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Identification of a Fossil Sterane Biomarker in Crude Oil – an Androstane with a Modified Carbon Skeleton

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Dedicated to Professor Dr. Karl-Heinz Dötz on the occasion of his 70th birthday

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Three constitutional isomers of androstane were prepared for comparison with three unknown fossil $C_{19}H_{32}$ organic biomarkers ("19A", "19B", and "19C" in elution order) in geological samples from Oman. 3β-Methyl-A-*nor*-androstane was prepared in six steps (8 % overall yield) from testosterone. The key steps of this sequence were an Eschenmoser fragmentation and recyclization of the A ring. A mixture of four stereoisomers of 3-methyl-A-*nor*-androstane (4 % overall yield) was prepared by ionic hydrogenation of the olefin after A-ring recyclization in three steps. 17-Methyl-18-*nor*-androstane was synthesized in four steps as a mixture of isomers (58 % overall yield) from dihydrotestosterone with a Wagner–Meerwein shift of the 13β-methyl group to C-17 as the key step. Pure 17β- and 17α-methyl-18-*nor*-13α-androstane (4 and 2 % overall yield, respectively) were obtained in three additional steps after α-oxidation of the Wagner–Meerwein rearrangement product and subsequent reduction. The synthesis of 18-*nor*-D-*homo*-13β-androstane (12 % yield over seven steps from dihydrotestosterone) involved oxidative cleavage of the C–C double bond in the Wagner–Meerwein rearrangement product from the previous synthesis and subsequent recyclization of the D ring followed by reduction. The relative configurations of all final products were confirmed by X-ray crystallography. A comparison of the synthetic standards with the saturated hydrocarbon fraction of an Oman crude oil by gas chromatography (GC–MS) coinjection on three different GC columns and comparison of mass spectra revealed that unknown compound 19C is 18-*nor*-D-*homo*-13β,14α-androstane, whereas the isomeric 3-methyl-A-*nor*-androstanes and 17-methyl-18-*nor*-androstanes elute close to 19A and 19B, respectively, but do not match the unknowns.

Introduction

Based on extended organic geochemical investigations, mass spectral information indicated that samples of approximately 550-million-year-old crude oils and sedimentary rocks from the Oman Salt Basin contains (at least) three gas chromatographically separated isomers of putative C_{19} steranes ($C_{19}H_{32}$, m/z = 260; abbreviated as 19A, 19B, and 19C in order of elution) with modified androstane carbon skeletons and unknown constitutions.[1] Coeval sediments from Eastern Siberia, India, and Australia contain the same hydrocarbons.[1c] As there is empirical evidence that the occurrence and isomer distribution of unknown biomarkers correlate with geological age and the salinity of the water during sediment accumulation, there is considerable interest in revealing the precise structures of the unknowns to trace them back to potential biogenic ancestors in specific precursor organisms. The concentrations of the unknown biomarkers in the Oman samples are too low for them to be readily isolated as pure compounds for rigorous spectroscopic structural identification.

In our previous synthetic studies, we prepared steranes **1**–**3** (Figure 1), all of which have m/z = 260 $[M]^+$.[2] Their mass spectra and gas chromatographic retention times were compared with those of the putative unknown C_{19} steranes. Neither the spectral data nor the GC data matched closely enough to infer a structural identity of the natural hydrocarbons as any one of the synthetic standards. In continuation of these efforts, we selected structures **4**–**6** as additional reference compounds. Compound **4** is a regioisomer of 2α-methyl-A-*nor*-androstane (**3**), in which we translocated the

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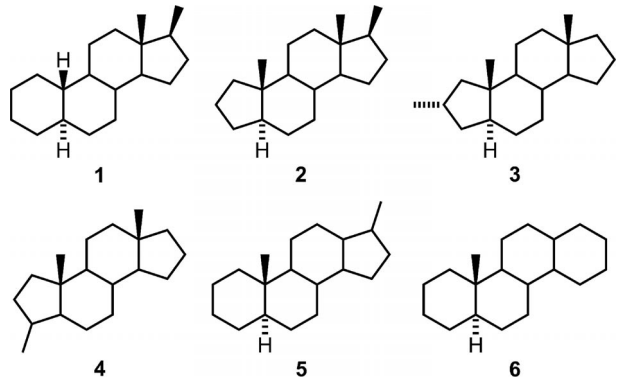


Figure 1. Target compounds of our previous (**1**–**3**) and present synthetic studies (**4**–**6**).

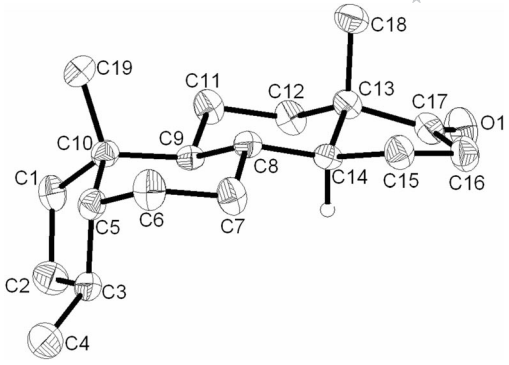


Figure 2. ORTEP representation of the molecular structure of ketone **12a**.

methyl group to the 3-position. 17-Methyl-18-*nor*-androstane (**5**) represents the shift of the 18-methyl group to the 17-position (for atom numbering, see ORTEP representations in Figures 2–4). Finally, the 18-methyl group was incorporated into the D ring to afford D-*homo*-18-*nor*-androstane (**6**), another synthetic target.

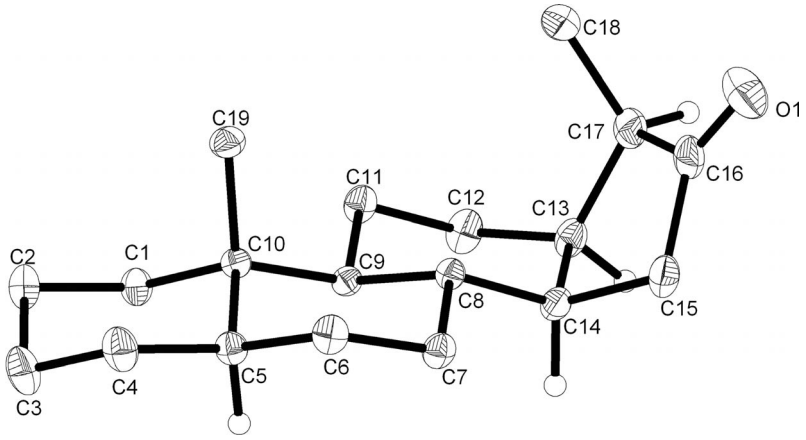


Figure 3. ORTEP representation of the molecular structure of ketone **18a**.

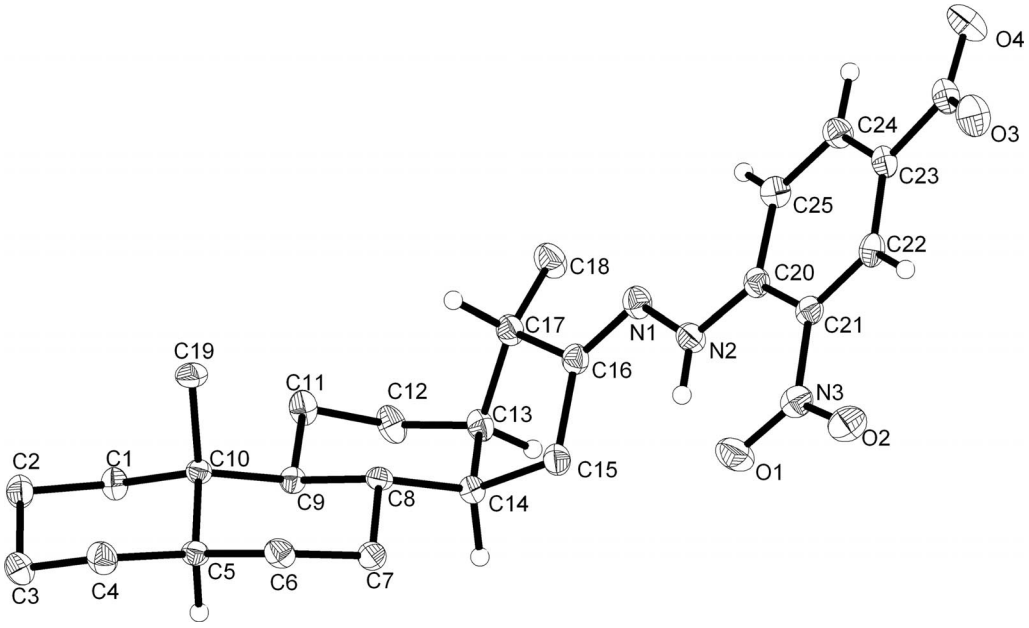
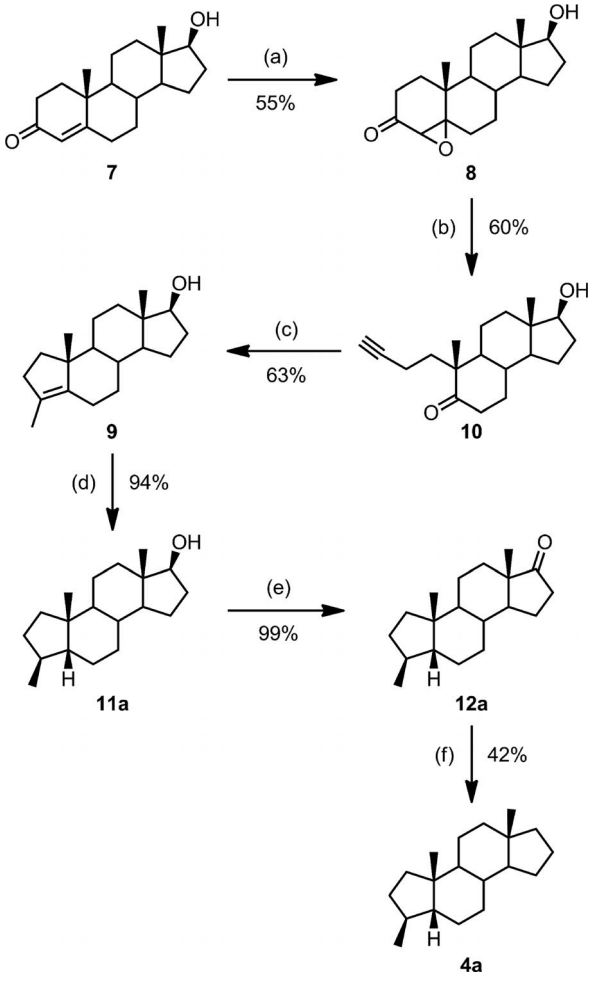


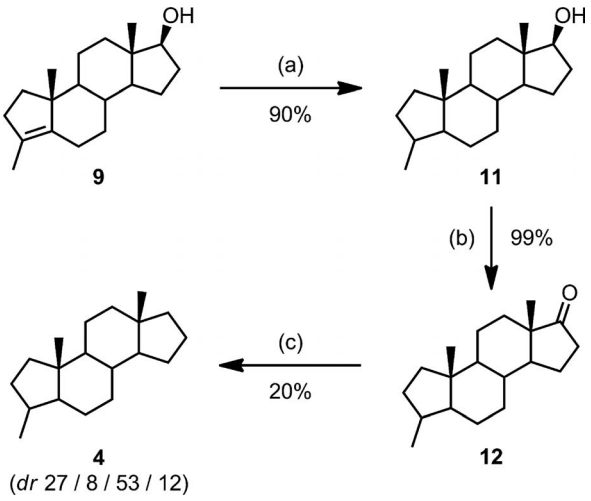
Figure 4. ORTEP representation of the molecular structure of hydrazone **19**.

