m, 6H, different CH_2), 1.37–1.34 (m, 1H, 8-C*H*), 1.34–1.30 (m, 1H, 5-C*H*), 1.27–1.15 (m, 3H, different CH_2 + 14-C*H*), 0.97–0.87 (m, 1H, CH_2), 0.84 (s, 3H, 18-CH_3), 0.77 (s, 3H, 19-CH_3), 0.72–0.63 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 221.3 (17-C_qO), 53.9 (+, 9-*C*H), 52.4 (+, 3-*C*HO), 51.4 (+, 14-*C*H), 51.0 (+, 2-*C*HO), 47.7 (13-C_q), 38.4 (–, 4-CH_2), 36.4 (+, 5-*C*H), 35.9 (–, 16-CH_2), 35.3 (+, 8-*C*H), 33.9 (10-C_q), 31.6 (–, CH_2), 30.6 (–, 1-CH_2), 29.1 (–, CH_2), 28.2 (–, CH_2), 21.9 (–, CH_2), 20.3 (–, CH_2), 13.8 (+, 19-CH_3), 13.1 (+, 18-CH_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2905 (w), 2851 (w), 1729 (m), 1442 (w), 1383 (w), 1294 (vw), 1257 (w), 1200 (vw), 1121 (ν-C-O, vw), 1052 (w), 1013 (w), 968 (w), 936 (vw), 912 (w), 811 (m), 771 (w), 698 (vw), 584 (w), 530 (vw), 507 (vw), 485 (w), 426 (vw) cm^{-1}. – **MS** (EI, 70 eV, 70 °C): *m/z* (%) = 288 (100) $[M]^{\bullet+}$, 273 (18) $[M–CH_3]^+$, 260 (27), 244 (16), 218 (13), 217 (14). – **HRMS** (EI, $C_{19}H_{28}O_2$): calc.: 288.2084; found: 288.2082.

NMR spectra show impurities of probably two further steroidal species and CH_2Cl_2.

The analytical and spectroscopical data match those reported in the literature.[9]

2*β*,3*α*-Dihydroxy-5*α*-androstane-17-on (**23**)



2*α*,3*α*-Epoxy-5*α*-androstane-17-on (**24**) (80 mg, 0.276 mmol, 1.00 equiv) was dissolved in a mixture of THF (2.9 mL) and a 1 M aqueous solution of sulfuric acid (0.70 mL). The reaction was stirred for 7 d at r.t. and then quenched with saturated aqueous $NaHCO_3$ solution (5.0 mL) followed by extraction with ethyl acetate (3×10 mL). The combined organic phases were washed with water (2×25 mL) and dried over Na_2SO_4. After filtration the solvent was evaporated and the crude product was purified by flash column

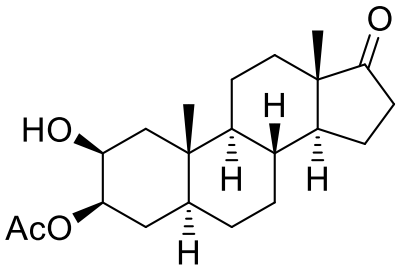
chromatography on silica gel (cyclohexane/acetone/triethylamine, 1:1:0.01) to afford the title compound **23** as colorless solid (46 mg, 0.151 mmol, 54%).

R_f = 0.31 (*c*Hex/acetone/NEt_3, 1:1:0.01). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.92–3.88 (m, 1H, 2-C*H*OH), 3.88–3.85 (m, 1H, 3-C*H*OH), 2.43 (dd, ^2J = 19.2 Hz, ^3J = 8.7 Hz, 1H, 16-CH_2^a), 2.07 (dd, ^2J = 18.7, ^3J = 9.5 Hz, 1H, 16-CH_2^b), 1.96–1.86 (m, 2H, 4-CH_2^a + CH_2), 1.83–1.45 (m, 8H, different CH_2 + 1-CH_2^a + 4-CH_2^b + 5-C*H* + 8-C*H*), 1.37–1.18 (m, 6H, different CH_2 + 1-CH_2^b + 14-C*H*), 1.06–1.00 (m, 1H, CH_2), 1.01 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 0.77 (ddd, *J* = 12.0, 11.7, 3.8 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 221.5 (17-C_qO), 71.4 (+, 3-*C*HOH), 70.2 (+, 2-*C*HOH), 55.4 (+, 9-*C*H), 51.5 (+, 14-*C*H), 48.0 (13-C_q), 45.5 (+, 5-*C*H), 43.2 (–, 1-*C*H_2), 36.0 (–, 16-*C*H_2), 35.6 (10-C_q), 34.6 (+, 8-*C*H), 32.5 (–, *C*H_2), 31.7 (–, *C*H_2), 30.9 (–, *C*H_2), 28.2 (–, *C*H_2), 21.9 (–, *C*H_2), 20.7 (–, *C*H_2), 14.6 (+, *C*H_3), 14.0 (+, *C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3558 (vw), 3475 (vw), 2906 (vw), 2847 (vw), 1705 (w), 1445 (vw), 1399 (vw), 1356 (vw), 1242, (vw), 1121 (vw), 1105 (vw), 1085 (vw), 1047 (w), 1008 (vw), 962 (vw), 847 (vw), 766 (vw), 608 (vw), 564 (vw), 470 (vw), 400 (vw), 385 (vw) cm^{-1}. – **MS** (EI, 70 eV, 140 °C): *m/z* (%) = 306 (100) $[M]^{\bullet+}$, 291 (9) $[M–CH_3]^+$, 288 (9), 273 (7), 262 (17). – **HRMS** (EI, $C_{19}H_{30}O_3$): calc.: 306.2189; found: 306.2187.

The analytical and spectroscopical data match those reported in the literature.[11]

2.2.5 Regioselective acetylation (Scheme 6)

2*β*-Acetoxy-3*β*-hydroxy-5*α*-androstane-17-on (**14**)

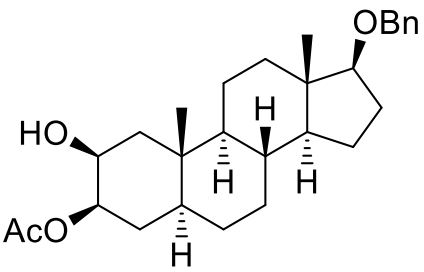


2*β*,3*β*-Dihydroxy-5*α*-androstane-17-on (**21**) (2.75 g, 8.97 mmol, 1.00 equiv) was dissolved in toluene (130 mL) and vinyl acetate (124 mL, 116 g, 1.35 mol, 150 equiv) and *candida rugosa* (770 units/mg, 2.26 g) was added. The reaction was stirred for 8 h at r.t. with 400 rpm before fresh *candida rugosa* (770 units/mg, 2.26 g) was added one more time. The suspension was stirred overnight at r.t. and the conversion was monitored *via* TLC. If necessary, *candida rugosa* (770 units/mg, 2.26 g) was added and stirred overnight at r.t. After filtration over celite® (ethyl acetate as eluent) and removal of the solvent under reduced pressure, the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 1:1) to give the title compound **14** as colorless solid (2.41 g, 6.92 mmol, 77%).

R_f = 0.51 (toluene/EtOAc, 1:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.77 (ddd, ^2J = 11.8, 4.7, 3.4 Hz, 1H, 3-C*H*OAc), 4.09 (bd, ^3J = 2.5 Hz, 1H, 2-C*H*OH), 2.42 (dd, ^2J = 19.3 Hz, ^3J = 8.5 Hz, 1H, 16-CH_2^a), 2.12–1.99 (m, 2H, 1-CH_2^a + 16-CH_2^b), 2.08 (s, 3H, COCH_3), 1.97–1.86 (m, 2H, CH_2 + O*H*), 1.85–1.73 (m, 3H, 2 different CH_2 + 4-CH_2^a), 1.68–1.42 (m, 4H, 2 different CH_2 + 4-CH_2^b + 8-C*H*), 1.40–1.12 (m, 7H, 3 different CH_2 + 1-CH_2^b + 5-C*H* + 14-C*H*), 1.05 (s, 3H, 19-CH_3), 1.03–0.90 (m, 1H, CH_2), 0.85 (s, 3H, 18-CH_3), 0.66 (ddd, ^3J = 12.2, 10.3 4.0 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 221.3 (17-C_qO), 170.2 (C_qO), 75.6 (+, 3-*C*HOAc), 68.7 (+, 2-*C*HOH), 55.4 (+, 9-*C*H), 51.4 (+, 14-*C*H), 48.0 (13-C_q), 45.6 (+,

5-*C*H), 43.0 (–, 1-*C*H$_2$), 35.9 (–, 16-*C*H$_2$), 35.7 (10-*C*$_q$), 34.6 (+, 8-*C*H), 31.7 (–, *C*H$_2$), 30.9 (–, *C*H$_2$), 28.7 (–, 4-*C*H$_2$), 28.0 (–, *C*H$_2$), 21.9 (–, *C*H$_2$), 21.5 (+, CO*C*H$_3$), 20.6 (–, *C*H$_2$), 14.6 (+, 18-*C*H$_3$), 14.0 (+, 19-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 3450 (bs), 2932 (w), 2917 (w), 2836 (w), 1737 (w), 1717 (m), 1452 (w), 1404 (vw), 1365 (w), 1331 (w), 1281 (vw), 1239 (w), 1167 (w), 1124 (w), 1024 (w), 970 (w), 913 (w), 895 (vw), 854 (vw), 831 (w), 737 (vw), 704 (vw), 664 (w), 588 (w), 554 (vw), 527 (w), 487 (vw), 467 (vw), 439 (vw) cm^{-1}. – **MS** (EI, 70 eV, 120 °C): *m/z* (%) = 348 (6) [M]$^{\bullet+}$, 288 (100) [M–OAc]$^+$, 260 (15), 242 (10), 218 (11). – **HRMS** (EI, $C_{21}H_{32}O_3$): calc.: 348.2295; found: 348.2293.

3*β*-Acetoxy-2*β*-hydroxy-17*β*-benzyloxy-5*α*-androstane-17-on (**14-Bn**)



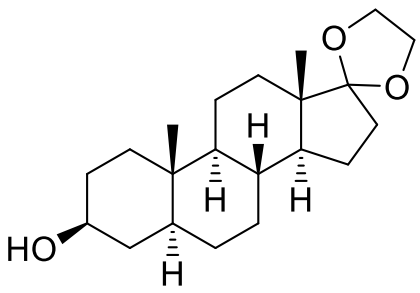
2*β*,3*β*-Dihydroxy-17*β*-benzyloxy-5*α*-androstane-17-on (**SI-08-Bn**) (740 mg, 1.86 mmol, 1.00 equiv) was dissolved in toluene (16 mL) and vinyl acetate (17.2 mL, 16.0 g, 186 mmol, 100 equiv) and *candida rugosa* (770 units/mg, 350 mg) were added. The mixture was stirred with 400 rpm at r.t. overnight before adding *candida rugosa* (770 units/mg, 350 mg) for a second time. The reaction was stirred 1 d at r.t. and then filtered over Celite® (ethyl acetate as eluent). After evaporation of the solvent, the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to give the title compound **14-Bn** as colorless solid (453 mg, 1.03 mmol, 55%).

***R*$_f$** = 0.52 (*c*Hex/EtOAc, 5:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 4H, 4 C*H*$_{Ar}$), 7.31–7.24 (m, 1H, C*H*$_{Ar}$), 4.79 (ddd, ^3J = 11.8, 4.8, 3.3 Hz, 1H, 3-C*H*OAc), 4.55 (s, 2H, OC*H*$_2$Ph), 4.14–4.08 (m, 1H, 2-C*H*OH), 3.43 (dd, ^3J = 8.4 Hz, 1H, 17-C*H*OBn), 2.11 (s, 3H, COC*H*$_3$), 2.09–1.89 (m, 3H, 3 different C*H*$_2$), 1.80 (q, *J* = 12.2 Hz, 1H, C*H*$_2$), 1.72–1.62 (m, 1H, C*H*$_2$), 1.63–1.50 (m, 3H, 3 different C*H*$_2$), 1.49–1.08 (m, 9H, 6 different C*H*$_2$ + 5-C*H* + 8-C*H*), 1.06 (s, 3H, C*H*$_3$), 1.03–0.84 (m, 2H, C*H*$_2$ + 14-C*H*), 0.84 (s, 3H, C*H*$_3$), 0.67–0.53 (m, 1H, 9-C*H*) ppm.

The analytical and spectroscopical data match those that are described on page 17.

2.3 Experimental procedures for the synthesis of 2*α*,3*β* -*trans*-diol 27 in Scheme 5

17,17-(Ethylendioxy)-5*α*-androstane-3*β*-ol (**SI-10**)[12]

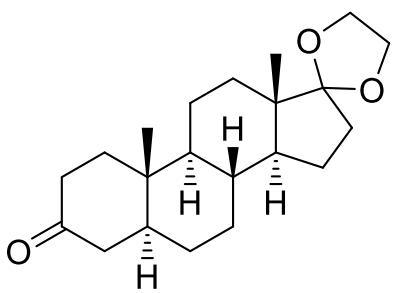


Epi-androsterone (**12**) (1.01 g, 3.48 mmol, 1.00 equiv) und *para*-toluenesulfonic acid monohydrate (132 mg, 695 µmol, 0.20 equiv) were dissolved in absolute dichloromethane (20 mL) and absolute ethylene glycol (3.9 mL, 4.32 g, 69.6 mmol, 20.0 equiv) and trimethyl orthoformate (3.8 mL, 3.69 g, 34.8 mmol, 10.0 equiv) were added. The solution was stirred overnight at r.t. Upon completion, the reaction was diluted with 1 M aqueous NaOH solution (250 mL) followed by extraction with dichloromethane (2×150 mL). The combined organic phases were washed with water (200 mL) and dried over Na_2SO_4. After filtration and removal of the solvents the crude product was purified by flash column chromatography (cyclohexane/ethyl acetate, 3:1) to give the title compound **SI-10** as colorless solid (1.02 g, 3.05 mmol, 88%).

R_f = 0.27 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.95–3.77 (m, 4H, 2×OCH_2), 3.57 (tt, ^3J = 10.8, 4.8 Hz, 1H, 3-C*H*OH), 1.95 (ddd, ^2J = 14.5, ^3J = 11.6, 3.1 Hz, 1H, CH_2), 1.83–1.72 (m, 2H, 2 different CH_2), 1.73–1.60 (m, 3H, 3 different CH_2), 1.58–1.46 (m, 3H, 3 different CH_2), 1.43–1.31 (m, 4H, 2 different CH_2 + 8-C*H* + 14-C*H*), 1.30–1.16 (m, 5H, 4 different CH_2), 1.13–1.02 (m, 1H, 5-C*H*), 0.95 (td, ^2J = 13.5, ^3J = 3.8 Hz, 1H, CH_2), 0.90–0.85 (m, 1H, CH_2), 0.82 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 0.66 (ddd, ^3J = 13.4, 9.8, 3.9 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 119.3 (17-C_qO), 71.1 (+, 3-*C*HOH), 65.0 (–, O*C*H_2), 64.4 (–, O*C*H_2), 54.0 (+, 9-*C*H), 50.2 (+, 14-*C*H), 45.8 (13-C_q), 44.7 (+, 5-*C*H), 38.0 (–, *C*H_2), 36.9 (–, *C*H_2), 35.6 (+, 8-*C*H), 35.4 (10-C_q), 34.0 (–, *C*H_2), 31.3 (–, *C*H_2), 31.2 (–, *C*H_2), 30.5 (–, *C*H_2), 28.4 (–, *C*H_2), 22.5 (–, *C*H_2), 20.5 (–, *C*H_2), 14.3 (+, *C*H_3), 12.2 (+, *C*H_3) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 3332 (br), 2920 (w), 2860 (w), 1469 (vw), 1384 (vw), 1366 (vw), 1308 (w), 1208 (vw), 1167 (w), 1104 (w), 1071 (w), 1038 (m), 1013 (w), 984 (vw), 955 (w), 913 (vw), 891 (vw), 794 (vw), 753 (vw) cm^{-1}. – **MS** (EI, 70 eV, 80 °C): *m/z* (%) = 334 (41) $[M]^{\bullet+}$, 99 (100). – **HRMS** ($C_{21}H_{34}O_3$): calc.: 334.2508; found: 334.2506.

Analytical data set can be compared with the literature, e.g. Chen, Steroids, 2019, 81-95[13].

17,17-(Ethylendioxy)-5*α*-androstane-3-on (**25**)



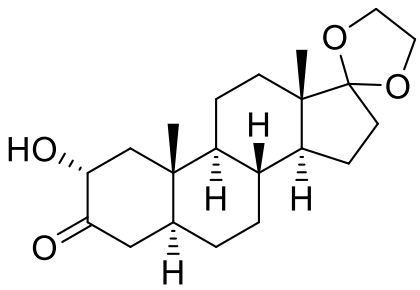
Under argon atmosphere, 17,17-(ethylendioxy)-5*α*-androstane-3*β*-ol (**SI-10**) (1.26 g, 3.76 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (24 mL) and at 0 °C Dess-Martin periodinane (2.07 g, 4.88 mmol, 1.30 equiv) was added portionwise. The solution was slowly allowed to warm to r.t. (90 min) and then stirred at r.t. for 90 min. The mixture was diluted with dichloromethane (30 mL) and quenched with a mixture of saturated aqueous $Na_2S_2O_3$ solution and

saturated aqueous $NaHCO_3$ solution (3:1, 60 mL). After phase separation, the aqueous phase was extracted with dichloromethane (2×200 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and filtered. The solvent was removed and the obtained crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 4:1) to afford the title compound **25** as colorless solid (1.00 g, 3.01 mmol, 80%).

***R*$_f$** = 0.35 (*c*Hex/EtOAc, 4:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.90–3.73 (m, 4H, 2×OCH_2), 2.37–2.26 (m, 1H, 2-CH_2^a), 2.23 (ddd, ^2J = 10.7 Hz, ^3J = 6.5, 2.5 Hz, 1H, 2-CH_2^b), 2.18 (d, ^2J = 14.4 Hz, 1H, 4-CH_2^a), 2.01 (ddd, ^2J = 15.2 Hz, 4.0, 2.2 Hz, 1H, 4-CH_2^b), 1.98–1.87 (m, 2H, 2 different CH_2), 1.82–1.41 (m, 6H, 5 different CH_2 + 5-C*H*), 1.38–1.13 (m, 8H, 5 different CH_2 + 8-C*H* + 14-C*H*), 0.94 (s, 3H, CH_3), 0.92–0.80 (m, 1H, CH_2), 0.80 (s, 3H, CH_3), 0.74–0.61 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 212.0 (C_qO), 119.2 (17-C_q), 65.1 (–, OCH_2), 64.4 (–, OCH_2), 53.4 (+, 9-*C*H), 50.0 (+, 14-*C*H), 46.5 (+, 5-*C*H), 45.8 (C_q), 44.6 (–, *C*H_2), 38.4 (–, *C*H_2), 38.0 (–, *C*H_2), 35.5 (C_q), 35.4 (+, 8-*C*H), 34.0 (–, *C*H_2), 30.8 (–, *C*H_2), 30.4 (–, *C*H_2), 28.7 (–, *C*H_2), 22.5 (–, *C*H_2), 20.7 (–, *C*H_2), 14.3 (+, *C*H_3), 11.3 (+, *C*H_3) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 2932 (vw), 2852 (vw), 1704 (w), 1445 (vw), 1376 (vw), 1302 (vw), 1273 (vw), 12108 (vw), 1165 (vw), 1109 (v), 1033 (w), 952 (w), 883 (vw), 749 (vw), 683 (vw), 595 (vw) cm^{-1}. – **MS** (EI, 70 eV, 100 °C): *m/z* (%) = 332 (41) $[M]^{\bullet+}$, 99 (100). – **HRMS** ($C_{21}H_{32}O_3$): calc.: 332.2346; found: 332.2345.

The analytical and spectroscopical data match those reported in the literature.[14]

17,17-(Ethylendioxy)-2α-hydroxy-5α-androstane-3-on (**26**)



Under argon atmosphere, 17,17-(ethylendioxy)-5α-androstane-3-on (**25**) (1.00 g, 3.15 mmol, 1.00 equiv) was dissolved in absolute dichloromethane (24 mL) and at 0 °C triethylamine (0.85 mL, 610 mg, 6.03 mmol, 2.00 equiv) and trimethylsilyl trifluoromethanesulfonate (0.65 mL, 804 mg, 3.62 mmol, 1.20 equiv) were added slowly. After 1 h, the reaction was quenched with water (40 mL) followed by an extraction with dichloromethane (2 × 200 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (40 mL), dried over Na_2SO_4 and filtered. After removal of the solvent, the residue was dissolved in *n*-hexane (40 mL) and at 0 °C sodium hydrogencarbonate (1.53 g, 18.1 mmol, 6.00 equiv) and *meta*-chlorperoxybenzoic acid (w/w = 70%, 1.10 g, 4.44 mmol, 1.41 equiv) were added consecutively. The suspension was stirred for 2 h at 0 °C. By adding saturated aqueous $NaHCO_3$ solution (30 mL) the reaction was quenched and extracted with diethyl ether (2×50 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (30 mL) and water (30 mL) and dried over Na_2SO_4. After filtration, the solvent was removed under reduced pressure.

Workup A:

The obtained residue was dissolved in absolute tetrahydrofuran (20 mL) and 1M solution of TBAF in tetrahydrofuran (6.0 mL, 1.57 g, 6.02 mmol, 2.00 equiv) was added. After 10 min stirring at r.t. for 10 min, the reaction was quenched with saturated aqueous $NHCl_4$ solution (80 mL) and extracted with diethyl ether (2×80 mL) and ethyl acetate (2×80 mL). The combined organic phases were washed with H_2O (120 mL) and brine (120 mL), dried over Na_2SO_4 and filtered. The solvent was evaporated and the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to obtain the title compound **26** as colorless solid (723 mg, 2.07 mmol, 66%).

Workup B:

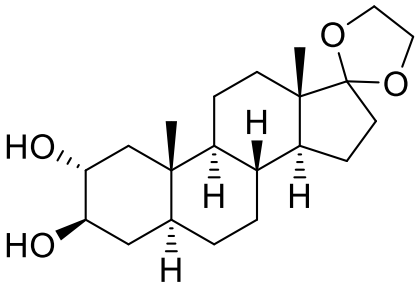
The obtained residue was dissolved in methanol (20 mL) and oxalic acid (27.6 mg, 0.302 mmol, 0.10 equiv) was added at r.t. After 5 min, the reaction was diluted with water (30 mL) and extracted with diethyl ether (20 mL) and ethyl acetate (20 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ solution (30 mL), dried over Na_2SO_4 and filtered. The solvent was evaporated and the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 5:1) to obtain the title compound **26** as colorless solid* (621 mg, 1.78 mmol, 56%).

R_f = 0.59 (*c*Hex/EtOAc, 1:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.24–4.11 (m, 1H, 2-C*H*OH), 3.89–3.72 (m, 4H, 2×OCH_2), 3.44 (d, ^3J = 3.3 Hz, 1H, O*H*), 2.41 (dd, ^2J = 12.5 Hz, ^3J = 7.1 Hz, 1H, 1-CH_2^a), 2.34 (td, ^2J = 13.9 Hz, ^3J = 1.0 Hz, 1H, 4-CH_2^a), 2.20 (dd, ^2J = 14.1 Hz, ^3J = 3.8 Hz, 1H, 4-CH_2^b), 1.91 (ddd, ^2J = 14.5, ^3J = 11.6, 3.1 Hz, 1H, 16-CH_2^a), 1.75–1.42 (m, 6H, 16-CH_2^b + 3 different CH_2 + C*H*), 1.41–1.08 (m, 7H, 4 different CH_2 + 8-C*H* + C*H*), 1.11 (t_{app}, *J* = 12.3 Hz, 1H, 1-CH_2^b) 1.03 (s, 3H, 19-CH_3), 0.92–0.82 (m, 1H, CH_2), 0.79 (s, 3H, 18-CH_3), 0.80–0.60 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 210.8 (3-C_qO), 119.1 (17-C_qO_2), 72.6 (+, 2-*C*HOH), 65.1 (–, *C*H_2O), 64.4 (–, *C*H_2O), 53.4 (+, 9-*C*H), 49.8 (+, *C*H), 48.3 (+, *C*H), 48.2 (–, 1-*C*H_2), 45.8 (13-C_q), 42.2 (–, 4-*C*H_2), 37.0 (10-C_q), 34.7 (+, 8-*C*H), 34.0 (–, 16-*C*H_2), 30.8 (–, *C*H_2), 30.4 (–, *C*H_2), 28.3 (–, 6-*C*H_2), 22.5 (–, 15-*C*H_2), 20.9 (–, 11-*C*H_2), 14.2 (+, *C*H_3), 12.7 (+, *C*H_3) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 3443 (vw), 2936 (w), 2856 (w), 1712 (w), 1441 (vw), 1386 (vw), 1307 (vw), 1278 (vw), 1259 (vw), 1207 (vw), 1167 (w), 1108 (w), 1086 (w), 1051 (w), 1034 (w), 1011 (w), 952 (w), 900 (vw), 883 (vw), 767 (vw), 689 (vw), 645 (vw), 604 (vw), 575 (vw) 535 (vw) cm^{-1}. – **MS** (EI, 70 eV, 110 °C): *m/z* (%) = 348 (34) $[M]^{\bullet+}$, 99 (100). – **HRMS** ($C_{21}H_{32}O_4$): calc.: 348.2292; found: 348.2295.

*The NMR spectra contain an unkown impurity.

Please note that a side product was observed. NMR analysis suggests that the structure corresponds to the regioisomer 17,17-(ethylendioxy)-4-hydroxy-5α-androstane-3-on.

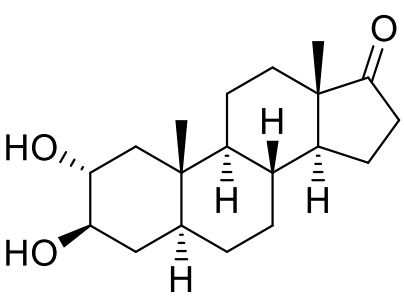
17,17-(Ethylendioxy)-2*α*,3*β*-dihydroxy-5*α*-androstane (**SI-11**)



Under argon atmosphere, 17,17-(Ethylendioxy)-2*α*-hydroxy-5*α*-androstane-3-on (**26**) (100 mg, 287 µmol, 1.00 equiv) was dissolved in a mixture of absolute dichloromethane and absolute methanol (4:1, 15 mL) and at –20 °C sodium borohydride (43 mg, 1.15 mmol, 4.00 equiv) was slowly added. The reaction was allowed to warm to r.t. and was stirred until TLC indicates full conversion. The reaction was quenched by adding saturated aqueous $NaHCO_3$ solution (25 mL) followed by extraction with dichloromethane (2×20 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and filtered. After solvent removal, the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 10:1 → 2:1) to give the title compound **SI-11** as colorless powder (66 mg, 189 µmol, 66%).

***R*$_f$** = 0.29 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.98–3.80 (m, 4H, 2×OC*H*$_2$), 3.58 (ddd, ^3J = 11.6, 9.0, 4.7 Hz, 1H, 2-C*H*OH), 3.39 (ddd,^3J = 11.1, 9.1, 5.2 Hz, 1H, 3-C*H*OH), 2.10 (bs, 2H, 2 × O*H*), 2.02–1.92 (m, 2H, 1-C*H*$_2^a$ + 16-C*H*$_2^a$), 1.81–1.74 (m, 1H, 16-C*H*$_2^b$), 1.72–1.55 (m, 5H, 5 different C*H*$_2$), 1.43–1.17 (m, 9H, 5 different C*H*$_2$ + 5-C*H* + 8-C*H* + 14-C*H*), 0.95 (m, 1H, 1-C*H*$_2^b$), 0.89–0.84 (m, 1H, C*H*$_2$), 0.84 (s, 3H, C*H*$_3$), 0.83 (s, 3H, C*H*$_3$), 0.79–0.70 (m, 1H, 9-C*H*) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 120.3 (17-*C*$_q$), 77.3 (+, 3-*C*H), 74.0 (+, 2-*C*H), 66.1 (–, O*C*H$_2$), 65.5 (–, O*C*H$_2$), 55.0 (+, 9-*C*H), 51.1 (+, 14-*C*H), 46.9 (13-*C*$_q$), 46.0 (–, 1-*C*H$_2$), 45.8 (+, 5-*C*H), 38.4 (10-*C*$_q$), 36.5 (–, *C*H$_2$), 35.9 (+, 8-*C*H), 35.1 (–, *C*H$_2$), 32.1 (–, *C*H$_2$), 31.5 (–, 4-*C*H$_2$), 28.7 (–, 6-*C*H$_2$), 23.5 (–, 13-*C*H$_2$), 21.7 (–, 11-*C*H$_2$), 15.3 (+, *C*H$_3$), 14.4 (+, *C*H$_3$) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 3413 (w), 2930 (w), 2863 (w), 1442 (w), 1385 (vw), 1354 (vw), 1306 (w), 1278 (vw), 1236 (vw), 1205 (vw), 1166 (vw), 1132 (w), 1103 (w), 1052 (m), 1031 (m), 1008 (w), 976 (w), 951 (w), 909 (vw), 885 (w), 791 (vw), 749 (vw), 622 (vw) cm^{-1}. – **MS** (EI, 70 eV, 110 °C): *m/z* (%) = 350 (42) [M]$^{\bullet+}$, 134 (22), 99 (100). – **HRMS** ($C_{21}H_{34}O_4$): calc.: 350.2452; found: 350.2453.

2*α*,3*β*-Dihydroxy-5*α*-androstane-17-on (**27**)



17,17-(Ethylendioxy)-2*α*,3*β*-dihydroxy-5*α*-androstane-3-on (**SI-11**) (247 mg, 0.700 mmol, 1.00 equiv) and *para*-toluenesulfonic acid·H_2O (581 mg, 3.38 mmol, 4.80 mmol) was dissolved in acetone (30 mL) and stirred at r.t. for 3 h. The solution was quenched by the addition of 5% aqueous $NaHCO_3$ solution and acetone was evaporated under reduced pressure. The aqueous phase was extracted with dichloromethane (3×50 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and filtered. After solvent removal, the crude product was purified by short flash column chromatography on silica gel (ethyl acetate) to give the title compound **SI-11** as colorless powder (188 mg, 0.615 mmol, 88%).

$\boldsymbol{R_f}$ = 0.30 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 3.57 (ddd, ^3J = 11.6, 9.0, 4.7 Hz, 1H, 2-C*H*OH), 3.39 (ddd, ^3J = 11.2, 9.0, 5.2 Hz, 1H, 3-C*H*OH), 2.54 (bs, 2H, 2×O*H*), 2.43 (ddd, ^2J = 19.2 Hz, ^3J = 9.0 Hz, J = 1.1 Hz, 1H, 16-CH_2^a), 2.11–2.00 (m, 1H, 16-CH_2^b), 1.98 (dd, J = 12.5, 4.8 Hz, 1H, 1-CH_2^a), 1.96–1.87 (m, 1H, CH_2^a), 1.84–1.75 (m, 2H, 2 different CH_2), 1.70–1.61 (m, 2H, 2 different CH_2), 1.56–1.46 (m, 2H, 4-CH_2^a + 8-C*H*), 1.43–1.16 (m, 7H, 3 different CH_2 + 4-CH_2^b + 5-C*H* + 14-C*H*), 1.02–0.92 (m, 2H, 1-CH_2^b + CH_2), 0.86 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 0.76 (ddd, J = 12.1, 10.4, 4.1 Hz, 1H, 9-C*H*) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 221.3 (C_qO), 76.2 (+, 2-C*H*OH), 72.9 (+, 3-C*H*OH), 54.4 (+, 9-C*H*), 51.3 (+, 14-C*H*), 47.8 (13-C_q), 45.0 (–, 1-CH_2), 44.8 (+, 5-C*H*), 37.6 (10-C_q), 35.9 (–, CH_2), 35.5 (–, CH_2), 34.4 (+, 8-C*H*), 31.5 (–, CH_2), 30.7 (–, CH_2), 27.6 (–, CH_2), 21.8 (–, CH_2), 20.7 (–, CH_2), 13.8 (+, CH_3), 13.5 (+, CH_3) ppm. – **IR (ATR)**: $\tilde{\nu}$ = 3480 (br), 2927 (w), 2857 (w), 1721 (w), 1452 (vw), 1409 (vw), 1377 (vw), 1292 (vw), 1249 (vw), 1202 (vw), 1131 (vw), 1099 (vw), 1057 (w), 1030 (w), 1010 (w), 981 (vw), 952 (vw), 924 (vw), 897 (vw), 815 (vw) cm^{-1}. – **MS** (EI, 70 eV, 90 °C): *m/z* (%) = 306 (7) $[M]^{\bullet+}$, 86 (87), 84 (100). – **HRMS** ($C_{19}H_{30}O_3$): calc.: 306.2195; found: 306.2194.

2.4 Experimental procedures for the introduction of the 2,3-*trans*-diol moiety and the oxygen functionality at C-19

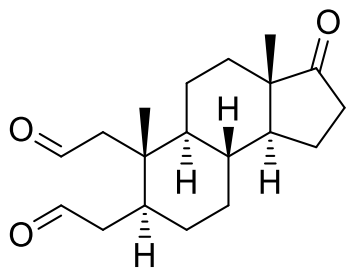
2.4.1 Experimental procedures for the hypoiodite reaction (Scheme 6 and Table 1)

If not stated otherwise, the protocols of this section are based on the general procedure **GP-2** described in the experimental section of the corresponding paper.

General procedure for the C–H activation *via* a hypoiodite reaction (GP-2)

A suspension of DIB (1.5 equiv) and I_2 (1.3 equiv) in a mixture of cyclo-hexane and benzene (10:1, 25–30 mM) was degassed by bubbling with argon (15 min) which was followed by the addition of the 2*β*-acetoxy-3*β*-hydroxyandrostane derivative (1.0 equiv.). The reaction was sonicated at the given temperature and for the given time before it was quenched with saturated aqueous $Na_2S_2O_3$ solution. After phase separation the aqueous phase was extracted with CH_2Cl_2 (3 ×) and the combined organic extracts were washed with brine and dried over Na_2SO_4. After filtration and evaporation the obtained crude product was purified by flash column chromatography on silica gel (*c*Hex/EtOAc) to afford the 2*β*,19-epoxy-5*α*-androstane derivative as colorless solid.

2,3-seco-5*α*-Androster-17-on-2,3-dial (**28**)

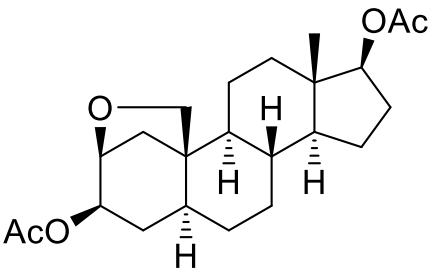


According to the general procedure **GP-2**, 2*β*,3*β*-dihydroxy-5*α*-androstane-17-on (**21**) (49 mg, 161 µmol, 1.00 equiv), DIB (79 mg, 245 µmol, 1.50 equiv) and I_2 (53 mg, 209 µmol, 1.30 equiv) were applied in cyclohexane (4.2 mL) and benzene (0.40 mL). The reaction was quenched after 80 minutes of sonication at 35 °C. The title compound **28** was obtained after flash column chromatography on silica gel (cyclohexane/ethyl acetate, 1:1) as colorless oil (24 mg, 77.6 µmol, 48%).

***R*$_f$** = 0.57 (*c*Hex/EtOAc, 1:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 9.83 (s, 1H, 3-C*H*O), 9.72 (s, 1H, 2-C*H*O), 2.66 (d, ^2J = 15.4 Hz, 1H, 1-CH_2^a), 2.55 (dd, ^2J = 15.5 Hz, ^3J = 1.6 Hz, 1H, 4-CH_2^a), 2.44 (dd, ^2J = 19.3 Hz, ^3J = 8.8 Hz, 1H, 16-CH_2^a), 2.29 (dd, ^2J = 15.5 Hz, ^3J = 2.8 Hz, 1H, 4-CH_2^b), 2.25–2.20 (m, 1H, C*H*), 2.19–2.13 (m, 1H, 1-CH_2), 2.07 (dd, ^2J = 18.9 Hz, ^3J = 9.5 Hz, 1H, 16-CH_2^b), 1.97–1.91 (m, 1H, CH_2), 1.86–1.77 (m, 2H, CH_2), 1.61 (dd, ^2J = 13.6 Hz, ^3J = 2.7 Hz, 1H, CH_2), 1.54–1.45 (m, 3H, 2 different CH_2 + 8-C*H*), 1.35–1.23 (m, 5H, 3 different CH_2 + C*H* + 14-C*H*), 1.06–0.97 (m, 1H, CH_2), 0.87 (s, 3H, 19-CH_3), 0.86 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR**† (126 MHz, $CDCl_3$): δ = 202.4 (2-*C*HO), 202.1 (3-*C*HO), 51.2 (+, 14-*C*H), 49.7 (–, 4-*C*H_2), 49.6 (+, *C*H), 47.5 (13-C_q), 45.6 (–, 1-*C*H_2), 40.5 (10-C_q), 38.4 (+, *C*H), 36.0 (–, 16-*C*H_2), 34.9 (+, 8-*C*H), 31.4 (–, *C*H_2), 30.3 (–, *C*H_2), 28.1 (–, *C*H_2), 21.8 (–, *C*H_2), 21.5 (–, *C*H_2), 15.7 (+, 19-*C*H_3), 13.8 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2918 (w), 2854 (w), 2723 (vw), 1733 (m), 1716 (m), 1451 (w), 1405 (w), 1374 (w), 1203 (w), 1116 (w), 1050 (w), 1008 (w), 919 (w), 893 (w), 831 (w), 729 (vw), 580 (vw), 537 (vw), 465 (vw), 382 (vw) cm^{-1}. – **MS** (EI, 70 eV, 100 °C): *m/z* (%) = 304 (26) $[M]^{\bullet+}$, 260 (44), 216 (100). – **HRMS** (EI, $C_{19}H_{28}O_3$): calc.: 304.2033; found: 304.2032.

