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SYNTHETIC STUDIES IN THE CARDENOLIDE SERIES—II

STEREOSPECIFIC INTRODUCTION OF C-17 SIDE CHAIN

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Abstract—Direct preparation of 14β-hydroxy steroids from 14α-H compounds is described; a 15β-hydroxy-14α-H compound is also obtained. Grignard reagents react with 14β-hydroxy-androstan-17-one in the "normal way", giving a 17β-side chain, but surprisingly organolithium reagents give the unexpected 17α-side chain.

In the course of our study of various pathways to cardenolides[1] we have been led to explore the not too well documented chemistry of ring D in the 14β-androstan-17-one series with a A/B trans or cis ring-junction. We wish to describe the rather unexpected results which have been found when 14β-hydroxy-5α-androstan-17-one **8** was used as a substrate. It turns out that the latter compound reacts with Grignard reagents from the less hindered β side of the steroid molecule ("normal" reaction), whereas the corresponding organolithium reagents approach exclusively from the α side. Both $LiAlH_4$ and $NaBH_4$ reduce compound **8** also from the β side, leading to 5α-androstan-14β, 17α-diol **15**. In sharp contrast, no such "abnormal" behaviour was found when there is no 14β hydroxyl group; 5α, 14β-androstan-17-one **16** react uniquely from the less hindered β face.

Synthesis of substrates

The introduction of a 14β-hydroxyl group in a steroid molecule has been reported via the 14β,15β epoxide or the related bromohydrin.[2] A more straightforward method has been used by Afonso[3] the oxidation by air or oxygen of 3β-acetoxy-5α-androst-14-ene-17-one which yields stereospecifically the desired 14β-hydroperoxide, easily reduced into the 14β-hydroxy compound. However, the preparation of the starting material, especially in large quantity, is not very convenient. The more accessible 5α-androst-15-ene-17-one **1a** oxidized under the same conditions also gives a 14β hydroperoxide[4-6] albeit rather sluggishly. In both cases, the probable intermediate is the allylic radical **4**, whose formation is very likely the rate determinating step. Removal of H-16 is apparently a very fast process, since the oxidation of **2** is completed in a few hours, whereas the oxidation of **1** requires several weeks.

Therefore, we became interested in finding conditions under which the migration of the double bond ($\Delta^{15} \rightarrow \Delta^{14}$) and the oxidation would simultaneously take place, regardless of its detailed mechanism. In the course of the purification of **1a** by chromatography on alumina, we noted the formation of a small amount of its Δ^{14} isomer, *which did not exist in the crude material.* Thus, pure androst-15-ene-17-one **1a** was adsorbed on slightly basic alumina (Grade III or IV) and the solvent (pentane) evaporated. Dry oxygen was gently blown from the bottom through the column, at room temperature.† After 5 days, the solid was extracted with chloroform, and the reaction produts were separated by TLC, leading to a mixture A of 14β-hydroperoxy and 14β-hydroxy-androst-15-ene-17-one **5a** and **6a** in addition to a small amount of 15β-hydroxy-5α, 14α-androstane-17-one **7a**‡ Reduction of mixture A with trimethyl phosphite led to pure 14β-hydroxy-5α-androst-15-ene-17-one **6a**. In order to improve the yield of the desired compound, the oxidation was carried out as indicated above, but every 24 hr, the organic material was dissolved in methylene chloride, and adsorbed on a new batch of alumina. An average 40% yield of 14β-hydroxy-5α-androst-15-ene-17-one **6a** could be isolated on a routine basis as well as a small amount of 5α,14-androst-14-ene-17-one **2a** and 5α,14β-androst-15-one **3a**. The latter compounds can be recycled in the oxidation device so that the actual yield of **6a** is at least 50%.

The occurrence of 15β-hydroxy-androstane-17-one **7a** is indicative of 1–4 addition of water to the unsaturated ketone.