Results and Discussion

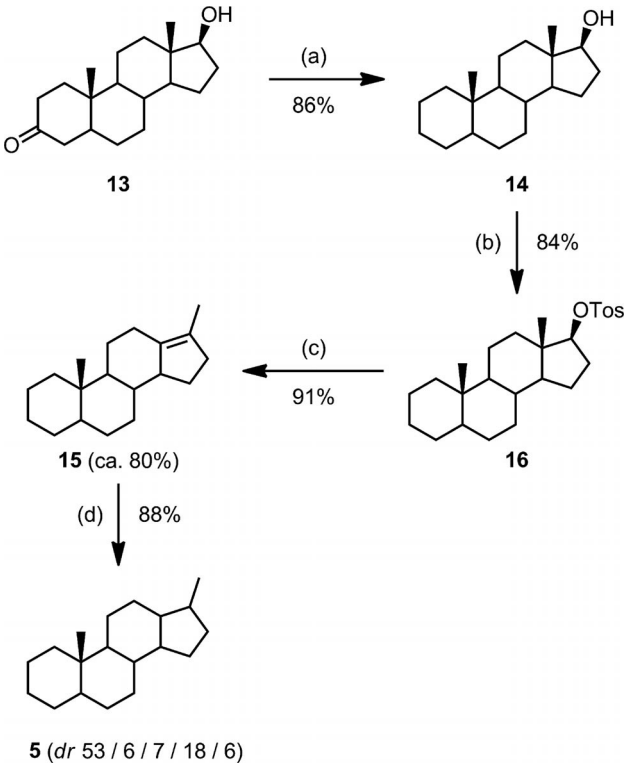
The synthesis of 3-methyl-A-*nor*-androstane (**4**) started with testosterone (**7**), which was submitted to a Weitz–Scheffer[3] oxidation to give epoxide **8**[4] (Scheme 1) as a mixture of two diastereomers [55% yield, diastereomeric ratio, dr (α/β)[5] = 30:70]. The latter was submitted to Eschenmoser fragmentation[6] with tosylhydrazine to give 4,5-*seco*-ynone **10**[7] in 60% yield, which was subsequently reductively cyclized to 3-methyl-A-*nor*-androst-3(5)-en-17-ol (**9**, 63%).[7] Catalytic hydrogenation of the C–C double bond furnished the so far unknown alcohol **11a** as a single diastereomer. Its configuration was established after pyridinium chlorochromate (PCC) oxidation[8] to ketone **12a** (99%), which is a solid material that yielded single crystals suitable for X-ray structure determination (Figure 2).[9] Surprisingly, the A and B rings of **12a** are *cis* fused with 3β-Me and 5β-H, which implies a formal *anti* dihydrogenation of olefin **9**. We actually presumed a *syn* hydrogenation from the α face to put the 3-Me group into the β configuration and the A/B rings fused *trans*. As this scenario provokes a 1,3-strain of two pseudoaxial methyl groups on the A ring, the hydrogenation may have been accompanied by palladium-catalyzed epimerization at C-5. Alternatively, prior to hydrogenation, the tetrasubstituted C-3(5) double bond in



Scheme 1. Synthesis of 3β-methyl-A-*nor*-5β-androstane (**4a**). Reagents and conditions: (a) H_2O_2, NaOH, H_2O, MeOH, 4 °C, 24 h; (b) *p*TosNHNH$_2$, CH_2Cl_2, AcOH, 0 to 23 °C, 2 h; (c) Li, NH_3(l), THF, –60 °C, 3 h, then excess NH_4Cl; (d) H_2 (3 bar), cat. Pd/C, EtOAc, 60 °C, 16 h; (e) PCC, CH_2Cl_2, 23 °C, 16 h; (f) excess $H_2NNH_2{\cdot}H_2O$, KOH, DEG, 200 °C, 16 h.



Scheme 2. Synthesis of four diastereomers of hydrocarbon **4** by ionic hydrogenation of olefin **9**. Reagents and conditions: (a) 1. 40 equiv. TFA, 20 equiv. Et_3SiH, CH_2Cl_2, –20 to 23 °C, 16 h; 2. KOH, MeOH, H_2O, 23 °C, 0.5 h; (b) PCC, CH_2Cl_2, 23 °C, 16 h; (c) excess. $H_2NNH_2{\cdot}H_2O$, KOH, DEG, 200 °C, 16 h.

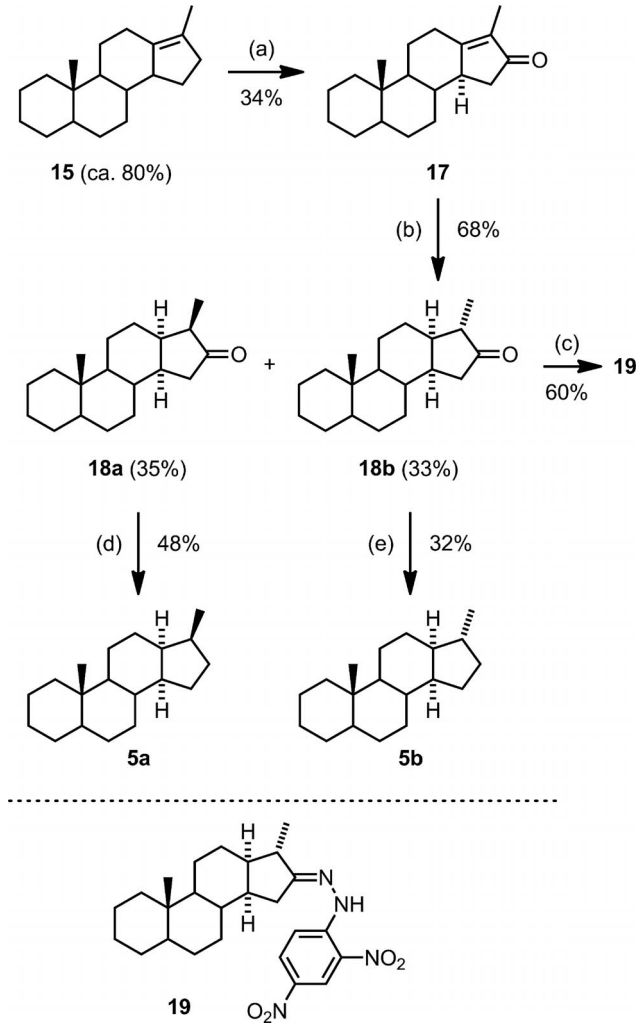


Scheme 3. Synthesis of five diastereomers of hydrocarbon **5** from dihydrotestosterone (**13**). Reagents and conditions: (a) excess $H_2NNH_2{\cdot}H_2O$, KOH, DEG, 200 °C, 16 h; (b) TosCl, cat. 4-dimethylaminopyridine (DMAP), pyridine, 55 °C, 5 d; (c) 5 equiv. EtMgBr, toluene, 110 °C, 4 h; (d) H_2 (1 bar), cat. Pd/C, EtOAc, 23 °C, 6 d.

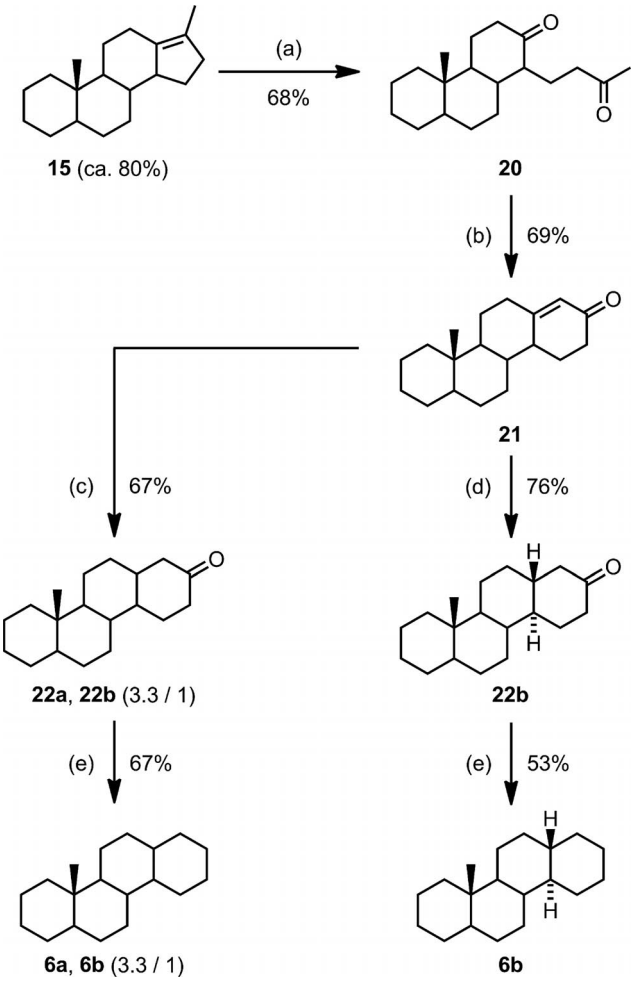
9 may have migrated (under Pd catalysis) to C-2–C-3 or C-3–C-4. A different diastereomer of **12a** (with 5α-H) was actually reported previously.[10] Finally, ketone **12a** was submitted to the Huang-Minlon version[11] of the Wolff–Kishner reduction in diethylene glycol (DEG) to give hydrocarbon **4a** (42%), again as a single diastereomer.

To access the diastereomers of **4a**, we decided to perform dihydrogenation of olefin **9** under ionic conditions via a carbenium ion at either C-3 or C-5 (Scheme 2). An appropriate protocol utilizes a mixture of trifluoroacetic acid (TFA) and Et_3SiH.[12] Indeed, the reaction basically proceeded without any stereoselectivity, and four diastereomers of alcohol **11** were obtained [ratio (**11a**/b/c/d) 27:8:53:12 by retention time order and relative intensity, GC]. PCC oxidation and Huang-Minlon reduction gave hydrocarbon **4**, again as a mixture of four diastereomers in the same ratio as **11**. Upon coinjection with the saturated hydrocarbon fraction of an Oman crude oil, product **4a** as well as its stereoisomers eluted close to 19A but did not match the naturally occurring unknown C_{19} compound. The mass spectra of the synthesis products slightly differed from that of 19A to different degrees.

The synthetic plan for 17-methyl-18-*nor*-androstane (**5**) envisaged a shift of the 13-methyl group to the 17-position by a Wagner–Meerwein rearrangement, as proposed by Miescher und Kägi.[13] Therefore, we started with commercially available dihydrotestosterone (**13**) and first removed the carbonyl group by a Huang-Minlon reduction (Scheme 3). Alcohol **14**[14] was activated by sulfonylation, and the tosylate **16**[15] was treated with an excess of ethyl Grignard reagent.[16] The methyl group shifted from the 13-position to the 17-position. A mixture of four tetrasubstituted olefins (ratio 4:12:80:4 by retention time order and relative intensity, GC) was obtained in 91% yield; compound **15**[14] is assumed to be the major component (ca. 80%) of this mixture. This rearrangement is presumed to



Scheme 4. Synthesis of single diastereomers **5a** and **5b** (17β- and 17α-methyl-18-*nor*-13α-androstane) of hydrocarbon **5**. Reagents and conditions: (a) 20 equiv. CrO_3, 40 equiv. pyridine, CH_2Cl_2, 23 °C, 16 h; (b) H_2 (4 bar), cat. Pd/C, EtOAc, 40 °C, 3 d; (c) 2,4-$(O_2N)_2C_6H_3NHNH_2$, H_2SO_4, EtOH, H_2O, 23 °C, 10 min; (d) excess $H_2NNH_2{\cdot}H_2O$, KOH, DEG, 200 °C, 16 h; (e) excess $H_2NNH_2{\cdot}H_2O$, KOH, toluene, DEG, 110 °C, 5 h; then 200 °C, 16 h.