† The range of the ^{13}C NMR spectrum was not extended which is why the signal of the carbonyl group at C-17 is missing (~ 220 ppm).

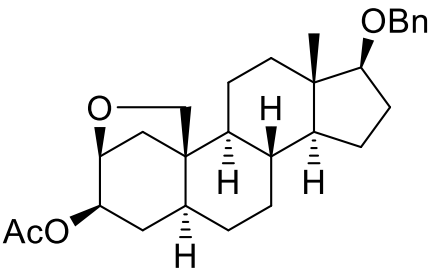
3*β*,17*β*-Diacetoxy-2*β*,19-epoxy-5*α*-androstane (**13-Ac**)



3*β*,17*β*-Diacetoxy-5*α*-androstane-2*β*-ol (**14-Ac**) (50 mg, 127 µmol, 1.00 equiv), DIB (49 mg, 157 µmol, 1.20 equiv) and I_2 (35 mg, 140 µmol, 1.10 equiv) were suspended in cyclohexane (13 mL) and then irradiated at 40 °C using an 10 W LED lamp with λ = 530 nm. After 120 min of irradiation the reaction was quenched with saturated aqueous $Na_2S_2O_3$ solution (5.0 mL). The phases were separated and the aqueous phase was extracted with dichloromethane (3×20 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4 and filtered. After evaporation of the solvents, the crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 2:1) to afford the title compound **13-Ac** as colorless solid (33 mg, 85.0 µmol, 67%). Due to problems with reproducibility the herein applied irradiation protocol was replaced by the sonication protocol given by the general procedure **GP-2**.

***R*$_f$** = 0.27 (*c*Hex/EtOAc, 2:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.67 (dd, ^3J = 9.9, 5.9 Hz, 1H, 3-C*H*OAc), 4.57 (dd, ^3J = 9.2, 7.9 Hz, 1H, 17-C*H*OAc), 4.21 (d, ^3J = 6.9 Hz, 1H, 2-C*H*O), 3.82 (d, ^2J = 8.2 Hz, 1H, 19-CH_2^aO), 3.71 (d, ^2J = 8.3 Hz, 1H, 19-CH_2^bO), 2.25 (dd, ^2J = 11.8 Hz, ^2J = 7.1 Hz, 1H, 1-CH_2^a), 2.22–2.07 (m, 1H, 16-CH_2^a), 2.05 (s, 3H, COCH_3), 2.03 (s, 3H, COCH_3), 1.98–1.88 (m, 1H, 4-CH_2^a), 1.76 (ddd, ^2J = 12.7 Hz, ^3J = 4.0, 2.7 Hz, 1H, CH_2), 1.70–1.53 (m, 4H, 3 different CH_2 + 16-CH_2^b), 1.51–1.10 (m, 9H, 5 different CH_2 + 1-CH_2^b + 4-CH_2^b + 5-C*H* + 9-C*H*), 1.04–0.79 (m, 3H, 14-C*H* + 8-C*H* + CH_2), 0.73 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.0 (*C*$_q$O), 170.6 (*C*$_q$O), 82.4 (+, 17-*C*HOAc), 76.9 (+, 2-*C*HO), 74.9 (+, 3-*C*HOAc), 67.7 (–, 19-*C*H_2O), 50.6 (+, 14-*C*H), 46.5 (10-*C*$_q$), 45.7 (+, 9-*C*H), 42.2 (13-*C*$_q$), 41.9 (+, 5-*C*H), 38.9 (–, 1-*C*H_2), 38.0 (+, 8-*C*H), 36.3 (–, *C*H_2), 32.2 (–, 4-*C*H_2), 30.7 (–, *C*H_2), 29.6 (–, *C*H_2), 27.3 (–, 16-*C*H_2), 23.3 (–, *C*H_2), 21.2 (+, COCH_3), 20.1 (+, COCH_3), 20.6 (–, 11-*C*H_2), 11.7 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2934 (w), 2857 (w), 1724 (s), 1445 (w), 1363 (m), 1287 (w), 1245 (s), 1119 (w), 1029 (m), 977 (m), 956 (w), 917 (w), 884 (w), 859 (vw), 783 (w), 729 (vw), 672 (vw), 625 (w), 551 (vw), 500 (w), 402 (w) cm^{-1}. – **MS** (EI, 70 eV): *m/z* (%) = 390 (100) [M]$^{\bullet+}$, 362 (47), 330 (96), 272 (16) [M–2×OAc]$^+$, 221 (25). – **HRMS** (EI, $C_{23}H_{34}O_5$): calc.: 390.2401; found: 390.2399.

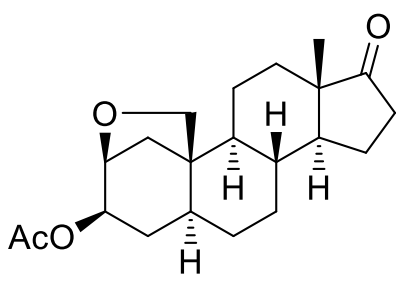
3*β*-Acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**)



The synthesis followed the **GP-2**: 2*β*,3*β*-Dihydroxy-17*β*-benzyloxy-5*α*-androstane-17-on (**14-Bn**) (120 mg, 272 mmol, 1.00 equiv), DIB (193 mg, 599 mmol, 2.20 equiv) and I_2 (104 mg, 408 mmol, 1.50 equiv) were suspended in a mixture of cyclohexane (10 mL) and benzene (1.0 mL). After 120 min of sonication at a temperature range of 20 – 30 °C the reaction was quenched and the work up followed the **GP-2**. The crude product was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) to afford the title compound **13-Bn** as colorless solid (57 mg, 131 mmol, 48%).

***R*$_f$** = 0.62 (*c*Hex/EtOAc, 3:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.33–7.32 (m, 4H, 4×C*H*$_{Ar}$), 7.28–7.22 (m, 1H, C*H*$_{Ar}$), 4.72–4.64 (m, 1H, 3-C*H*OAc), 4.53 (s, 2H, OC*H*$_2$Ph), 4.21 (d, ^3J = 7.0 Hz, 1H, 2-C*H*O), 3.83 (d, ^2J = 8.3 Hz, 1H, 19-C*H*$_2^a$O), 3.73 (d, ^2J = 8.2 Hz, 1H, 19-C*H*$_2^b$O), 3.40 (dd, ^3J = .9 Hz, 1H, 17-C*H*OBn), 2.26 (dd, ^2J = 11.8 Hz, ^3J = 7.1 Hz, 1H, 1-C*H*$_2^a$), 2.06 (s, 3H, COC*H*$_3$), 2.03–1.88 (m, 3H, 4-C*H*$_2^a$ + 16-C*H*$_2^a$ + C*H*$_2$), 1.72–1.63 (m, 2H, 2 different C*H*$_2$), 1.61–1.49 (m, 3H, 2 different C*H*$_2$ + 16-C*H*$_2^b$), 1.43–1.33 (m, 3H, C*H*$_2$ + 4-C*H*$_2^b$ + 5-C*H*), 1.30–1.05 (m, 5H, 3 different C*H*$_2$ + 1-C*H*$_2^b$ + 9-C*H*), 0.97–0.83 (m, 3H, C*H*$_2$ + 8-C*H* + 14-C*H*), 0.78 (s, 3H, 18-C*H*$_3$) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 170.7 (*C*$_q$O), 139.1 (1'-*C*$_q$), 128.1 (+, 3',5'-*C*H$_{Ar}$), 127.1 (+, 4'-*C*H$_{Ar}$), 127.1 (+, 2',6'-*C*H$_{Ar}$), 87.9 (+, 17-*C*HOBn), 74.4 (+, *C*HOAc), 71.4 (–, *C*H$_2$OPh), 67.7 (–, 19-*C*H$_2$O), 51.0 (+, 14-*C*H), 46.5 (10-*C*$_q$), 45.9 (+, 9-*C*H), 42.7 (13-*C*$_q$), 41.9 (+, 5-*C*H), 38.8 (–, 1-*C*H$_2$), 38.0 (+, 8-*C*H), 37.3 (–, *C*H$_2$), 32.3 (–, 4-*C*H$_2$), 30.8 (–, *C*H$_2$), 29.6 (–, 16-*C*H$_2$), 27.7 (–, *C*H$_2$), 26.7 (–, *C*H$_2$), 23.2 (–, 12-*C*H$_2$), 21.2 (+, CO*C*H$_3$), 20.8 (–, *C*H$_2$), 11.5 (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2933 (vw), 2846 (vw), 1778 (vw), 1728 (w), 1496 (vw), 1450 (vw), 1367 (vw), 1245 (w), 1132 (w), 1111 (vw), 1070 (vw), 1025 (w), 985 (w), 958 (vw), 912 (vw), 883 (vw), 787 (vw), 738 (w), 695 (w), 618 (vw), 495 (vw) cm^{-1}. – **MS** (+FAB, 3-NBA): *m/z* (%) = 439 (100) $[M+H]^+$. – **HRMS** (+FAB, $C_{28}H_{38}O_4$, $[M+H]^+$): calc.: 439.2843; found: 439.2845.

3*β*-Acetoxy-2*β*,19-epoxy-5*α*-androstane-17-on (**13**)



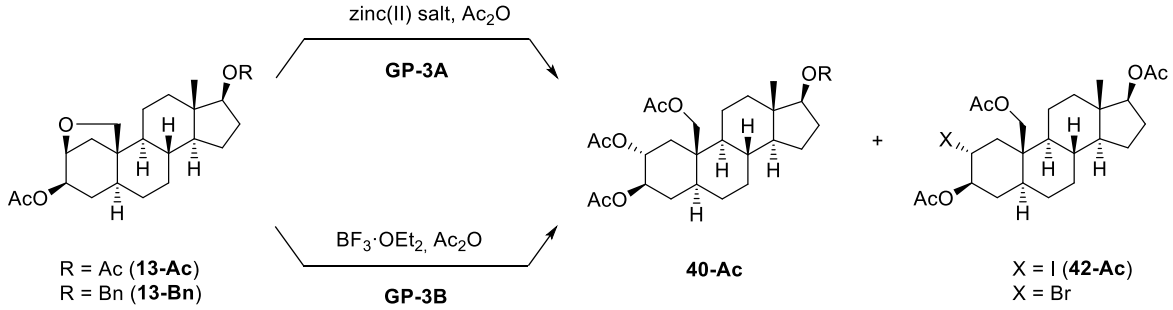
The synthesis followed the **GP-2** given in the experimental section of corresponding paper. 3*β*-Acetoxy-2*β*-hydroxy-5*α*-androstane-17-on (**14**) (100 mg, 287 µmol, 1.00 equiv), DIB (201 g, 0.631 mmol, 2.20 equiv) and I_2 (87 mg, 0.344 mmol, 1.20 equiv) were suspended in a mixture of cyclohexane (10 mL) and benzene (1 mL). The reaction was sonicated for 200 min at a temperature range of 20–30 °C. After purification by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) the title compound **13** was obtained as colorless solid (106 mg, in 1:0.2 mixture with **32**, 72%).

$\boldsymbol{R_f}$ = 0.28 (*c*Hex/EtOAc, 2:1). – **^{1}H NMR (**500 MHz, $CDCl_3$): δ = 4.62 (dd, ^3J = 9.5, 6.6 Hz, 1H, C*H*OAc), 4.16 (d, ^3J = 7.0 Hz, 1H, 2-C*H*O), 3.79 (d, ^2J = 8.2 Hz, 1H, 19-CH_2^aO), 3.66 (d, J = 8.2 Hz, 1H, 19-CH_2^bO), 2.38 (dd, ^2J = 19.5 Hz, ^3J = 8.5 Hz, 1H, 16-CH_2^a), 2.20 (dd, ^2J = 11.7 Hz, ^3J = 7.1 Hz, 1H, CH_2), 2.08–1.97 (m, 1H, 16-CH_2^b), 2.00 (s, 3H, COCH_3), 1.94–1.84 (m, 2H, 2 different CH_2), 1.82–1.69 (m, 3H, 3 different CH_2), 1.61–1.54 (m, 1H, CH_2), 1.47–1.28 (m, 4H, 3 different CH_2 + C*H*), 1.26–1.11 (m, 5H, 3 different CH_2 + 2 different C*H*), 1.07–0.99 (m, 1H, C*H*), 0.95–0.84 (m, 1H, CH_2), 0.76 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 221.0 (17-C_qO), 170.7 (C_qO), 77.0 (+, 3-*C*HOAc), 74.4 (+, 2-*C*HO), 67.7 (–, 19-*C*H_2O), 51.3 (+, *C*H), 47.3 (C_q), 46.6 (C_q), 46.0 (+, *C*H), 41.9 (+, *C*H), 38.8 (–, *C*H_2), 37.7 (+, *C*H), 35.7 (–, *C*H_2), 32.3 (–, *C*H_2), 31.1 (–, *C*H_2), 30.1 (–, *C*H_2), 29.5 (–, *C*H_2), 21.6 (–, *C*H_2), 21.2 (+, CO*C*H_3), 20.5 (–, *C*H_2), 13.5 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2906 (vw), 2854 (vw), 2926 (vw), 1724 (w), 1450 (vw), 1368 (vw), 1241 (w), 1134 (w), 1022 (w), 987 (w), 910 (w), 877 (vw), 786 (vw), 725 (vw), 596 (vw), 513 (vw), 400 (vw) cm^{-1}. – **MS** (EI, 70 eV, 100 °C): *m/z* (%) = 346 (100) $[M]^{\bullet+}$, 331 (10) $[M–CH_3]^+$, 318 (41) $[M–CO]^+$, 288 (100) $[M–OAc]^+$, 237 (54), 217 (35), 181 (51), 131 (56). – **HRMS** (EI, $C_{21}H_{30}O_4$): calc.: 346.2139; found: 346.2139.

2.4.2 Experimental procedures for the Lewis-acid mediated ring opening (Table 2)

All reaction protocols of this section are based on the general procedure **GP-3** described in the experimental section of the corresponding paper. For better clarity, in **GP-3A** zinc(II) salts were used while for **GP-3B** boron trifluoride diethyl etherate was used.

Synthesis of 2*α*,3*β*,17*β*,19-tetraacetoxy-5*α*-androstane (**29-Ac**)



For both substrates **13-Ac** and **13-Bn**, only **29-Ac** (R = OAc) was obtained. The formation of the corresponding 17-benzyl protected **29-Bn** (R = Bn) was not observed, since a selective ether cleavage of the THF was not achieved under the tested reaction conditions.

- Starting from 3*β*,17*β*-diacetoxy-2*β*,19-epoxy-5*α*-androstane (**13-Ac**)

According to **GP-3A**, 3*β*,17*β*-diacetoxy-2*β*,19-epoxy-5*α*-androstane (**13-Ac**) (25 mg, 62.7 µmol, 1.00 equiv) and zinc(II) iodide (70 mg, 219 µmol, 3.50 equiv) were dissolved in acetic anhydride (3.0 mL) and stirred in the dark overnight at 40 °C. Following the **GP-3** the crude product was purified by flash column chromatography on silica gel (cyclohexane/ ethyl acetate, 3:1) to obtain 3*β*,17*β*,19-triacetoxy-2*α*-iodo-5*α*-androstane (**34-Ac**) (16 mg, 28.2 µmol, 45%) and the title compound **29-Ac** (5.6 mg, 11.4 µmol, 18%) both as yellowish solids.

According to **GP-3B**, 3*β*,17*β*-diacetoxy-2*β*,19-epoxy-5*α*-androstane (**13-Ac**) (25 mg, 57.2 µmol, 1.00 equiv) was dissolved in acetic anhydride (2.0 mL) and $BF_3 \cdot OEt_2$ (0.11 mL, 572 mmol, 10.0 equiv) was added dropwise. Following the **GP-3B**, the title compound **29-Ac** was obtained after flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) as slightly yellow solid (20 mg, 40.6 µmol, 70%).

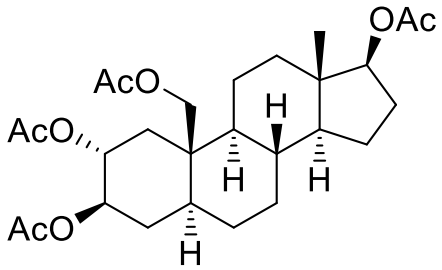
- Starting from 3*β*-acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**)

Entry	Reagent	General procedure	Yield 29-Ac
1	1.50 equiv ZnI_2	GP-3A	39%
2	1.15 equiv $ZnOTf_2$	GP-3A	92%
3	10.0 equiv $BF_3 \cdot OEt_2$	GP-3B	77%
4	1.00 equiv $BF_3 \cdot OEt_2$	GP-3B	0% (no conversion)

Following **GP-3A** 3*β*-acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**) (80 mg, 182 µmol, 1.00 equiv) and zinc(II) triflate (76 mg, 209 µmol, 1.15 equiv) was dissolved in acetic anhydride (2.0 mL). The reaction was stirred overnight at 40 °C and then 2 h at 60 °C. The work up followed the general procedure **GP-3** afford the crude product which was then purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) to give the title compound **29-Ac** as slightly yellow solid (82 mg, 167 µmol, 92%).

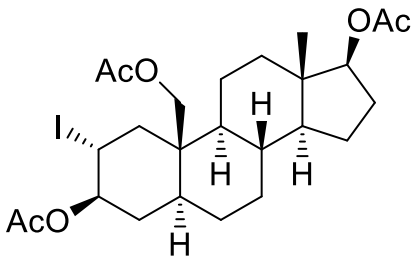
According to **GP-3B**, 3*β*-acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**) (40 mg, 91.2 µmol, 1.00 equiv) was dissolved in acetic acid (3.0 mL) (0.09 mL 343 µmol, 3.80 equiv) and $BF_3{\cdot}OEt_2$ was added dropwise. Following the instructions of the general procedure **GP-3** led to the crude product which was then purified by column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1) to obtain the title compound **29-Ac** as yellowish solid (34 mg, 69.8 µmol, 77%).

2*α*,3*β*,17*β*,19-Tetraacetoxy-5*α*-androstane (**29-Ac**)



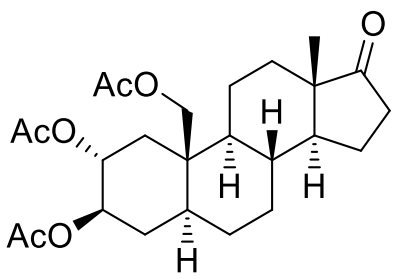
***R*$_f$** = 0.40 (*c*Hex/EtOAc, 2:1). – **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.93 (ddd, ^3J = 11.5, 9.9, 4.6 Hz, 1H, 2-C*H*OAc), 4.84 (td, ^3J = 10.3, 5.5 Hz, 1H, 3-C*H*OAc), 4.57 (dd, ^3J = 9.2, 7.8 Hz, 1H, 17-C*H*OAc), 4.22 (s, 2H, 19-CH_2OAc), 2.49 (dd, ^2J = 12.7 Hz, ^3J = 4.7 Hz, 1H, CH_2^a), 2.17 (m, 1H, 16-CH_2^a), 2.14 (s, 3H, COCH_3), 2.02 (s, 3H, COCH_3), 2.01 (s, 3H, COCH_3), 2.00 (s, 3H, COCH_3), 1.87 (ddd, ^2J = 12.9 Hz, ^3J = 5.6, 2.9 Hz, 1H, CH_2^a), 1.76–1.67 (m, 2H, 2 different CH_2), 1.66–1.56 (m, 2H, 2 different CH_2), 1.54–0.79 (m, 13H, 16-CH_2^b, 7 different CH_2 + 4 different C*H*), 0.77 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR** (101 MHz, $CDCl_3$): δ = 171.2 (C_qO), 171.0 (C_qO), 170.4 (C_qO), 170.1 (C_qO), 82.3 (+, 17-*C*HOAc), 73.6 (+, 3-*C*HOAc), 71.5 (+, 2-*C*HOAc), 62.1 (–, 19-*C*H_2OAc), 53.9 (+, *C*H), 50.5 (+, *C*H), 44.1 (+, *C*H), 42.5 (C_q), 39.5 (C_q), 37.3 (–, 16-*C*H_2), 36.7 (–, *C*H_2), 34.9 (+, *C*H), 32.8 (–, *C*H_2), 30.9 (–, *C*H_2), 27.3 (–, *C*H_2), 27.0 (–, *C*H_2), 23.3 (–, *C*H_2), 21.5 (–, *C*H_2), 21.0 (+, 4×CO*C*H_3), 12.1 (+, 18-*C*H_3) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2924 (w), 1731 (m), 1449 (w), 1366 (w), 1230 (m), 1028 (m), 918 (w), 645 (vw), 605 (w) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 493 (100) $[M]^{\bullet+}$, 432 (18) $[M–HOAc]^+$, 390 (44), 372 (37), 359 (45), 330 (100), 317 (30), 312 (29), 300 (24), 239 (43). – **HRMS** (EI, $C_{27}H_{40}O_8$): calc.: 492.2724; found: 492.2797.

3*β*,17*β*,19-triacetoxy-2*α*-iodo-5*α*-androstane (**34-Ac**)



***R*$_f$** = 0.60 (*c*Hex/EtOAc, 2:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.95–4.87 (m, 1H, 3-*C*HOAc), 4.57 (t, ^3J = 8.5 Hz, 1H, 17-C*H*OAc), 4.28 (d, ^2J = 12.3 Hz, 1H, 19-CH_2^a), 4.21–4.19 (m, 1H, 2-C*H*I), 4.17 (d, ^2J = 12.0 Hz, 1H, 19-CH_2^b), 2.91 (dd, ^2J = 13.5, ^3J = 4.3 Hz, 1H, CH_2), 2.16 (ddd, ^2J = 14.0 Hz, ^3J = 6.9, 3.9 Hz, 1H, CH_2), 2.10 (s, 3H, COCH_3), 2.08 (s, 3H, COCH_3), 2.03 (s, 3H, COCH_3), 1.80 (dd, *J* = 9.7, 5.3 Hz, 1H, CH_2), 1.77–1.67 (m, 3H, 3 different CH_2 + 5-C*H*), 1.64–1.57 (m, 2H, 2 different CH_2), 1.54–1.37 (m, 3H, 2 different CH_2 + 8-C*H*), 1.37–1.23 (m, 4H, 3 different CH_2 + 14-C*H*), 1.21–1.00 (m, 3H, 2 different CH_2 + 9-C*H*), 0.98–0.88 (m, 1H, CH_2), 0.87–0.81 (m, 1H, C*H*), 0.77 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 171.3 (*C*$_q$O), 171.1 (*C*$_q$O), 170.2 (*C*$_q$O), 82.6 (+, 17-*C*HOAc), 77.6 (+, 3-*C*HOAc), 62.4 (–, 19-*C*H_2OAc) , 53.9 (+, 9-*C*H), 50.9 (+, 14-*C*H), 46.3 (–, *C*H_2), 44.5 (+, 5-*C*H), 42.7 (*C*$_q$), 42.3 (*C*$_q$), 37.1 (–, *C*H_2), 35.5 (+, 8-*C*H), 34.9 (–, *C*H_2), 31.1 (–, *C*H_2), 29.0 (+, 2-*C*HI), 27.6 (–, *C*H_2), 27.6 (–, *C*H_2), 23.6 (–, *C*H_2), 21.7 (–, *C*H_2), 21.3 (+, CO*C*H_3), 21.3 (+, CO*C*H_3), 21.3(+, CO*C*H_3), 12.3 (+, 18-*C*H_3) ppm. – **MS** (ESI): *m/z* (%) = 583 $[M+Na]^+$. – **HRMS** (ESI, $[C_{25}H_{37}IO_6+Na]^+$): calc.: 583.1527; found: 583.1512.

2*α*,3*β*,19-Triacetoxy-5*α*-androstane-17-on (**29**)

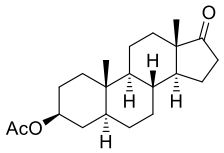


According to the **GP-3A** 3*β*-acetoxy-2*β*,19-epoxy-5*α*-androstane-17-on (**13**) (61 mg, 178 mmol, 1.00 equiv) and zinc(II) trifluoromethanesulfonate (94 mg, 266 mmol, 1.50 equiv) were dissolved in acetic acid (2.0 mL) and heated to 45 °C overnight. Then reaction was heated for another two hours to 65 °C. After cooling to r.t., the instructions of **GP-3** led to the crude product which was purified by flash column chromatography on silica gel (cyclohexane/ethyl acetate, 3:1→3:2) to give the title compound **29** as slightly yellow solid (54 mg, 120 µmol, 68%).

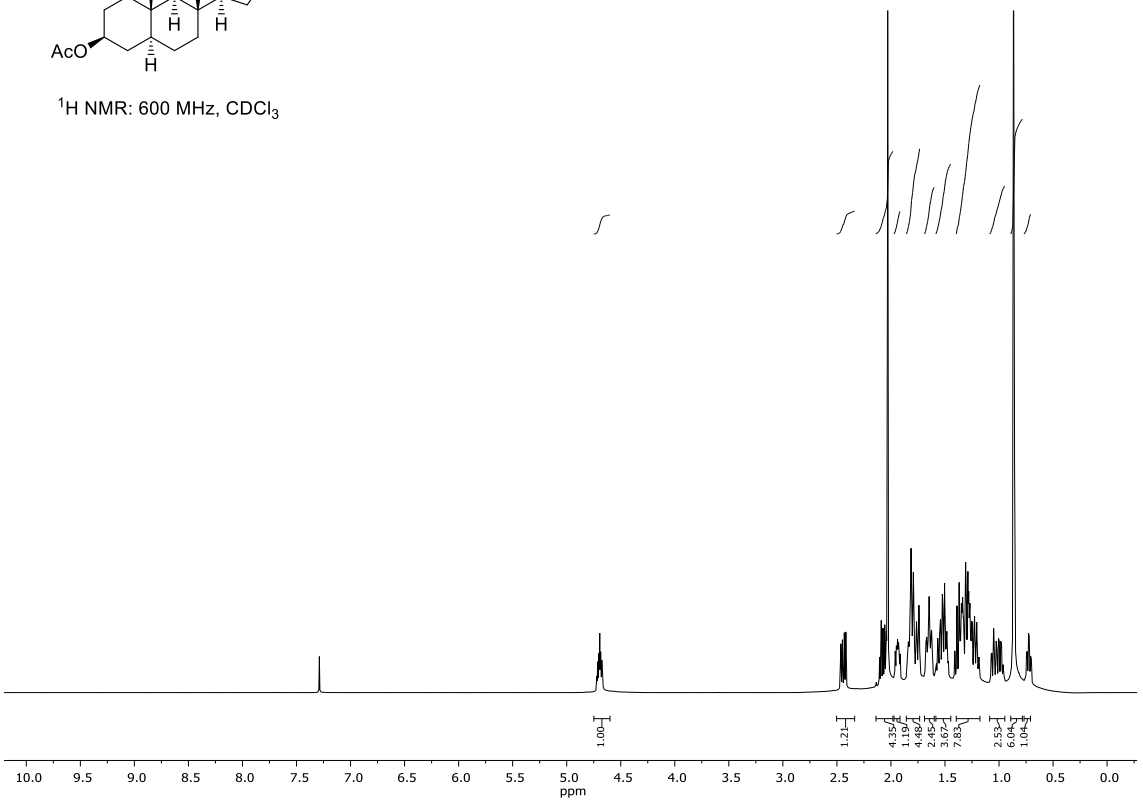
***R*$_f$** = 0.28 (*c*Hex/EtOAc, 2:1). – **^{1}H NMR** (500 MHz, $CDCl_3$): δ = 4.91 (ddd, ^3J = 11.4, 9.8, 4.6 Hz, 1H, 2-C*H*OAc), 4.84 (td, ^3J = 10.4, 5.4 Hz, 1H, 3-C*H*OAc), 4.24 (d, ^2J = 12.4 Hz, 1H, 19-CH_2^aOAc), 4.21 (d, ^2J = 12.4 Hz, 1H, 19-CH_2^bOAc), 2.50 (dd, ^2J = 12.7 Hz, ^3J = 4.6 Hz, 1H, 16-CH_2^a), 2.44 (dd, ^2J = 19.3 Hz, ^3J = 8.8 Hz, 1H, 1-CH_2^a), 2.15 (s, 3H, COCH_3), 2.10–2.04 (m, 1H, 16-CH_2^b), 2.01 (s, 3H, COCH_3), 2.00 (s, 3H, COCH_3), 1.96–1.69 (m, 5H, 5 different CH_2), 1.64–1.15 (m, 9H, 5 different CH_2 + C*H* + C*H* + C*H*), 1.07–0.91 (m, 2H, 1-CH_2^b + CH_2), 0.88–0.83 (m, 1H, C*H*), 0.85 (s, 3H, 18-CH_3) ppm. – **^{13}C NMR** (126 MHz, $CDCl_3$): δ = 220.6 (17-C_qO), 171.5 (C_qO), 170.8 (C_qO), 170.4 (C_qO), 73.8 (+, 3-*C*HOAc), 71.6 (+, 2-*C*HOAc), 62.2 (–, *C*H$_2$OAc), 54.3 (+, *C*H), 51.4 (+, *C*H), 47.9 (13-C_q), 44.4 (+, 5-*C*H), 39.9 (10-C_q), 37.5 (–, 1-*C*H$_2$), 35.8 (–, 16-*C*H$_2$), 35.0 (+, *C*H), 33.0 (–, 4-*C*H$_2$), 31.7 (–, *C*H$_2$), 30.5 (–, *C*H$_2$), 27.1 (–, *C*H$_2$), 21.8 (+, 3 × CO*C*H$_3$), 21.5 (–, *C*H$_2$), 21.3 (–, *C*H$_2$), 14.1. (+, 18-*C*H$_3$) ppm. – **IR** (ATR): $\tilde{\nu}$ = 2922 (vw), 1733 (m), 1448 (vw), 1367 (w), 1225 (m), 1031 (w), 911 (w), 731 (vw), 647 (vw), 604 (vw), 576 (vw), 458 (vw) cm^{-1}. – **MS** (EI, 70 eV, 130 °C): *m/z* (%) = 448 (24) [M]$^{\bullet+}$, 346 (22), 286 (50), 255 (25), 84 (100). – **HRMS** (EI, $C_{25}H_{36}O_7$): calc.: 448.2451; found: 448.2461.

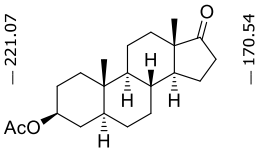
3. NMR spectra of the synthesized compounds

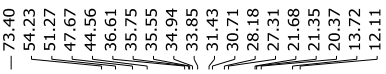
3*β*-Acetyloxy-5*α*-androstane-17-on (**SI-01**)



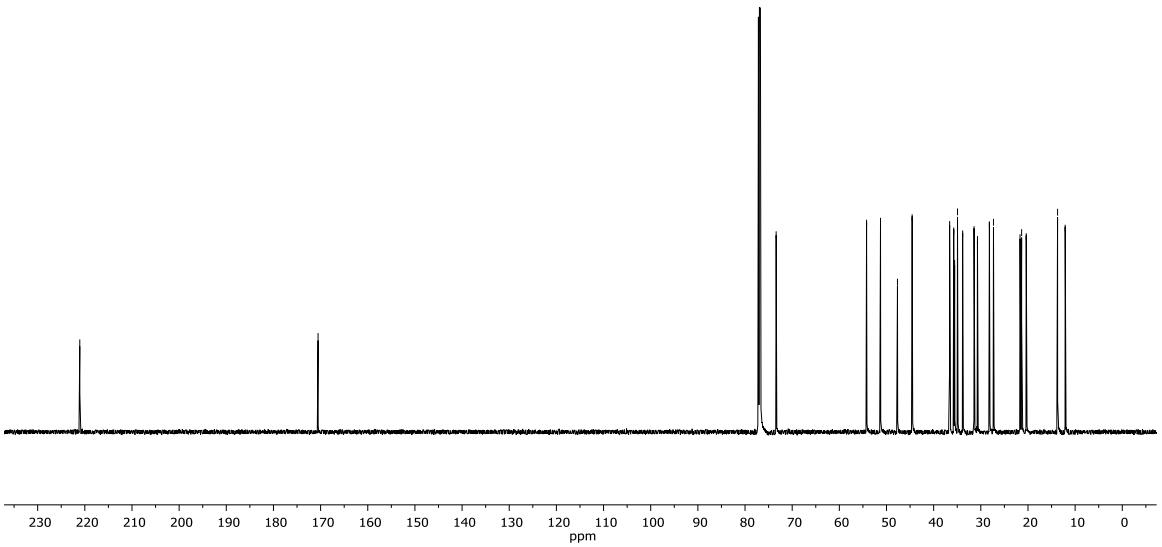
^{1}H NMR: 600 MHz, $CDCl_3$



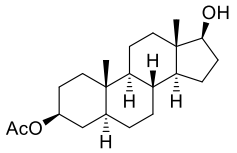




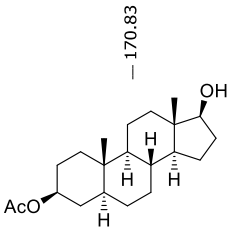
^{13}C NMR: 126 MHz, $CDCl_3$



3*β*-Acetoxy-5*α*-androstane-17*β*-ol (**SI-02**)

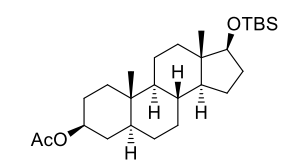


^{1}H NMR: 400 MHz, $CDCl_3$

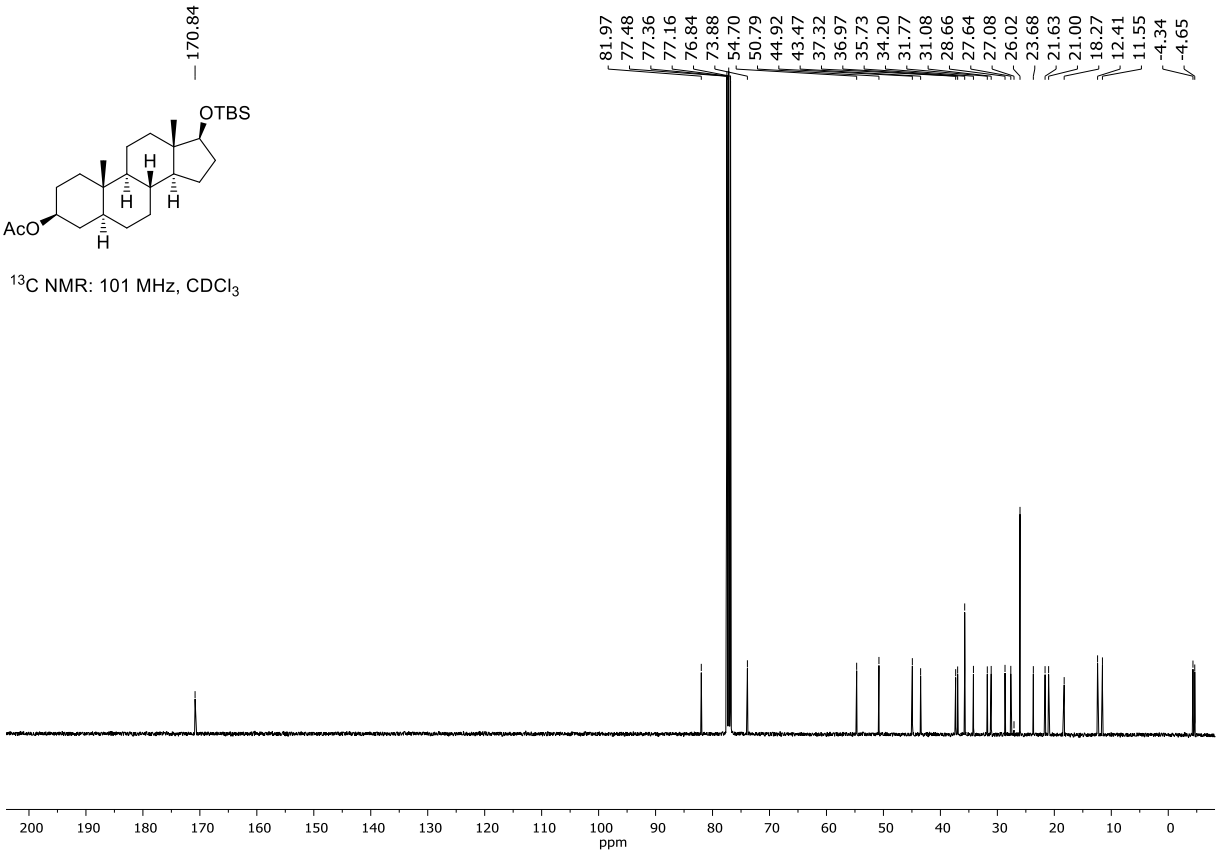


^{13}C NMR: 101 MHz, $CDCl_3$

3*β*-Acetoxy-17*β*-[[(*tert*-butyl)dimethylsilyl]oxy]-5*α*-androstane (**SI-03-TBS**)[3]