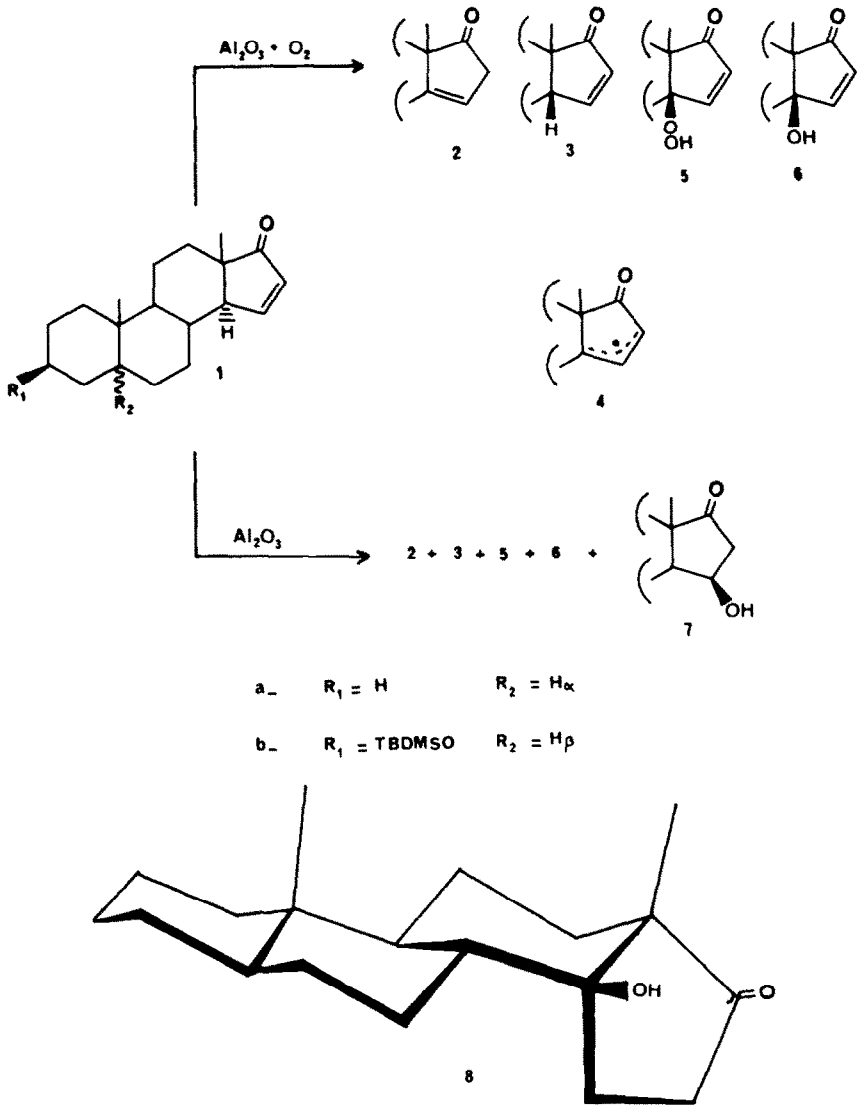
To the best of our knowledge, no such reaction *under homogenous conditions* has ever been reported. When air was replaced by argon, the amount of **7a** rose sharply. A fair quantity of the mixture of **5a** and **6a** was still isolated, thereby showing that oxygen is strongly adsorbed on alumina, since it was not flushed even after several hours of exposure at room temperature to a stream of argon.

On starting from 3β-t-butyldimethylsilyloxy-5β-androst-15-ene-17-one **1b**[1] a 50% yield of the related 14β-hydroxy-compound **6b** with cardenolide configuration was formed.

On silica gel, no such migration-oxidation process takes place, even after a long period of time.

†The device was not sheltered from light. Similar results were obtained when the tube was wrapped in aluminium foil.

‡The structure of this compound was elucidated by comparison with an authentic sample, kindly sent to us by Dr G. D. Meakins, whom we thank.