Scheme 5. Synthesis of hydrocarbons **6a** and **6b**. Reagents and conditions: (a) $KMnO_4$, Me_3NBnCl, CH_2Cl_2, 40 °C, 20 h; (b) cat. KOH, H_2O, MeOH, 40 °C, 7 h; (c) H_2 (4 bar), cat. Pd/C, pyridine, 23 °C, 1 d; (d) Li, NH_3(l), THF, –60 °C, 3 h; (e) excess $H_2NNH_2{\cdot}H_2O$, KOH, DEG, 200 °C, 16 h.

proceed via a secondary carbenium ion, and the role of the Grignard reagent is proposed to be that of a Lewis acid, which is definitely unusual for such a reagent. Therefore, we wondered whether the rearrangement could also be induced by anhydrous $MgBr_2 \cdot OEt_2$. Indeed, a mixture of tetrasubstituted olefins was obtained (77% yield), but only 66% of this mixture was **15**. However, catalytic hydrogenation of **15** and its isomers gave hydrocarbon **5** as a mixture of five stereoisomers (ratio 53:6:7:28:6 by retention time order and intensity, GC). Upon investigation by GC–MS, the second isomer of this mixture exhibited a GC retention time and mass spectrum very similar to those of unknown Oman biomarker 19B.[1a]

To prepare a single stereoisomer of **5** with known configuration, the mixture of olefin **15** (ca. 80%) and its regioisomers was submitted to Collins oxidation[17] in the α position to the C–C double bond (Scheme 4). Upon this transformation, the minor isomers of **15** appear to be completely removed, and enone **17** was obtained as a single isomer (34%; its constitution was established by 2D NMR experiments). Catalytic hydrogenation gave ketone **18**[18] as a mixture of two stereoisomers **18a** and **18b** (ratio ca. 1:1). This mixture was difficult to separate, but pure isomers **18a** (35%) and **18b** (33%) were obtained by repeated column chromatography. The relative configurations of both materials were elucidated by X-ray crystallography. Although we directly obtained single crystals of **18a**, we failed to obtain single crystals of **18b**. Therefore, we prepared hydrazone **19**, which fortuitously showed good crystallinity. ORTEP representations of both structures are depicted in Figures 3 and 4. Rings C and D are *cis* annulated in **18a** (Figure 3) and the 17-methyl group is in the β configuration; therefore, *syn* dihydrogenation of **17** occurred from the α face, which seemed to be less shielded by the axial 10β methyl group. To our surprise, we found hydrazone **19** also with *cis* annulation of the C and D rings and the 17-methyl group in the α configuration (Figure 4); thus, compound **18b** would be the product of an *anti* dihydrogenation. Therefore, we first checked whether product **19** has the same configuration as starting material **18b**, because epimerization could have occurred during hydrazone formation. Reductive cleavage of hydrazone **19** with $SnCl_2$ in tetrahydrofuran (THF)[19] gave ketone **18**, which was identical to diastereomer **18b** by NMR and according to GC retention time. Thus, epimerization at C-17 must have occurred after *syn* dihydrogenation of **17** from the α face. Such epimerizations were observed previously under Pd/C catalysis[20] in an apparently formal *anti* dihydrogenation.

Ketones **18a** and **18b** were submitted to Huang-Minlon reduction, and hydrocarbons **5a** (48%) and **5b** (32%) were obtained. Actually, when a mixture of **18a** and **18b** was submitted to this reduction, isomer **18a** was converted significantly faster than **18b**; thus, the latter was recovered together with product **5a**. Compound **5a** perfectly coelutes with Oman crude oil component 19B[1a] on capillary columns coated with DB-1MS and DBXLB, but has a slightly shorter retention time on a DB-5MS column and, thus, the two compounds are not structurally identical. Hydrocarbon **5b** has a GC retention time very similar to that of **5a**; it actually elutes as a trailing shoulder of **5a** and was initially not recognized as the sixth component in the original isomer mixture of **5**. Nevertheless, upon coinjection with the Oman petroleum hydrocarbons on the DB-5MS column, compound **5b** elutes slightly earlier than 19B and, thus, also

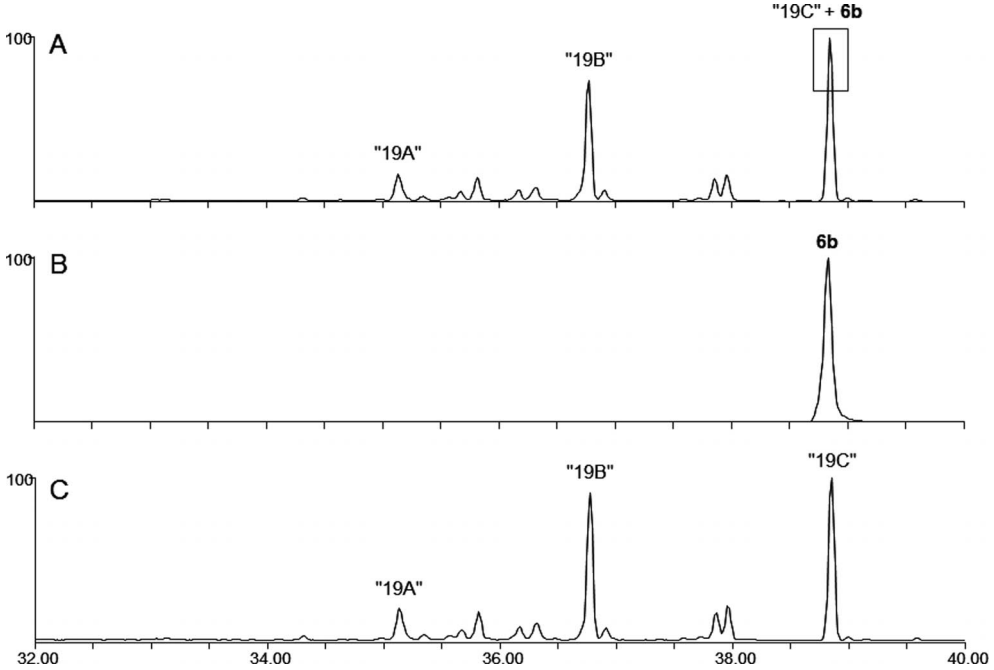


Figure 5. GC–MS coinjection experiments of **6b** and 19C.[1a] Chromatogram C is the $m/z = 260 \rightarrow 203$ transition for the saturated hydrocarbon fraction of an Oman crude oil (OMO 021), chromatogram B is compound **6b**, and chromatogram A is the admixture of the crude oil hydrocarbons containing 19C plus **6b**.The box at the top of the GC peak shows a perfect match on a DB-5MS column.

does not match the unknown. The mass spectra of 19B, **5a**, and **5b** are virtually identical. The use of GC columns with even higher polarity was considered but discarded because the dominant factor for the GC retention time of an apolar saturated hydrocarbon is its boiling point.

18-*nor*-D-*homo*-Androstane (**6**) is another androstane isomer that formally involves use of the 13-methyl group for D-ring extension. Starting with a mixture of olefin **15** and its regioisomers, we oxidatively cleaved the C–C double bond[21] to obtain diketone **20**, which was subsequently recyclized to give enone **21** (Scheme 5). Catalytic hydrogenation in pyridine as solvent gave saturated ketone **22** (73% yield) as a mixture of *cis* and *trans* isomers (**22a**/**22b** 77:23). Huang-Minlon reduction furnished the target hydrocarbon **6**[22] also as a mixture of *cis* and *trans* isomers (**6a**/**6b** 3.3:1). A comparison of the analytical data revealed a match of *trans* compound **6b** with Oman crude oil constituent 19C[1a] on three different gas chromatographic columns (example in Figure 5) and identical mass spectra.

We elucidated the relative configurations of **22a**/**22b** and **6a**/**6b** as follows: The reduction of enone **21** under Birch conditions[23] gave a single ketone **22b**, which was identical to the minor isomer of **22** obtained by hydrogenation. This compound **22b** gave single crystals suitable for X-ray structure determination. Figure 6 shows an ORTEP representation of its molecular structure in the solid state; *trans* fusion of the C and D rings is clearly visible. Consequently, hydrocarbon **6b** was obtained after Huang-Minlon reduction and we were also able to grow single crystals of this compound (Figure 7).

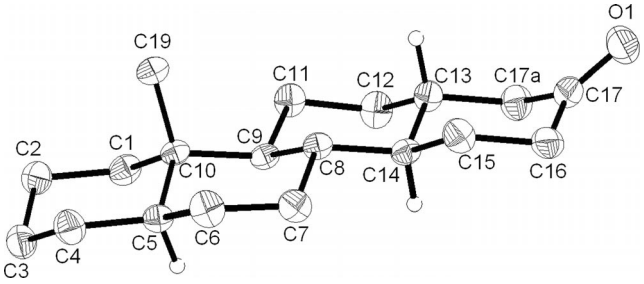


Figure 6. ORTEP representation of the molecular structure of ketone **22b**.

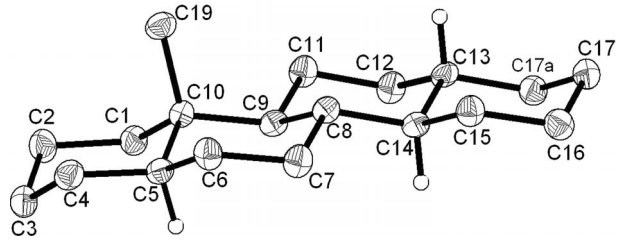


Figure 7. ORTEP representation of the molecular structure of hydrocarbon **6b**.

Conclusions

We identified a new steroidal hydrocarbon as a constituent of crude oil. The mass spectra and gas chromatographic retention times of synthetic androstane derivatives **4**, **5**, and **6** were compared with those of three putative unknown $C_{19}H_{32}$ steranes (named 19A, 19B and 19C) in sediments and crude oils from the Oman Salt Basin. 3-Methyl-A-*nor*-androstane (**4**, four diastereomers were investigated) and 17-methyl-18-*nor*-androstane (**5**, six diastereomers) had GC retention times close to those of 19A and 19B, respectively, but did not match those of the unknowns closely enough to infer the structural identity of one of these two natural hydrocarbons. On the other hand, one of the diastereoisomers of **6**, namely, 18-*nor*-D-*homo*-13β,14α-androstane (**6b**), is identical to the hitherto unknown compound 19C, which was (apart from an identical mass spectrum) proved by co-injection of the natural material on three different GC columns. Compounds **4**, **5**, and **6** were synthesized in several steps from testosterone (**7**) or dihydrotestosterone (**13**), and the constitutions and relative configurations of diastereomerically pure final products were established by X-ray crystallography. Further investigation will focus on the elucidation of constituents 19A and 19B by conceptualization of alternative target compounds for synthesis and the preparation of all-isomer mixtures of the products to account for eventual geochemical epimerization reactions during diagenesis (low-temperature geochemical transformation, usually <50 °C) and catagenesis (higher temperatures, "oil window") in the course of the geological history.

Experimental Section

General: Preparative column chromatography was performed with Merck SiO_2 (35–70 μm, type 60 A) with hexane, *tert*-butyl methyl ether (MTBE), and ethyl acetate (EtOAc) as eluents. TLC was performed with Merck aluminium plates coated with SiO_2 F_{254}. ^1H and ^{13}C NMR spectra were recorded with a Bruker Avance DRX 500 instrument. The multiplicities of carbon signals were determined with DEPT experiments. MS and HRMS spectra of synthesis products were obtained with a Finnigan MAT 95 (EI and CI) and a Waters Q-TOF Premier (ESI) spectrometer. IR spectra were recorded with a Bruker Tensor 27 spectrometer equipped with a "GoldenGate" diamond attenuated total reflectance (ATR) unit. GC–MS retention time experiments on petroleum hydrocarbons, both alone and in admixtures with synthetic standards, were conducted in multiple reaction monitoring (MRM) mode, and the compound-specific 260 Da molecular ion to 203 Da fragment transition was targeted. We used a Micromass AutoSpec Ultima mass spectrometer interfaced to an Agilent 6890 N gas chromatograph, and the GC was fitted with a fused silica capillary column (60 m; 0.25 mm i.d.; 0.25 μm film thickness; J&W Scientific) with He as carrier gas. The phases tested were DB-5MS, DB-1MS, and DB-XLB (30 m for this column), and identity was assured by co-elution on all three. The GC temperature program was 60 (2 min) to 150 °C at 10 K/min and to 330 °C (held 19 min) at 3 K/min. The AutoSpec source was operated in electron ionization (EI, 70 eV) mode at 250 °C with 8 kV accelerating voltage. Additional full scan analyses were conducted over a range of m/z = 50–600. The data were acquired and processed by using MassLynx 4.0 (Micromass Ltd.).