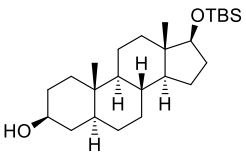


^{1}H NMR: 400 MHz, $CDCl_3$

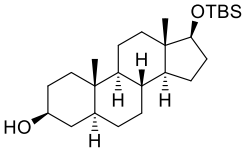


^{13}C NMR: 101 MHz, $CDCl_3$

17*β*-[(*tert*-Butyl)dimethylsilyl)oxy]-5*α*-androstane-3*β*-ol (**SI-04-TBS**)

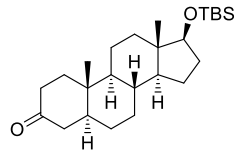


^{1}H NMR: 400 MHz, $CDCl_3$

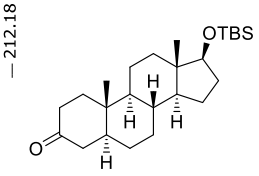


^{13}C NMR: 101 MHz, $CDCl_3$

17*β*-[(*tert*-Butyldimethylsilyl]oxy]-5*α*-androstane-3-on (**17-TBS**)

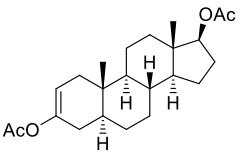


^{1}H NMR: 400 MHz, $CDCl_3$

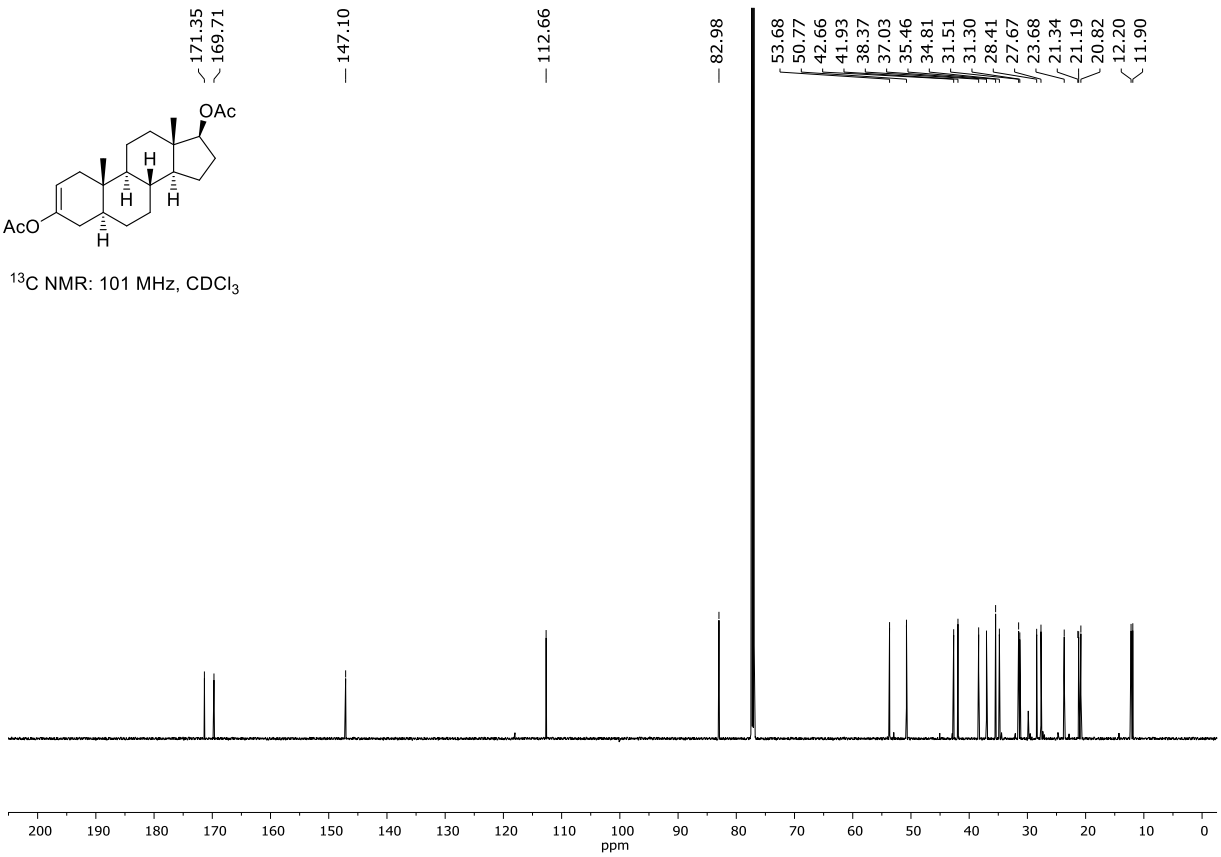


^{13}C NMR: 101 MHz, $CDCl_3$

3,17β-Diacetoxy-5α-androst-2-ene (**16**-**Ac**)

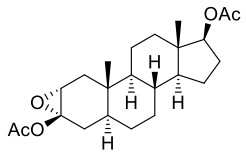


^{1}H NMR: 400 MHz, $CDCl_3$

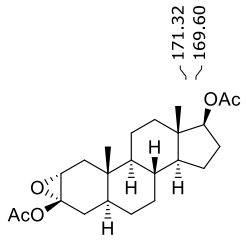


^{13}C NMR: 101 MHz, $CDCl_3$

3*β*,17*β*-Diacetoxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Ac**)[5]

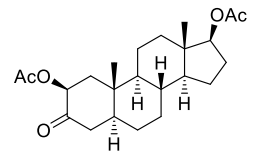


^{1}H NMR: 400 MHz, $CDCl_3$

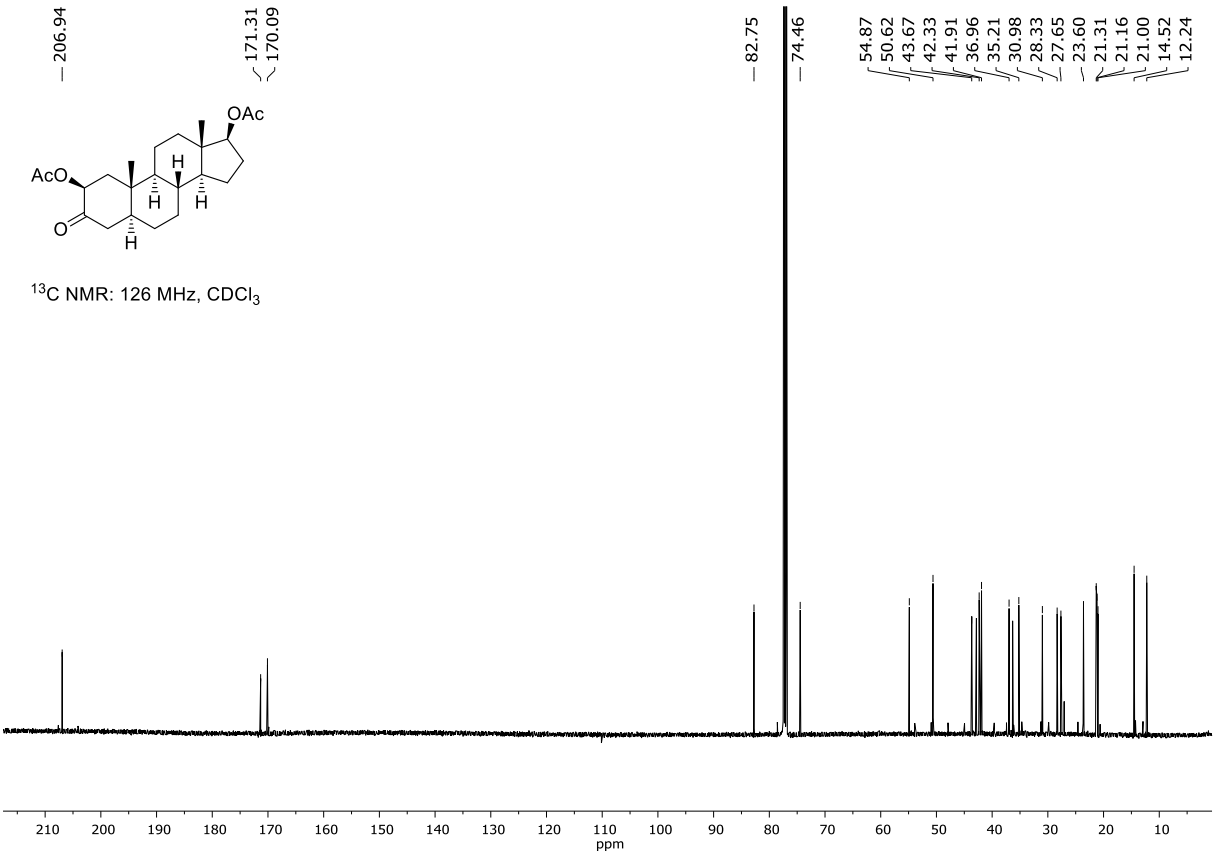


^{13}C NMR: 101 MHz, $CDCl_3$

2*β*,17*β*-Diacetoxy-5*α*-androstane-3-on (**19-Ac**)

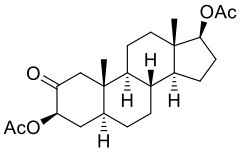


^{1}H NMR: 500 MHz, $CDCl_3$

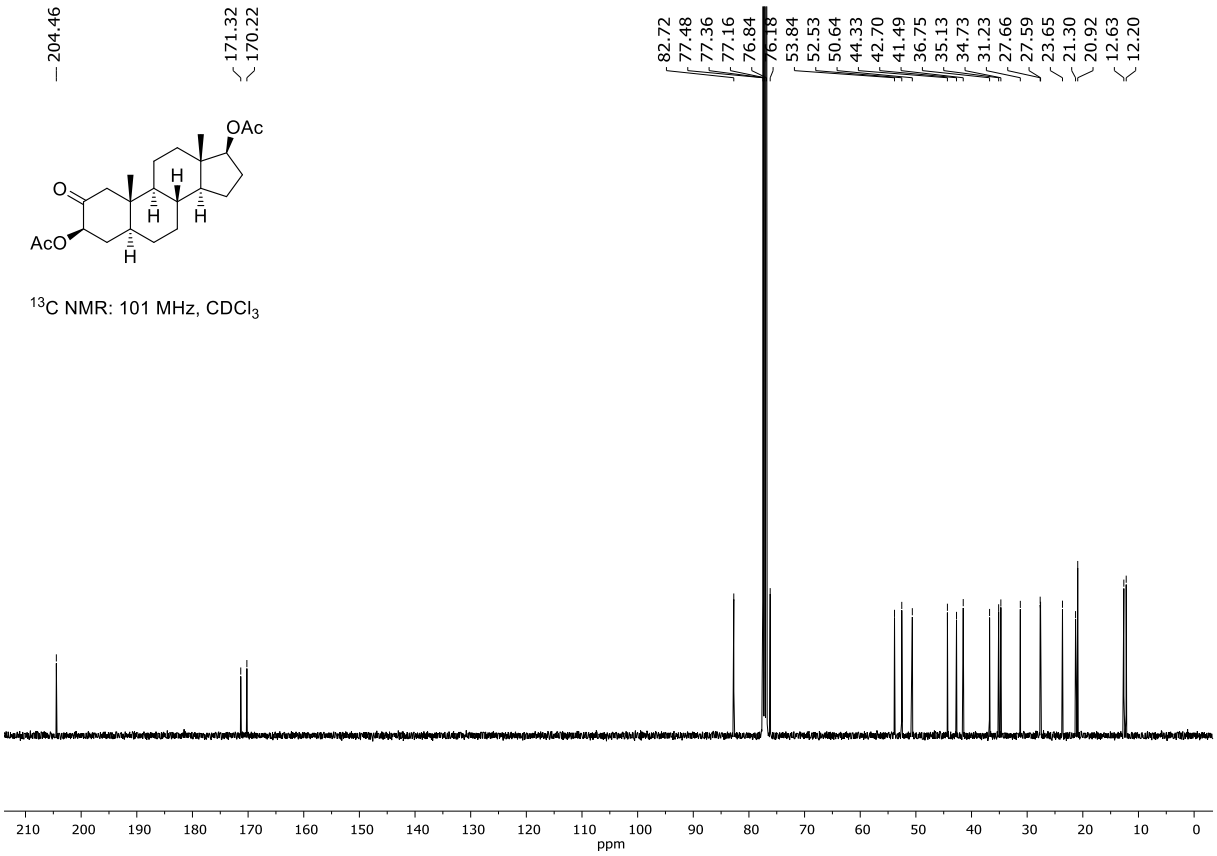


^{13}C NMR: 126 MHz, $CDCl_3$

3*β*,17*β*-Diacetoxy-5*α*-androstane-2-on (**20-Ac**)

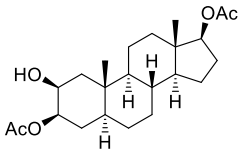


^{1}H NMR: 400 MHz, $CDCl_3$

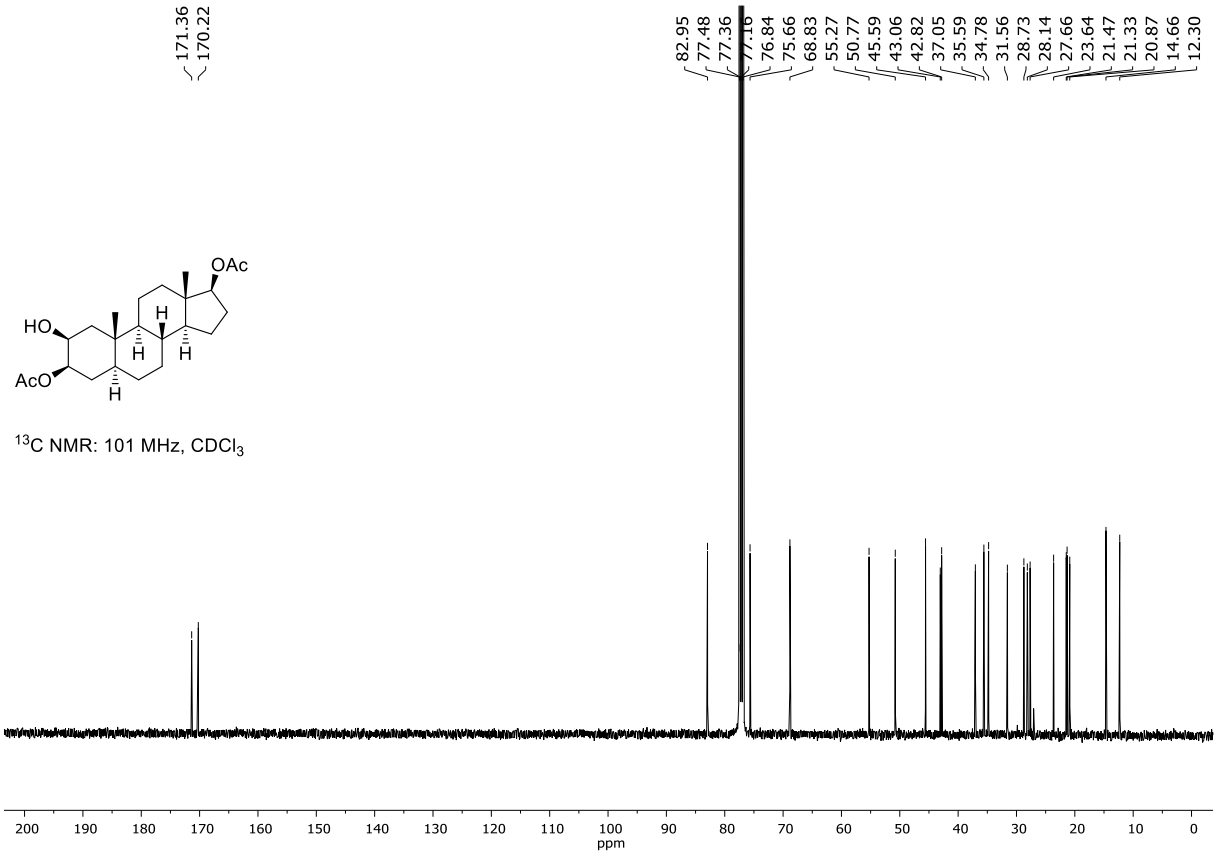


^{13}C NMR: 101 MHz, $CDCl_3$

3*β*,17*β*-Diacetoxy-5*α*-androstane-2*β*-ol (**14-Ac**)

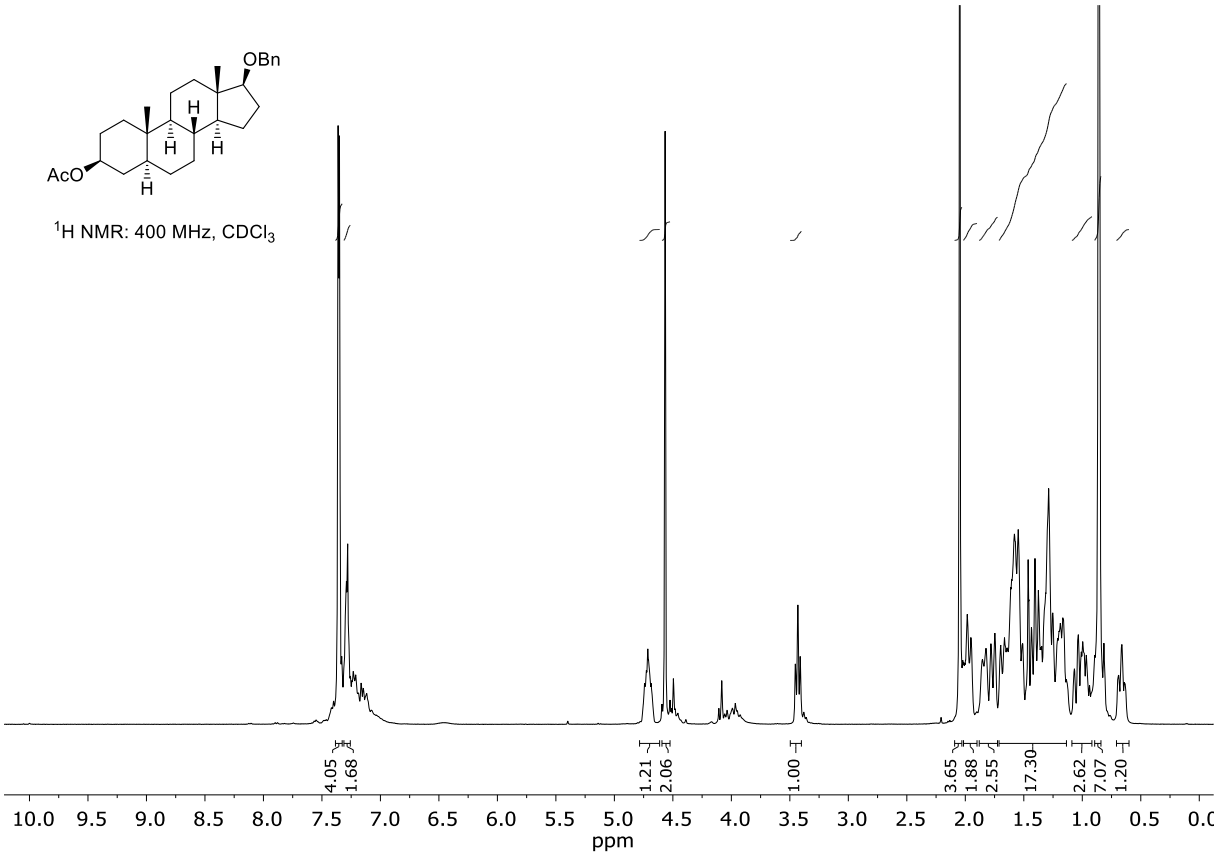


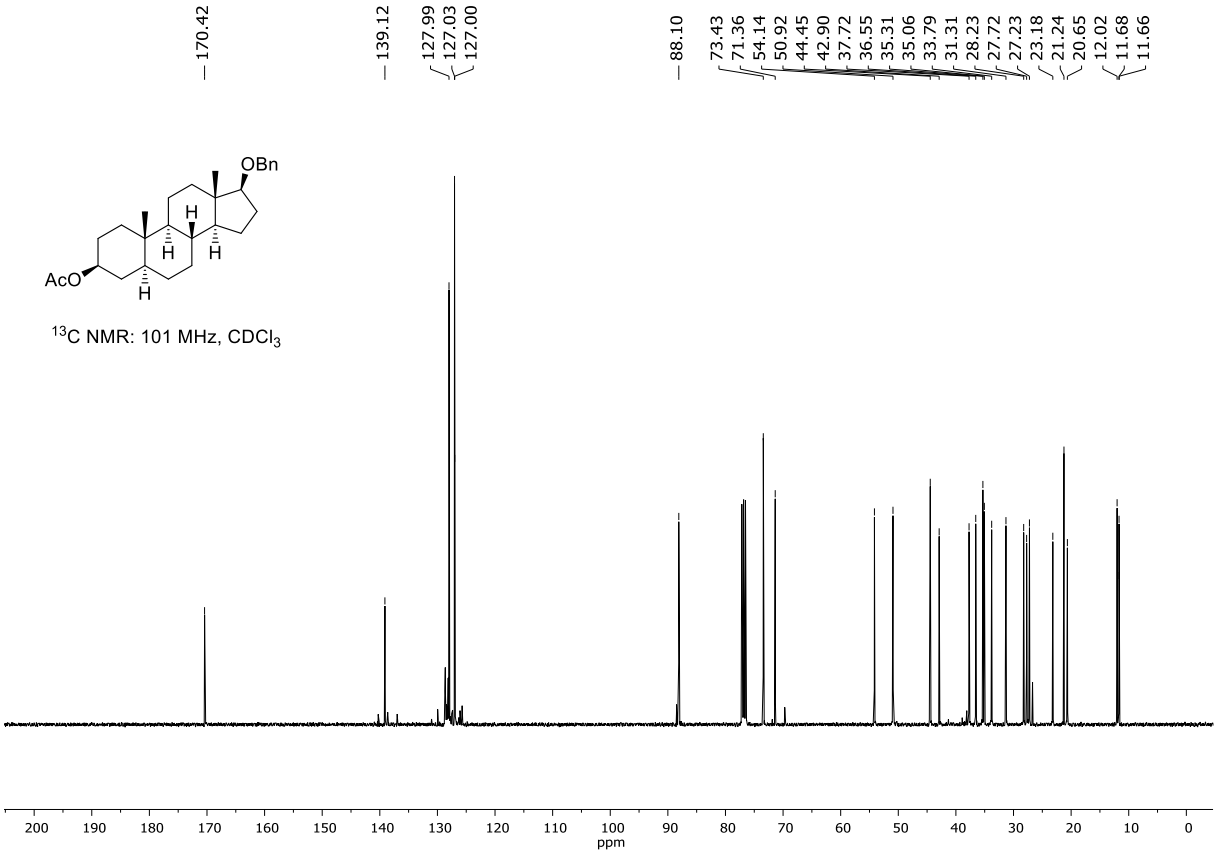
^{1}H NMR: 400 MHz, $CDCl_3$



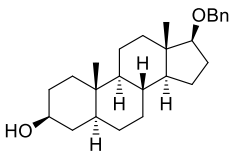
^{13}C NMR: 101 MHz, $CDCl_3$

3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane (**SI-03-Bn**)

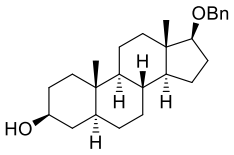


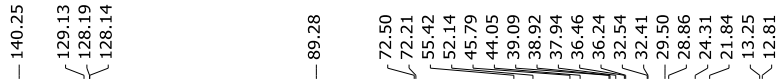


17*β*-Benzyloxy-5*α*-androstane-3*β*-ol (**SI-04-Bn**)

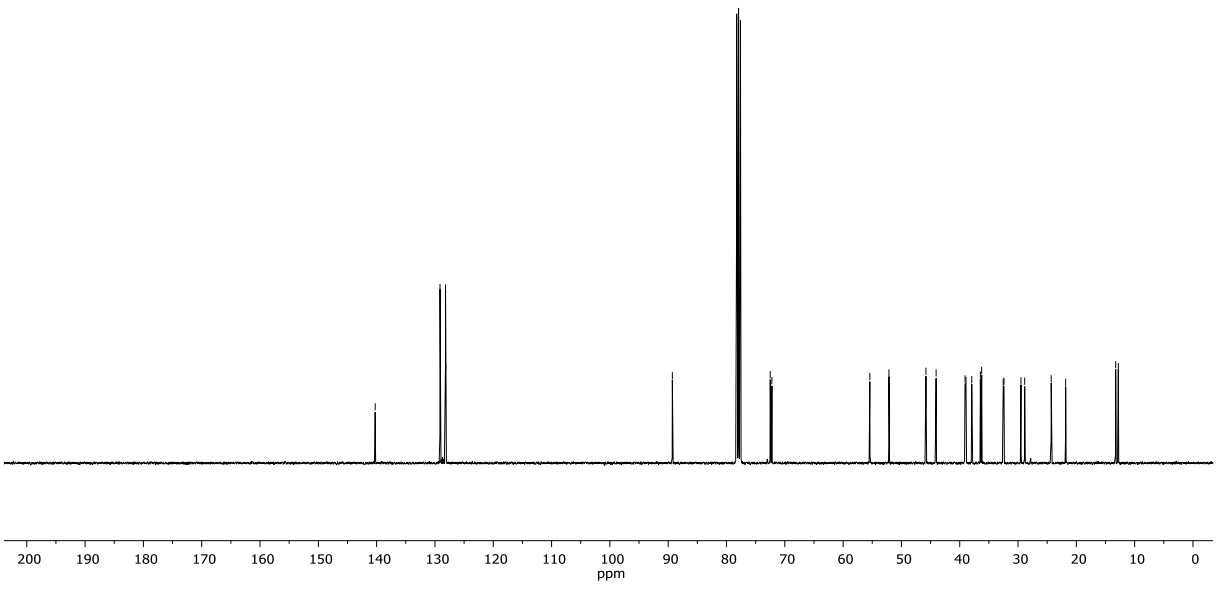


^{1}H NMR: 400 MHz, $CDCl_3$

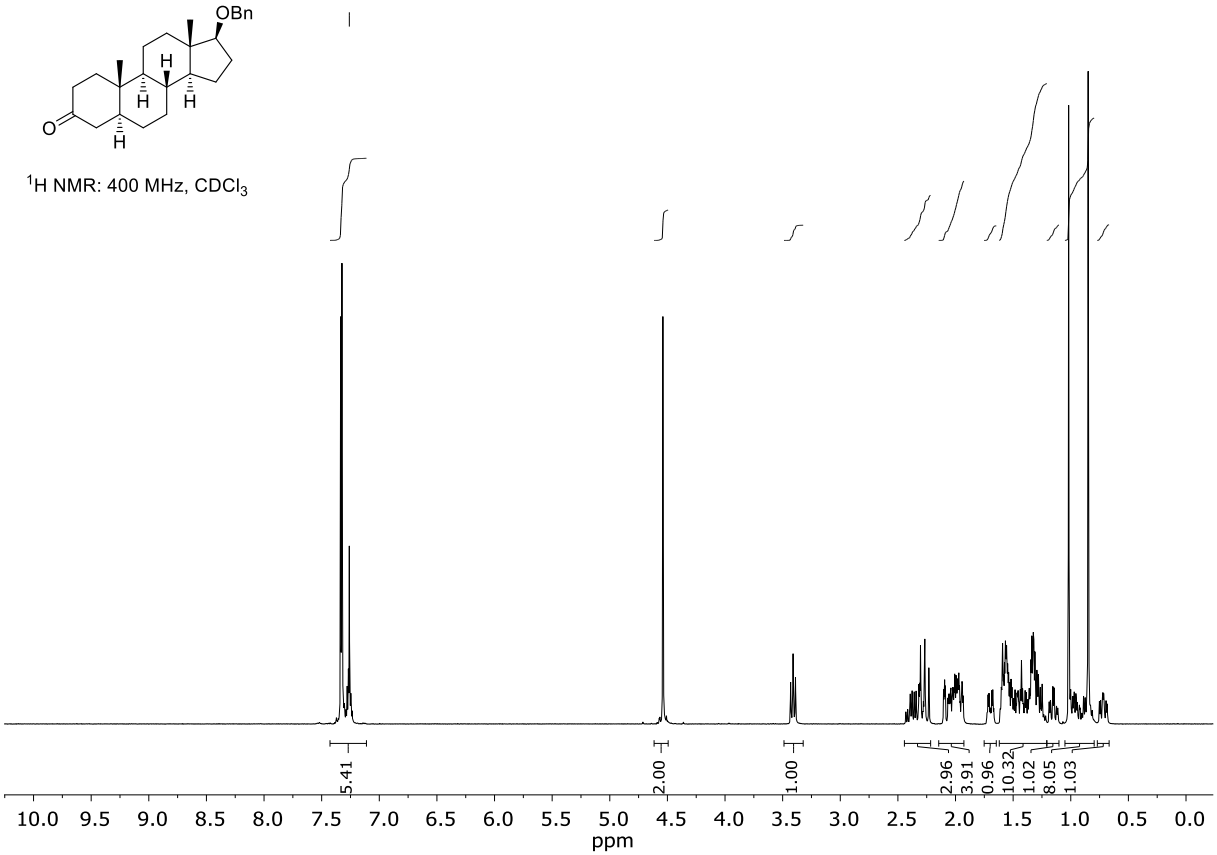


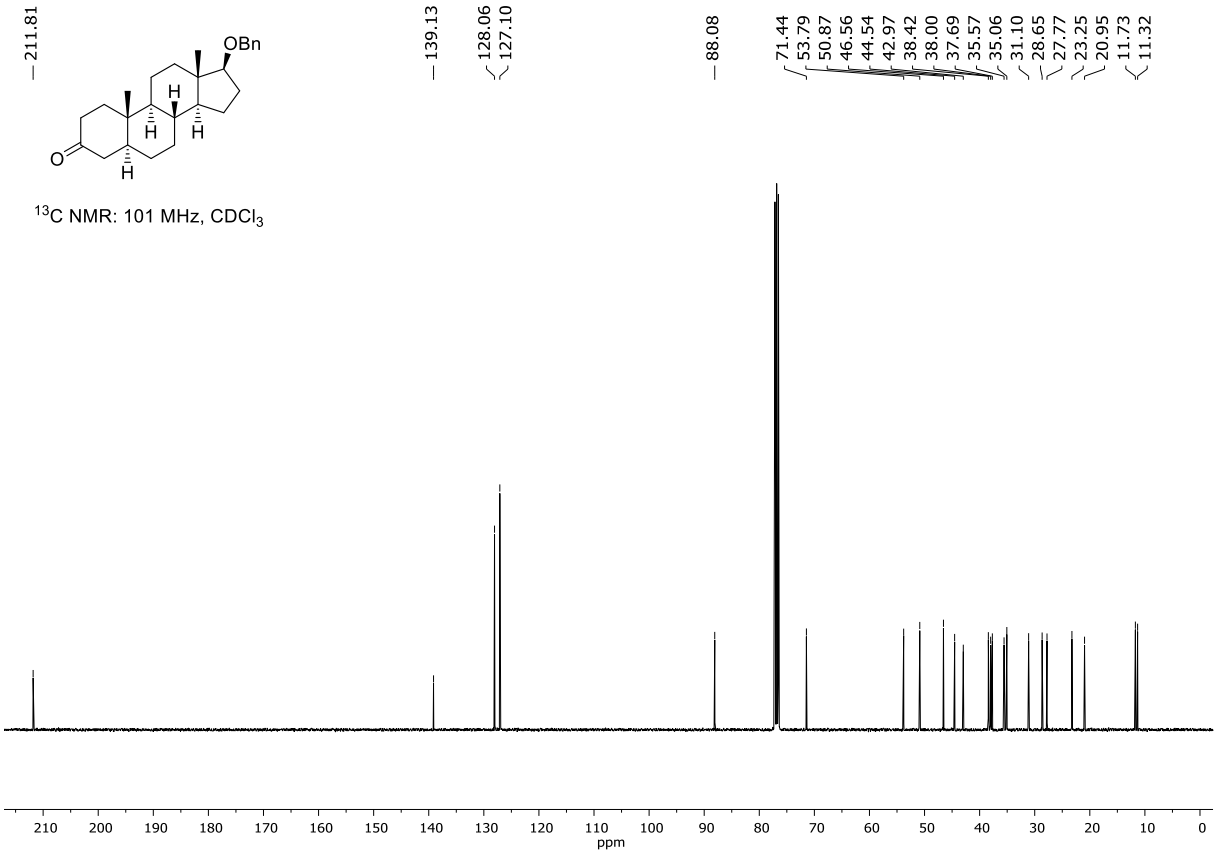


^{13}C NMR: 101 MHz, $CDCl_3$

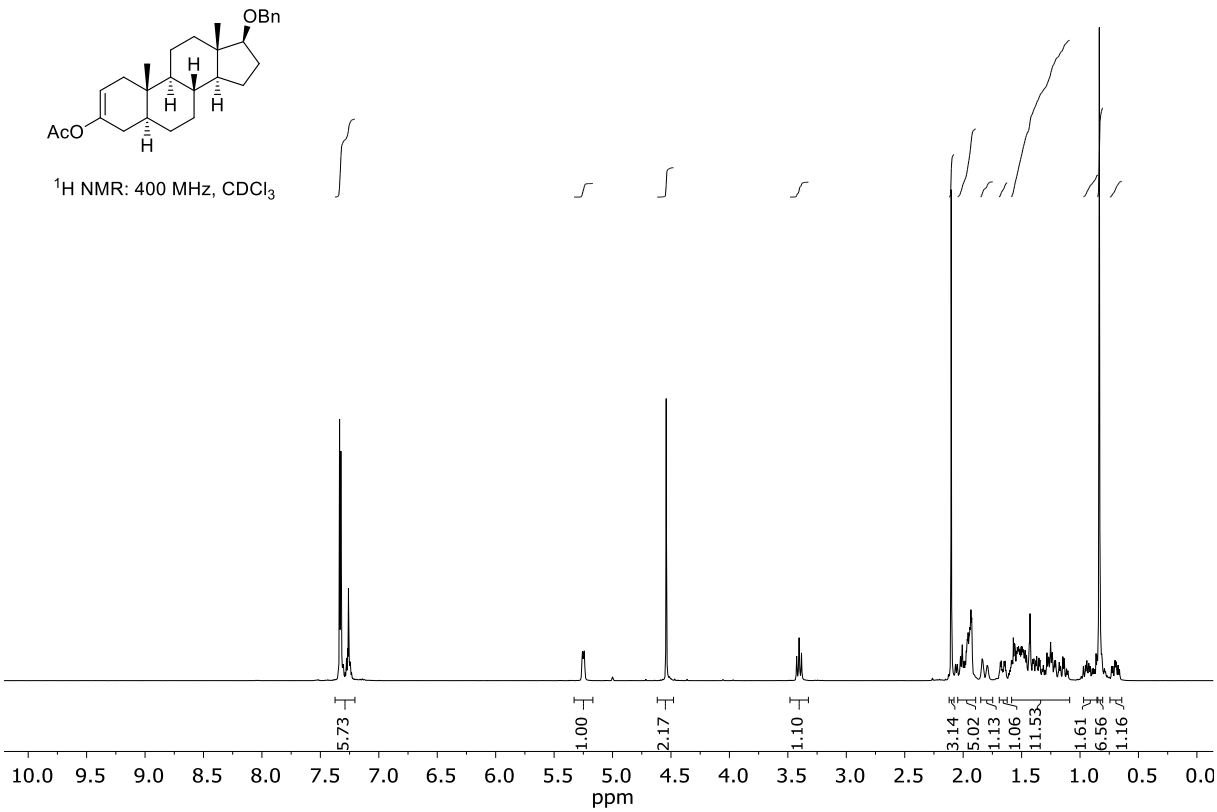


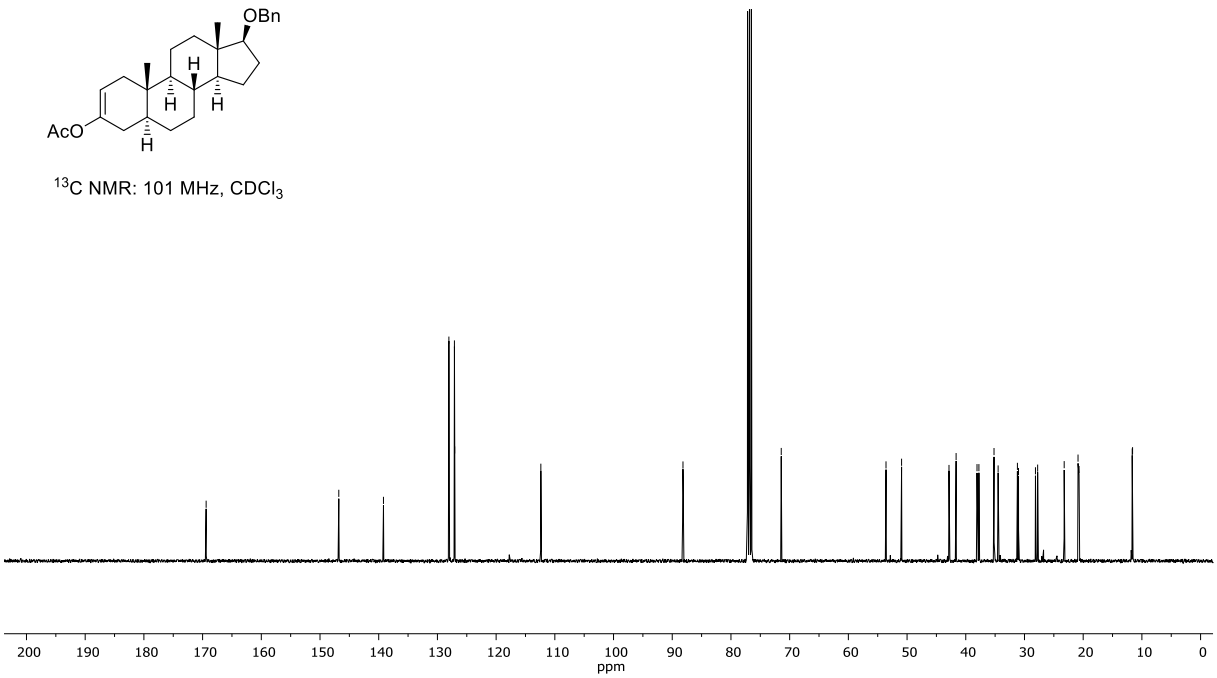
17*β*-Benzyloxy-5*α*-androstane-3-on (**17-Bn**)