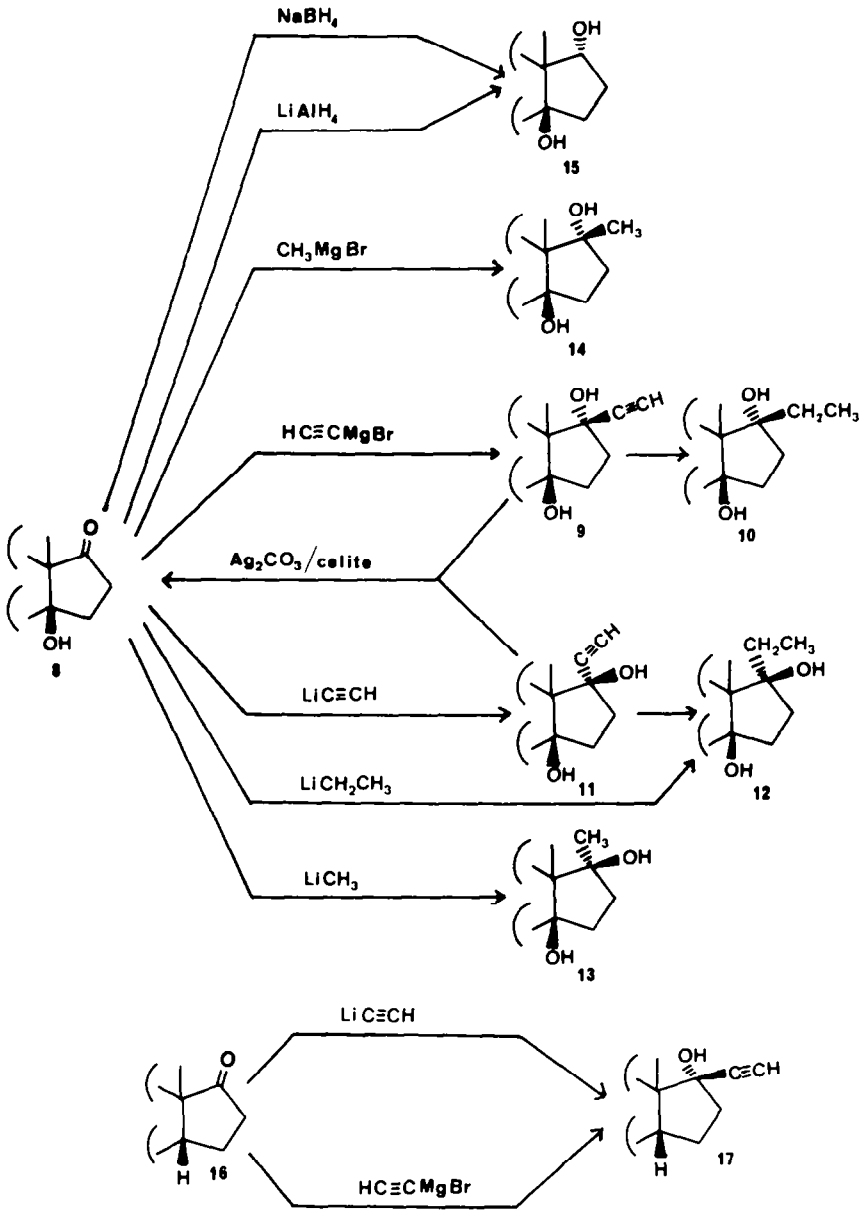
Reactions of 14β-hydroxy-androstan-17-ones with organolithium or organomagnesium derivatives

From a very naive point of view, due to its peculiar shape (see Fig. 2), 14β-hydroxy-androstan-17-one **8** should react with nucleophiles in a stereoselective manner: the β face is relatively unhindered, whereas the α side is fairly crowded. Thus, at first sight, organolithium (R–Li) and Grignard reagents (R–Mg–Br) should lead to the same compound. Ethynyl magnesium bromide and methyl magnesium bromide in tetrahydrofuran react from the β side, as expected.[8] Ethyl magnesium bromide acts as a reducting agent rather than as a nucleophile;[9] no addition to the carbonyl group was detected. In order to avoid difficulties arising from the nature of various solvents THF was used throughout.

When the ethynyl Grignard reagent was used, the yield was rather low, but the major compound was the 17α tertiary alcohol **9** contaminated with a very small amount of its 17β isomer **11**.

The infrared spectrum of the dominant compound led to no clear-cut conclusion, since weak intramolecular hydrogen bonding could be detected. ^1H and ^{13}C NMR were also inconclusive. Thus, its structure was established from its X-ray diffraction pattern.[10]

Ethynyllithium, either prepared *in situ*, or as its commercially available tetramethylethylenediamine complex, gave a single compound **11** different from **9**. Since the starting material is a β hydroxy ketone, the possibility of a retroaldol ring opening, under basic conditions, followed by aldolisation and then by nucleophilic reaction on the carbonyl group has to be ruled out. Thus, compounds **9** and **11** were treated with silver carbonate on Celite.[11] Both lead to the same substance **8**. Hence, the reaction product with ethylnylithium should simply be the diol formed when the nucleophilic attack takes place from the "rear" that is from the hindered α face of the substrate. Although the ^1H NMR spectra were in good agreement with this conclusion, as well as the existence of strong intramolecular hydrogen bonding, as shown by the near IR spectrum, the structure of **11** was firmly established by X-ray diffraction analysis.[10] Methyl and ethyllithium also afforded *single* compounds **13** and **12**. Very strong hydrogen bonding, according to the near IR spectra, lacking in compounds **14** and **10**, is in favour of the proposed stereochemistry of **12** and **13**. Moreover hydrogenation of the triple bond of **11** led to a substance identical with the reaction product between ethyllithium and 14β-hydroxy-androstan-17-one **8**.