17β-Hydroxy-4ξ,5ξ-epoxyandrostan-3-one (8): A solution of testosterone (**7**, 2.50 g, 8.67 mmol) in MeOH (100 mL) was treated at 0 °C successively with H_2O_2 (17 mL, 30% in H_2O) and NaOH solution (10 mL, 2% in H_2O). The resulting mixture was stirred for

24 h at 0 °C, and the solvent was evaporated under vacuum. The crude material was treated with H_2O (40 mL) and extracted with EtOAc (3× 50 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under vacuum. After chromatography (SiO_2, MTBE, R_f = 0.44), epoxytestosterone **8** (1.45 g, 4.76 mmol, 55%) was obtained as a mixture of α- and β-epoxides (α/β 0.3:0.7).[5] ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.75 (s, 0.7×3 H, β isomer), 0.77 (s, 0.3×3 H, α isomer), 0.95–1.12 (m, 4 H), 1.06 (s, 0.3×3 H, α isomer), 1.15 (s, 0.7×3 H, β isomer), 1.18–1.33 (m, 2.3 H), 1.35–1.48 (m, 2.9 H), 1.52–1.65 (m, 3.9 H), 1.68–1.73 (m, 0.3 H), 1.80–1.86 (m, 2.6 H), 2.02–2.25 (m, 3 H), 2.26–2.41 (m, 1 H), 2.96 (s, 0.7 H, β isomer), 3.02 (s, 0.3 H, α isomer), 3.63 (t, J = 8.6 Hz, 0.7 H, β isomer), 3.66 (t, J = 8.6 Hz, 0.3 H, α isomer) ppm. $^{13}C\{^1H\}$NMR (125 MHz, $CDCl_3$): β isomer: δ = 11.04 (CH_3), 18.93 (19-CH_3), 21.11 (CH_2), 23.31 (CH_2), 26.08 (CH_2), 29.70 (CH_2), 29.87 (CH_2), 30.31 (CH_2), 32.49 (CH_2), 35.43 (CH), 36.18 (CH_2), 37.23 (C), 43.00 (C), 46.57 (CH), 50.40 (CH), 62.62 (CH), 70.26 (C), 81.51 (CH), 206.83 (C) ppm; α isomer: δ = 11.04 (CH_3), 16.49 (19-CH_3), 20.97 (CH_2), 23.31 (CH_2), 28.45 (CH_2), 29.07 (CH_2), 29.57 (CH_2), 30.36 (CH_2), 33.05 (CH_2), 35.43 (CH), 36.42 (CH_2), 36.74 (C), 42.87 (C), 50.19 (CH), 50.75 (CH), 62.82 (CH), 70.10 (C), 81.64 (CH), 206.99 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3401 (br m), 2938 (s), 2871 (m), 2851 (m), 1709 (s), 1468 (m), 1448 (m), 1379 (m), 1341 (m), 1319 (w), 1307 (w), 1266 (m), 1248 (m), 1205 (m), 1182 (m), 1138 (m), 1114 (m), 1079 (m), 1055 (s), 1020 (m), 984 (w), 953 (m), 937 (w), 911 (w), 884 (m), 861 (m) cm^{-1}. MS (ESI+): m/z = 327 $[M + Na]^+$.

17β-Hydroxy-5-oxo-4,5-*seco*-androst-3-yne (10):[7] A solution of epoxy ketone **8** (2.6 g, 8.5 mmol) in a mixture of CH_2Cl_2 and AcOH (1:1, 45 mL) was added dropwise over a period of 1 h to a cooled (ice/water bath) solution of *p*-tosylhydrazine (1.7 g, 8.9 mmol) in CH_2Cl_2/AcOH (1:1, 45 mL). The solution was warmed to ambient temperature and stirred for a further 2 h. After removal of the solvent under vacuum, the mixture was redissolved in CH_2Cl_2 (100 mL) and successively washed with saturated $NaHCO_3$ solution (100 mL) and water (100 mL). The solution was dried ($MgSO_4$) and filtered. After evaporation, the residue was chromatographed (SiO_2, hexane/MTBE 1:1, R_f = 0.23) to furnish **10** (1.47 g, 5.10 mmol, 60%) as a yellow oil. $[\alpha]_D^{20}$ = 31.6 (CH_2Cl_2, 1 g dm^{-3}). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.79 (s, 3 H), 0.98 (td, J = 11.5, 7.3 Hz, 1 H), 1.05–1.10 (m, 1 H), 1.08 (s, 3 H), 1.12–1.19 (m, 1 H), 1.22–1.36 (m, 2 H), 1.42–1.54 (m, 4 H), 1.59–1.65 (m, 1 H), 1.73 (dq, J = 11.0, 3.3 Hz, 2 H), 1.83 (dt, J = 12.6, 3.3 Hz, 1 H), 1.90–1.95 (m, 2 H), 2.00–2.17 (m, 4 H), 2.24–2.28 (m, 1 H), 2.51 (td, J = 14.5, 6.3 Hz, 1 H), 3.64 (t, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.07 (CH_3), 13.68 (CH_2), 20.58 (CH_3), 21.13 (CH_2), 23.34 (CH_2), 30.25 (CH_2), 30.57 (CH_2), 33.54 (CH_2), 34.84 (CH), 36.02 (CH_2), 37.95 (CH_2), 42.91 (C), 47.41 (CH), 50.36 (CH), 50.73 (C), 68.07 (CH), 81.42 (CH), 84.85 (CH), 214.46 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3405 (br w), 3306 (w), 2939 (m), 2872 (w), 2855 (w), 2118 (w), 1700 (s), 1454 (w), 1429 (w), 1378 (w), 1348 (w), 1319 (w), 1278 (w), 1249 (w), 1208 (w), 1160 (w), 1132 (w), 1070 (m), 1054 (m), 1023 (w), 952 (w), 921 (w), 852 (w), 831 (w), 737 (w), 704 (w), 627 (m) cm^{-1}. MS (CI, isobutane): m/z (%) = 289 (23) $[M + H]^+$, 271 (14), 236 (100). HRMS (ESI+): calcd. for $C_{19}H_{28}NaO_2$ $[M + Na]^+$ 311.1987; found 311.1981.

17β-Hydroxy-3-methyl-A-*nor*-androst-3(5)-ene (9): Absolute THF (1 mL) was added to a solution of Li (36 mg, 5.20 mmol) in liquid NH_3 (ca. 5 mL) at –78 °C. The mixture was stirred for 30 min, and a solution of 4,5-*seco*-ynone **10** (150 mg, 0.52 mmol) in absolute THF (4 mL) was added dropwise. The reaction mixture was stirred for 3 h at –78 to –50 °C. Solid NH_4Cl (556 mg, 10.4 mmol) was added in small portions, and the solution was warmed to ambient temperature overnight, and the NH_3 evaporated. Water (5 mL) was added, and the solution was extracted with MTBE (3× 30 mL). The combined organic solvents were dried ($MgSO_4$) and filtered, and the solvent was evaporated. The residue was chromatographed (SiO_2, hexane/MTBE 1:1, R_f = 0.37) to furnish olefin **9** (90 mg, 0.32 mmol, 63%) as colorless solid, m.p. 117–119 °C. $[\alpha]_D^{20}$ = 61.7 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.69–0.80 (m, 2 H), 0.76 (s, 3 H), 0.88–0.94 (m, 1 H), 0.90 (s, 3 H), 1.02–1.08 (m, 1 H), 1.27 (qd, J = 12.5, 6.2 Hz, 1 H), 1.36–1.51 (m, 6 H), 1.57 (s, 3 H), 1.58–1.73 (m, 3 H), 1.78–1.84 (m, 2 H), 2.00–2.11 (m, 2 H), 2.26–2.36 (m, 2 H), 3.62 (t, J = 7.8 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.07 (CH_3), 13.56 (CH_3), 18.02 (CH_3), 22.26 (CH_2), 22.56 (CH_2), 23.54 (CH_2), 30.37 (CH_2), 31.57 (CH_2), 35.41 (CH_2), 36.07 (CH), 36.67 (CH_2), 38.14 (CH_2), 43.17 (C), 49.72 (C), 50.59 (CH), 55.22 (CH), 81.85 (CH), 125.99 (C), 141.44 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3282 (br m), 2956 (m), 2921 (s), 2871 (m), 2840 (m), 1469 (w), 1448 (m), 1436 (m), 1378 (w), 1366 (w), 1349 (m), 1333 (w), 1318 (w), 1278 (w), 1261 (w), 1205 (w), 1183 (w), 1160 (w), 1133 (m), 1114 (m), 1075 (m), 1054 (s), 1034 (m), 1018 (m), 987 (w), 963 (w), 937 (w), 923 (w), 910 (w), 892 (w), 875 (w), 830 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 274 (21) $[M]^+$, 259 (100), 241 (7), 164 (6), 147 (12), 122 (10), 109 (14), 93 (14). HRMS (EI): calcd. for $C_{19}H_{30}O$ $[M]^+$ 274.2297; found 274.2299.

17β-Hydroxy-3-methyl-A-*nor*-5β-androstane (11a): A suspension of olefin **9** (90 mg, 0.32 mmol) and Pd/C (35 mg, 33 µmol, 10% w/w Pd) in EtOAc (8 mL) was hydrogenated with H_2 (3 bar) for 16 h at 60 °C. The mixture was filtered through SiO_2 (hexane/MTBE 1:1, R_f = 0.41), and the solvent was evaporated to yield **11a** (83 mg, 0.30 mmol, 94%) as a colorless solid, m.p. 69 °C. $[\alpha]_D^{20}$ = 45.2 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.73 (s, 3 H), 0.83–0.98 (m, 3 H), 0.90 (d, J = 6.6 Hz, 3 H), 0.94 (s, 3 H), 1.00–1.06 (m, 2 H), 1.09–1.16 (m, 1 H), 1.20–1.34 (m, 4 H),1.36–1.43 (m, 2 H), 1.45–1.50 (m, 2 H), 1.52–1.60 (m, 3 H), 1.65–1.70 (m, 1 H), 1.76–1.86 (m, 2 H), 1.95–2.07 (m, 2 H), 3.61 (t, J = 8.5 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.18 (CH_3), 20.27 (CH_3), 21.83 (CH_2), 21.87 (CH_3), 21.88 (CH_2), 23.40 (CH_2), 26.13 (CH_2), 30.60 (CH_2), 30.76 (CH_2), 33.62 (CH), 36.25 (CH), 36.91 (CH_2), 37.09 (CH_2), 43.19 (C), 43.84 (C), 45.50 (CH), 51.10 (CH), 55.68 (CH), 81.98 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 3328 (br w), 2946 (m), 2927 (m), 2866 (m), 1449 (m), 1373 (m), 1345 (w), 1321 (w), 1310 (w), 1246 (w), 1205 (w), 1121 (m), 1051 (s), 1036 (m), 994 (w), 963 (w), 927 (w), 906 (w), 863 (w), 831 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 276 (63) $[M]^+$, 261 (25), 244 (7), 234 (14), 218 (16), 217 (100), 203 (7), 201 (6), 163 (8), 149 (46), 122 (16), 109 (37), 81 (26), 67 (18), 55 (21). HRMS (EI): calcd. for $C_{19}H_{32}O$ $[M]^+$ 276.2453; found 276.2448.