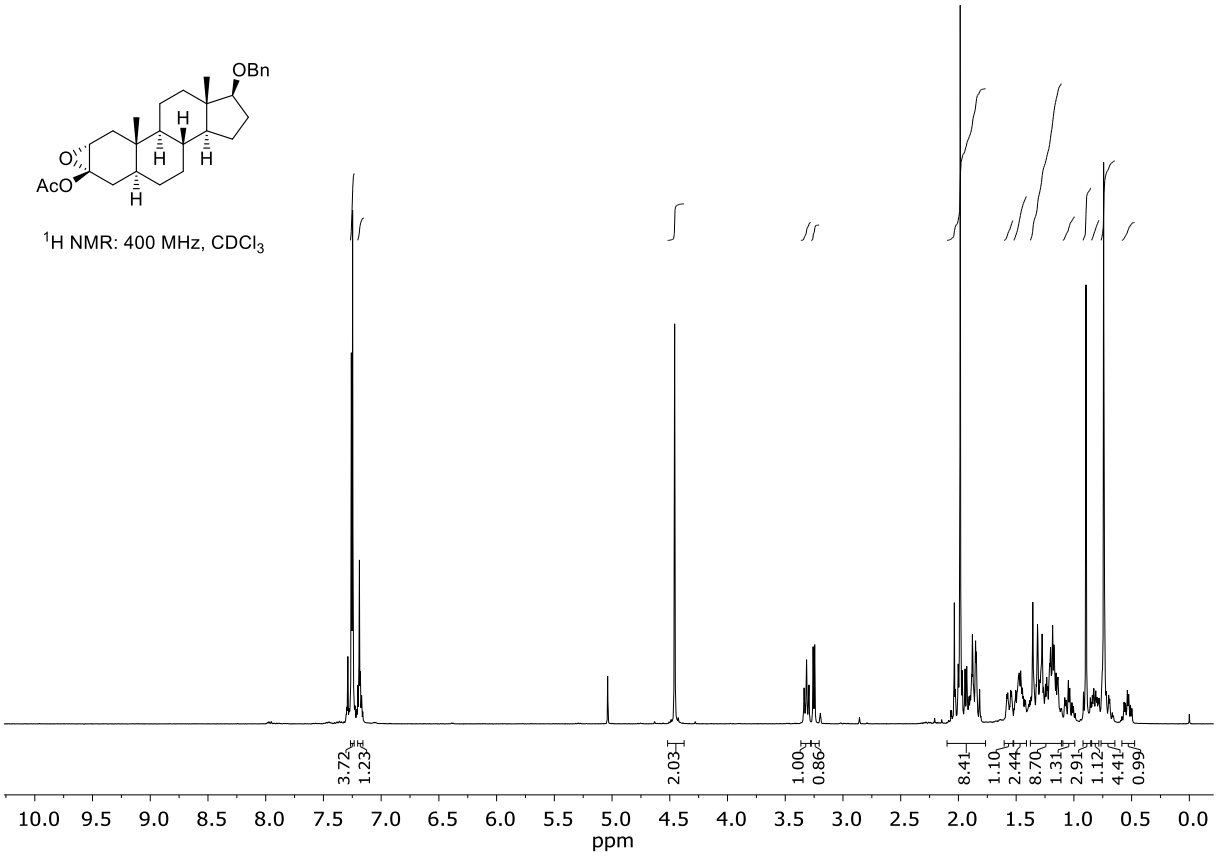


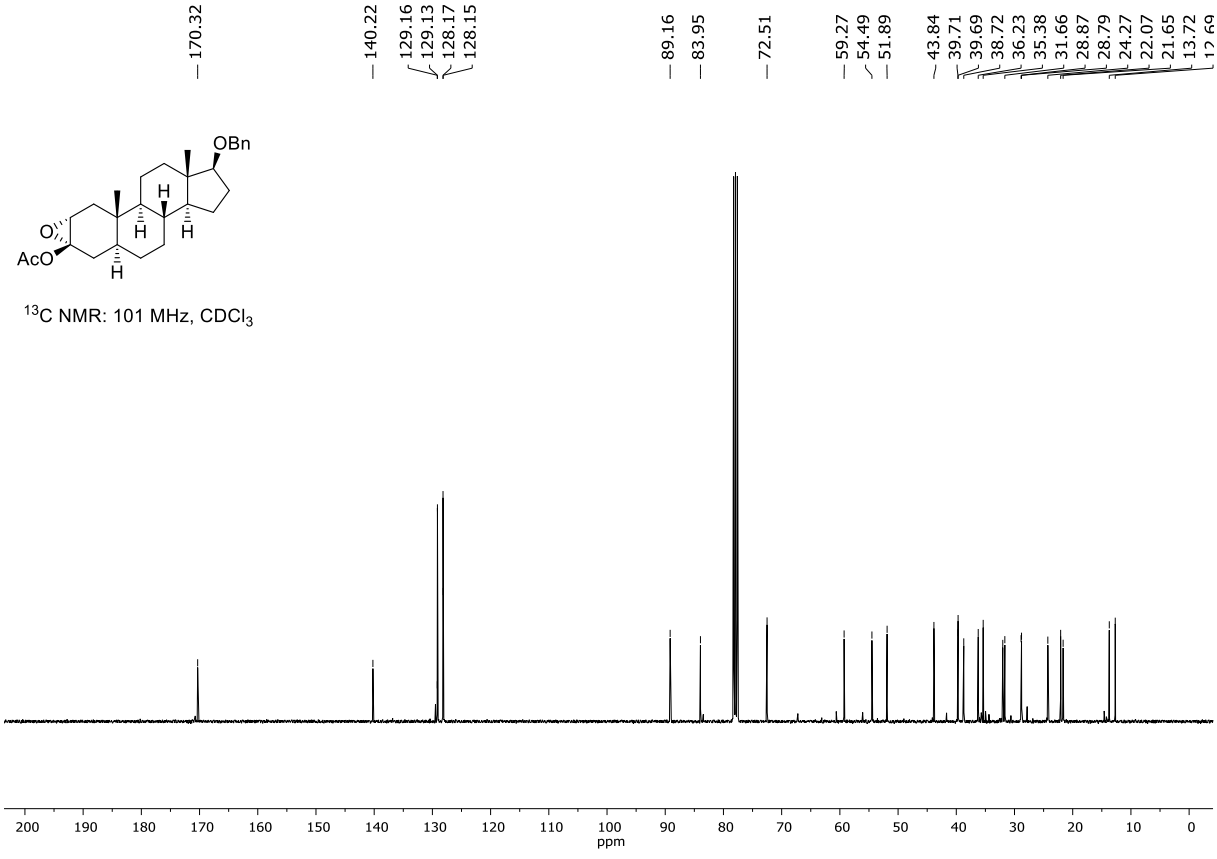
3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androst-2-ene (**16-Bn**)



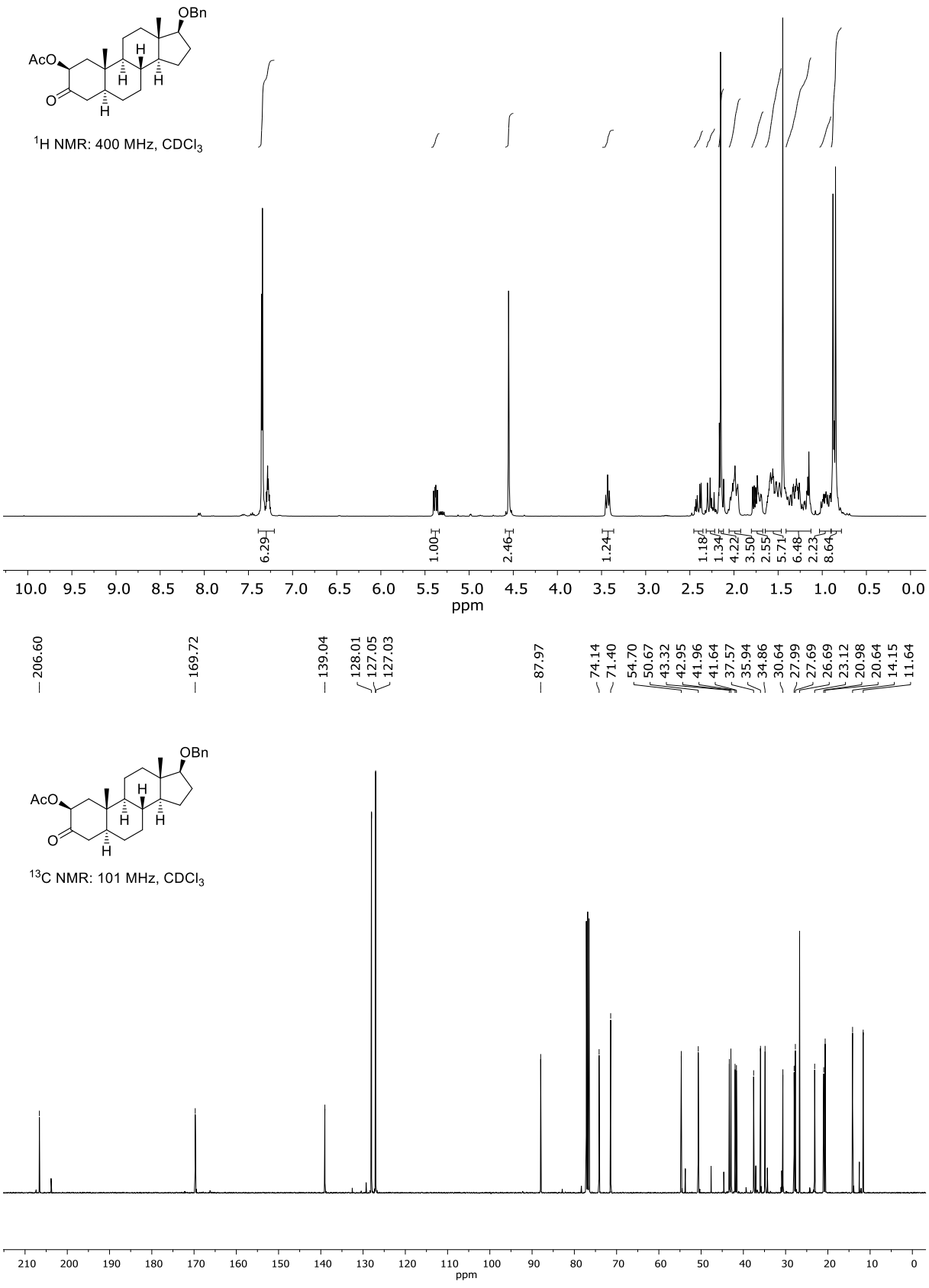


3*β*-Acetoxy-17*β*-benzyloxy-2*α*,3*α*-epoxy-5*α*-androstane (**18-Bn**)

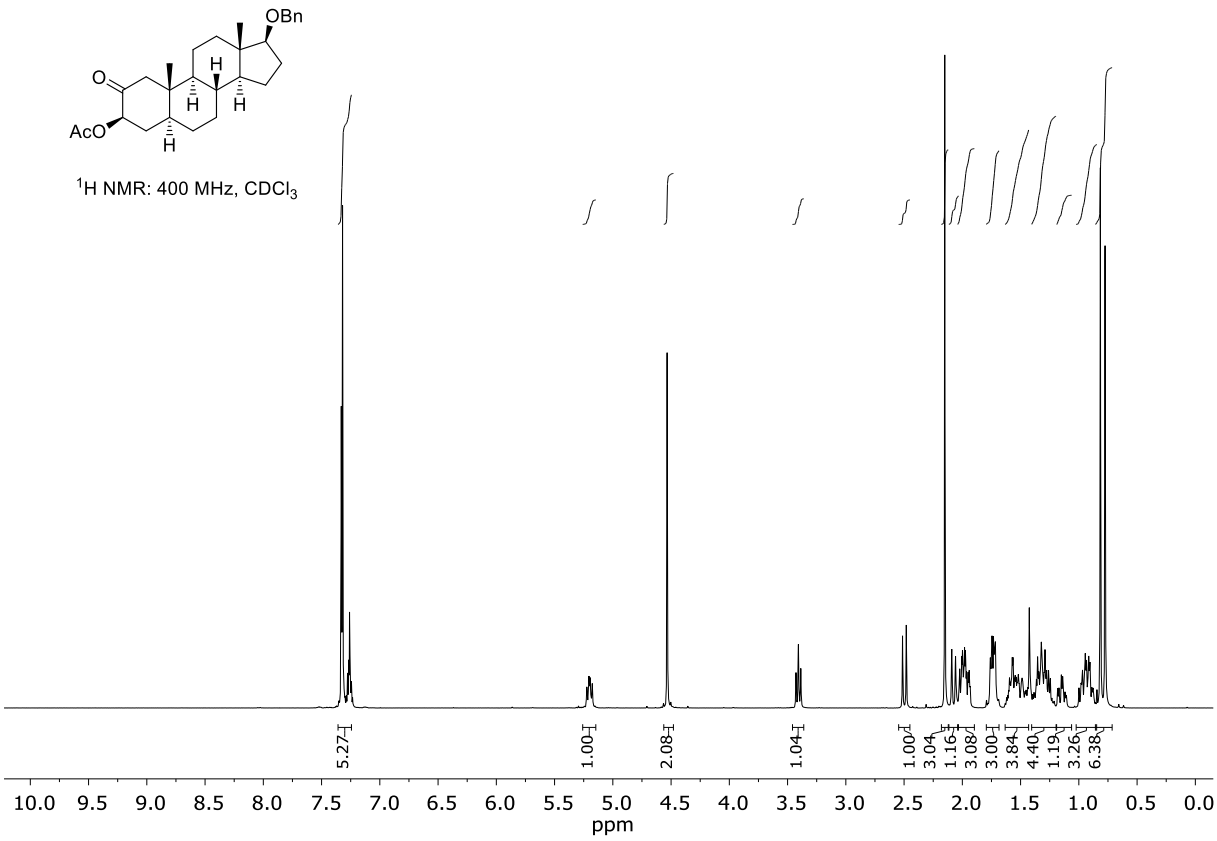


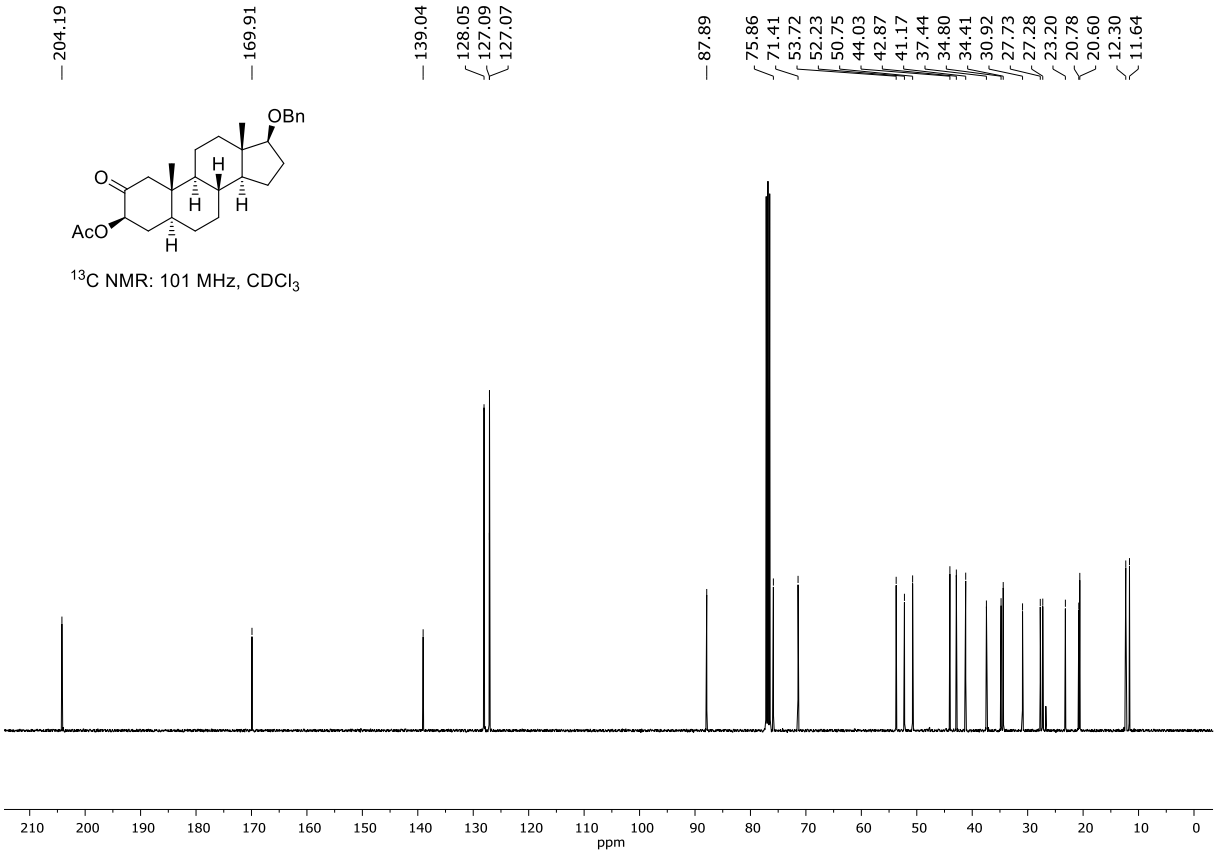


2*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-3-on (**19-Bn**)

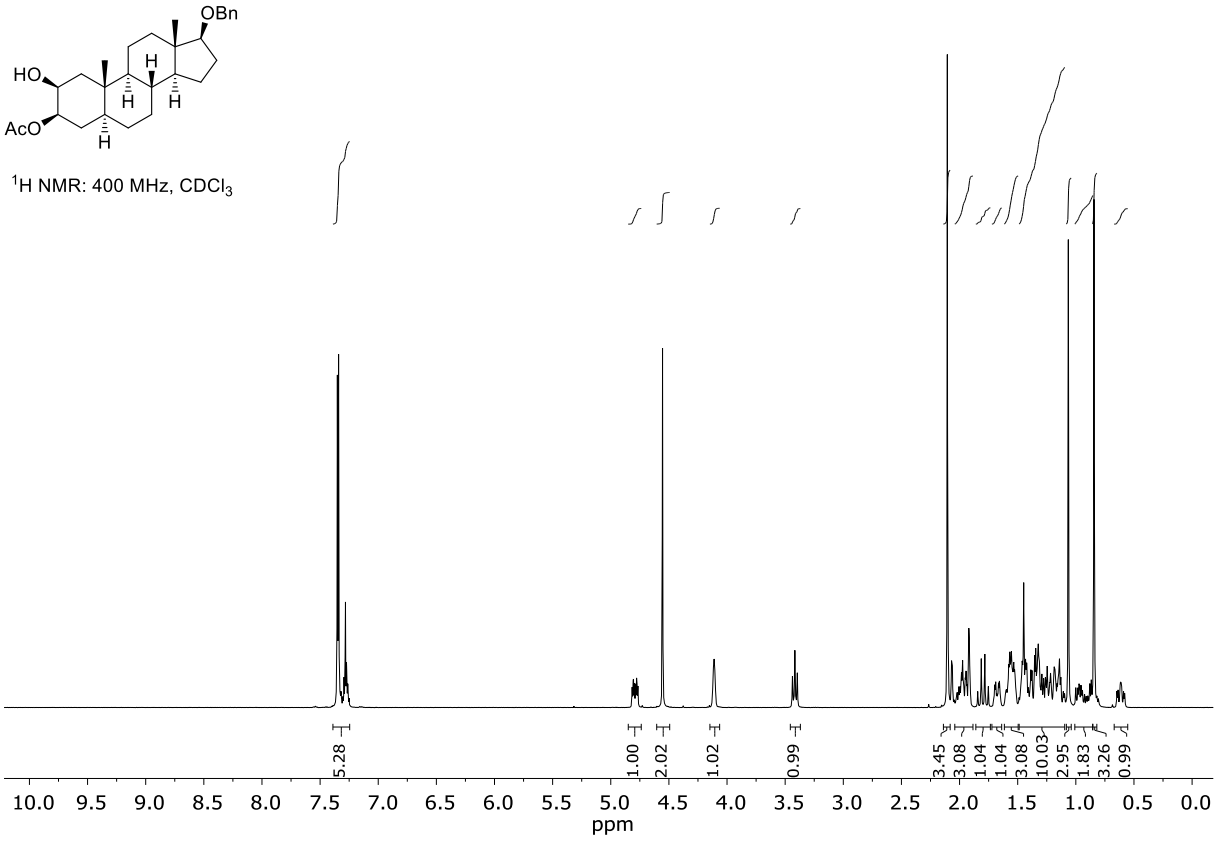


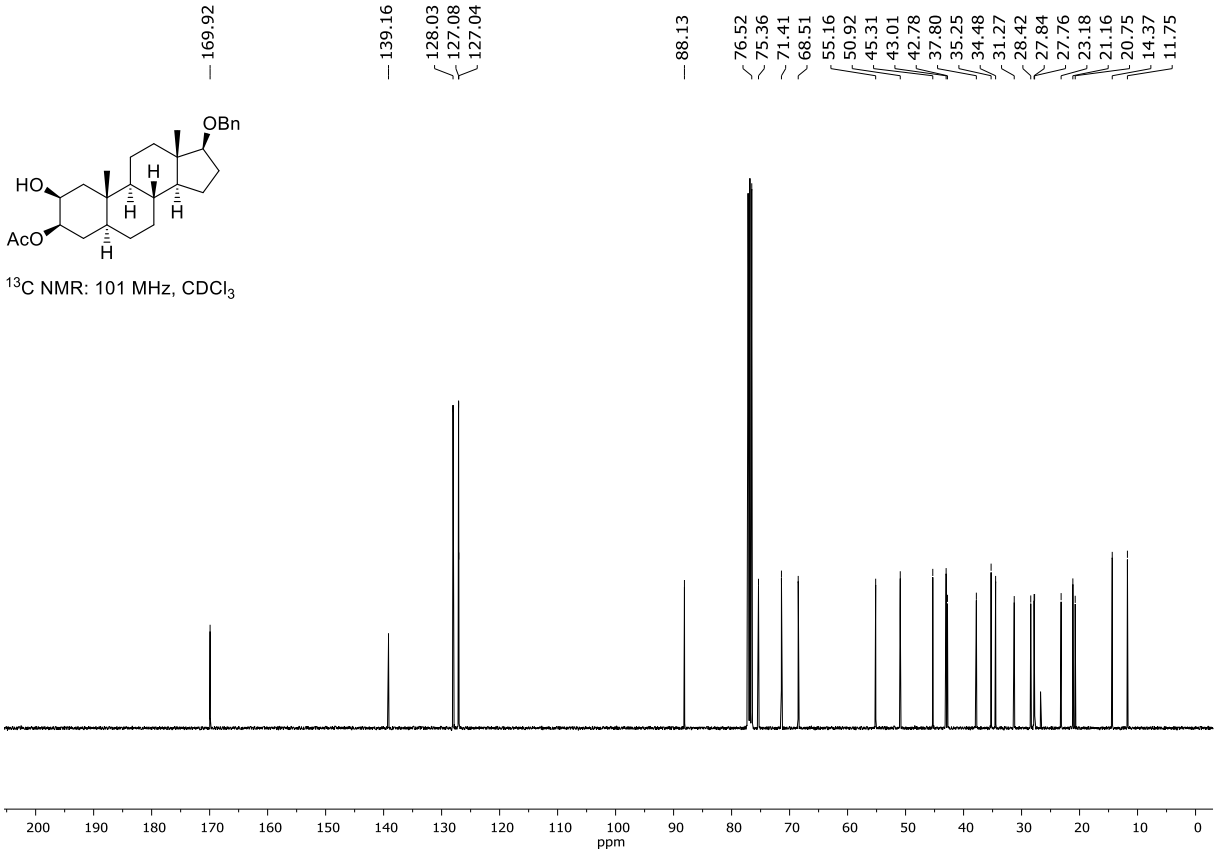
3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-2-on (**20-Bn**)



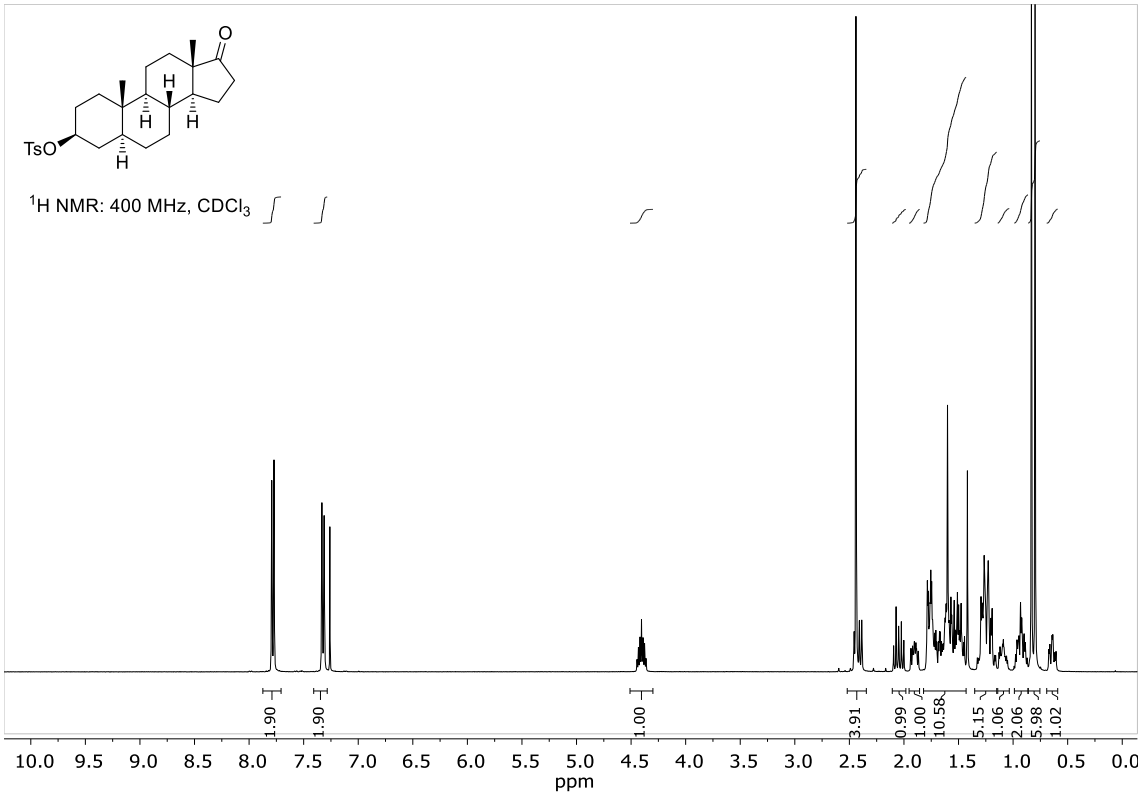


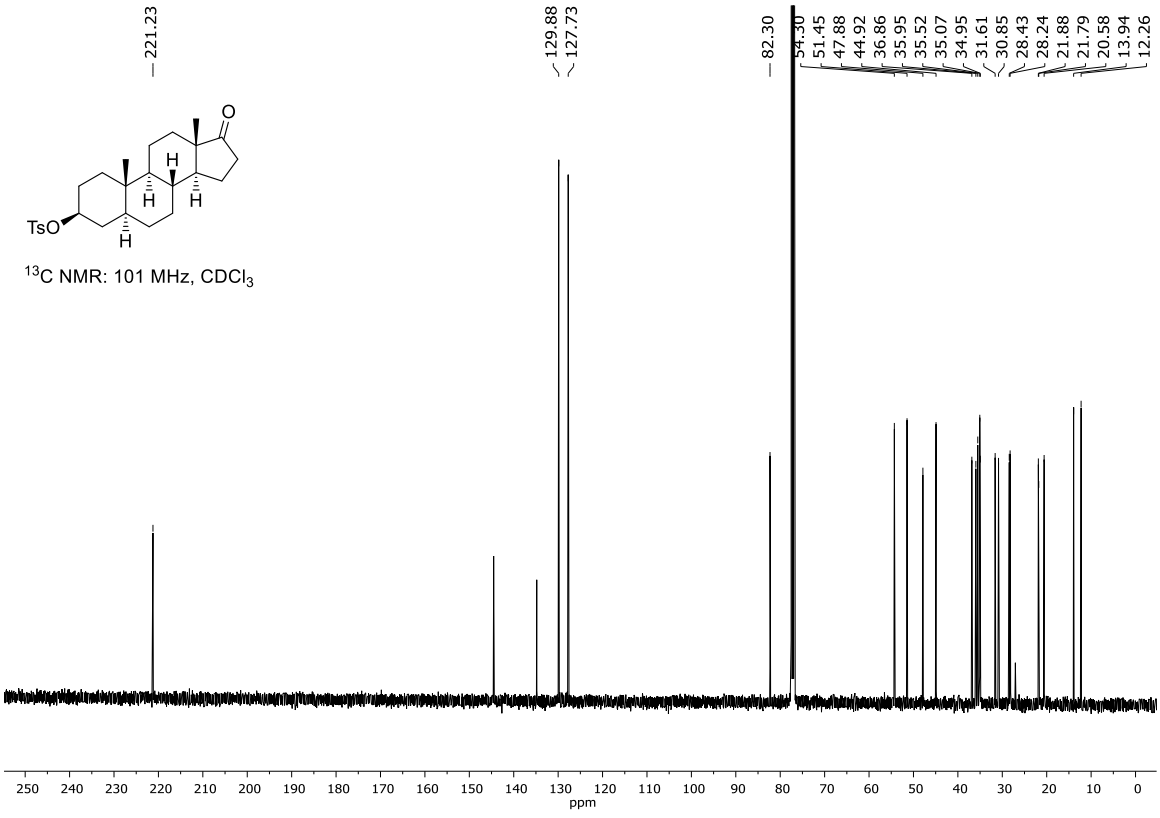
3*β*-Acetoxy-17*β*-benzyloxy-5*α*-androstane-2*β*-ol (**14-Bn**)



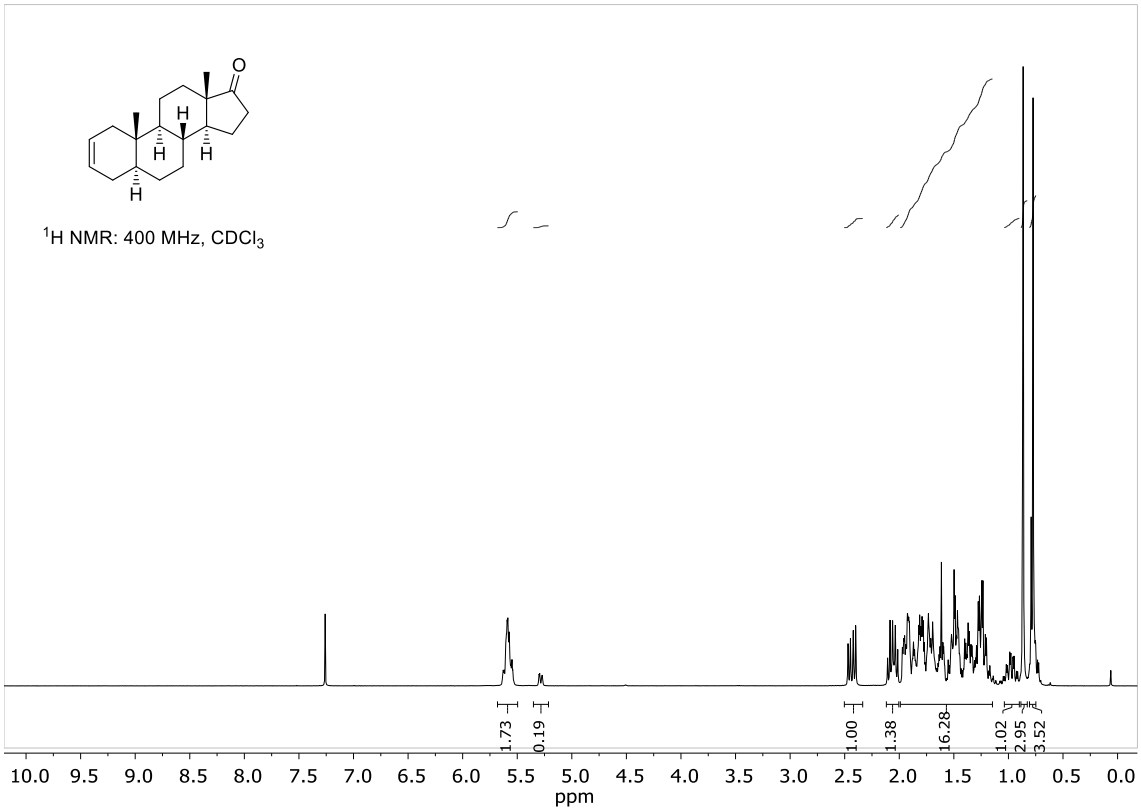


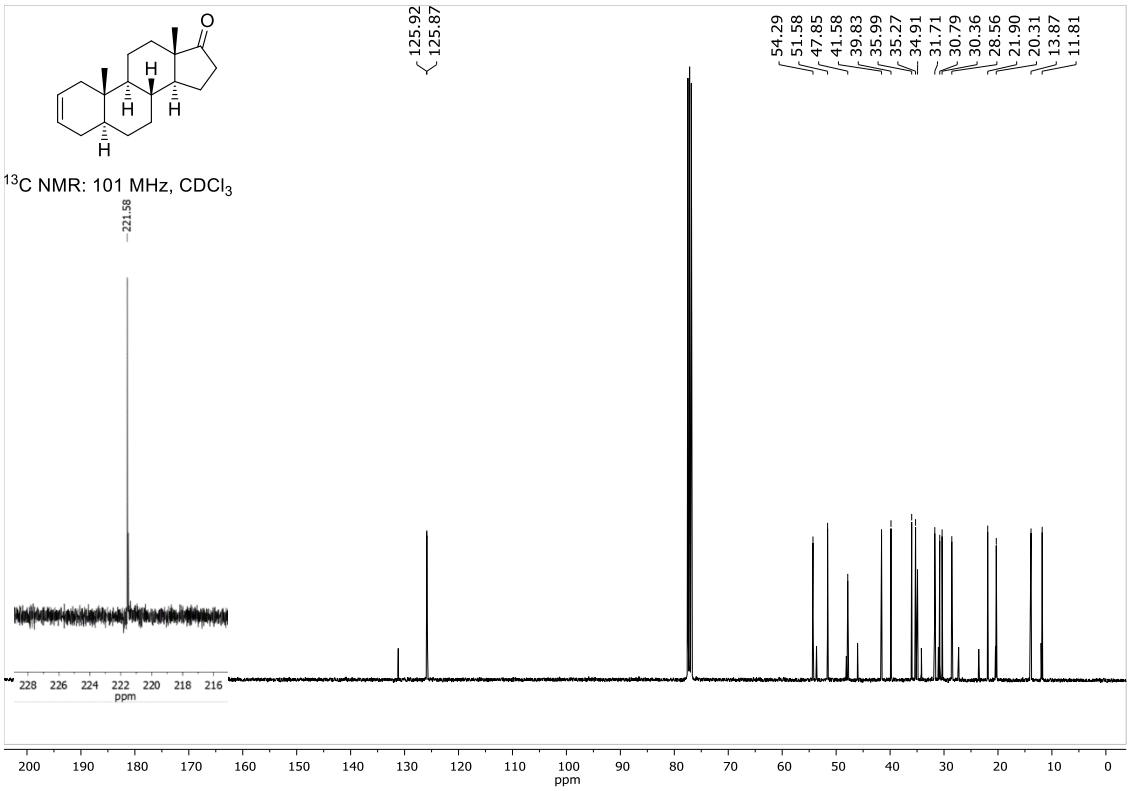
3*β*-[[(4-Methylphenyl)sulfonyl]oxy]-5*α*-androstane-17-on (**SI-03**)