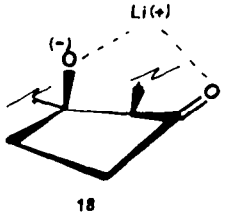


When 5α,14β-androstan-17-one **16** was used as a substrate (Fig. 4), instead of the 14β hydroxy compound, everything becomes "normal", that is, nucleophilic attack takes place from the less hindered β face; Grignard[8] and organo-lithium reagents give the same product **17**. Thus, the 14β OH group, as expected, plays a determining role in the reaction mechanism.

The first step, obviously, involves the acidic 14β-hydroxyl proton and one mole of organometallic reagent.

It has been shown that lithium cation complexes a carbonyl group much more readily than does magnesium cation.[12] The lithium alcoholate should therefore be represented as **18** (Fig. 5). A strong Li/carbonyl interaction has two effects: the stable complex shelters the β face, and, simultaneously, helps change the hydridisation of C-17 from sp_2 in the carbonyl to sp_3 in the tertiary alcohol, provided the nucleophilic attack by the second molecule of R-Li comes from the α side.

According to (Cram's study of reactions of Grignard and lithium derivatives on α hydroxyketones[13], Li reagents



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easily give rise to cyclic intermediates wherein the metal is bonded with the alkoxide and the carbonyl group. No such strong complexing effect is likely when magnesium derivatives are used; moreover, steric requirements and in particular the presence of the bulky C-18 rather difficult.

The loose interaction between Mg and the carbonyl group is certainly not strong enough to overcome the energy barrier due to steric effect.

Such a striking difference between the behaviour of organolithium and Grignard reagents on the same substrate seems to be worth noting.

In our case, it enables us to introduce in a stereospecific manner a 17β side chain on a C/D cis androstane derivative, that is in the less thermodynamically favourable configuration.

EXPERIMENTAL

M.ps were determined on a Reichert apparatus, and were not corrected. IR spectra were taken on a Perkin Elmer 577 spectrophotometer. Mass spectra were measured with a VG ZAB2F spectrometer. NMR spectra were recorded at 400 MHz in $CDCl_3$ on a Bruker WM.400 spectrometer, chemical shifts are in ppm (ref TMS). Microanalyses have given results ± 0.3% from theory for underlined elements.

Preparation of 14β-hydroxy-androst-15-en-17-one **6a**

A soln of androst-15-en-17-one **1a** (0.400 g, 1.46 mmol) in 50 ml CH_2Cl_2 was evaporated to dryness on 30 g of basic alumina (Merck, grade IV) under vacuum. This material in a chromatographic column, was submitted to a stream of oxygen. The solid phase was extracted once a day and the resulting soln was deposited again on alumina. After 5 days it was extracted by chloroform; a yellow oil (0.400 g) was obtained, giving a positive test with potassium iodide. ^{1}H NMR Spectra of the mixture showed a doublet at 6.2 ppm and at 7.5 ppm corresponding to the olefinic protons on carbons 15 and 16 of **6a**.[1] It exhibited a doublet at 5.32 ppm and at 7.30 ppm corresponding to **5a**.[3] In order to reduce the hydroperoxide, this oil was treated for 12 hr with 2 ml of trimethylphosphite in 4 ml of pyridine. The following substances were isolated (TLC: $CHCl_3$ 100, MeOH 0.5; 5 elutions): Androst-14-en-17-one **2a** (0.048 g, yield 12%),[4,6] IR (KBr): 1740 cm^{-1} (C=O); 1640 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$): δ = 2.90 (m, 2H, H16); δ = 5.50 (m, 1H, H15). $C_{19}H_{28}O$ (C, H).

14β-*Androst-15-en-17-one* **3a** (0.032 g, yield 8%),[4,6] IR (KBr): 1700 cm^{-1} (C=O); 1586 cm^{-1} (C=C); ^{1}H NMR ($CDCl_3$): δ = 6.15 (m, 1H, H16); δ = 7.70 (m, 1H, H15). $C_{19}H_{28}O$(C, H).