3-Methyl-A-*nor*-5β-androstan-17-one (12a): PCC (83 mg, 0.38 mmol) was added to a solution of alcohol **11a** (43 mg, 0.16 mmol) in CH_2Cl_2 (5 mL). The solution was stirred for 16 h at ambient temperature, then treated with MTBE (10 mL) and filtered through a short pad of SiO_2 (washed with 100 mL MTBE). The solvent was removed under vacuum to give ketone **12a** (44 mg, 0.16 mmol, 99%) as a crystalline solid (m.p. 96 °C), which was used without further purification. $[\alpha]_D^{20}$ = 108.3 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85 (s, 3 H), 3.02 (d, J = 7.1 Hz, 3 H), 0.95 (s, 3 H), 1.00–1.17 (m, 3 H), 1.19–1.45 (m, 6 H), 1.46–1.64 (m, 5 H), 1.65–1.70 (m, 1 H), 1.76–1.86 (m, 2 H), 1.89–1.94 (m, 1 H), 1.96–2.08 (m, 2 H), 2.42 (dd, J = 19.3, 9.0 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 13.80 (CH_3), 20.22 (CH_3), 21.49 (CH_2), 21.74 (CH_3), 21.76 (CH_2), 21.77 (CH_2), 25.45 (CH_2), 30.68 (CH_2), 31.89 (CH_2), 33.59 (CH), 35.71 (CH), 35.91 (CH_2), 36.85 (CH_2), 43.86 (C), 45.52 (CH), 47.99 (C), 51.54 (CH), 55.58 (CH), 221.42 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2950 (m), 2931 (m), 2899 (m), 2862

(m), 2821 (w), 1736 (vs), 1455 (m), 1408 (w), 1380 (m), 1339 (w), 1304 (w), 1291 (w), 1269 (w), 1212 (w), 1170 (w), 1150 (w), 1116 (w), 1063 (m), 1053 (m), 1015 (m), 966 (w), 916 (w), 899 (w), 863 (w), 833 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 274 (100) $[M]^+$, 259 (20), 242 (10), 230 (39), 203 (41), 164 (6), 149 (15), 121 (11), 109 (37), 108 (43), 95 (26), 81 (21). HRMS (EI): calcd. for $C_{19}H_{30}O$ $[M]^+$ 274.2297; found 274.2295.

3β-Methyl-A-*nor*-5β-androstane (4a): A solution of ketone **11a** (30 mg, 0.11 mmol), $H_2NN_2H{\cdot}H_2O$ (0.2 mL, 1.1 mmol, 65% hydrazine), and toluene (1 mL) was heated to 100 °C for 2 h. DEG (4 mL) was added, and the toluene was removed by distillation. The reaction mixture was treated with KOH (15 mg, 0.27 mmol) and then stirred at 200 °C for 16 h. After cooling to ambient temperature, the solution was diluted with brine (10 mL) and extracted with hexane (2× 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. After chromatography (SiO_2, hexane, R_f = 0.76), the hydrocarbon **4a** (12 mg, 46 μmol, 41%) was obtained as a colorless oil. $[\alpha]_D^{20}$ = 60 (CH_2Cl_2, 1 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.69 (s, 3 H), 0.88–0.93 (m, 1 H), 0.91 (d, *J* = 6.1 Hz, 3 H), 0.95 (s, 3 H), 0.98–1.06 (m, 2 H), 1.07–1.16 (m, 5 H), 1.18–1.25 (m, 2 H), 1.27–1.36 (m, 2 H), 1.39–1.46 (m, 3 H), 1.53–1.57 (m, 2 H), 1.61–1.72 (m, 4 H), 1.80–1.88 (m, 1 H), 1.97–2.07 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 17.57 (CH_3), 20.33 (CH_3), 20.61 (CH_2), 21.95 (CH_3), 22.08 (CH_2), 22.30 (CH_2), 25.53 (CH_2), 26.98 (CH_2), 30.83 (CH_2), 33.65 (CH), 36.56 (CH), 36.97 (CH_2), 39.27 (CH_2), 40.50 (CH_2), 41.09 (C), 43.94 (C), 45.63 (CH), 54.68 (CH), 55.71 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 2947 (m), 2925 (m), 2858 (m), 1451 (m), 1376 (m), 1297 (w), 1260 (w), 1215 (w), 1191 (w), 1162 (w), 1088 (w), 1063 (w), 1015 (w), 968 (w), 946 (w), 928 (w), 911 (w), 902 (w), 799 (w) cm^{-1}. MS (EI, 70 eV): *m/z* (%) = 260 (50) $[M]^+$, 245 (46), 232 (7), 217 (40), 203 (100), 189 (22), 175 (59), 161 (10), 149 (34), 135 (38), 121 (22), 109 (24), 107 (25), 95 (58), 81 (34), 67 (20). HRMS (EI): calcd. for $C_{19}H_{32}$ $[M]^+$ 260.2504; found 260.2501.

Four Isomers of 3-Methyl-A-*nor*-androstan-17β-ol (11): TFA (2.47 g, 21.7 mmol) was added to a solution of olefin **9** (149 mg, 0.54 mmol) in CH_2Cl_2 (20 mL) at –20 °C. The solution was stirred for 10 min, treated with Et_3SiH (1.26 g, 10.9 mmol) at –20 °C, and then stirred for 16 h at ambient temperature. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3× 20 mL). The solvent was removed under vacuum to give the trifluoroacetates of the title compounds (186 mg, 0.49 mmol) as a mixture of four diastereomers (ratio a/b/c/d 27:8:53:12), which were analyzed by GC–MS (EI, 70 eV). (a): *m/z* (%) = 372 (6) $[M]^+$, 357 (7), 315 (15), 287 (6), 258 (10), 243 (20), 217 (18), 201 (25), 173 (13), 149 (32), 133 (22), 109 (40), 95 (100), 81 (91), 69 (69), 55 (91); (b): *m/z* (%) = 372 (4) $[M]^+$, 357 (28), 315 (23), 287 (7), 258 (13), 243 (72), 217 (25), 201 (25), 173 (14), 149 (74), 133 (22), 109 (42), 95 (67), 81 (100), 81 (90), 69 (87), 55 (95); (c): *m/z* (%) = 372 (5) $[M]^+$, 357 (5), 344 (9), 315 (47), 287 (3), 258 (5), 243 (14), 217 (14), 201 (47), 173 (7), 149 (21), 133 (20), 109 (29), 107 (46), 95 (67), 81 (95), 69 (78), 55 (100); (d): *m/z* (%) = 372 (8) $[M]^+$, 357 (5), 330 (4), 315 (25), 287 (15), 258 (5), 243 (25), 217 (10), 201 (22), 173 (21), 149 (26), 133 (19), 109 (29), 107 (32), 95 (62), 81 (82), 69 (86), 55 (100). The trifluoroacetates were then treated with a solution of KOH (10 mL, 10% w/w in MeOH/H_2O, 9:1), and the mixture was stirred for 30 min at ambient temperature. The reaction mixture was diluted with H_2O (20 mL) and extracted with MTBE (3× 50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under vacuum to give alcohol **11** (135 mg, 0.49 mmol, 90%) as a colorless oil. Two peaks [a/b 23:77] were detected by GC–MS (EI, 70 eV). (a): *m/z* (%) = 276 (17) $[M]^+$, 261 (19), 217 (100), 203 (7), 175 (7), 166 (11), 149 (55), 147 (22), 133 (12), 121 (19), 109 (45), 95 (45), 81 (54), 67 (46), 55 (51); (b): *m/z* (%) = 276 (18) $[M]^+$, 261 (22), 243 (7), 217 (100), 201 (29), 175 (13), 166 (15), 149 (43), 147 (21), 133 (14), 121 (27), 109 (41), 107 (43), 95 (44), 81 (71), 79 (59), 67 (48), 55 (73).

Four Isomers of 3-Methyl-A-*nor*-5β-androstan-17-one (12): PCC (142 mg, 0.66 mmol) was added to a solution of alcohol **11** (73 mg, 0.26 mmol) in CH_2Cl_2 (10 mL). The solution was stirred for 16 h at ambient temperature, treated with MTBE (20 mL), and filtered through a short pad of SiO_2 (washed with 100 mL MTBE). The solvent was removed under vacuum to obtain ketone **12** (70 mg, 0.25 mmol, 99%) as a mixture of four diastereomers [ratio **12a/**b/c/d 27:8:53:12]. GC–MS (EI, 70 eV): **12a**: *m/z* (%) = 274 (100) $[M]^+$, 259 (20), 242 (10), 230 (39), 203 (41), 164 (6), 149 (15), 121 (11), 109 (37), 108 (43), 95 (26), 81 (21); (b): *m/z* (%) = 274 (28) $[M]^+$, 259 (18), 241 (22), 230 (16), 217 (21), 203 (55), 199 (9), 189 (5), 175 (9), 161 (21), 149 (45), 147 (33), 133 (24), 122 (35), 108 (84), 95 (66), 93 (72), 81 (80), 79 (82), 67 (100); (c): *m/z* (%) = 274 (36) $[M]^+$, 259 (11), 241 (19), 230 (40), 217 (31), 203 (43), 199 (26), 189 (11), 175 (12), 161 (30), 149 (33), 147 (30), 133 (22), 121 (47), 108 (91), 95 (87), 93 (86), 81 (76), 79 (85), 67 (100); (d): *m/z* (%) = 274 (30) $[M]^+$, 259 (13), 241 (15), 230 (17), 217 (17), 203 (45), 199 (7), 189 (9), 175 (13), 161 (19), 149 (35), 147 (41), 133 (24), 122 (39), 108 (100), 109 (98), 95 (61), 93 (75), 81 (67), 79 (86), 67 (970).

Four Isomers of 3-Methyl-A-*nor*-5β-androstane (4): A solution of ketone **12** [62 mg, 0.23 mmol; four isomers, ratio **12a/b/c/d** 27:8:53:12], KOH (32 mg, 0.58 mmol), and $H_2NNH_2{\cdot}H_2O$ (111 mg, 2.23 mmol) in DEG (5 mL) was heated for 16 h to 200–220 °C. After cooling to ambient temperature, the mixture was diluted with brine (15 mL) and extracted with MTBE (3× 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated after filtration. The residue was purified by chromatography (SiO_2, hexane/MTBE 1:1, R_f = 0.62) to yield **4** (12 mg, 46 μmol, 20%; four isomers, ratio **4a**/b/c/d 27:8:53:12) as a colorless oil. MS (EI, 70 eV): **4a**: *m/z* (%) = 260 (50) $[M]^+$, 245 (46), 232 (7), 217 (40), 203 (100), 189 (22), 175 (59), 161 (10), 149 (34), 135 (38), 121 (22), 109 (24), 107 (25), 95 (58), 81 (34), 67 (20); isomer b: *m/z* (%) = 260 (26) $[M]^+$, 245 (74), 232 (5), 217 (26), 203 (100), 189 (23), 175 (34), 163 (10), 149 (55), 135 (30), 121 (17), 107 (20), 95 (35), 81 (24), 67 (18), 55 (13); isomer c: *m/z* (%) = 260 (10) $[M]^+$, 245 (12), 232 (10), 217 (13), 203 (100), 189 (9), 175 (9), 161 (6), 149 (12), 135 (13), 121 (12), 107 (17), 95 (22), 81 (16), 67 (10); isomer d: *m/z* (%) = 260 (29) $[M]^+$, 245 (22), 232 (3), 217 (10), 203 (100), 189 (10), 175 (40), 162 (10),149 (33), 135 (22), 121 (11), 107 (13), 95 (25), 81 (17), 67 (13), 55 (10).

5α-Androstan-17β-ol (14):[14] A solution of dihydrotestosterone (**13**, 2.00 g, 6.89 mmol), KOH (965 mg, 17.2 mmol), and $H_2NNH_2{\cdot}H_2O$ (3.45 g, 68.9 mmol) in DEG (35 mL) was heated for 16 h to 200–220 °C. After cooling to ambient temperature, the mixture was diluted with hydrochloric acid (ca. 15 mL, 2 mol/L) and extracted with MTBE (3× 100 mL). The combined organic layers were dried ($MgSO_4$) and concentrated after filtration. The residue was purified by chromatography (SiO_2, hexane/MTBE 2:1, R_f = 0.38) to yield **14** (1.63 g, 5.90 mmol, 86%) as a colorless solid, m.p. 160 °C. $[\alpha]_D^{20}$ = 11.7 (CH_2Cl_2, 1 g dm^{-3}). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.66 (td, *J* = 12.3, 4.1 Hz, 1 H), 0.73 (s, 3 H), 0.79 (s, 3 H), 0.84–0.98 (m, 3 H), 1.01–1.06 (m, 2 H), 1.15–1.30 (m, 8 H), 1.35–1.45 (m, 3 H), 1.48–1.68 (m, 6 H), 1.78 (dt, *J* = 12.2, 3.1 Hz, 1 H), 2.01–2.08 (m, 1 H), 3.63 (t, *J* = 8.0 Hz, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.12 (CH_3), 12.23 (CH_3), 20.36 (CH_2), 22.15 (CH_2), 23.35 (CH_2), 26.78 (CH_2), 28.92 (CH_2), 29.02 (CH_2), 30.50 (CH_2), 31.71 (CH_2), 35.55 (CH), 36.32 (C), 36.80 (CH_2),

38.70 (CH_2), 42.96 (C), 47.09 (CH), 51.12 (CH), 54.87 (CH), 82.01 (CH, C-17) ppm. IR (ATR): $\tilde{\nu}$ = 3276 (br m), 2975 (w), 2918 (s), 2868 (m), 2845 (m), 1468 (w), 1447 (w), 1375 (w), 1353 (w), 1336 (w), 1323 (w), 1246 (w), 1136 (w), 1116 (w), 1087 (w), 1053 (s), 1010 (m) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 276 (74) $[M]^+$, 261 (36), 219 (18), 217 (100), 203 (9), 166 (11), 150 (23), 149 (72), 109 (48), 81 (36), 55 (33), 41 (16). HRMS (EI): calcd. for $C_{19}H_{32}O$ $[M]^+$ 276.2453; found 276.2460.