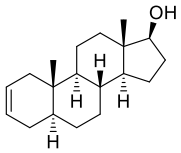
5*α*-Androst-2-ene-17-on (**15**)



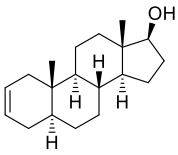


Inseparable mixture of regioisomers (10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum); for the ^{13}C NMR spectrum only the signals for the major isomers were picked**.**

5*α*-Androst-2-ene-17*β*-ol (**SI-06-OH**)



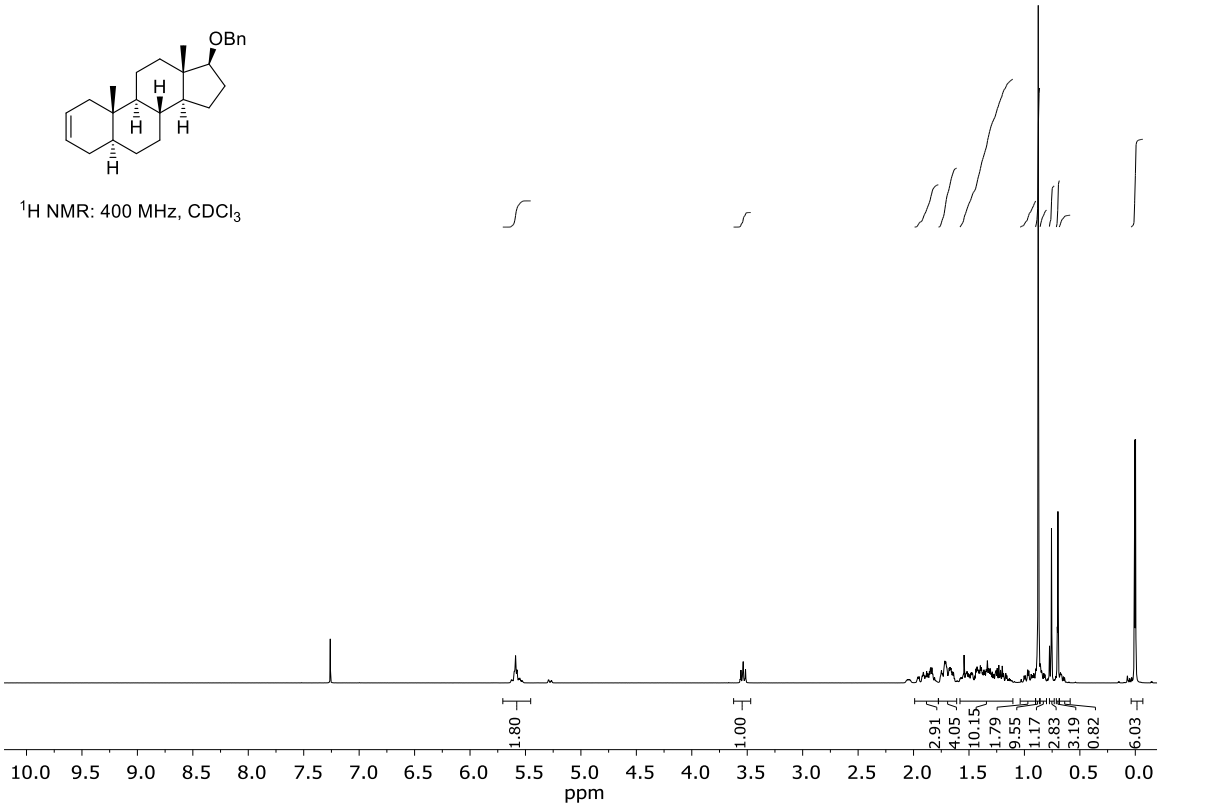
^{1}H NMR: 400 MHz, $CDCl_3$ + CD_3OD

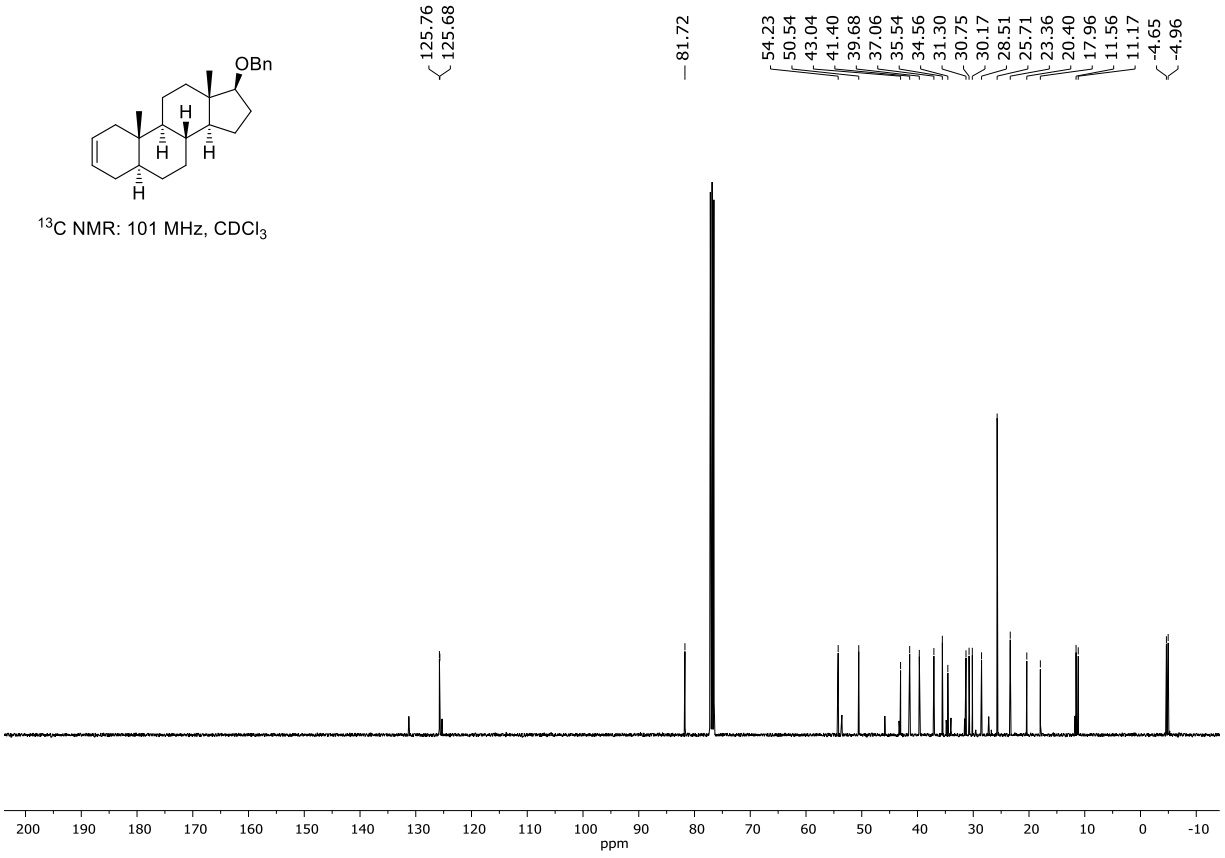


^{13}C NMR: 101 MHz, $CDCl_3$ + CD_3OD

Inseparable mixture of regioisomers (10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum); for the ^{13}C NMR spectrum only the signals for the major isomers were picked

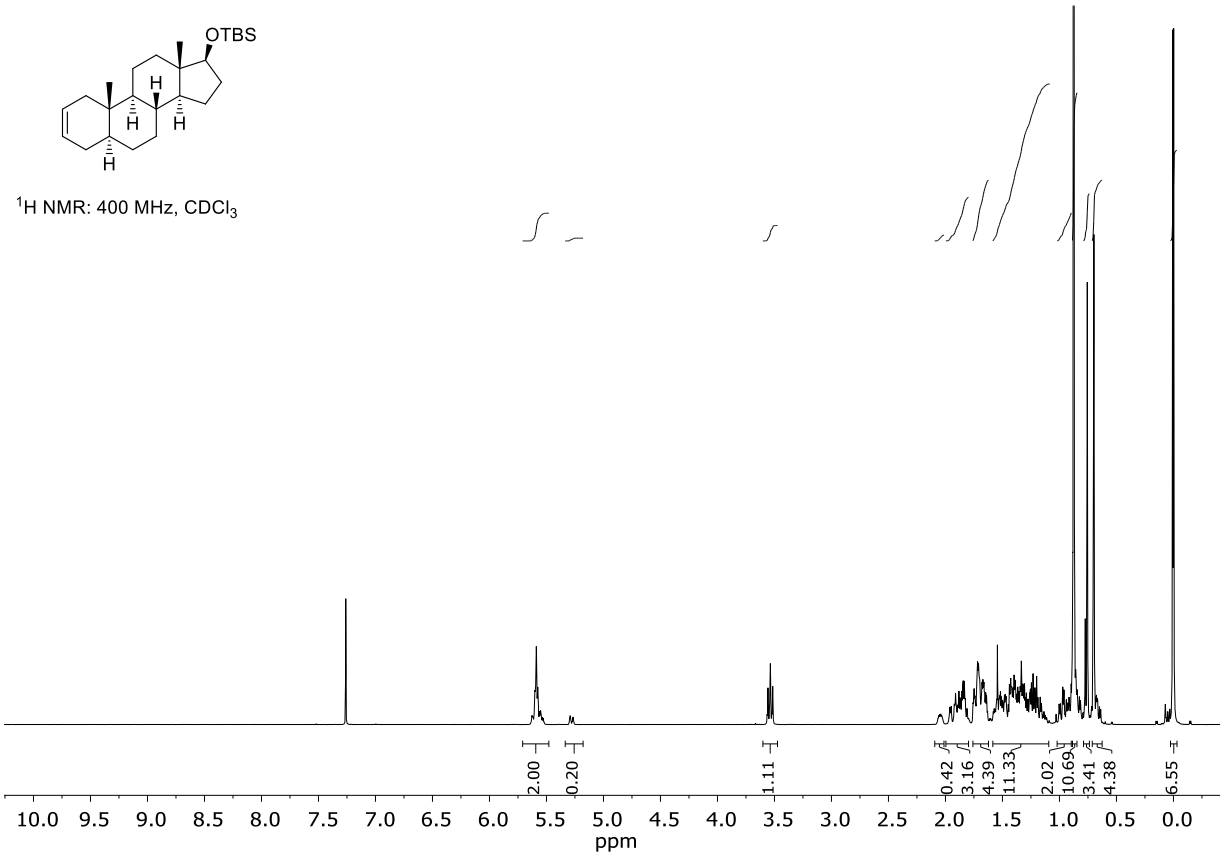
17*β*-Benzyloxy-5*α*-androst-2-ene (**SI-06-Bn**)

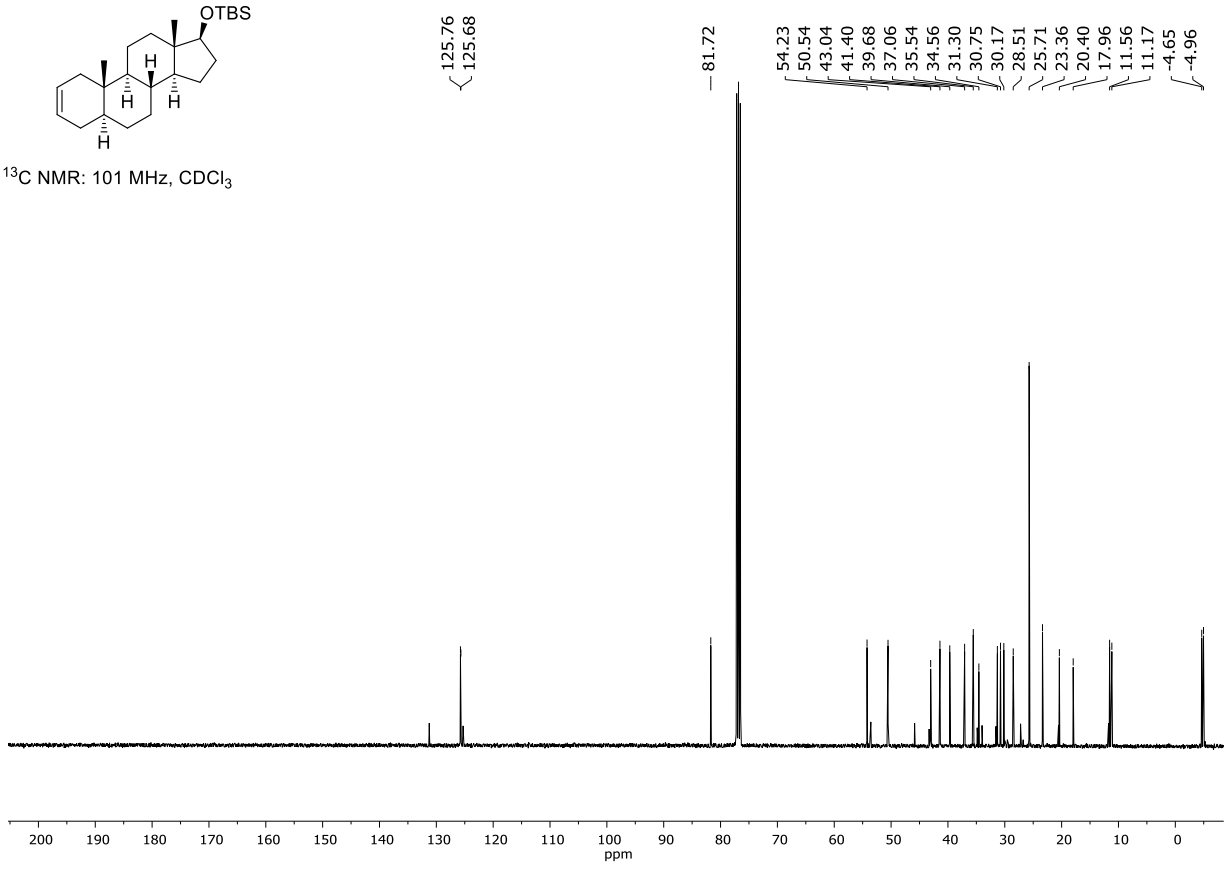




Inseparable mixture of regioisomers (10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum); for the ^{13}C NMR spectrum only the signals for the major isomers were picked)

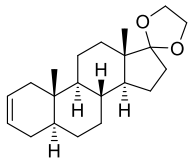
17*β*-[[(*tert*-butyl)dimethylsilyl]oxy]-5*α*-androst-2-ene (**SI-06-TBS**)



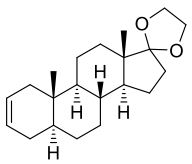


Inseparable mixture of regioisomers (10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum); for the ^{13}C NMR spectrum only the signals for the major isomers were picked.

17,17-(Ethylendioxy)-5*α*-androst-2-ene (**SI-07**)



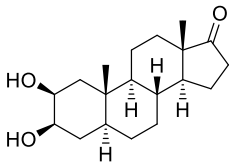
^{1}H NMR: 500 MHz, $CDCl_3$



^{13}C NMR: 125 MHz, $CDCl_3$

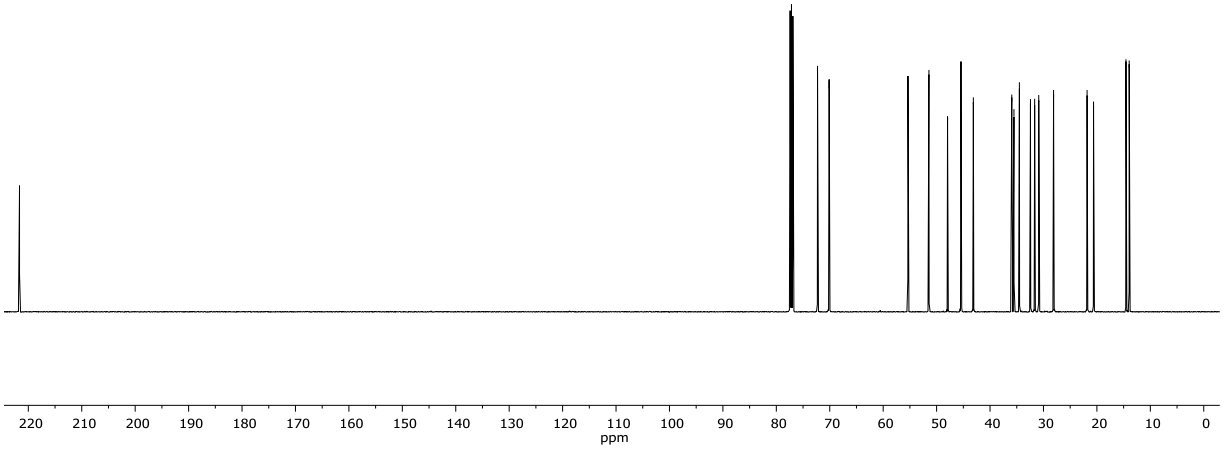
Inseparable mixture of regioisomers (10:1 according to the integration of olefinic signals from the ^{1}H NMR spectrum); for the ^{13}C NMR spectrum only the signals for the major isomers were picked.

2*β*,3*β*-Dihydroxy-5*α*-androstane-17-on (**21**)

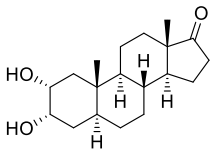


^{1}H NMR: 500 MHz, $CDCl_3$

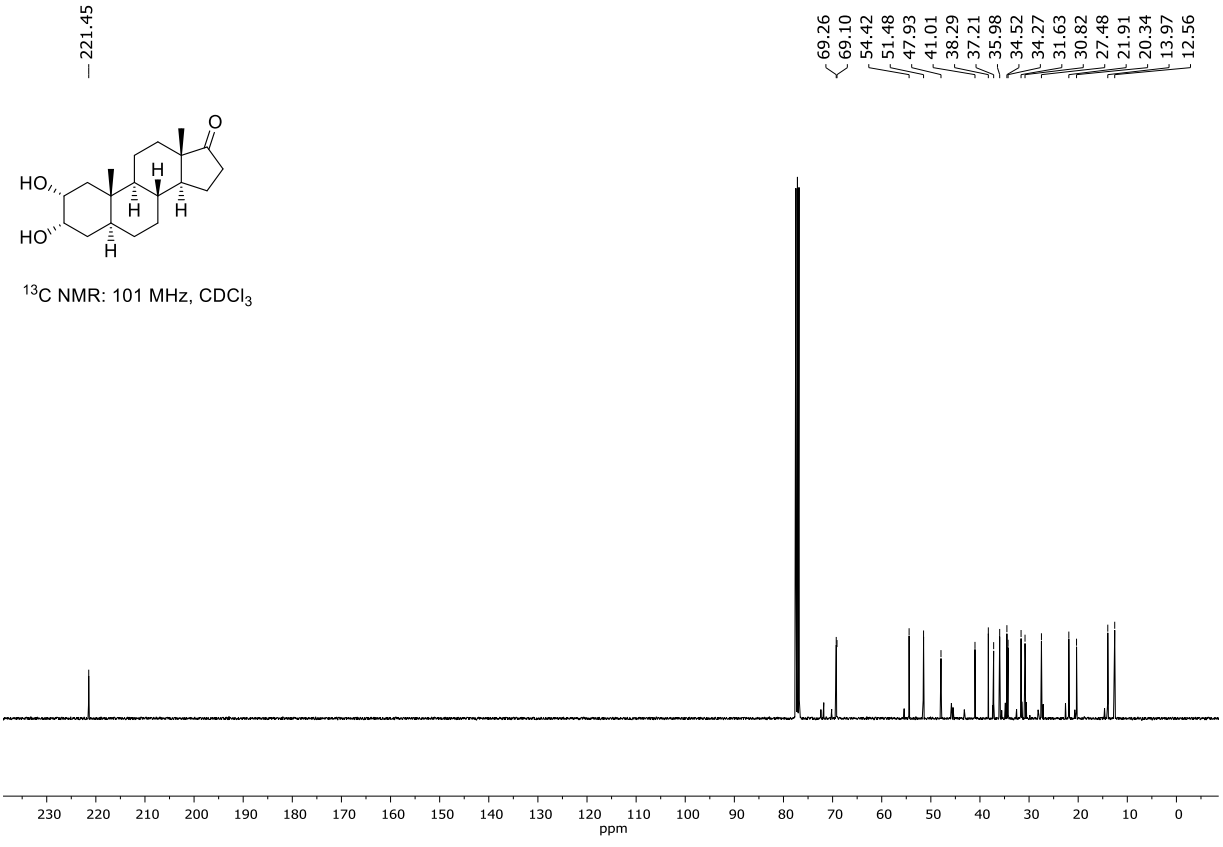
^{13}C NMR: 101 MHz, $CDCl_3$



2*α*,3*α*-Dihydroxy-5*α*-androstane-17-on (**22**)



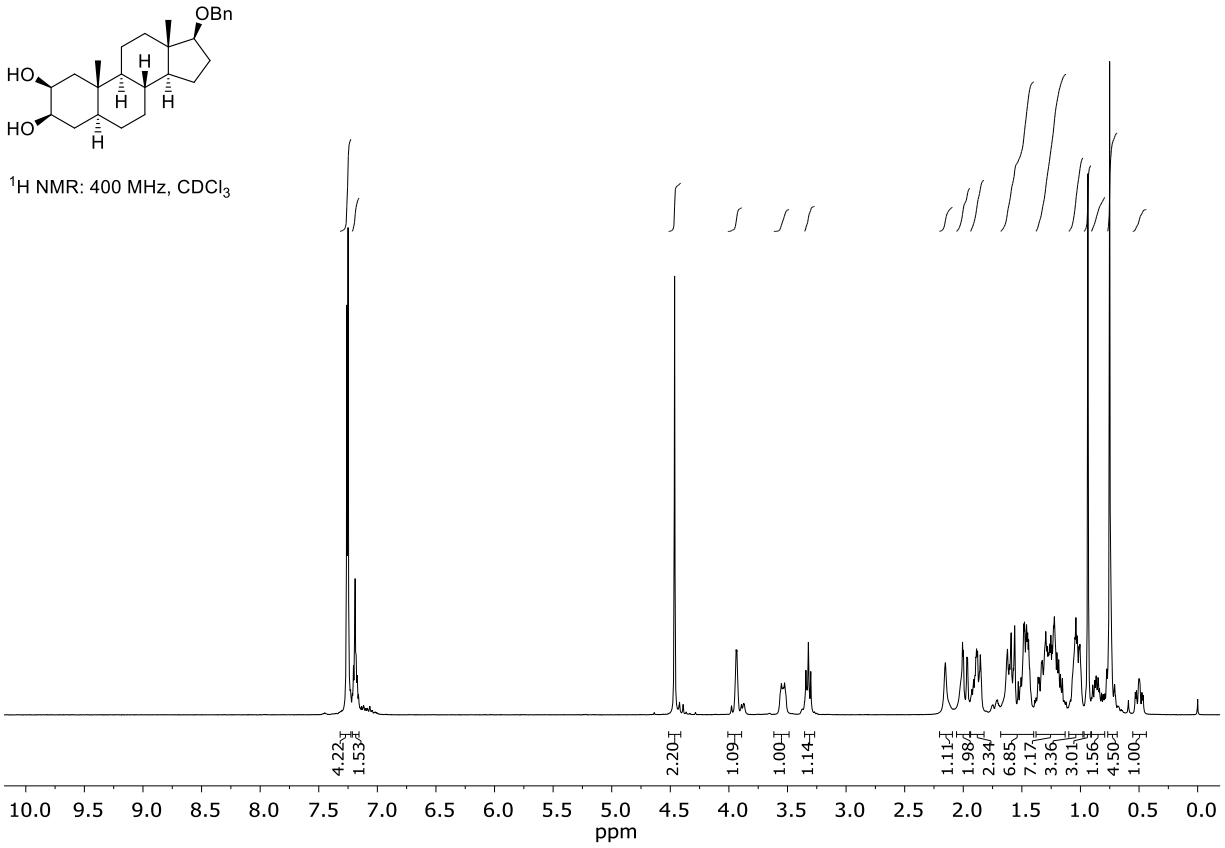
^{1}H NMR: 400 MHz, $CDCl_3$

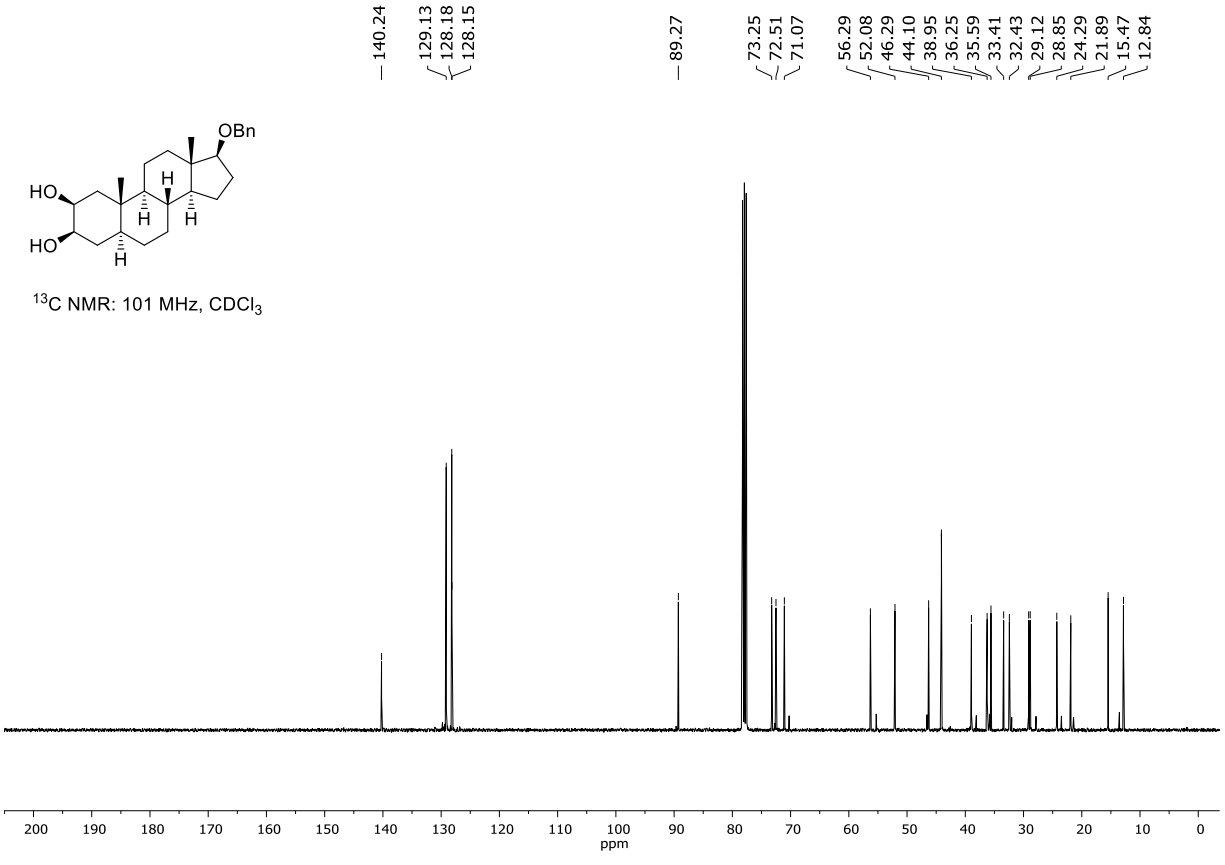


^{13}C NMR: 101 MHz, $CDCl_3$

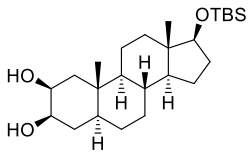
Mixture of isomers (only partially separable via normal flash column chromatography on silica gel); for the ^{13}C NMR spectrum only the signals for the major isomers were picked.

2*β*,3*β*-Dihydroxy-17*β*-benzyloxy-5*α*-androstane-17-on (**SI-08-Bn**)

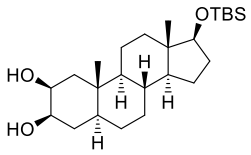




2*β*,3*β*-Dihydroxy-17*β*-[(*tert*-Butyldimethylsilyl)oxy]-5*α*-androstane-17-on (**SI-08-OTBS**)

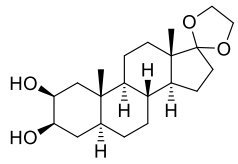


^{1}H NMR: 400 MHz, $CDCl_3$

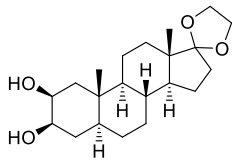


^{13}C NMR: 101 MHz, $CDCl_3$

17,17-(Ethylendioxy)-2*β*,3*β*-dihydroxy-5*α*-androstane (**SI-09**)



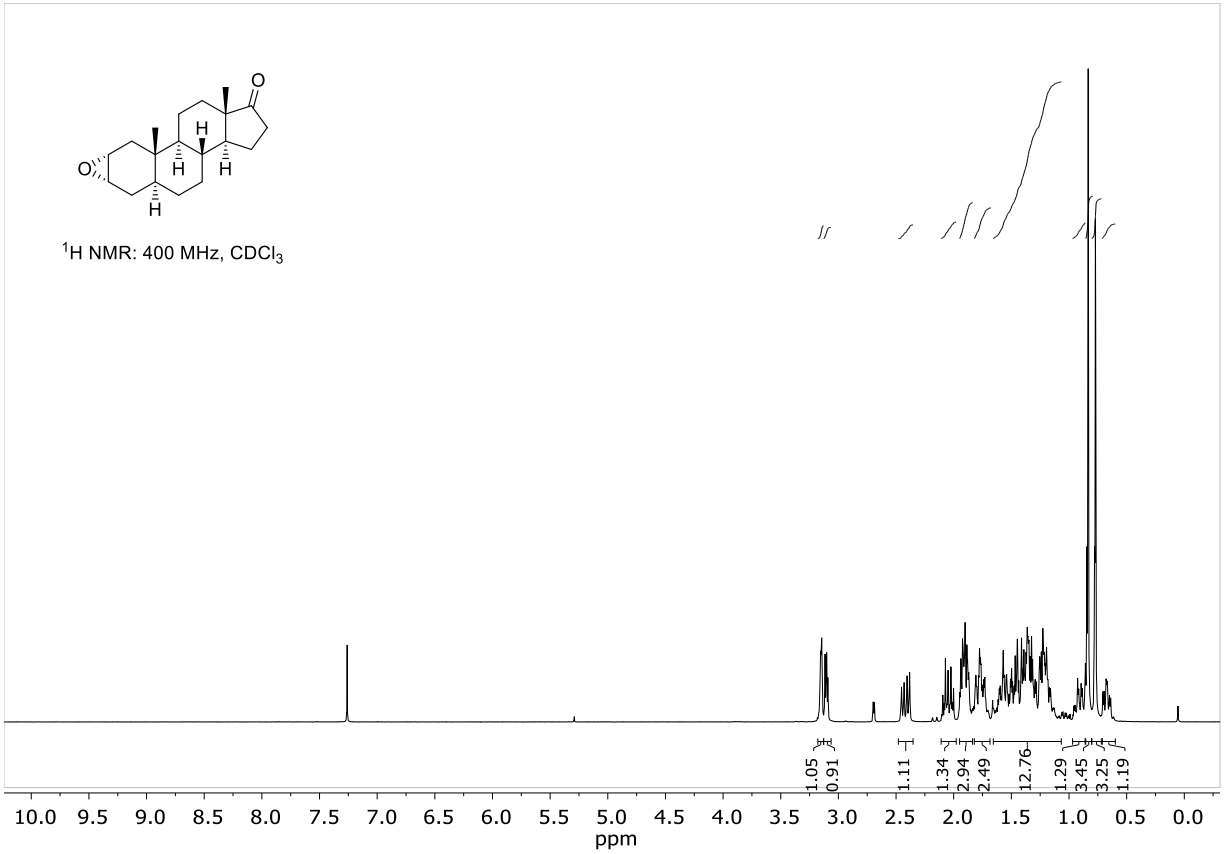
^{1}H NMR: 500 MHz, $CDCl_3$

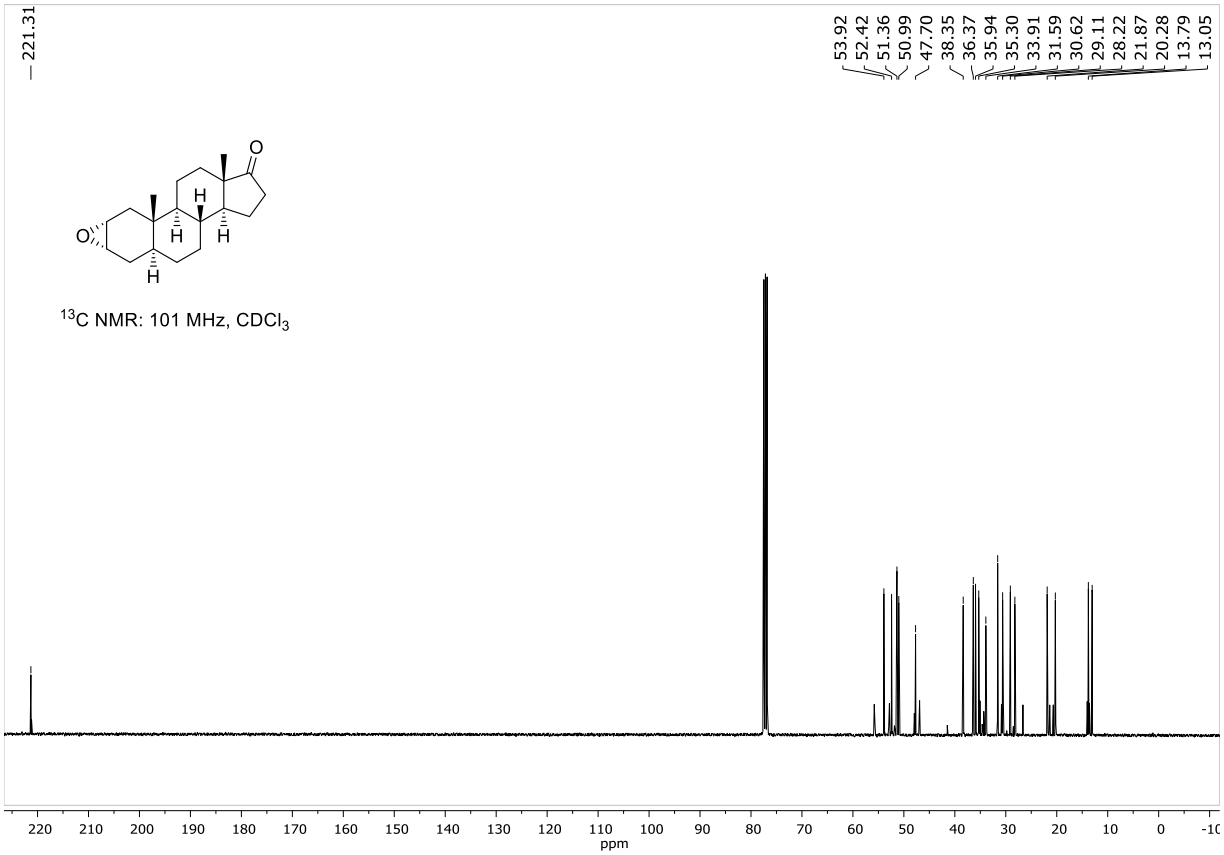


^{13}C NMR: 126 MHz, $CDCl_3$

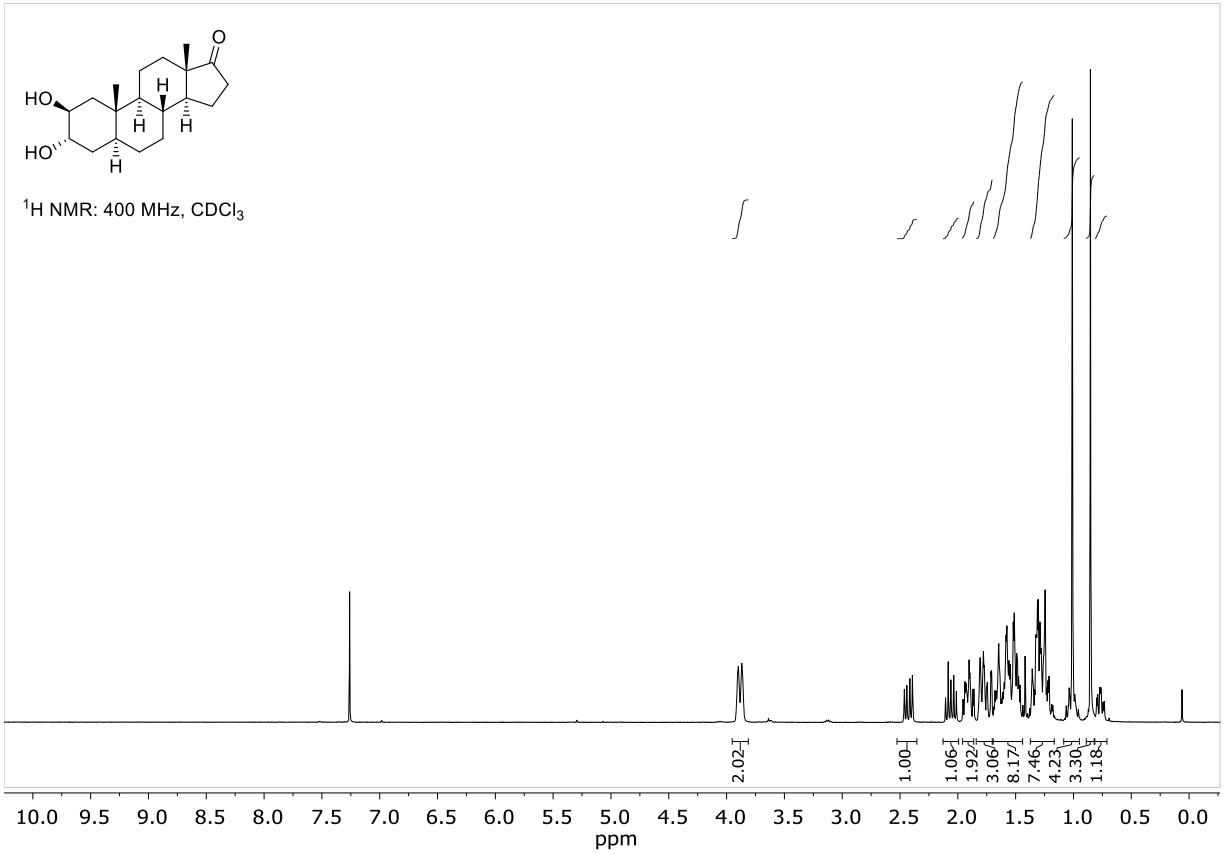
Mixture of isomers (only partially separable via normal flash column chromatography on silica gel); for the ^{13}C NMR spectrum only the signals for the major isomers were picked.