14β-Hydroxy-Androst-15-en-17-one **6a** (0.160 g, yield: 38%). Yield 50% with respect to **2a** and **3a**, identical with authentic material.[14]

Preparation of 3β-t-butyldimethylsilyloxy-14β-hydroxy-(5β) androst-15-en-17-one **6b**

6b was prepared in the same way as **6a** (yield 40%, 50% with respect to isomerised androstenones obtained) m.p. 156–158° (hexane). $\{\alpha\}_D^{24} = +98°$ ($CHCl_3$, c = 0.3); IR (CS_2): 3600 cm^{-1} (OH); 1715 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$): δ = 0.0 (s, 6H, $-(CH_3)_2Si-$), 0.87 (s, 9H, $(CH_3)_3C-Si-$). $C_{25}H_{42}SiO_3$ (C, H).

Preparation of 15β-hydroxy-androstan-17-one **7a**

Androst-15-en-17-one **1a** (0.200 g, 0.73 mmol) in 20 ml of pentane was adsorbed on 60 g of alumina (Merck grade IV). The solvent was evaporated in a stream of nitrogen. The mixture was kept for 5 days under argon, in the dark. It was extracted with chloroform. The residue (0.190 g) giving a positive test with potassium iodide, was separated by TLC ($CHCl_3$ – 100/MeOH 0.5, 5 elutions).

The following compounds were be isolated: Androst-14-en-17-one **2a** (0.028 g, yield: 14%). 14β-*androst-15-en-17-one* **3a** (0.020 g, yield: 10%). *Mixture A* (0.046 g, yield: 23%), oxidation products: hydroperoxide **5a** and alcohol **6a**. 15β-*hydroxy-androstan-17-one* **7a** (0.030 g, yield: 15%), identical with authentic material.[7]

ACTION OF GRIGNARD REAGENTS

Ethynyl magnesium bromide

General procedure. A stream of purified and dried acetylene was bubbled through 100 cm^3 of anhydrous THF for 1/2 hr 60 cm^3 of 3M soln of methylmagnesium bromide in ether was then added dropwise. Then the solution was stirred and kept saturated with acetylene for 1 hr. The ketone in THF was added dropwise to the soln of ethynyl magnesium bromide (60 equiv). The mixture was then refluxed for 15 min. After cooling, the reaction mixture was poured into phosphate buffer (KH_2PO_4 0.025 M, Na_2HPO_4 0.025 M, pH 7). Extraction with CH_2Cl_2 and usual workup gave the crude product.

Reaction with 14β-hydroxy-androstan-17-one **8**. Unsaturated hydroxy ketone **6a** was quantitatively hydrogenated (Pd/C) to given **8**.[14] Preparative TLC (cyclohexane–ether: 1/1) of the crude product of the reaction of ethynyl magnesium bromide with 0.152 g of **8** afforded 0.031 g of starting material, 0.002 g of 17α-ethynyl-androstan-14β, 17β diol **11** and 0.052 g of 17β-ethynyl-androstan-14β, 17α diol **9** (31.4% yield, 39.5% with respect to the recovered starting material).

17β-*ethynyl-androstan-14β, 17α-diol* **9**, m.p. 170–172° (pentane–ether), $\{\alpha\}_D^{24} = -19.4°$ ($CHCl_3$, C = 1.09). IR (CCl_4, 1 mm cell): 3612, 3580 cm^{-1} (free OH); 3500 cm^{-1}, broad (OH, H bonded 3310 cm^{-1} (≡CH). IR (CCl_4, 20 mm cell, $C < 10^{-3}$ M): 3500 cm^{-1}, became very weak but didn't vanish (OH---C≡C intramolec.).[15] ^{1}H NMR ($CDCl_3$): δ = 0.79 (s, 3H, 19-CH_3); δ = 1.18 (s, 3H, 18-CH_3); δ = 2.77 (s, 1H, ≡CH). MS (EI: M^+ = 316, *m/e* = 298, 283, 280. $C_{21}H_{32}O_2$: C, H.

9 was hydrogenated in a classical way on palladium/charcoal catalyst to give **10**.

17β-*ethyl-androstan-14β, 17α-diol* **10**, m.p. 220–222° (cyclohexane-$CHCl_3$), $\{\alpha\}_D^{24} = -9.1°$ ($CHCl_3$, C = 0.4). IR (CCl_4, 1 mm cell): 3610, 3625 cm^{-1} (free OH) (no H bonded OH absorption). ^{1}H NMR ($CDCl_3$): δ = 0.78 (s, 3H, 19-CH_3); δ = 0.91 (s, 3H, 18-CH_3); δ = 0.97 (t, 3H, 21-CH_3); δ = 2.04 (q, 2H, 20-CH_2). MS (EI): $M^{+\cdot}$ = 320, *m/e* = 302, 191, 184. $C_{21}H_{36}O_2$: C, H.