5α-Androstan-17β-yl-4-toluenesulfonate (16):[15] A solution of alcohol **14** (3.50 g, 12.7 mmol), *p*-TosCl (9.68 g, 50.8 mmol), and 4-dimethylaminopyridine (DMAP, 155 mg, 1.27 mmol) in absolute pyridine (40 mL) was stirred for 5 d at 55 °C. The solution was diluted with MTBE (100 mL) and washed successively with hydrochloric acid (1 mol/L, 100 mL), H_2O (100 mL), saturated $NaHCO_3$ solution (100 mL), and water (100 mL). The organic phase was dried ($MgSO_4$) and filtered. After evaporation of the solvent, the crude solid was recrystallized from MeOH (ca. 200 mL) to give tosylate **16** (4.61 g, 10.7 mmol, 84%) as a colorless solid, m.p. 137 °C. $[\alpha]_D^{20}$ = –8.3 (MTBE, 1 g dm^{-3}). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.56–0.61 (m, 1 H), 0.75 (s, 3 H), 0.77 (s, 3 H), 0.80–0.91 (m, 4 H), 0.96–1.02 (m, 1 H), 1.11–1.30 (m, 6 H), 1.31–1.43 (m, 2 H), 1.47–1.68 (m, 9 H), 1.87–1.95 (m, 1 H), 2.44 (s, 3 H), 4.24 (t, *J* = 8.4 Hz, 1 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 7.77 (d, *J* = 8.2 Hz, 2 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 11.77 (CH_3), 12.15 (CH_3), 20.03 (CH_2), 21.61 (CH_3), 22.07 (CH_2), 23.23 (CH_2), 26.70 (CH_2), 27.65 (CH_2), 28.74 (CH_2), 28.92 (CH_2), 31.47 (CH_2), 35.18 (C), 36.17 (CH), 36.24 (CH_2), 38.62 (CH_2), 43.00 (C), 46.95 (CH), 50.05 (CH), 54.53 (CH), 90.17 (CH), 127.78 (2 × CH), 129.60 (2 × CH), 134.29 (C), 144.29 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2971 (w), 2921 (m), 2904 (w), 2879 (w), 2846 (w), 1598 (w), 1444 (w), 1371 (m), 1358 (s), 1292 (w), 1188 (m), 1171 (s), 1097 (m), 993 (m), 966 (s), 889 (m), 868 (s), 844 (m), 827 (m), 814 (s), 667 (s), 575 (s), 551 (s) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 430 (10) $[M]^+$, 415 (11), 258 (100), 243 (61), 217 (27), 175 (9), 161 (17), 149 (56), 148 (59), 121 (17), 109 (33). HRMS (EI): calcd. for $[M]^+$ $C_{26}H_{38}O_3S$ 430.2542; found 430.2537.

17-Methyl-18-*nor*-5α-androst-13(17)-ene (15):[14] EtMgBr (19.5 mmol, 6.50 mL, 3 M solution in Et_2O) was added to a stirred solution of tosylate **16** (1.68 g, 3.90 mmol) in absolute toluene (20 mL) at 100 °C. After the Et_2O was removed by distillation, the suspension was stirred for 4 h at 110 °C. The suspension was cooled to 0 °C, treated with cold water (10 mL), and extracted with MTBE (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated after filtration under high vacuum to give a mixture of olefins (all with *m*/*z* = 258, GC–MS; 919 mg, 3.56 mmol, 91%) containing compound **15** in 80% purity. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.21 (CH_3), 13.44 (CH_3), 22.25 (CH_2), 25.30 (CH_2), 25.77 (CH_2), 26.84 (CH_2), 28.18 (CH_2), 28.86 (CH_2), 29.06 (CH_2), 32.52 (CH_2), 36.39 (C), 37.16 (CH_2), 38.87 (CH_2), 45.46 (CH), 46.61 (CH), 52.78 (CH), 54.01 (CH), 127.34 (C), 136.82 (C) ppm. MS (EI, 70 eV): *m*/*z* (%) = 258 (44) $[M]^+$, 243 (25), 201 (7), 188 (7), 175 (6), 162 (10), 161 (12), 149 (59), 148 (64), 133 (21), 119 (20), 107 (40), 94 (100), 79 (88), 67 (45), 55 (51).

Five Isomers of 17-Methyl-18-*nor*-androstane (5): A suspension of **15** (50 mg, 0.19 mmol; 80% purity) and Pd/C (10 mg, 10 μmol, 10% w/w Pd) in EtOAc (1 mL) was hydrogenated with H_2 (1 atm) at ambient temperature for 6 d. The mixture was filtered through SiO_2 (washed with 50 mL MTBE), and the solvent was removed under vacuum to give a mixture of five isomers of **5** [44 mg, 0.17 mmol, 89%; ratio a/b (**5a**)/c/d/e 53:6:7:18:9] as a colorless oil, which was analyzed by GC–MS. GC–MS (EI, 70 eV): (a): *m*/*z* (%) = 260 (62) $[M]^+$, 245 (40), 231 (5), 218 (4), 217 (3), 204 (55), 203 (100), 189 (12), 175 (13), 164 (9), 163 (11), 162 (8), 161 (18), 149 (32), 148 (28), 135 (51), 121 (21), 109 (31), 107 (37), 95 (52), 81 (49), 67 (32), 55 (17); (b, **5a**): *m*/*z* (%) = 260 (49) $[M]^+$, 245 (39), 231 (5), 218 (2), 217 (2), 204 (41), 203 (100), 189 (9), 175 (10), 164 (22), 163 (12), 162 (4), 161 (16), 149 (29), 148 (23), 135 (80), 121 (28), 107 (41), 95 (57), 81 (58), 67 (40), 55 (21); (c): *m*/*z* (%) = 260 (59) $[M]^+$, 245 (100), 232 (6), 218 (13), 217 (37), 204 (40), 203 (72), 190 (15), 189 (30), 175 (16), 164 (9), 163 (15), 162 (7), 161 (18), 149 (50), 148 (25), 135 (50), 121 (36), 109 (44), 107 (41), 95 (80), 81 (54), 67 (43), 55 (25); (d): *m*/*z* (%) = 260 (53) $[M]^+$, 245 (41), 218 (4), 217 (3), 204 (51), 203 (100), 189 (13), 175 (9), 164 (9), 163 (11), 162 (6), 161 (17), 149 (27), 148 (24), 135 (57), 121 (22), 109 (31), 107 (34), 95 (52), 81 (47), 67 (31), 55 (18); (e): *m*/*z* (%) = 260 (56) $[M]^+$, 245 (35), 231 (7), 218 (9), 217 (4), 204 (37), 203 (95), 189 (11), 175 (15), 164 (20), 163 (11), 162 (7), 161 (21), 149 (44), 148 (30), 135 (100), 121 (40), 109 (36), 107 (48), 95 (73), 81 (66), 67 (45), 55 (29).

17-Methyl-5α-androst-13-en-16-one (17): Anhydrous CrO_3 (774 mg, 7.74 mmol) was added to a solution of absolute pyridine (1.22 g, 15.5 mmol) in absolute CH_2Cl_2 (4 mL) at 0 °C. The mixture was stirred for 10 min at 0 °C and then for 40 min at ambient temperature. After the addition of a solution of olefin **15** (100 mg, 0.39 mmol) in absolute CH_2Cl_2 (0.5 mL), the reaction mixture was stirred for 16 h at ambient temperature. After decantation from the brown precipitate, the solution was treated with MTBE (10 mL). The mixture was filtered through a short pad of SiO_2 (washed with 100 mL MTBE), and the resulting filtrate was concentrated under vacuum. The residue was chromatographed (SiO_2, hexane/MTBE 1:1, R_f = 0.26) to give enone **17** (36 mg, 0.13 mmol, 34%) as a colorless solid, m.p. 121 °C. $[\alpha]_D^{20}$ = 30 (CH_2Cl_2, 1 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.70 (s, 3 H), 0.95 (td, *J* = 13.1, 4.1 Hz, 1 H), 1.04–1.16 (m, 5 H), 1.18–1.29 (m, 5 H), 1.36–1.45 (m, 1 H), 1.48–1.56 (m, 1 H), 1.65 (s, 3 H), 1.68–1.75 (m, 2 H), 1.79–1.85 (m, 1 H), 1.96–2.13 (m, 3 H), 2.16–2.22 (m, 1 H), 2.49 (dd, *J* = 18.5, 6.5 Hz, 1 H), 2.83–2.85 (m, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 7.55 (CH_3), 12.06 (CH_3), 22.00 (CH_2), 25.61 (CH_2), 26.66 (CH_2), 28.38 (CH_2), 28.58 (CH_2), 28.78 (CH_2), 33.10 (CH_2), 36.50 (C), 38.70 (CH_2), 39.94 (CH_2), 44.72 (CH), 46.55 (CH), 46.94 (CH), 52.58 (CH), 132.16 (C), 175.45 (C), 209.27 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2975 (w), 2920 (m), 2857 (m), 1693 (s), 1633 (s), 1451 (m), 1441 (m), 1398 (w), 1385 (w), 1357 (w), 1341 (w), 1327 (w), 1311 (w), 1295 (w), 1285 (w), 1267 (w), 1251 (w), 1238 (w), 1200 (w), 1733 (w), 1153 (w), 1095 (w), 1064 (w), 1027 (w), 985 (w), 968 (w), 909 (w), 891 (w), 845 (w) cm^{-1}. MS (EI, 70 eV): *m*/*z* (%) = 272 (100) $[M]^+$, 244 (13), 175 (6), 162 (16), 149 (42), 135 (9), 110 (50), 79 (10), 67 (9), 55 (8). HRMS (EI, 70 eV): calcd. for $C_{19}H_{28}O$ $[M]^+$ 272.2140; found 272.2143.