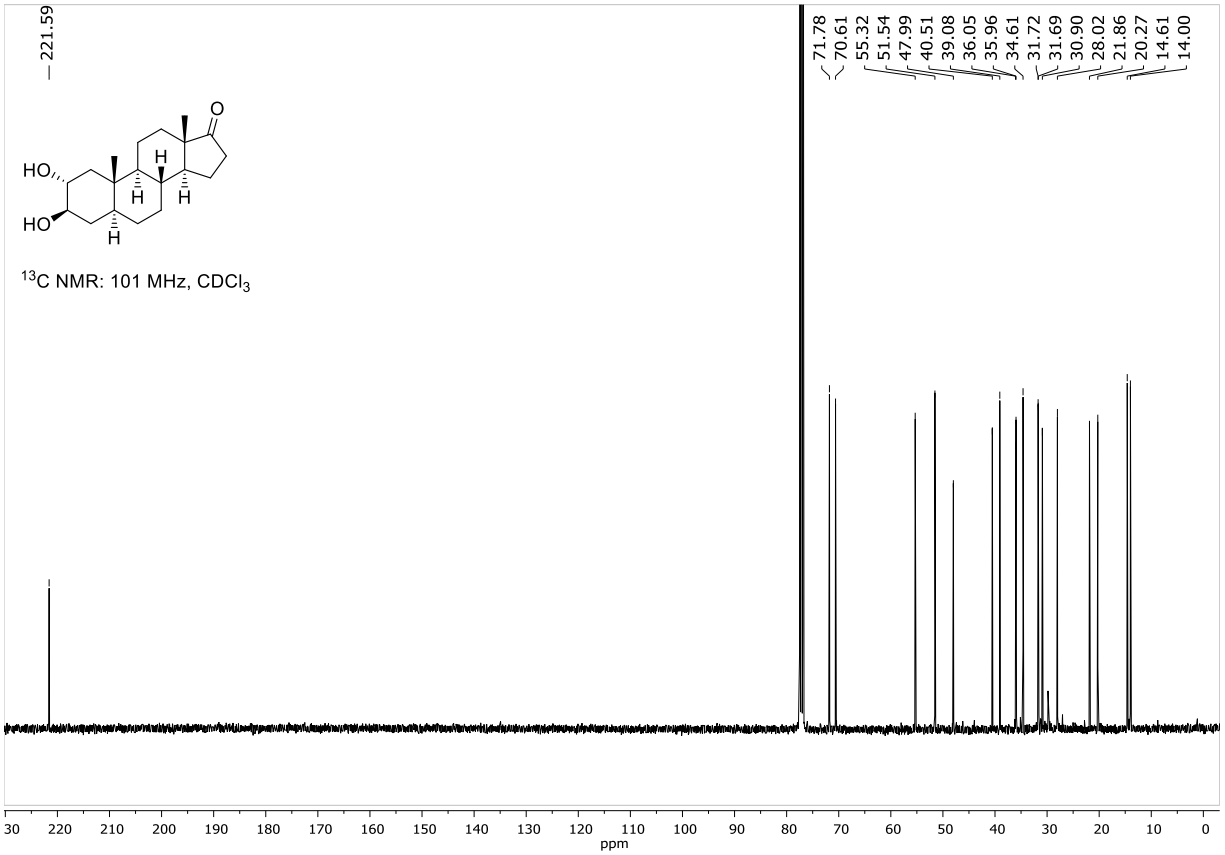
2*α*,3*α*-Epoxy-5*α*-androstane-17-on (**24**)[9]



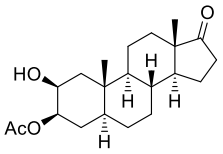


2*β*,3*α*-Dihydroxy-5*α*-androstane-17-on (**23**)

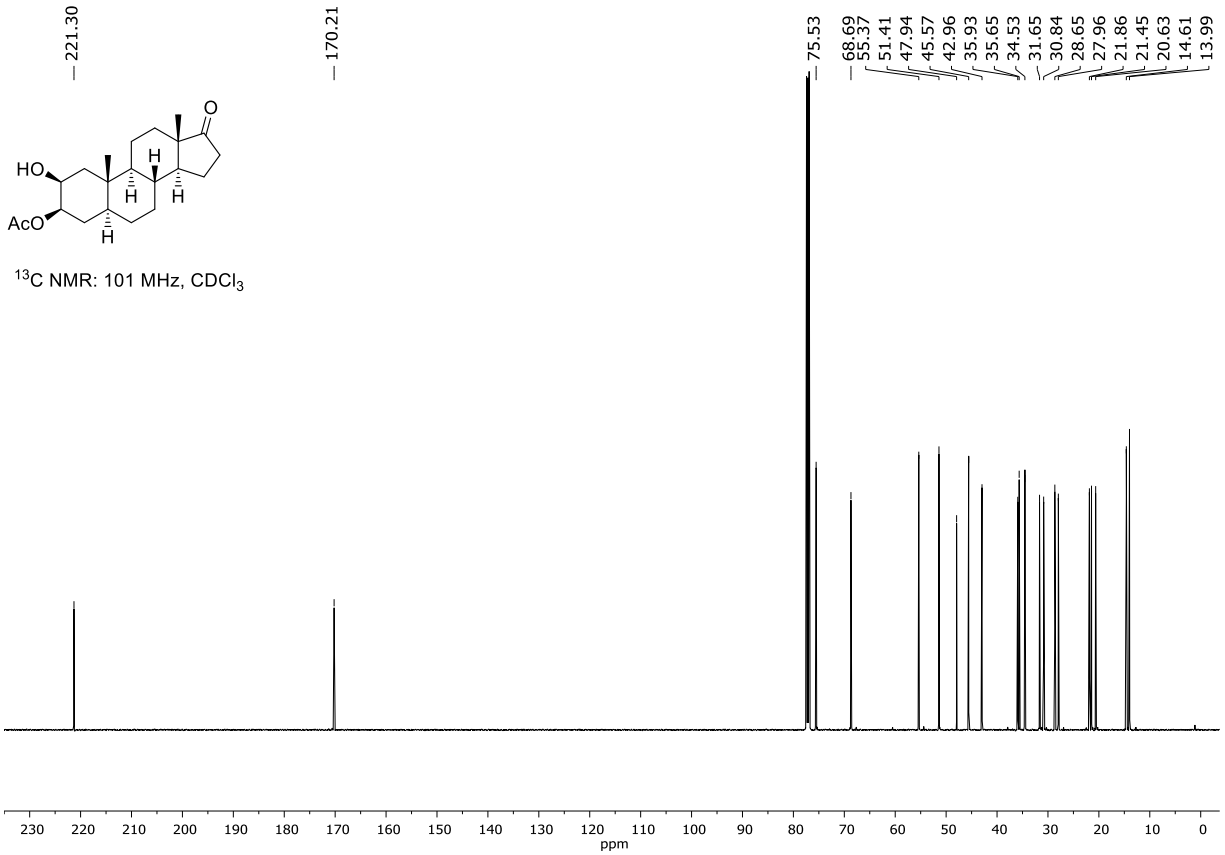




2*β*-Acetoxy-3*β*-hydroxy-5*α*-androstane-17-on (**14**)

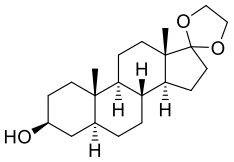


^{1}H NMR: 400 MHz, $CDCl_3$

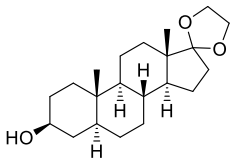


^{13}C NMR: 101 MHz, $CDCl_3$

17,17-(Ethylendioxy)-5*α*-androstane-3*β*-ol (**SI-10**)[12]

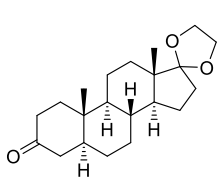


^{1}H NMR: 500 MHz, $CDCl_3$

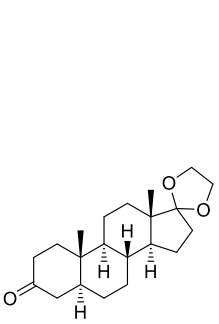


^{13}C NMR: 126 MHz, $CDCl_3$

17,17-(Ethylendioxy)-5*α*-androstane-3-on (**25**)[12]

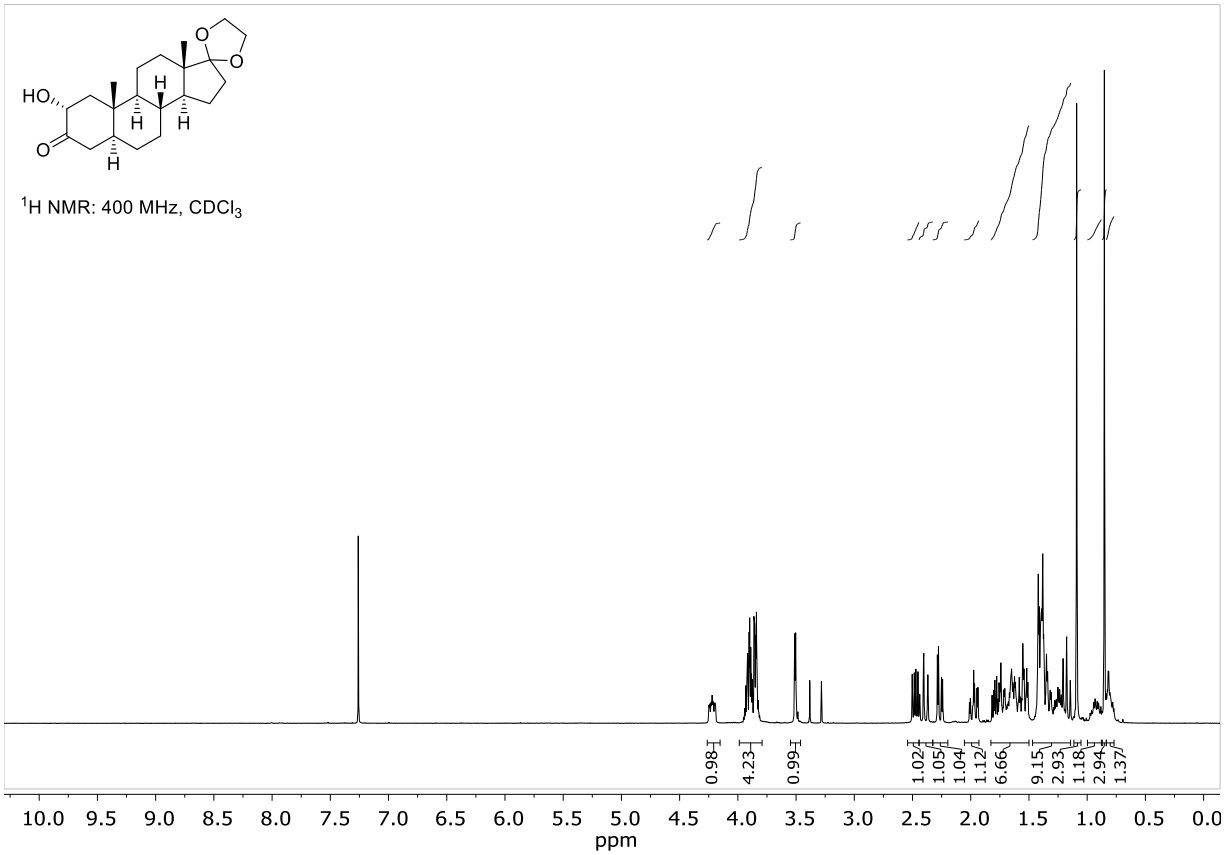


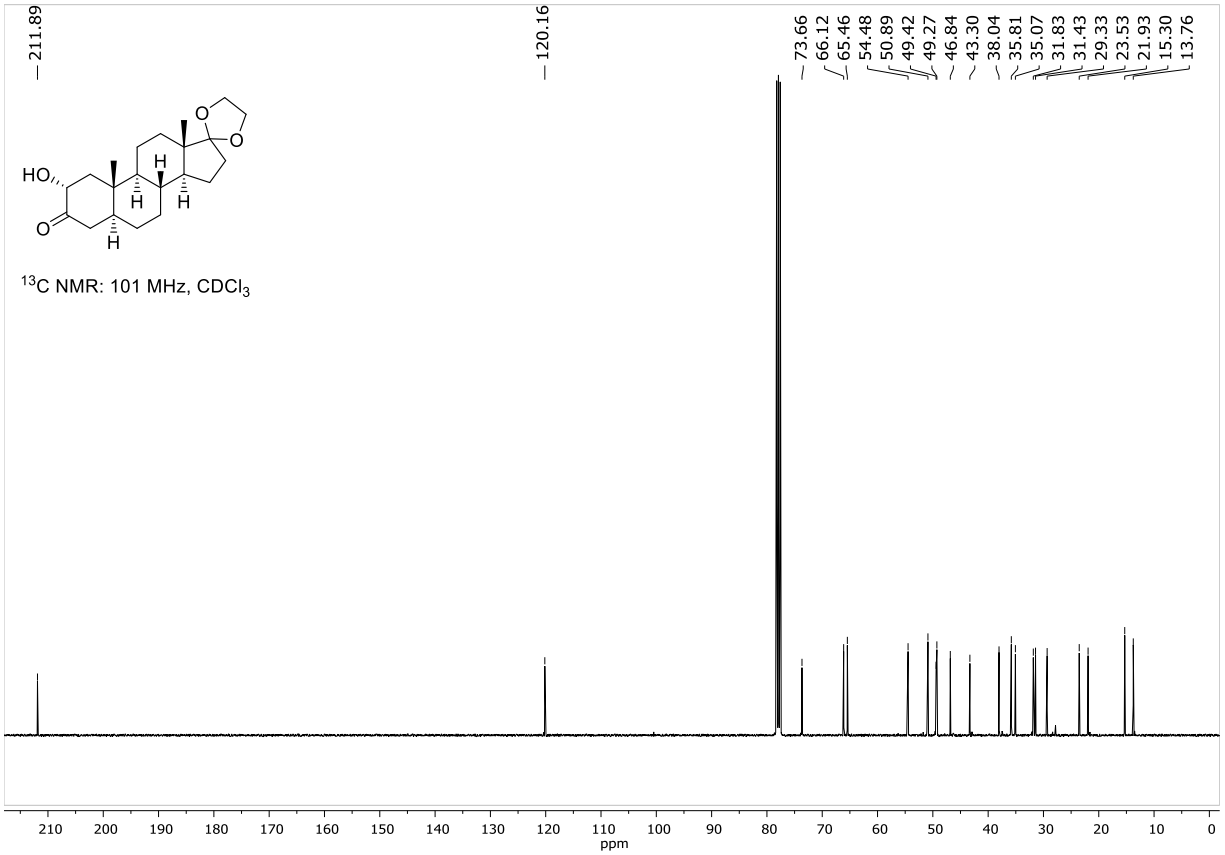
^{1}H NMR: 500 MHz, $CDCl_3$



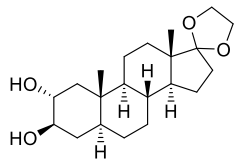
^{13}C NMR: 126 MHz, $CDCl_3$

17,17-(Ethylendioxy)-2*α*-hydroxy-5*α*-androstane-3-on (**26**)

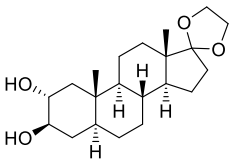




17,17-(Ethylendioxy)-2*α*,3*β*-dihydroxy-5*α*-androstane (**SI-11**)

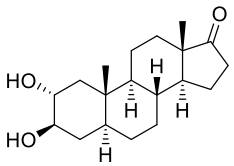


^{1}H NMR: 400 MHz, $CDCl_3$

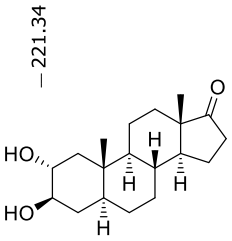


^{13}C NMR: 101 MHz, $CDCl_3$

2*α*,3*β*-Dihydroxy-5*α*-androstane-17-on (**27**)

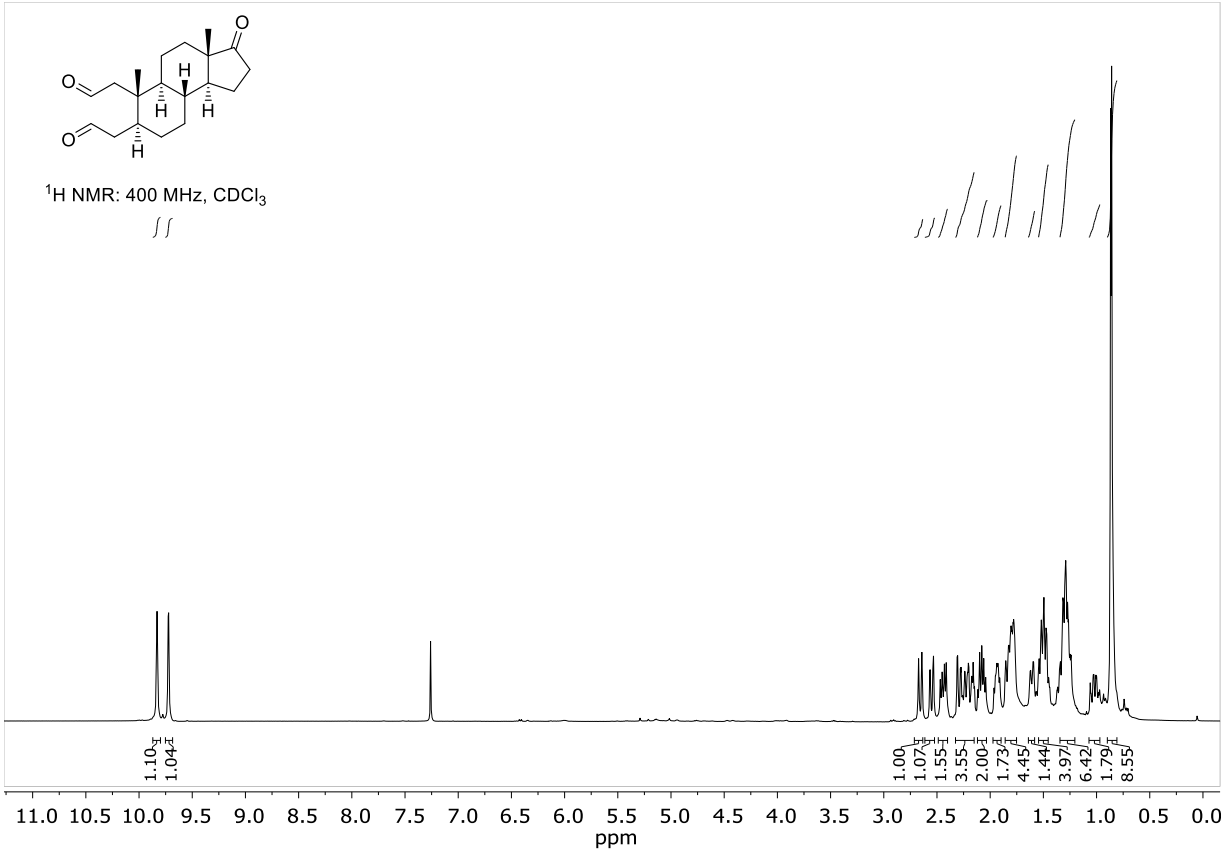


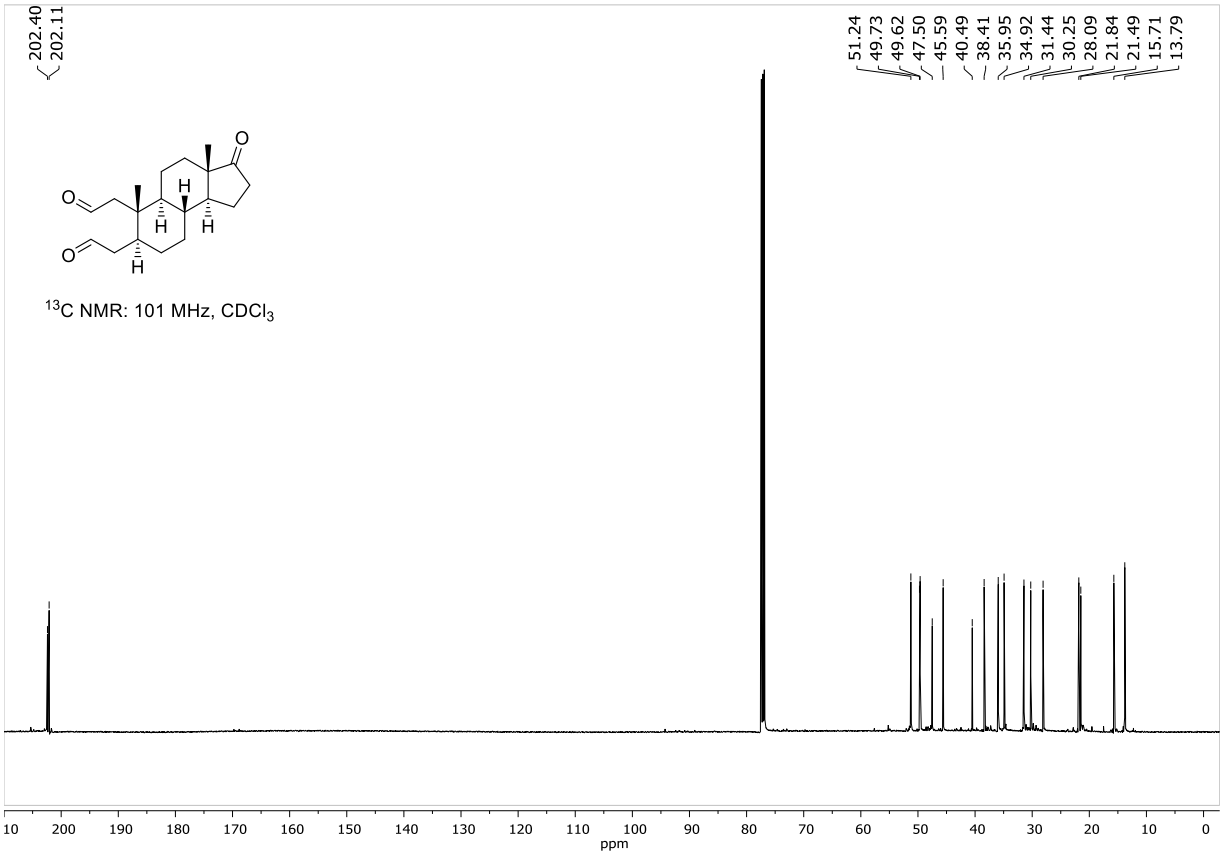
^{1}H NMR: 500 MHz, $CDCl_3$



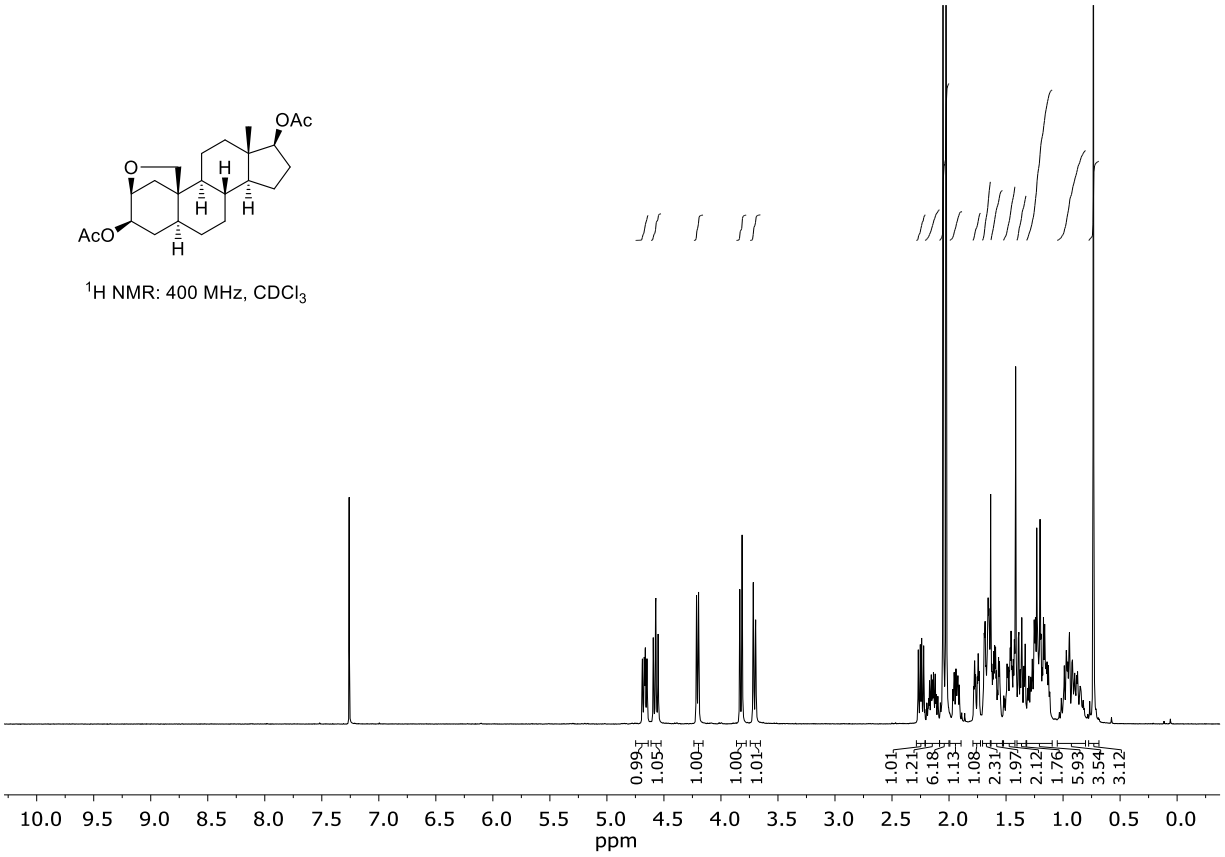
^{13}C NMR: 126 MHz, $CDCl_3$

2,3-seco-5*α*-Androstan-17-on-2,3-dial (**28**)

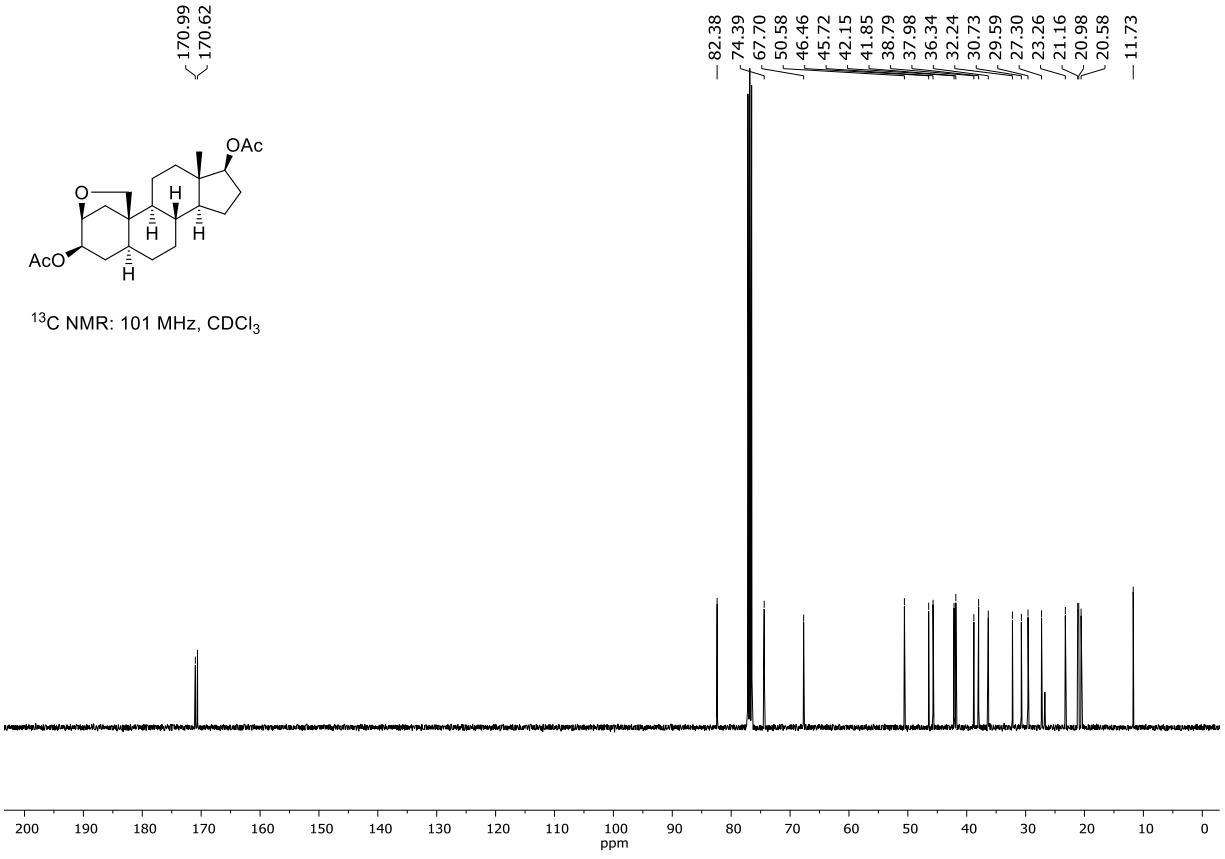




3*β*,17*β*-Diacetoxy-2*β*,19-epoxy-5*α*-androstane (**13-Ac**)

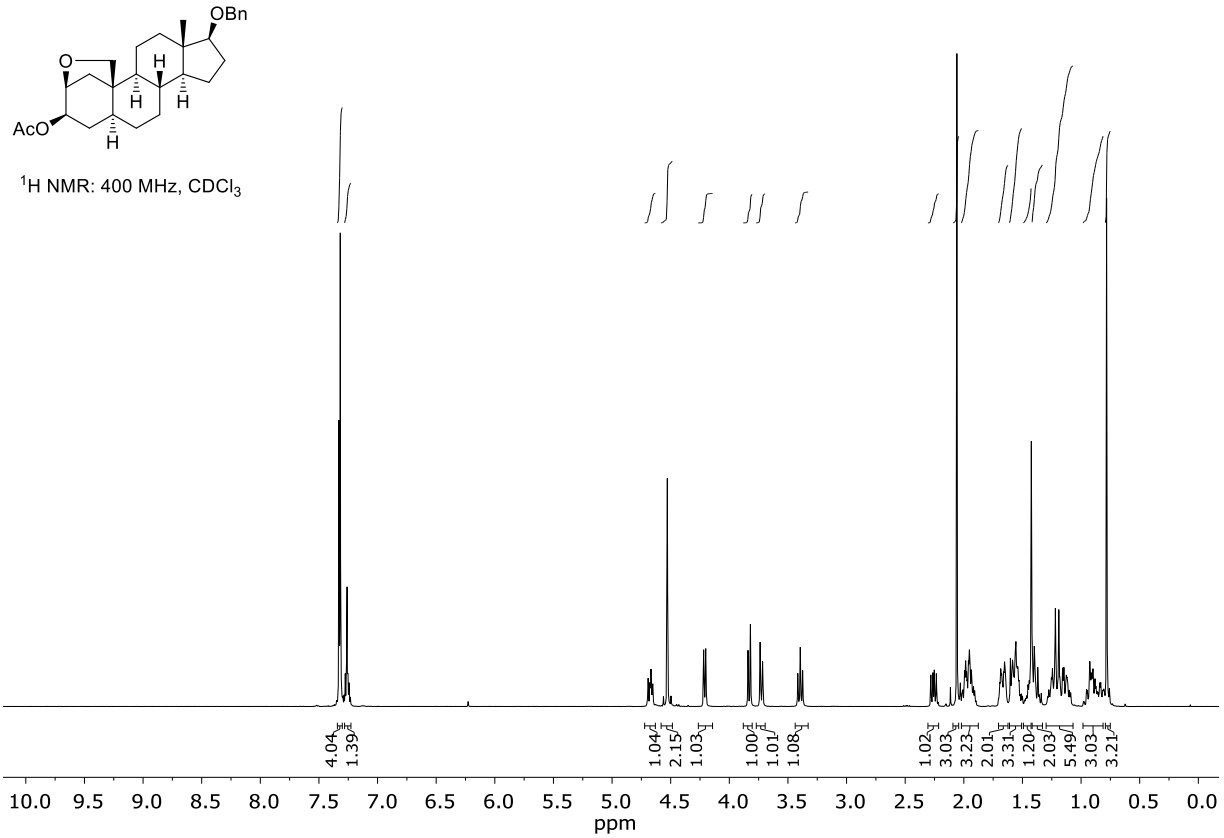


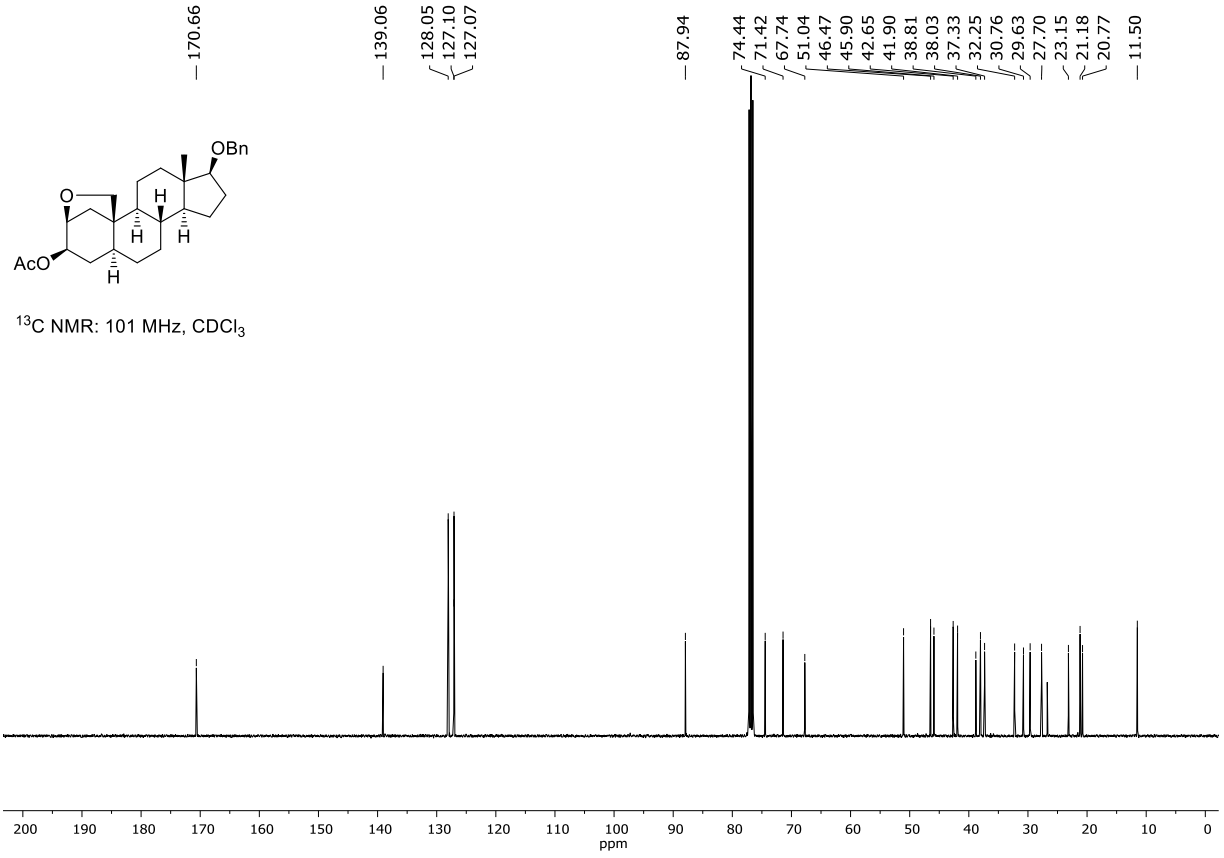
^{1}H NMR: 400 MHz, $CDCl_3$



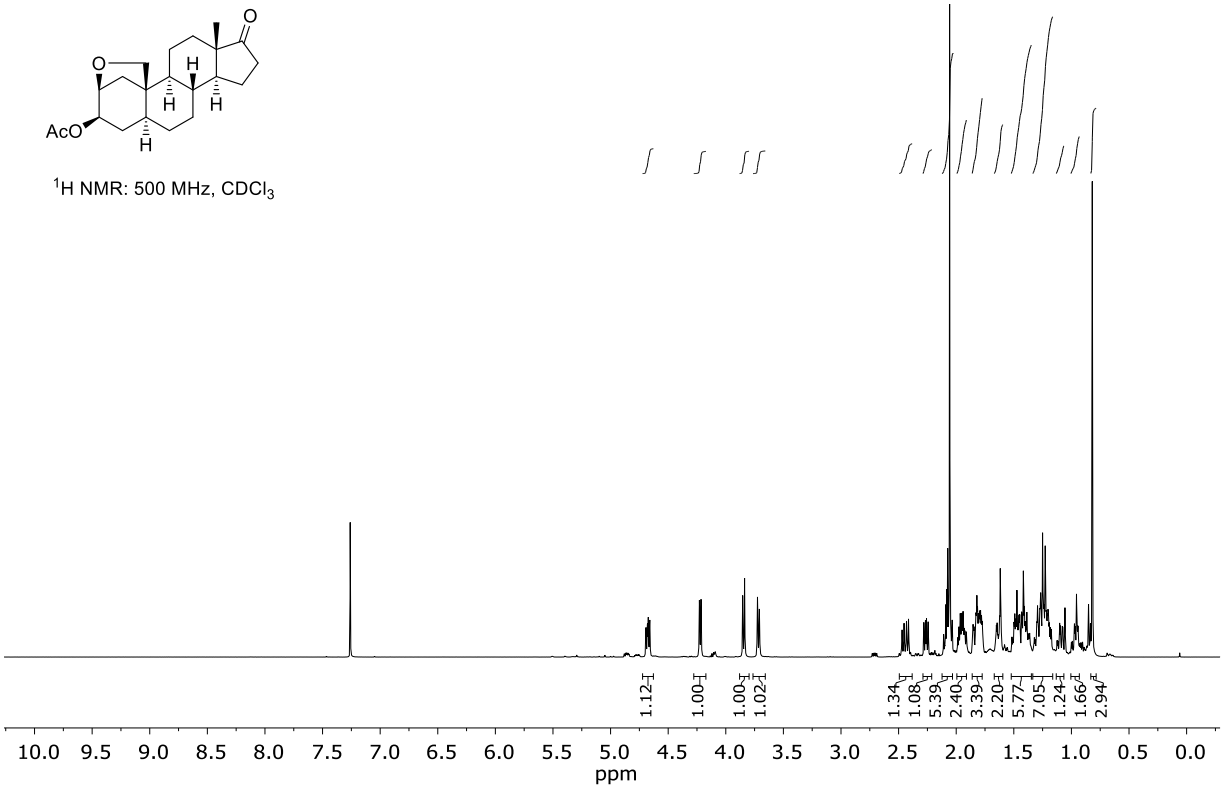
^{13}C NMR: 101 MHz, $CDCl_3$

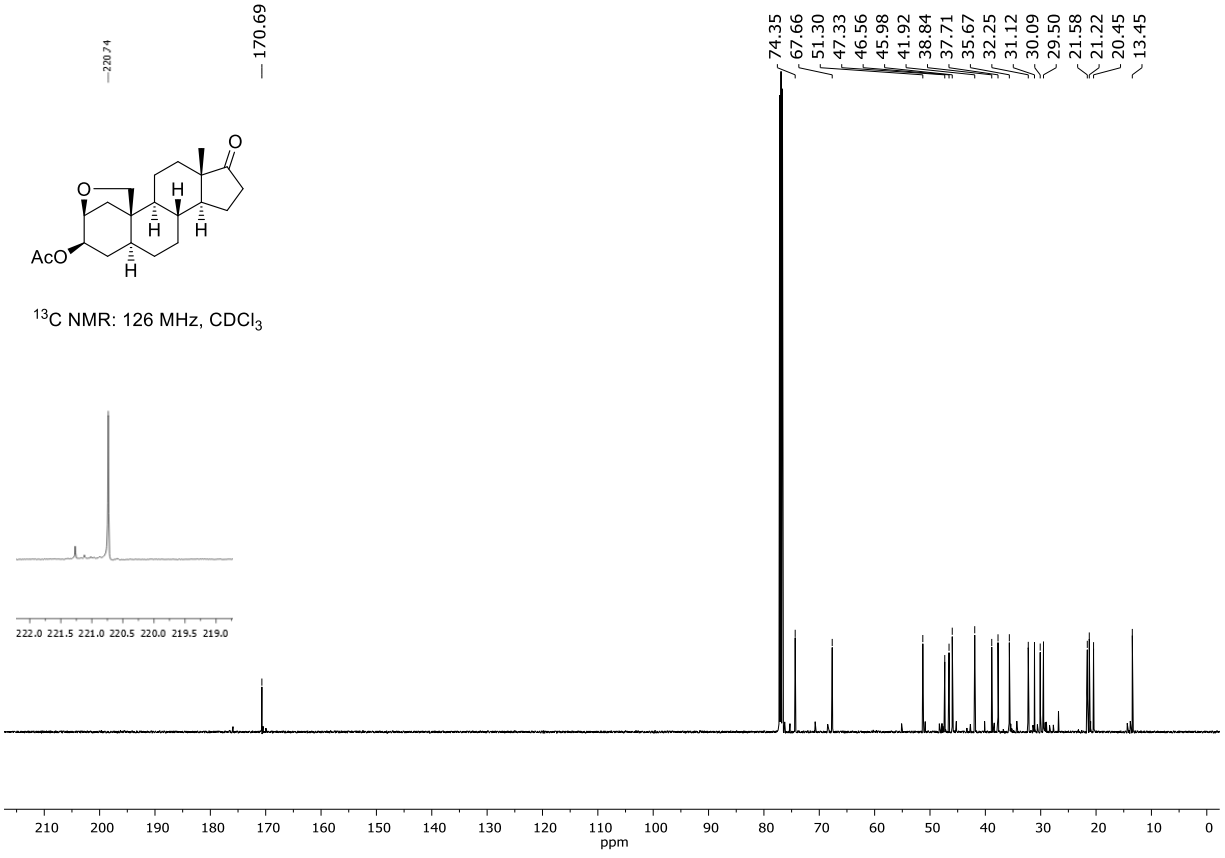
3*β*-Acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**)



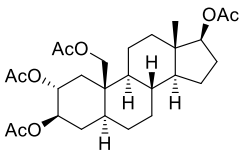


3*β*-Acetoxy-2*β*,19-epoxy-5*α*-androstane-17-on (**13**)

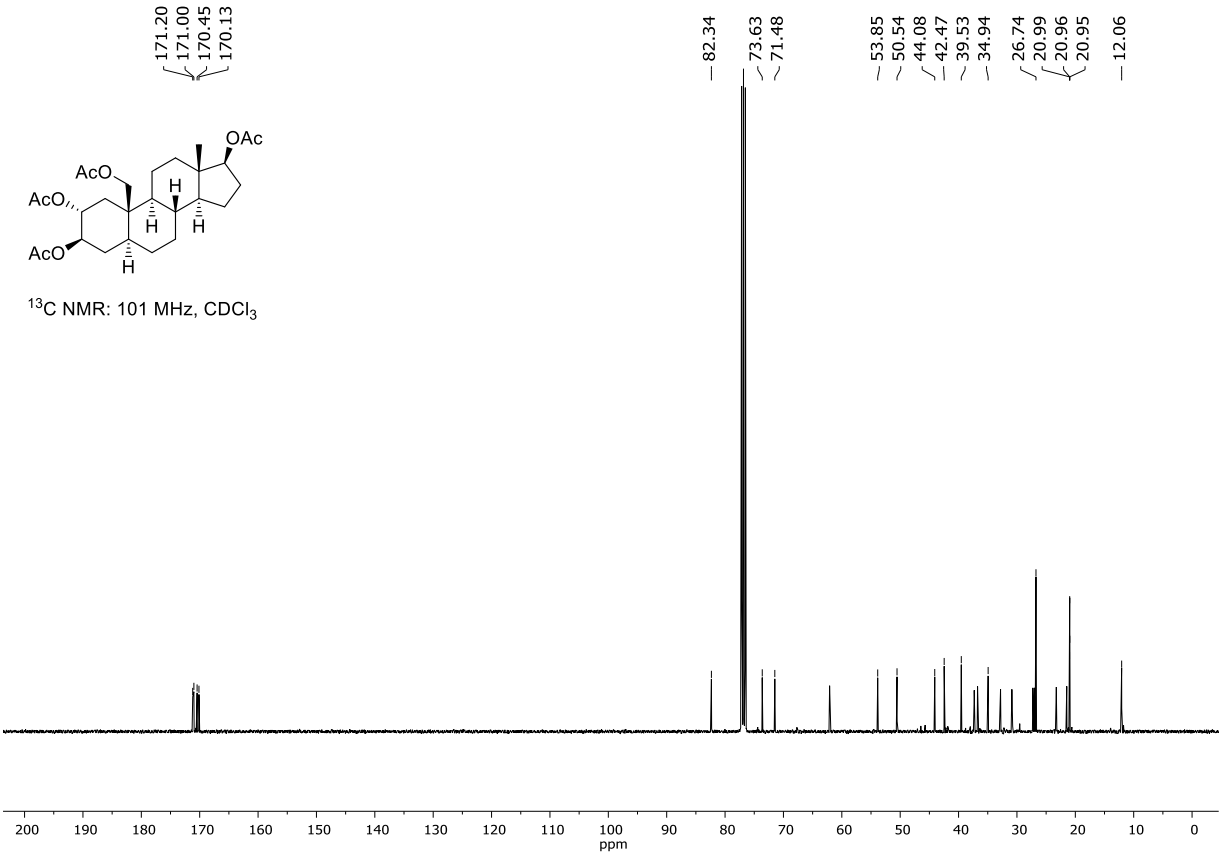




2*α*,3*β*,17*β*,19-Tetraacetoxy-5*α*-androstane (**513**)

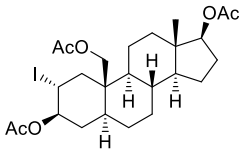


^{1}H NMR: 400 MHz, $CDCl_3$

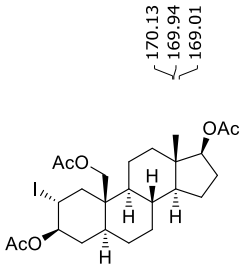


^{13}C NMR: 101 MHz, $CDCl_3$

3*β*,17*β*,19-Triacetoxy-2*α*-iodo-5*α*-androstane (**513-I**)

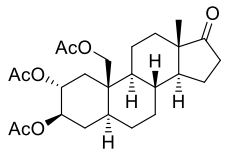


^{1}H NMR: 400 MHz, $CDCl_3$

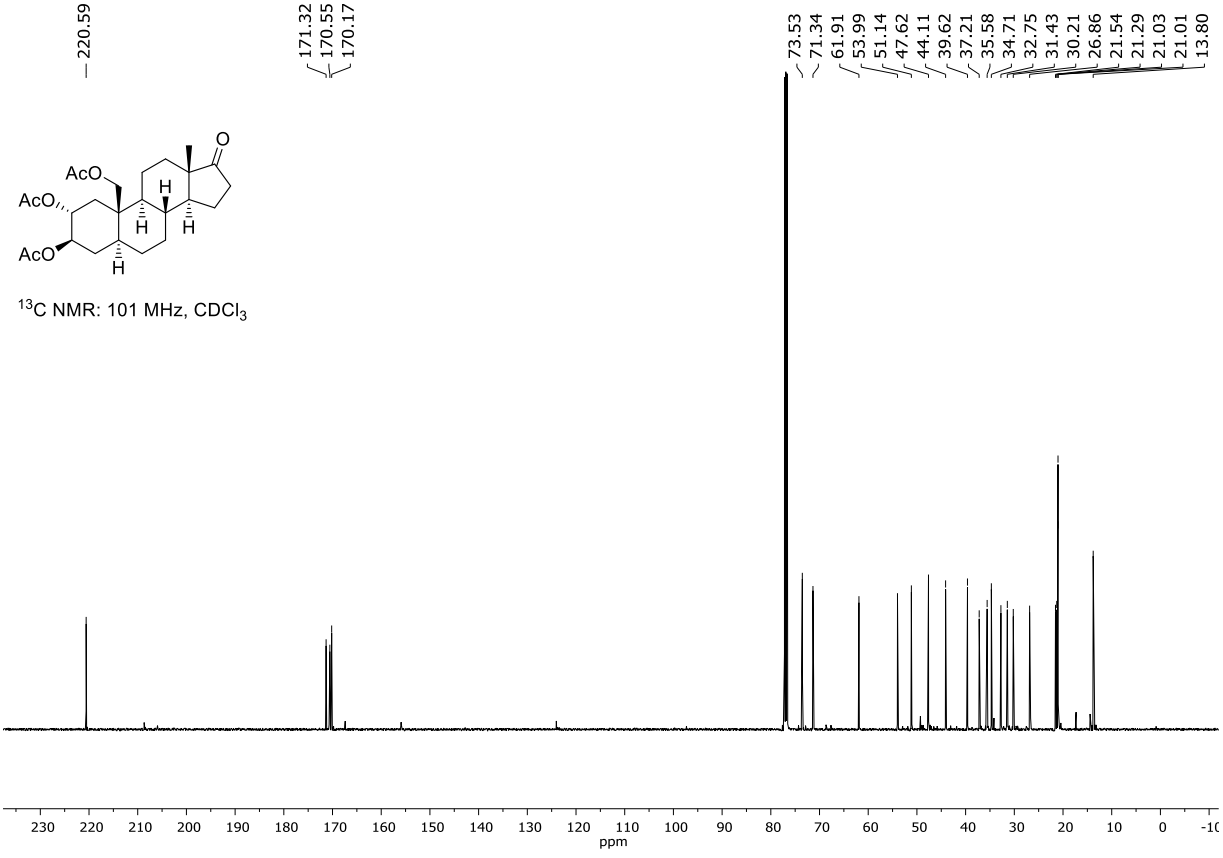


^{13}C NMR: 101 MHz, $CDCl_3$

2*α*,3*β*,19-Triacetoxy-5*α*-androstane-17-on (**29**)



^{1}H NMR: 400 MHz, $CDCl_3$

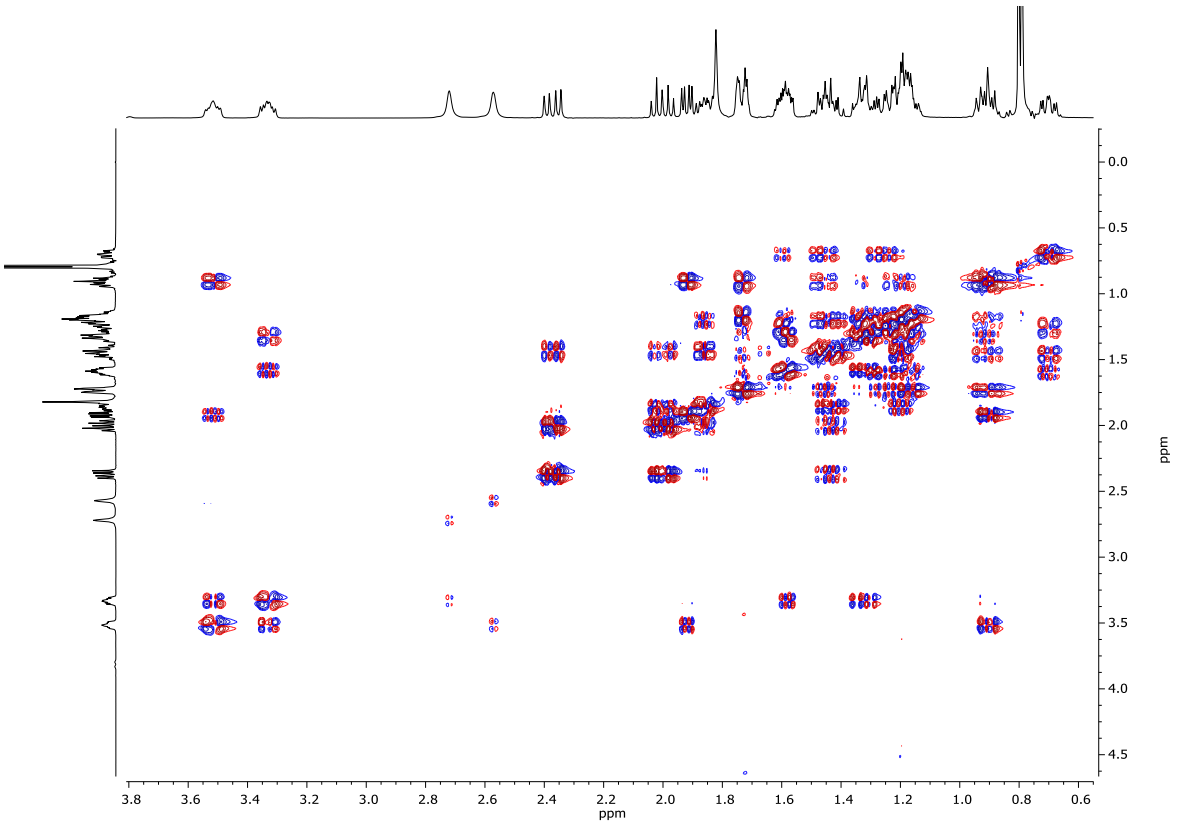


^{13}C NMR: 101 MHz, $CDCl_3$

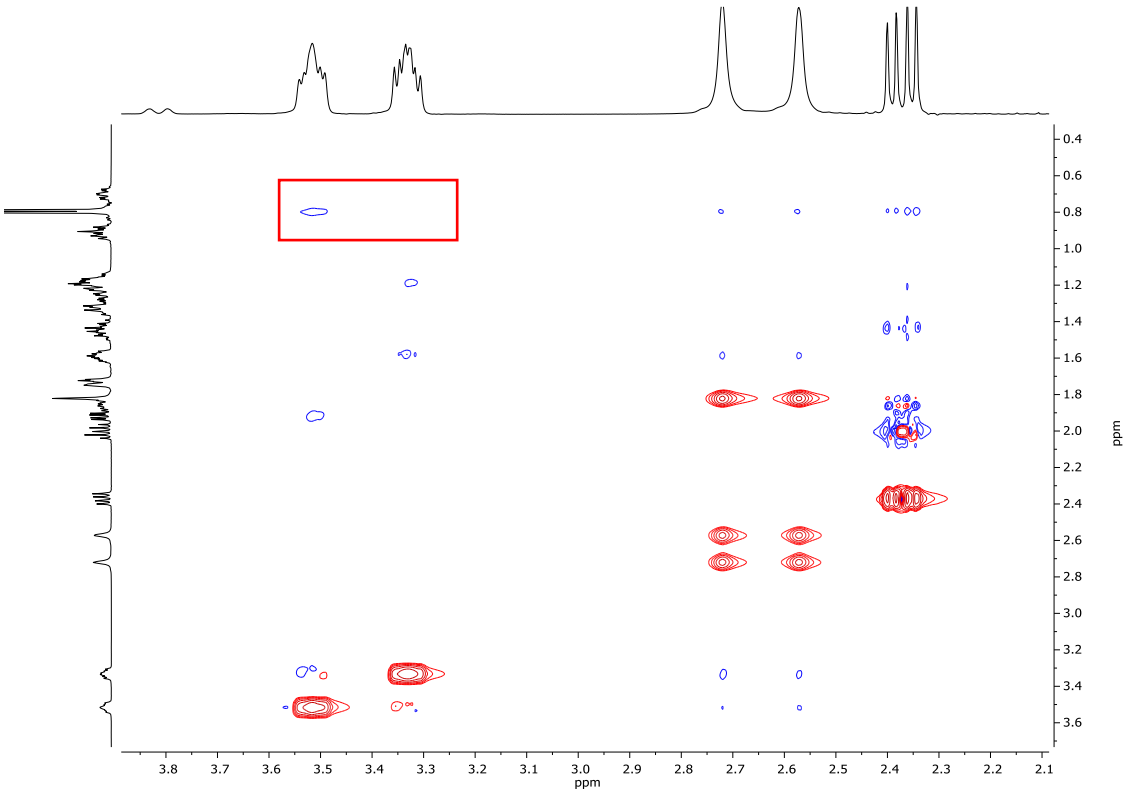
4. Selected full NMR data set of key compounds including 2D NMR and DEPT spectra

2*α*,3*β*-Dihydroxy-5*α*-androstane-17-on (**27**)

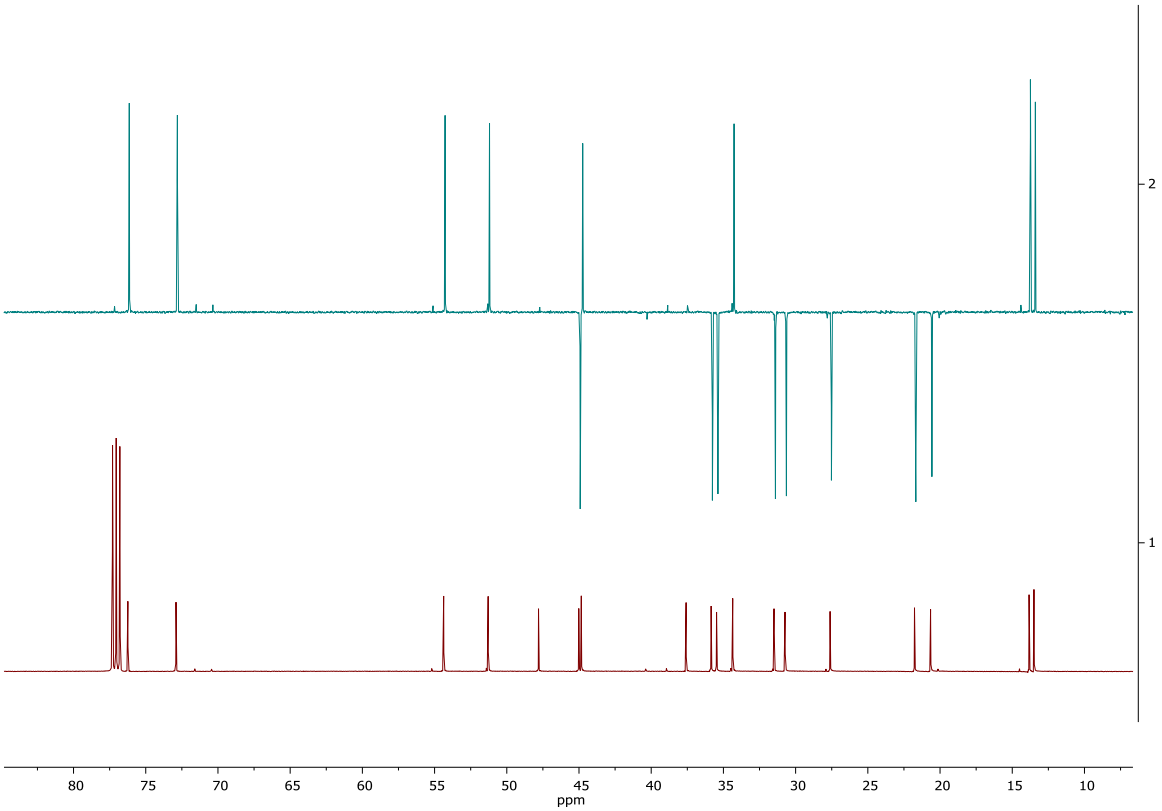
COSY spectrum



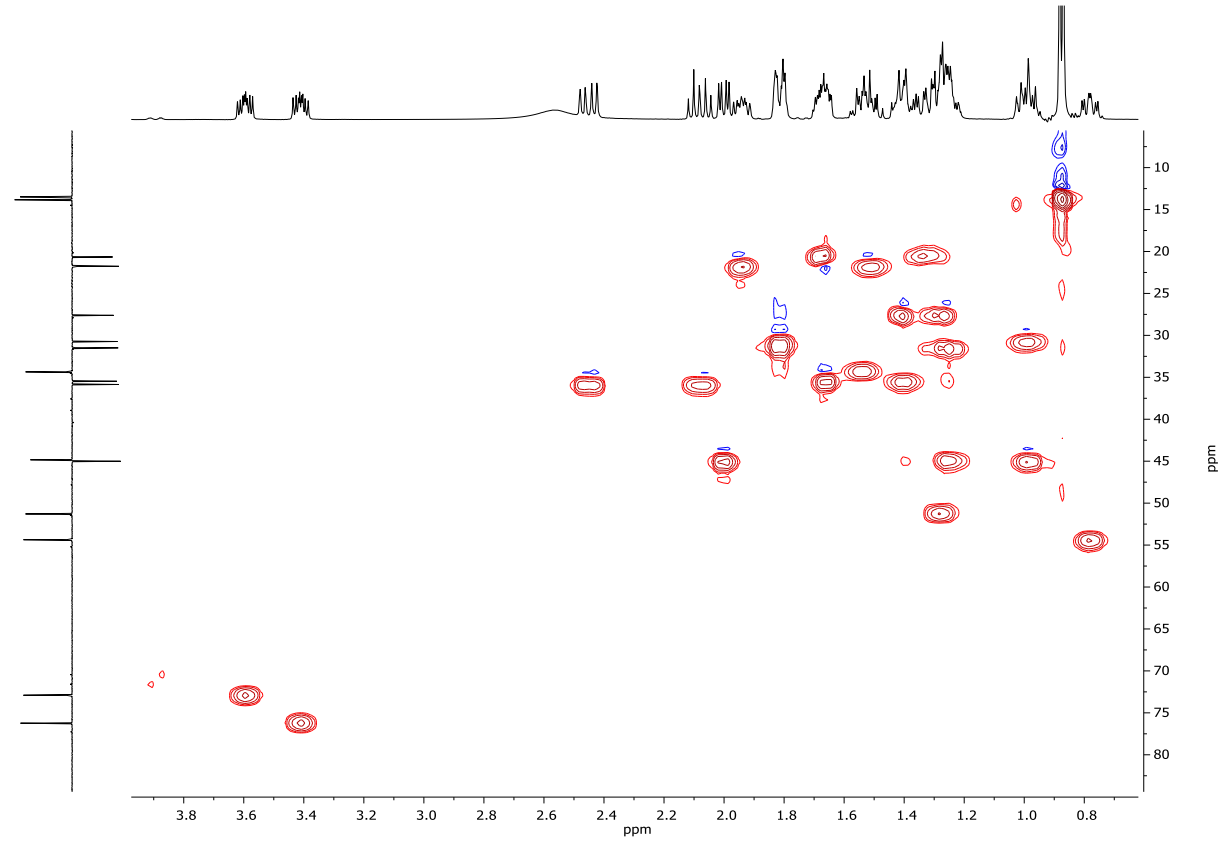
NOESY spectrum (selected part)



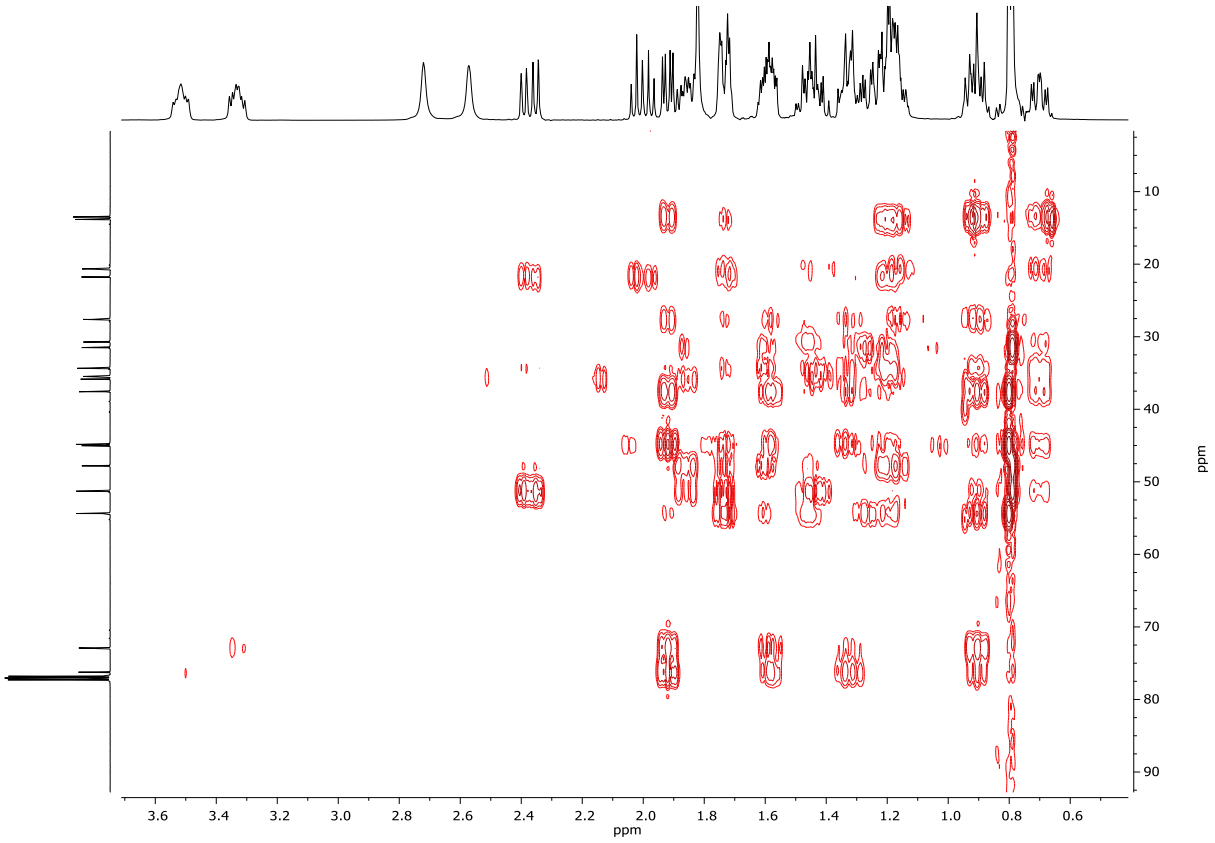
135-DEPT spectrum (above, 1) and ^{13}C NMR spectrum (below, 2)



HSQC spectrum

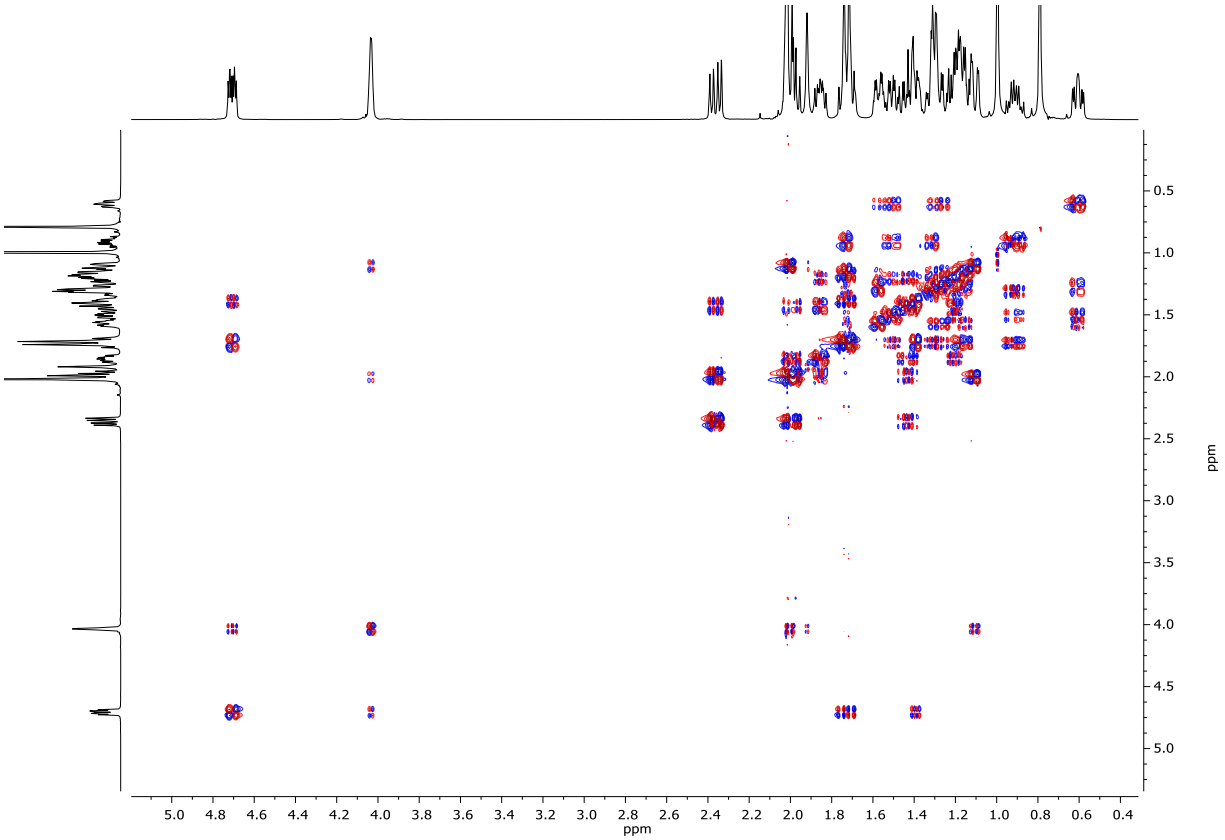


HMBC spectrum

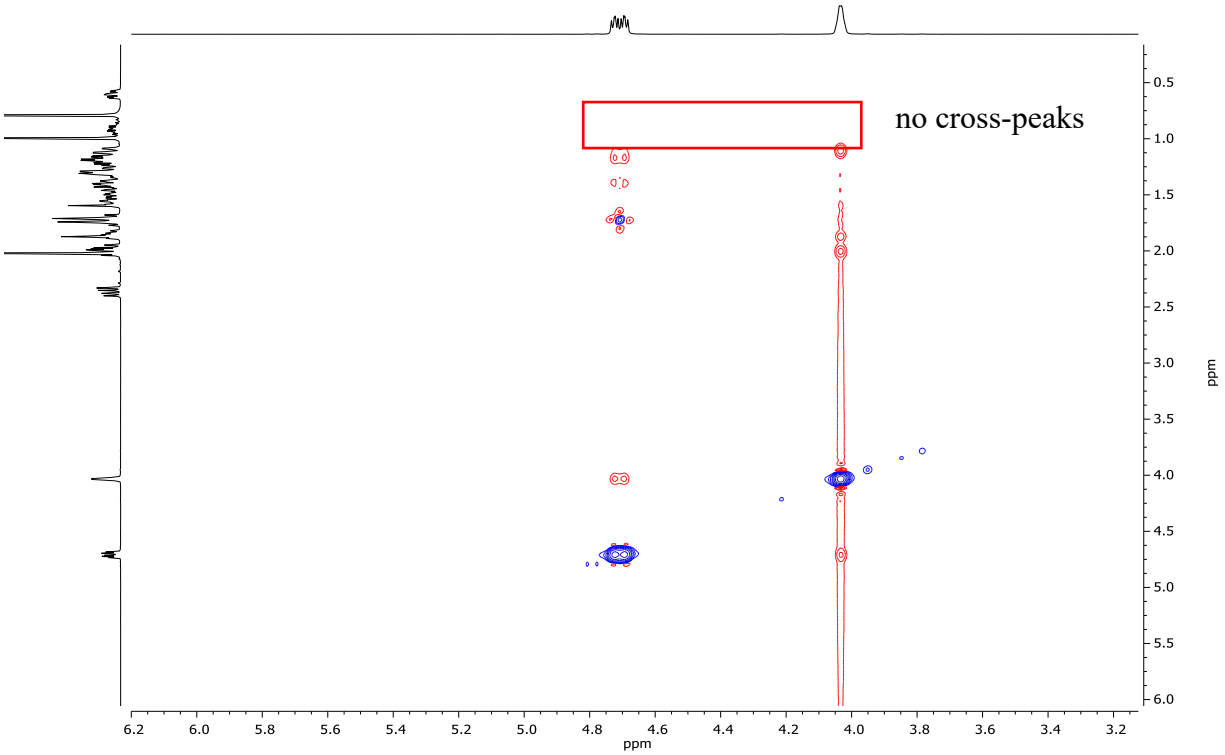


2*β*-Acetoxy-3*β*-hydroxy-5*α*-androstane-17-on (**14**)