17-Methyl-5α-androstan-16-one (18a and 18b): A suspension of enone **17** (200 mg, 0.73 mmol) and Pd/C (78 mg, 73 μmol, 10% w/w Pd) in EtOAc (10 mL) was hydrogenated (4 bar H_2) for 3 d at 40 °C. The mixture was filtered through SiO_2 (washed with 100 mL MTBE). The solvent was removed under vacuum, and the crude material was chromatographed (SiO_2, hexane/MTBE 5:1) to give ketone **18b** (40 mg, 15 mmol, 20%) in the first fraction (R_f = 0.53) as a colorless solid. The second fraction (R_f = 0.42–0.53) was a mixture of ketones **18a** and **18b** [120 mg, 0.44 mmol, 60%, **18a**/**18b** 70:30 (by ^{13}C NMR)]. The mixed fraction was chromatographed three times to give pure ketone **18a** (68 mg, 0.25 mmol, 35%) as a colorless solid and another portion of ketone **18b** (28 mg, 0.10 mmol, 13%). Isomer **18a**: M.p. 76 °C. $[\alpha]_D^{20}$ = 35 (CH_2Cl_2, 1 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.68 (s, 3 H), 0.82–0.90 (m, 3 H), 0.99–1.06 (m, 2 H), 1.07 (d, *J* = 7.6 Hz, 3 H), 1.12–1.25 (m, 6 H), 1.32–1.41 (m, 1 H), 1.47–1.49 (m, 1 H), 1.57–1.70 (m, 5 H),

1.81–1.86 (m, 2 H), 2.17 (dd, J = 18.4, 3.2 Hz, 1 H), 2.32 (pent, J = 8.0 Hz, 1 H), 2.41–2.46 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.05 (CH_3), 13.06 (CH_3), 21.66 (CH_2), 21.92 (CH_2), 23.39 (CH_2), 26.64 (CH_2), 28.57 (CH_2), 28.89 (CH_2), 33.38 (CH_2), 36.47 (C), 37.42 (CH), 38.14 (CH), 38.54 (CH_2), 42.68 (CH), 43.64 (CH_2), 45.46 (CH), 46.45 (CH), 49.90 (CH), 223.04 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2971 (w), 2934 (m), 2919 (m), 2848 (m), 1732 (vs), 1455 (w), 1444 (w), 1408 (w), 1380 (w), 1370 (w), 1353 (w), 1309 (w), 1281 (w), 1158 (w), 1145 (w), 1131 (w), 1039 (w), 1024 (w), 1000 (w), 977 (w), 957 (w), 918 (w), 898 (w), 852 (w), 795 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 274 (100) $[M]^+$, 259 (21), 245 (5), 217 (42), 203 (11), 189 (10), 175 (6), 163 (40), 149 (15), 135 (7), 123 (8), 121 (11), 110 (19), 95 (20), 86 (30), 84 (48), 67 (23), 55 (20), 49 (51). HRMS (EI): calcd. for $C_{19}H_{30}O$ $[M]^+$ 274.2291; found 274.2283. Isomer **18b**: M.p. 64 °C. $[\alpha]_D^{20}$ = 58 (CH_2Cl_2, 1 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.69 (s, 3 H), 0.78 (td, J = 11.0, 2.0 Hz, 1 H), 0.84–0.91 (m, 2 H), 1.01 (d, J = 7.0 Hz, 3 H), 1.02–1.26 (m, 8 H), 1.34–1.44 (m, 1 H), 1.49–1.52 (m, 1 H), 1.58–1.67 (m, 3 H), 1.72–1.86 (m, 5 H), 2.07–2.14 (m, 1 H), 2.19–2.29 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.13 (CH_3), 12.70 (CH_3), 18.85 (CH_2), 22.03 (CH_2), 25.65 (CH_2), 26.67 (CH_2), 28.77 (CH_2), 28.89 (CH_2), 32.52 (CH_2), 36.34 (C), 36.88 (CH), 38.50 (CH_2), 41.74 (CH), 42.96 (CH), 43.60 (CH_2), 43.75 (CH), 46.59 (CH), 52.74 (CH), 222.05 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2979 (w), 2918 (m), 2874 (m), 2853 (w), 1730 (vs), 1442 (m), 1402 (w), 1374 (w), 1175 (w), 1154 (w), 1133 (w), 1061 (w), 1061 (w), 1038 (w), 1011 (w), 978 (w), 959 (w), 902 (w), 869 (w), 844 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 274 (44) $[M]^+$, 259 (10), 217 (29), 203 (9), 189 (9), 175 (5), 163 (58), 149 (21), 147 (16), 133 (11), 123 (19), 110 (48), 95 (69), 81 (96), 67 (100), 55 (85). HRMS (EI): calcd. for $C_{19}H_{30}O$ $[M]^+$ 274.2297; found 274.2288.

17α-Methyl-5α-androstane-16-(2,4-dinitrophenyl)hydrazone (19): A solution of ketone **18b** (20 mg, 7.3 μmol) in EtOH (2.5 mL) was added to a solution of 2,4-dinitrophenylhydrazine (100 mg, 0.50 mmol) and H_2SO_4 (0.5 mL) in H_2O (0.75 mL). The reaction mixture was stirred for 10 min at 23 °C. The orange precipitate was collected by filtration, washed with EtOH/H_2O (5 mL, 1:1), and dried in high vacuum to give phenylhydrazone **19b** (20 mg, 4.4 μmol, 60%) as an orange solid, m.p. 154 °C. Single crystals were obtained from CH_2Cl_2/hexane. ^1H NMR (500 MHz, $CDCl_3$): δ = 0.70 (s, 3 H), 0.76–0.80 (m, 1 H), 0.86–0.96 (m, 2 H), 1.01–1.16 (m, 4 H), 1.19 (d, J = 6.5 Hz, 3 H), 1.22–1.30 (m, 4 H), 1.34–1.43 (m, 1 H), 1.50–1.53 (m, 1 H), 1.57–1.68 (m, 3 H), 1.73–1.75 (m, 2 H), 1.81–1.91 (m, 3 H), 2.44–2.53 (m, 2 H), 2.62–2.70 (m, 1 H), 7.97 (d, J = 9.9 Hz, 1 H), 8.28 (dd, J = 9.9, 2.1 Hz, 1 H), 9.12 (d, J = 2.1 Hz, 1 H), 10.86 (s, 1 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.15 (CH_3), 15.10 (CH_3), 18.90 (CH_2), 22.02 (CH_2), 24.84 (CH_2), 26.63 (CH_2), 28.70 (CH_2), 28.85 (CH_2), 32.56 (CH_2), 32.96 (CH_2), 36.35 (CH), 36.88 (C), 38.43 (CH_2), 38.78 (CH), 43.77 (CH), 45.36 (CH), 46.51 (CH), 52.77 (CH), 116.29 (CH), 123.59 (CH), 128.72 (C), 129.91 (CH), 137.43 (C), 145.14 (C), 170.58 (C) ppm. IR (ATR): $\tilde{\nu}$ = 3314 (w), 3107 (w), 2920 (m), 2855 (m), 1623 (s), 1590 (s), 1519 (m), 1501 (m), 1426 (m), 1412 (m), 1366 (w), 1335 (s), 1333 (s), 1271 (s), 1269 (m), 1220 (m), 1134 (m), 1070 (m), 1050 (m), 1022 (m), 923 (m), 831 (m), 743 (m), 702 (m), 686 (m) cm^{-1}. MS (ESI+): m/z = 493 $[M + K]^+$, 477 $[M + Na]^+$, 455 $[M + H]^+$. HRMS (ESI): calcd. for $C_{25}H_{34}N_4NaO_4$ $[M + Na]^+$ 477.2478; found 477.2489.

17β-Methyl-18-*nor*-13α-androstane (5a): A suspension of ketones **18a** and **18b** [34 mg, 0.12 mmol; **18a/18b** 70:30], $H_2NNH_2{\cdot}H_2O$ (240 mg, 4.8 mmol, 65% hydrazine), and KOH (97 mg, 1.73 mmol) in DEG (1.5 mL) was heated for 16 h to 200 °C. After cooling to ambient temperature, the solution was diluted with hydrochloric acid (10 mL, 2 mol/L) and extracted with MTBE (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. The crude product was chromatographed (SiO_2, hexane, R_f = 0.77) to give **5a** (15 mg, 60 μmol, R_f = 0.80, 48%) in the first fraction as a colorless oil. In the second fraction, ketone **18b** (11 mg, 40 μmol, R_f = 0.47, 33%) was recovered. $[\alpha]_D^{20}$ = –31.7 (CH_2Cl_2, 1 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.66 (td, J = 11.1, 2.6 Hz, 1 H), 0.70 (s, 3 H), 0.73–0.88 (m, 3 H), 0.91 (d, J = 6.5 Hz, 3 H), 0.97–1.05 (m, 3 H), 1.08–1.16 (m, 2 H), 1.18–1.26 (m, 4 H), 1.31–1.35 (m, 1 H), 1.38–1.51 (m, 5 H), 1.62–1.80 (m, 5 H), 1.81–1.90 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.16 (CH_3), 19.21 (CH_3), 19.89 (CH_2), 22.15 (CH_2), 25.39 (CH_2), 26.84 (CH_2), 28.19 (CH_2), 29.09 (CH_2), 29.19 (CH_2), 32.72 (CH_2), 32.83 (CH_2), 33.72 (CH), 36.42 (C), 37.78 (CH), 38.62 (CH_2), 46.77 (CH), 47.29 (CH), 47.60 (CH), 53.17 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 2920 (s), 2853 (s), 1445 (m), 1378 (w), 1305 (w), 1259 (m), 1192 (w), 1162 (w), 1094 (m), 1030 (m), 974 (w), 958 (w), 930 (w), 922 (w), 840 (w) 801 (m), 705 (w), 686 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 260 (70) $[M]^+$, 245 (39), 231 (5), 204 (40), 203 (100), 189 (8), 175 (12), 164 (18), 161 (16), 149 (22), 148 (22), 135 (60), 121 (20), 109 (18), 107 (28), 95 (34), 81 (38), 67 (28), 55 (18). HRMS (EI): calcd. for $C_{19}H_{32}$ $[M]^+$ 260.2499; found 260.2491.

17α-Methyl-18-*nor*-13α-androstane (5b): A solution of ketone **18b** (48 mg, 0.17 mmol), $H_2NNH_2{\cdot}H_2O$ (85 mg, 1.7 mmol, 65% hydrazine), KOH (24 mg, 0.43 mmol), and toluene (2 mL) in DEG (8 mL) was heated to reflux for 5 h. The water/toluene azeotrope was removed by distillation, and the remaining reaction mixture was heated to 200 °C for 16 h. After cooling to ambient temperature, the solution was diluted with hydrochloric acid (5 mL, 2 M) and extracted with MTBE (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. The crude product was chromatographed (SiO_2, hexane, R_f = 0.77) to give **5b** (15 mg, 54 μmol, 32%) as a colorless oil. $[\alpha]_D^{20}$ = –45 (CH_2Cl_2, 3 g/l). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.65 (td, J = 11.4, 2.3 Hz, 1 H), 0.69 (s, 3 H), 0.72–0.88 (m, 2 H), 0.90 (d, J = 6.5 Hz, 3 H), 0.94–1.04 (m, 3 H), 1.07–1.15 (m, 2 H), 1.18–1.25 (m, 4 H), 1.30–1.35 (m, 1 H), 1.37–1.54 (m, 6 H), 1.61–1.80 (m, 5 H), 1.81–1.89 (m, 2 H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): δ = 12.16 (CH_3), 19.22 (CH_3), 19.85 (CH_2), 22.13 (CH_2), 25.35 (CH_2), 26.82 (CH_2), 28.13 (CH_2), 29.06 (CH_2), 29.16 (CH_2), 32.67 (CH_2), 32.80 (CH_2), 33.64 (CH), 36.38 (C), 37.73 (CH), 38.57 (CH_2), 46.71 (CH), 47.24 (CH), 47.55 (CH), 53.13 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 2919 (s), 2853 (s), 1445 (m), 1378 (m), 1351 (w), 1306 (w), 1264 (w), 1247 (w), 1192 (w), 1107 (w), 1086 (w), 1055 (w), 1029 (w), 975 (w), 958 (w), 930 (w), 922 (w), 893 (w), 844 (w), 794 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 260 (76) $[M]^+$, 245 (40), 231 (8), 218 (3), 217 (3), 204 (43), 203 (100), 189 (9), 175 (11), 164 (17), 161 (14), 149 (22), 148 (22), 135 (61), 121 (20), 109 (18), 107 (28), 95 (39), 81 (45), 67 (35), 55 (26). HRMS (EI): calcd. for $C_{19}H_{32}$ $[M]^+$ 260.2499; found 260.2504.