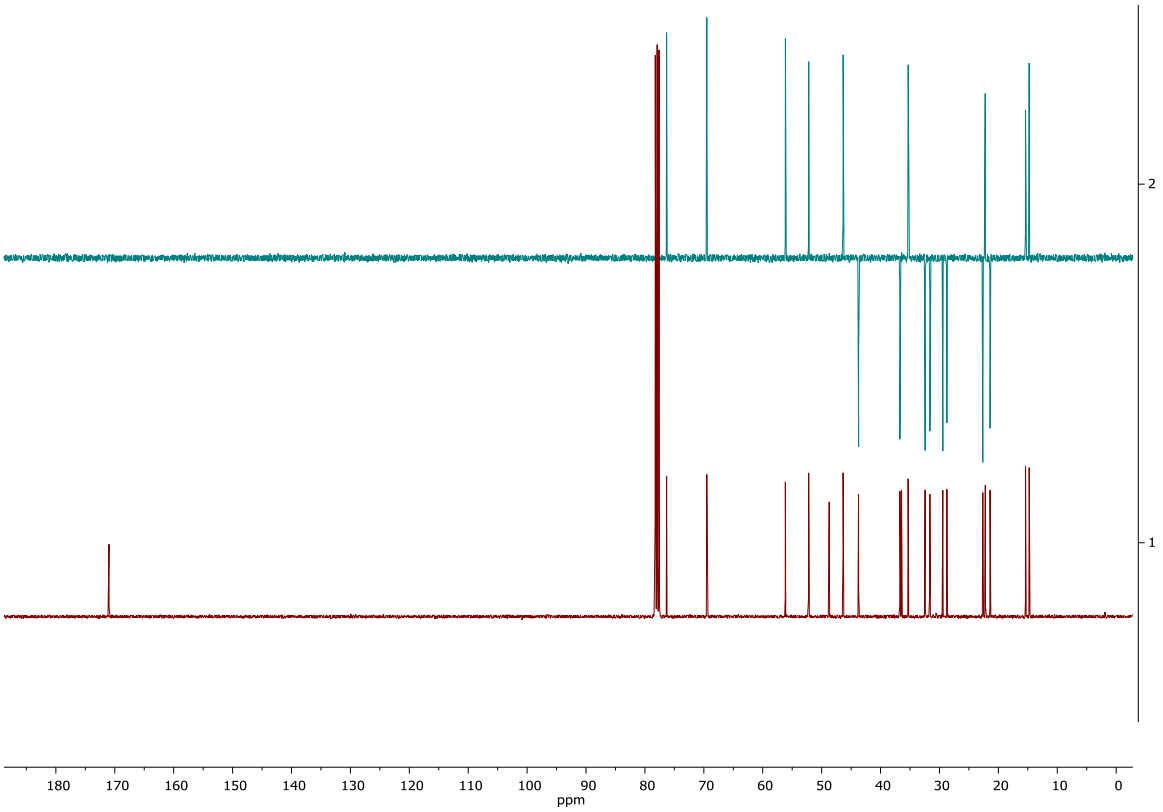
COSY spectrum



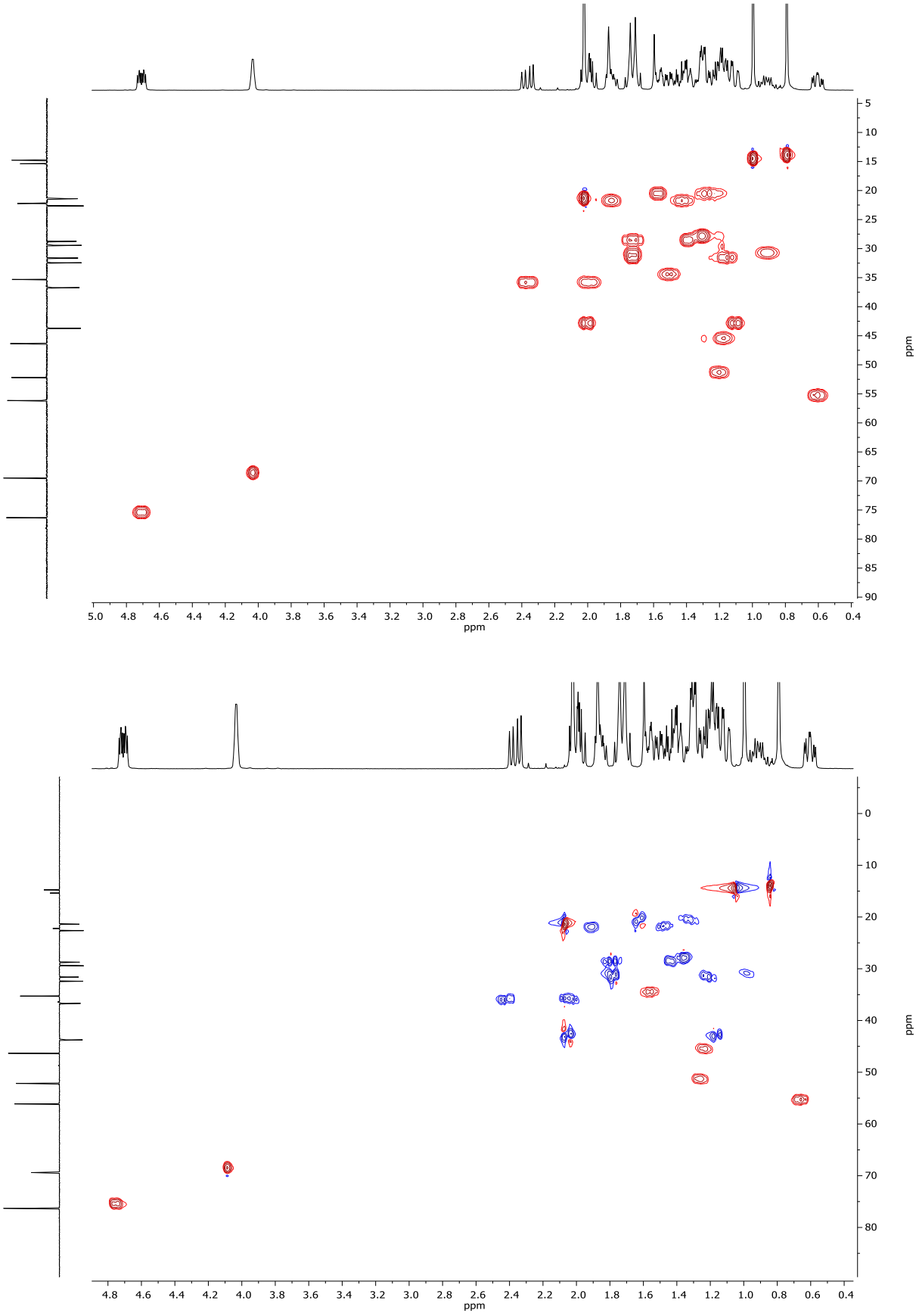
NOESY spectrum (selected part)



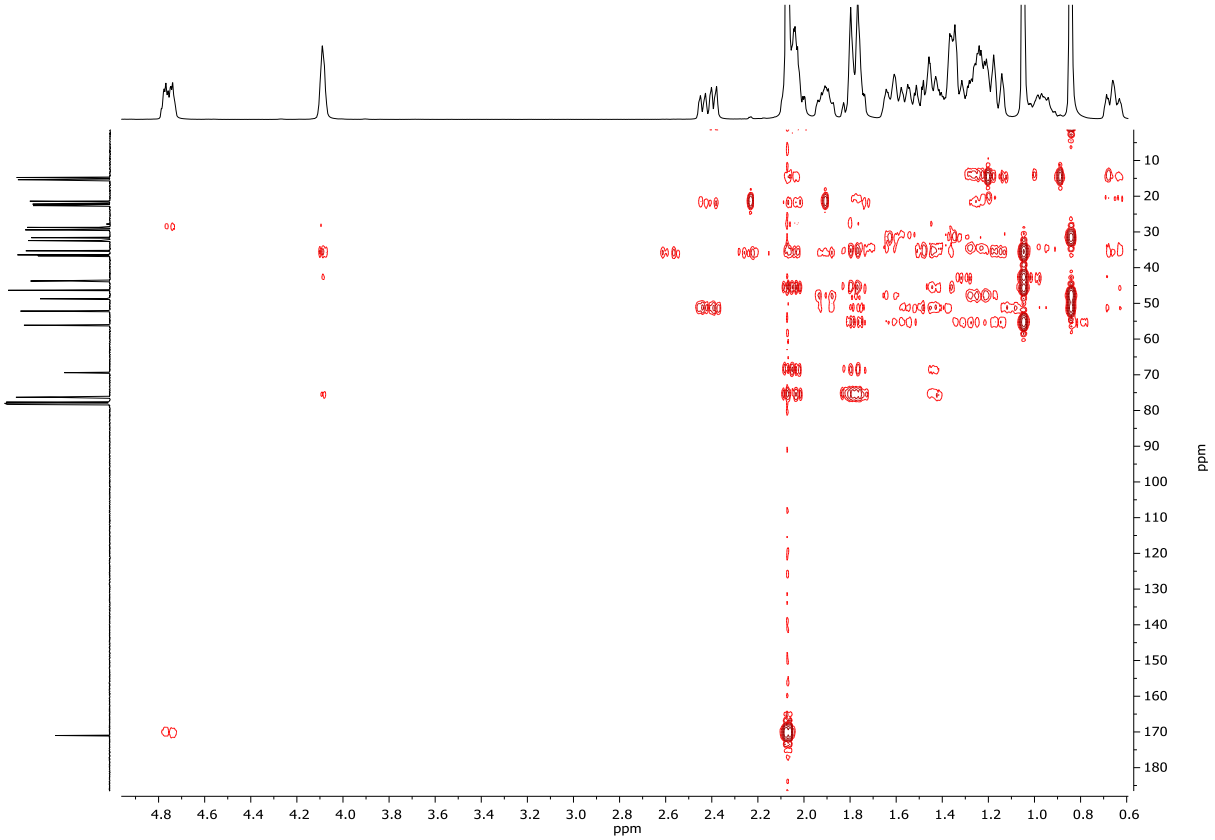
135-DEPT spectrum (above, 1) and ^{13}C NMR spectrum (below, 2)



HSQC spectrum



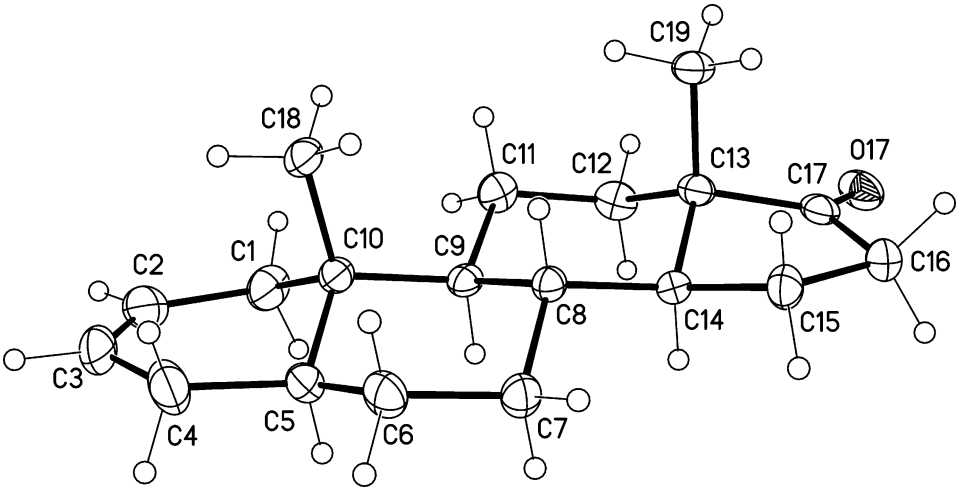
HMBC spectrum


4.8
4.6
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
ppm
10
20
30
40
50
60
70
80
90
100
110
120
130
140
150
160
170
180
ppm

5. Crystallographic Data

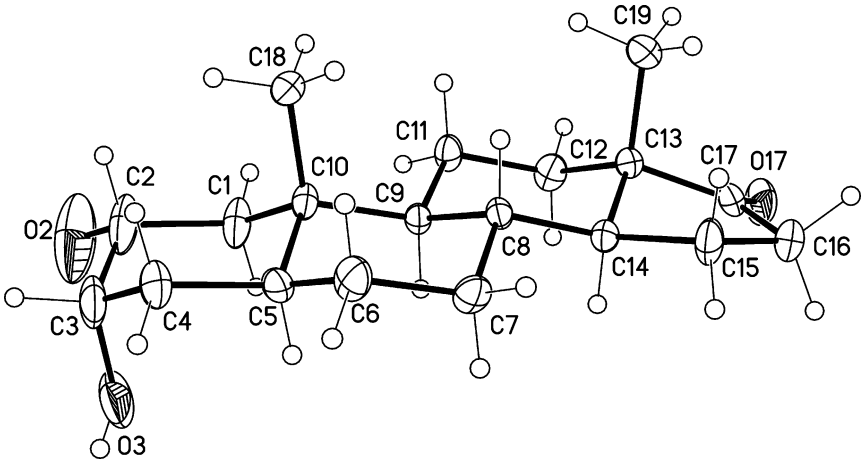
The single-crystal X-ray diffraction study was carried out on a Bruker D8 Venture diffractometer with Photon100 or PhotonII CPAD (for (**27**) detector at 123(2) K using Cu-Kα radiation (λ = 1.54178 Å. Direct Methods (SHELXS-97)[15] or dual space methods (SHELXT for **13** and **27**)[16] were used for structure solution and refinement was carried out using SHELXL-2014 (full-matrix least-squares on F^2)[16]. Hydrogen atoms were localized by difference electron density determination and refined using a riding model (H(O) free, except **21**). Semi-empirical absorption corrections were applied. For **15**, **27**, **SI-01** and **SI-04** an extinction correction were applied. The absolute configuration was determined by refinement of Parsons' x-parameter[17] or the enantiomer has been assigned by reference to an unchanging chiral center in the synthetic procedure (see cif-files for details). In **21** there seems to be a possible disorder of the OH-groups at C3 and C4 (see cif-files for details).

5α-Androst-2-ene-17-on (**15**)



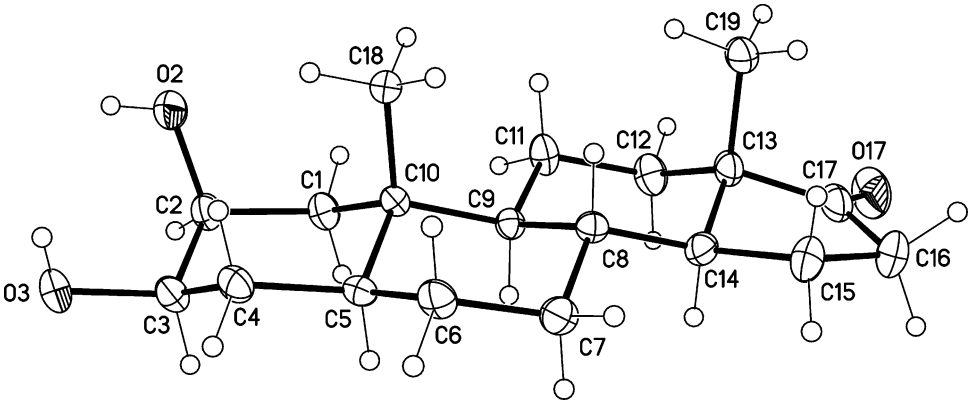
15: colorless crystals, $C_{19}H_{28}O$, M_r = 272.41, crystal size 0.36 × 0.20 × 0.08 mm, orthorhombic, space group $P2_12_12_1$ (No. 19), a = 6.4188(2) Å, b = 8.9046(3) Å, c = 26.9419(9) Å, V = 1539.91(9) Å^3, Z = 4, ρ = 1.175 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.527 mm^{-1}, F(000) = 600, $2\theta_{max}$ = 144.2°, 13756 reflections, of which 3011 were independent (R_{int} = 0.021), 182 parameters, R_1 = 0.031 (for 2981 I > 2σ(I)), wR_2 = 0.079 (all data), S = 1.08, largest diff. peak / hole = 0.287 / -0.172 e Å^{-3}. x = -0.05(5).

2*β*,3*β*-Dihydroxy-5*α*-androstane-17-on (**21**)



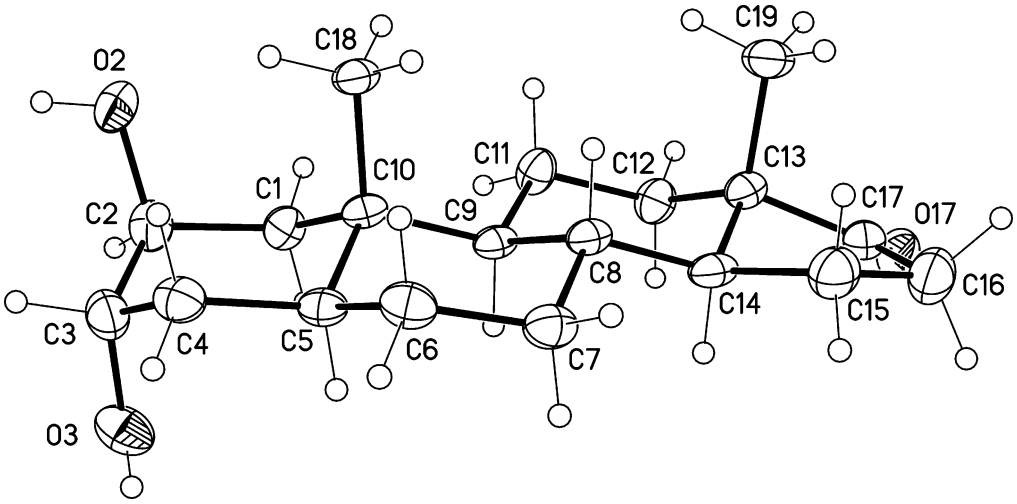
21: colorless crystals, $C_{19}H_{30}O_3$, M_r = 306.43, crystal size 0.08 × 0.06 × 0.02 mm, monoclinic, space group *P2₁* (No. 4), *a* = 6.0976(2) Å, *b* = 22.7525(7) Å, *c* = 6.2997(2) Å, *β* = 108.857(3)°, *V* = 827.08(5) Å^3, *Z* = 2, *ρ* = 1.230 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.638 mm^{-1}, *F*(000) = 336, $2\theta_{max}$ = 143.8°, 8766 reflections, of which 3222 were independent (R_{int} = 0.042), 199 parameters, 1 restraint, R_1 = 0.063 (for 2741 I > 2σ(I)), wR_2 = 0.169 (all data), *S* = 1.04, largest diff. peak / hole = 1.003 / -0.282 e Å^{-3}. x = -0.2(2).

2*α*,3*α*-Dihydroxy-5*α*-androstane-17-on (**22**)



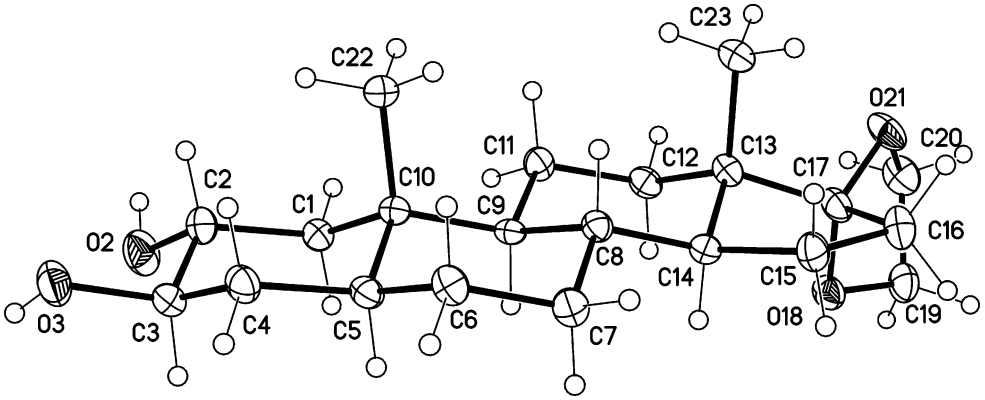
22: colorless crystals, $C_{19}H_{30}O_3$, M_r = 306.43, crystal size 0.16 × 0.10 × 0.02 mm, triclinic, space group *P1* (No. 1), *a* = 7.0823(2) Å, *b* = 10.2458(3) Å, *c* = 12.0686(3) Å, *α* = 73.204(2)°, *β* = 89-279(2)°, *γ* = 84.178(2)°, *V* = 833.93) Å^3, *Z* = 2, *ρ* = 1.220 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.633 mm^{-1}, *F*(000) = 336, $2\theta_{max}$ = 144.6°, 15480 reflections, of which 6149 were independent (R_{int} = 0.032), 409 parameters, 7 restraints, R_1 = 0.042 (for 5585 I > 2σ(I)), wR_2 = 0.104 (all data), *S* = 1.03, largest diff. peak / hole = 0.240 / -0.179 e Å^{-3}. x = 0.08(17).

2*β*,3*α*-Dihydroxy-5*α*-androstane-17-on (**23**)



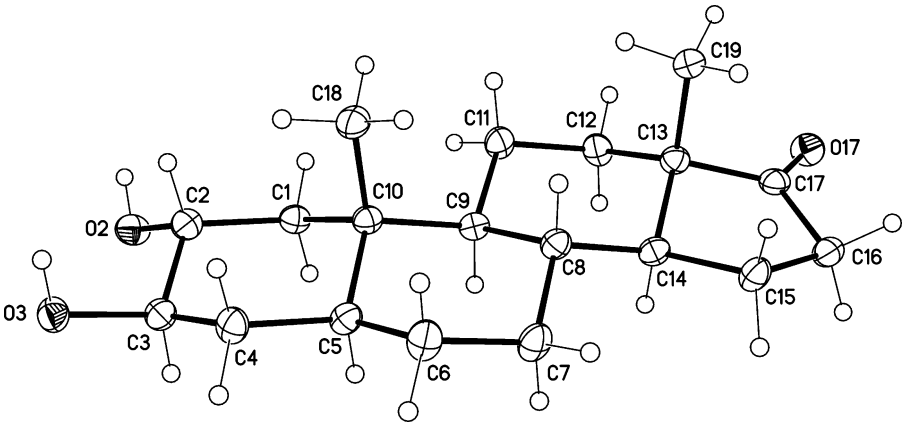
23: colorless crystals, $C_{19}H_{30}O_3$, M_r = 306.43, crystal size 0.26 × 0.24 × 0.02 mm, monoclinic, space group *P2₁* (No. 4), *a* = 9.5164(4) Å, *b* = 7.7586(3) Å, *c* = 11.9999(5) Å, *β* = 111.939(3)°, *V* = 822.11(6) Å^3, *Z* = 2, *ρ* = 1.238 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.642 mm^{-1}, *F*(000) = 336, *2θ*$_{max}$ = 144.4°, 9462 reflections, of which 3203 were independent (R_{int} = 0.044), 205 parameters, 3 restraints, R_1 = 0.052 (for 2917 I > 2σ(I)), wR_2 = 0.136(all data), *S* = 1.05, largest diff. peak / hole = 0.270 / -0.290 e Å^{-3}. x = 0.0(2).

17,17-(Ethylendioxy)-2*α*,3*β*-dihydroxy-5*α*-androstane (**SI-11**)



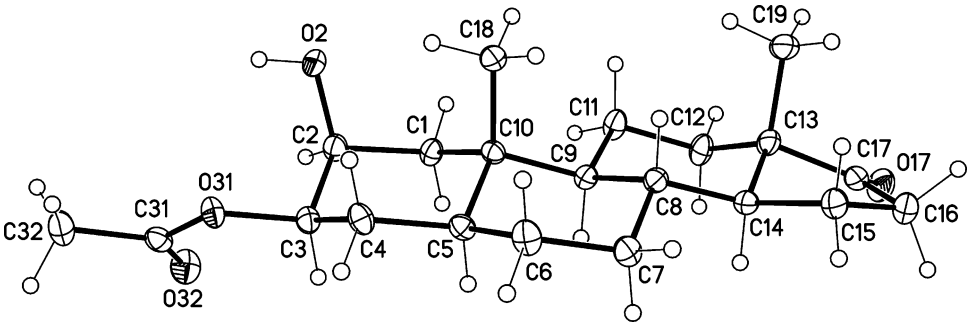
SI-11: colorless crystals, $C_{21}H_{34}O_4$, M_r = 350.48, crystal size 0.22 × 0.16 × 0.04 mm, monoclinic, space group *P2₁* (No. 4), *a* = 11.0162(3) Å, *b* = 6.7430(2) Å, *c* = 12.6811(3) Å, *β* = 103.877(2)°, *V* = 914.49(4) Å^3, *Z* = 2, *ρ* = 1.273 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.684 mm^{-1}, *F*(000) = 384, *2θ*$_{max}$ = 143.6°, 14546 reflections, of which 3541 were independent (R_{int} = 0.044), 232 parameters, 3 restraints, R_1 = 0.045 (for 3243 I > 2σ(I)), wR_2 = 0.109 (all data), *S* = 1.04, largest diff. peak / hole = 0.317 / -0.191 e Å^{-3}. x = 0.14(18).

2*α*,3*β*-Dihydroxy-5*α*-androstane-17-on (**27**)



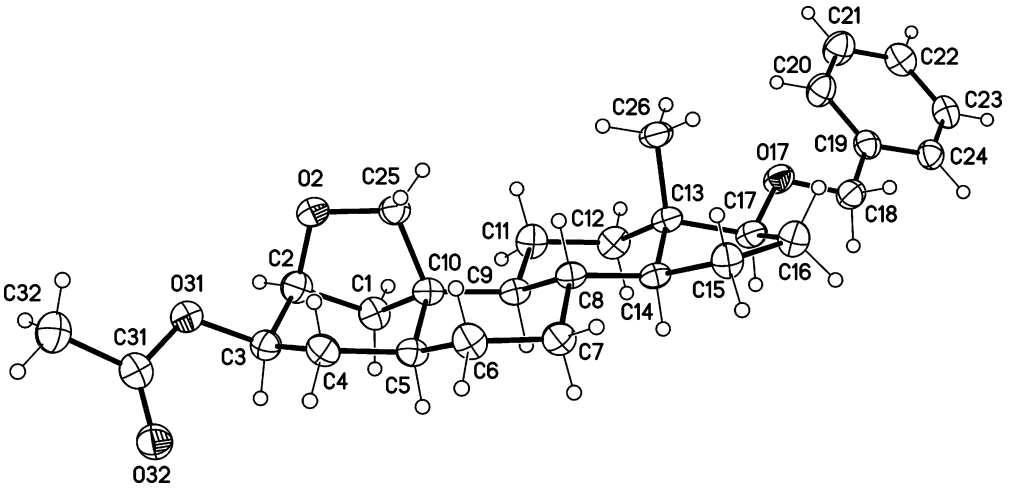
27: colourless crystals, $C_{19}H_{30}O3 \cdot H_2O$, M_r = 324.44, crystal size 0.28 × 0.14 × 0.06 mm, orthorhombic, space group $P2_12_12_1$ (No. 19), a = 6.3125(4) Å, b = 13.3434(8) Å, c = 10.8575(12) Å, V = 1756.83(18) Å^3, Z = 4, ρ = 1.227 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.671 mm^{-1}, F(000) = 712, $2\theta_{max}$ = 144.4°, 17174 reflections, of which 3469 were independent (R_{int} = 0.025), 220 parameters, 5 restraints, R_1 = 0.032 (for 3439 I > 2σ(I)), wR_2 = 0.087 (all data), S = 1.05, largest diff. peak / hole = 0.302 / -0.267 e Å^{-3}. x = -0.09(4).

2*β*-Acetoxy-3*β*-hydroxy-5*α*-androstane-17-on (**14**)



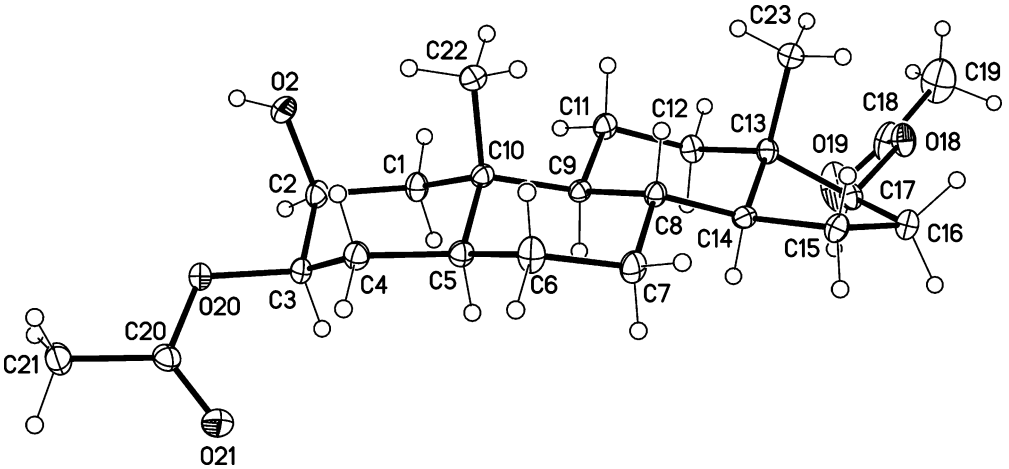
14: colorless crystals, $C_{21}H_{32}O_4$, M_r = 348.46, crystal size 0.22 × 0.20 × 0.06 mm, monoclinic, space group $P2_1$ (No. 4), a = 9.8746(3) Å, b = 7.6958(2) Å, c = 12.2229(4) Å, β = 92.870(1)°, V = 928.36(5) Å^3, Z = 2, ρ = 1.247 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.673 mm^{-1}, F(000) = 380, $2\theta_{max}$ = 144.6°, 12308 reflections, of which 3655 were independent (R_{int} = 0.030), 230 parameters, 2 restraints, R_1 = 0.029 (for 3588 I > 2σ(I)), wR_2 = 0.076 (all data), S = 1.04, largest diff. peak / hole = 0.187 / -0.160 e Å^{-3}. x = 0.01(6).

3*β*-Acetoxy-17*β*-benzyloxy-2*β*,19-epoxy-5*α*-androstane (**13-Bn**)



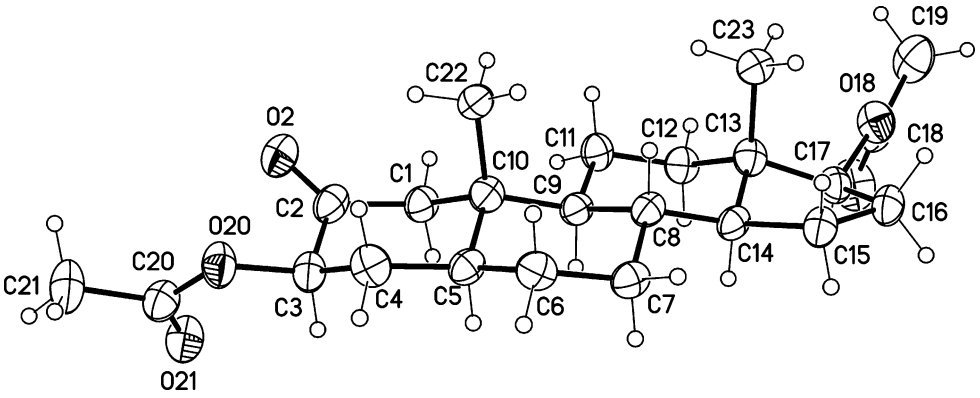
13-Bn: colorless crystals, $C_{28}H_{38}O_4$, M_r = 438.58, crystal size 0.20 × 0.16 × 0.08 mm, monoclinic, space group *P2₁* (No. 4), *a* = 9.6663(3) Å, *b* = 7.5343(2) Å, *c* = 16.3096(5) Å, *β* = 96.857(2)°, *V* = 1179.31(6) Å^3, *Z* = 2, *ρ* = 1.235 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.637 mm^{-1}, *F*(000) = 476, $2\theta_{max}$ = 144.4°, 17473 reflections, of which 4591 were independent (R_{int} = 0.024), 290 parameters, 1 restraint, R_1 = 0.031 (for 4482 I > 2σ(I)), wR_2 = 0.086 (all data), *S* = 1.05, largest diff. peak / hole = 0.260 / -0.161 e Å^{-3}. x = 0.13(6).

3*β*,17*β*-Diacetoxy-5*α*-androstane-2*β*-ol (**14-Ac**)



SI-01 – sb920: colorless crystals, $C_{23}H_{36}O_5$, M_r = 392.52, crystal size 0.50 × 0.35 × 0.25 mm, orthorhombic, space group $P2_12_12_1$(No. 19), *a* = 7.7219(3) Å, *b* = 13.4724(4) Å, *c* = 20.1540(7) Å, *V* = 2096.67(13) Å^3, *Z* = 4, *ρ* = 1.243 Mg/m^{-3}, *μ*(Cu-K$_\alpha$) = 0.689 mm^{-1}, *F*(000) = 856, $2\theta_{max}$ = 144.2°, 20103 reflections, of which 4140 were independent (R_{int} = 0.025), 260 parameters, R_1 = 0.028 (for 4106 I > 2σ(I)), wR_2 = 0.075 (all data), *S* = 1.07, largest diff. peak / hole = 0.236 / -0.167 e Å^{-3}. x = -0.02(4).

3*β*,17*β*-Diacetoxy-5*α*-androstane-2-on (**20-Ac**)



20-Ac – sb903: colorless crystals, $C_{23}H_{34}O_5$, M_r = 390.50, crystal size 0.15 × 0.03 × 0.01 mm, monoclinic, space group $P2_1$ (No. 4), a = 7.1015(3) Å, b = 25.1361(8) Å, c = 11.8745/4) Å, β = 92.269(2)°, V = 2117.98(13) Å^3, Z = 4, ρ = 1.225 Mg/m^{-3}, μ(Cu-K$_\alpha$) = 0.682 mm^{-1}, F(000) = 848, $2\theta_{max}$ = 136.4°, 12893 reflections, of which 7180 were independent (R_{int} = 0.047), 510 parameters, 1 restraint, R_1 = 0.064 (for 5010 I > 2σ(I)), wR_2 = 0.147 (all data), S = 1.02, largest diff. peak / hole = 0.178 / -0.173 e Å^{-3}. x = 0.4(3).

CCDC Numbers

CCDC 1822521 (**15**), CCDC 1822522 (**21**), CCDC 1822523 (**22**), CCDC 1822524 (**23**), CCDC 1822525 (**SI-11**), CCDC 1822526 (**14**), CCDC 1822527 (**13**), CCDC 1822528 (**14-Ac**), 1822529 (**20-Ac**), and CCDC 1998175 (**27**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

6. References

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