13,17-*seco*-18-*nor*-17-*homo*-Androsta-13,17-dione (20): A solution of the mixture of olefins containing **15** (470 mg, 1.82 mmol: 80% purity, 1.45 mmol of **15**) in absolute CH_2Cl_2 (5 mL) was added to a solution of $KMnO_4$ (711 mg, 4.50 mmol) and dry benzyltrimethylammonium chloride (835 mg, 4.50 mmol) in absolute CH_2Cl_2 (45 mL) at 23 °C. The solution was heated for 20 h to 40 °C. After cooling to ambient temperature, the solution was diluted with aqueous AcOH (50%, 50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvents were evaporated. The residue was chromatographed (SiO_2, hexane/MTBE 1:1, R_f = 0.37) to furnish diketone **20** (288 mg,

0.99 mmol, 68%) as a yellow oil. $[\alpha]_D^{20}$ = 6.7 (MTBE, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.70 (s, 3 H), 0.95 (td, J = 12.9, 3.9 Hz, 1 H), 1.05–1.43 (m, 11 H), 1.45–1.52 (m, 2 H), 1.63–1.73 (m, 3 H), 1.82–1.88 (m, 1 H), 1.96–1.99 (m, 1 H), 2.04–2.08 (m, 1 H), 2.10 (s, 3 H), 2.65 (td, J = 13.3, 5.5 Hz, 1 H), 2.34–2.40 (m, 2 H), 2.46–2.53 (m, 1 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.91 (CH_3), 19.38 (CH_2), 21.95 (CH_2), 26.39 (CH_2), 26.59 (CH_2), 28.52 (CH_2), 28.63 (CH_2), 29.83 (CH_3), 32.30 (CH_2), 36.62 (C), 38.67 (CH_2), 41.02 (CH_2), 41.99 (CH_2), 42.60 (CH), 46.11 (CH), 52.68 (CH), 54.84 (CH), 209.12 (C), 212.73 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2920 (m), 2854 (w), 1708 (vs), 1445 (w), 1354 (w), 1284 (w), 1213 (w), 1196 (w), 1162 (w), 1109 (w), 1089 (w), 960 (w), 925 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 290 (100) $[M]^+$, 272 (33), 257 (14), 233 (33), 220 (50), 219 (53), 149 (22), 109 (56). HRMS (EI): calcd. for $C_{19}H_{30}O_2$ $[M]^+$ 290.2246; found 290.2240.

D-*homo*-Androst-13(17a)-en-17-one (21): Aqueous NaOH solution (10%, 0.04 mL) was added to a solution of diketone **20** (300 mg, 1.03 mmol) in MeOH/H_2O (10:1, 11 mL), and the resulting mixture was subsequently stirred for 7 h at 40 °C. Water (20 mL) was then added, and the mixture was allowed to stand at ambient temperature for 16 h. The precipitate was collected by filtration and washed with H_2O (5 mL). The crude solid was purified by chromatography (SiO_2, hexane/MTBE 2:1; R_f = 0.43) to give compound **21** (196 mg, 0.71 mmol, 69%) as a colorless solid, m.p. 143 °C. $[\alpha]_D^{20}$ = –43.3 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.69 (s, 3 H), 0.90 (td, J = 12.9, 3.9 Hz, 1 H), 0.95–1.31 (m, 10 H), 1.34–1.42 (m, 1 H), 1.46–1.57 (m, 2 H), 1.65–1.72 (m, 2 H), 1.90–2.01 (m, 3 H), 2.12–2.27 (m, 3 H), 2.23–2.45 (m, 2 H), 5.77 (br s, 1 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 11.92 (CH_3), 21.90 (CH_2), 25.61 (CH_2), 26.23 (CH_2), 26.56 (CH_2), 28.57 (CH_2), 28.63 (CH_2), 31.51 (CH_2), 35.95 (CH_2), 36.42 (C), 36.43 (CH_2), 38.55 (CH_2), 43.25 (CH), 43.87 (CH), 46.00 (CH), 52.63 (CH), 123.79 (CH), 167.03 (C), 199.99 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2947 (m), 2918 (m), 2855 (m), 2811 (w), 1663 (vs), 1620 (m), 1466 (w), 1445 (w), 1429 (w), 1380 (w), 1361 (w), 1261 (m), 1209 (m), 1178 (w), 1122 (w), 970 (w), 957 (w), 902 (w), 880 (m) cm^{-1}. MS (EI, 70 eV): m/z (%) = 272 (48) $[M]^+$, 230 (16), 163 (50), 164 (22), 149 (21), 135 (14), 110 (100). HRMS (EI): calcd. for $C_{19}H_{28}O$ $[M]^+$ 272.2140; found 272.2137.

D-*homo*-Androstan-17-ones (22a and 22b): A suspension of enone **21** (40 mg, 0.15 mmol) and Pd/C (8 mg, 7 μmol, 10% w/w Pd) in pyridine (3 mL) was hydrogenated for 24 h with H_2 (4 bar) at ambient temperature. The mixture was filtered through SiO_2 (washed with 100 mL MTBE). After evaporation of the solvent, the crude product was chromatographed (hexane/MTBE 4:1, R_f = 0.42–0.39) to give the ketones **22a** and **22b** (ratio 3.3:1, 27 mg, 0.10 mmol, 67%) as a colorless oil. Isomer **22a**: ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 12.78 (CH_3), 19.54 (CH_2), 22.51 (CH_2), 27.08 (CH_2), 27.85 (CH_2), 29.22 (CH_2), 29.37 (CH_2), 31.33 (CH_2), 31.42 (CH_2), 31.95 (CH), 38.81 (C), 37.00 (CH_2), 38.53 (CH), 38.93 (CH_2), 42.00 (CH), 43.34 (CH_2), 46.73 (CH), 54.18 (CH), 213.17 (C) ppm. MS (EI, 70 eV): m/z (%) = 274 (60) $[M]^+$, 259 (15), 256 (30), 241 (32), 227 (4), 218 (33), 217 (49), 204 (23), 199 (27), 189 (11), 171 (9), 159 (13), 149 (100), 147 (30), 131 (21), 119 (17), 110 (22), 109 (24), 108 (25), 107 (26), 95 (35), 93 (29), 91 (35), 81 (50), 79 (40), 67 (40), 55 (25).

D-*homo*-Androstanes (6a and 6b): A suspension of ketones **22a** and **22b** (34 mg, 0.12 mmol), $H_2NNH_2{\cdot}H_2O$ (0.06 mL, 1.2 mmol, 65% hydrazine), and KOH (17 mg, 0.31 mmol) in DEG (1 mL) was heated to 200 °C for 16 h. After cooling to ambient temperature, the solution was diluted with hydrochloric acid (5 mL, 2 M) and extracted with hexane (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. After chromatography (SiO_2, hexane, R_f = 0.77), the alkanes **6a** and **6b** (ratio 3.3:1, 20 mg, 80 μmol, 65%) were obtained as a colorless oil. MS (EI, 70 eV), **6a**: m/z (%) = 260 (100) $[M]^+$, 245 (48), 231 (9), 218 (4), 204 (47), 203 (92), 189 (9), 175 (15), 164 (27), 149 (22), 148 (35), 135 (53), 121 (30), 109 (17), 107 (22), 95 (34), 81 (46), 67 (32), 55 (18); data for isomer **6b** vide infra.

D-*homo*-13β,14α-Androstan-17-one (22b): Absolute THF (1 mL) was added to a solution of Li (18 mg, 2.6 mmol) in NH_3 (4 mL) at –78 °C, and the resulting solution was stirred for 30 min. A solution of enone **21** (140 mg, 0.51 mmol) in absolute THF (3 mL) was then added dropwise. After 2.5 h of stirring at –78 to –50 °C, the reaction mixture was treated with solid NH_4Cl (275 mg, 5.14 mmol) in small portions. The solution was warmed to ambient temperature overnight, and the NH_3 evaporated. The slurry was dissolved in H_2O (5 mL) and extracted with MTBE (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvents were evaporated. The crude material was chromatographed (SiO_2, hexane/MTBE 4:1, R_f = 0.39) to give **22b** (107 mg, 0.39 mmol, 76%) as a colorless solid, m.p. 106 °C. $[\alpha]_D^{20}$ = –38.9 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.72 (s, 3 H), 0.78–1.30 (m, 14 H), 1.32–1.43 (m, 2 H), 1.49–1.52 (m, 1 H), 1.66–1.72 (m, 3 H), 1.78 (dq, J = 12.7, 3.2 Hz, 1 H), 1.98 (dq, J = 12.7, 3.2 Hz, 1 H), 2.02–2.07 (m, 1 H), 2.23–2.31 (m, 3 H), 2.35–2.40 (m, 1 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 12.09 (CH_3), 22.07 (CH_2), 24.67 (CH_2), 26.66 (CH_2), 28.77 (CH_2), 28.87 (CH_2), 30.35 (CH_2), 31.15 (CH_2), 34.43 (CH_2), 36.43 (C), 38.53 (CH_2), 40.90 (CH), 41.33 (CH_2), 43.30 (CH), 46.31 (CH), 47.50 (CH), 48.67 (CH_2), 53.40 (CH), 212.12 (C) ppm. IR (ATR): $\tilde{\nu}$ = 2950 (m), 2916 (s), 2851 (s), 1705 (vs), 1444 (m), 1419 (w), 1379 (w), 1326 (w), 1274 (w), 1263 (w), 1246 (w), 1205 (w), 1186 (w), 1103 (w), 1089 (w), 1024 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 274 (75) $[M]^+$, 259 (38), 256 (12), 241 (31), 230 (32), 218 (45), 217 (100), 201 (13), 199 (34), 189 (16), 175 (12), 171 (11), 162 (21), 149 (66), 147 (32), 131 (26), 119 (25), 110 (29), 109 (34), 108 (24), 107 (37), 105 (32), 95 (49), 93 (41), 91 (58), 81 (75), 79 (60), 67 (58), 55 (40). HRMS (EI): calcd. for $C_{19}H_{30}O$ $[M]^+$ 274.2297; found 274.2290.

D-*homo*-13β,14α-Androstane (6b): A mixture of ketone **22b** (40 mg, 0.15 mmol), $H_2NNH_2{\cdot}H_2O$ (0.07 mL, 1.5 mmol, 65% hydrazine), and KOH (21 mg, 0.38 mmol) in DEG (2 mL) was heated for 16 h to 200 °C. After cooling to ambient temperature, the solution was diluted with hydrochloric acid (10 mL, 2 mol/L) and extracted with hexane (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and filtered, and the solvent was removed under reduced pressure. After chromatography (SiO_2, hexane, R_f = 0.77), sterane **6b** (20 mg, 80 μmol, 53%) was obtained as a colorless solid, m.p. 53 °C. $[\alpha]_D^{20}$ = –21.7 (CH_2Cl_2, 1 g/l). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.54–0.61 (m, 1 H), 0.66–0.70 (m, 1 H), 0.71 (s, 3 H), 0.72–1.03 (m, 8 H), 1.10–1.25 (m, 8 H), 1.34–1.42 (m, 1 H), 1.47–1.51 (m, 1 H), 1.55–1.59 (m, 2 H), 1.63–1.73 (m, 5 H), 1.91–1.97 (m, 2 H) ppm. ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$): δ = 12.17 (CH_3), 22.17 (CH_2), 24.92 (CH_2), 26.45 (CH_2), 26.80 (CH_2), 26.91 (CH_2), 29.01 (CH_2), 29.03 (CH_2), 30.01 (CH_2), 30.79 (CH_2), 34.52 (CH_2), 34.54 (CH_2), 36.38 (C), 38.56 (CH_2), 41.43 (CH), 42.80 (CH), 46.45 (CH), 49.14 (CH), 53.84 (CH) ppm. IR (ATR): $\tilde{\nu}$ = 2946 (m), 2915 (s), 2846 (s), 1464 (w), 1442 (w), 1376 (w), 1346 (w), 1304 (w), 1289 (w), 1263 (w), 1238 (w), 1190 (w), 1172 (w), 1134 (w), 1103 (w), 1082 (w), 1053 (w), 1042 (w), 1016 (w), 986 (w), 972 (w), 964 (w), 945 (w), 931 (w), 906 (w), 883 (w), 869 (w), 847 (w), 838 (w), 808 (w), 794 (w) cm^{-1}. MS (EI, 70 eV): m/z (%) = 260 (100) $[M]^+$, 246 (6), 245 (35), 218 (5), 204 (36), 203 (78), 189 (5), 176 (6), 175 (7), 164 (13), 149 (13), 135 (26), 121 (15), 109 (20), 95 (36), 81 (40), 67

(27), 55 (18), 41 (10). HRMS (EI): calcd. for $C_{19}H_{32}$ $[M]^+$ 260.2504; found 260.2508.

Supporting Information (see footnote on the first page of this article): ^1H and ^{13}C NMR spectra of all reported compounds.

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