Reaction with 14β-androstan-17-one **16**.[8] Unsaturated ketone **3a** was quantitatively hydrogenated (Pd/C) to give **16**.[4,6]

Only one product was detected after reaction of **16** (0.3 g) with ethynyl-magnesium bromide. Column chromatography (PE. 3/1) gave 0.160 g of **17** (49% yield).

17β-*ethynyl-14β-androstan-17α-ol* **17**. m.p. =80–82° (pentane), $\{\alpha\}_D^{20} = +27.9°$ ($CHCl_3$, C = 1.09), IR (CCl_4): 3610 cm^{-1} (free OH); 3450 cm^{-1} (OH, intermolec. H bond); 3310 cm^{-1} (≡CH). ^{1}H NMR ($CDCl_3$): δ = 0.77 (s, 3H, 19–CH_3): δ = 1.12 (s, 3H, 18–CH_3); δ = 2.53 (s, 1H, ≡CH). $C_{21}H_{32}O$: C, H.

Methyl magnesium bromide. The reaction was performed under dry nitrogen atmosphere.

Reaction with 14β-hydroxy-androstan-17-one **8**. 3 cm^3 of a 3M soln of CH_3MgBr in ether were added dropwise to 0.263 g of **8** in 8 cm^3 of dried THF, stirring was kept for 1 hr at room temp. Then the mixture was refluxed for 12 hr, cooled, hydrolysed with water and extracted with CH_2Cl_2 · 0.275 g of crude product were obtained. TLC separation (pentane–ether: 1/2, 2 elutions) gave 0.071 g of **8** and 0.028 g of **14** (10.1% yield, 13.8% with respect to the recovered starting material).

17β-*methyl-androstan-14β, 17α-diol* **14**. m.p. = 200–202° (pentane-ether), $\{\alpha\}_D^{24} = -7.4°$ ($CHCl_3$, C = 1.4). IR (CCl_4, 1 mm cell): 3620 (free OH) (no H bonded OH absorption). ^{1}H NMR ($CDCl_3$): δ = 0.77 (s, 3H, 19-CH_3); δ = 0.92 (s, 3H, 18-CH_3); δ = 1.47 (s, 3H, 20-CH_3). MS (EI): M^+ = 306, *m/e* = 288, 270, 255. $C_{20}H_{34}O_2$: C, H.

ACTION OF ORGANOLITHIUM REAGENTS

Lithium acetylide. 40 cm^3 of dry THF previously saturated with acetylene was added dropwise to a mixture of 7 cm^3 of commercial 15% soln of butyllithium in hexane and 10 cm^3 of THF. Then bubbling of acetylene was maintained for 1 hr. 0.5 g of ketone **8** in 15 cm^3 of THF was added dropwise to the soln of

lithium acetylide (10 equiv) at 0°C. Stirring was continued for 2 hr at room temp. Saturated Na_2SO_4 soln was then added. Extraction with ether and usual workup gave the crude product.

Preparative TLC (cyclohexane–ether: 2/1) afforded 0.185 g of 17α-ethynyl-androstan-14β, 17β-diol **11** (34% yield, 77% with respect to the recovered starting material) and 0.280 g of **8**.

17α-ethynyl-androstan-14β, 17β-diol **11**. m.p. = 166–168° (pentane–ether), $\{\alpha\}_D^{24} = -17.0$ ($CHCl_3$, C = 0.5).

IR (CCl_4, 1 mm cell): 3602 cm^{-1} (free OH); 3536 cm^{-1} (H bonded OH, intramolecular); 3500 cm^{-1}, broad (H bonded OH, intermolecular); 3320 cm^{-1} (≡CH). IR (CCl_4, 20 mm cell, C < 10^{-3} M): 3540 cm^{-1} sharp (OH, H bonded, intramolecular) (no 3500 cm^{-1} absorption).

^1H NMR ($CDCl_3$): δ = 0.79 (s, 3H, 19-CH_3); δ = 1.11 (s, 3H, 18-CH_3); δ = 2.47 (s, 1H, ≡CH). MS (EI): $M^{+\cdot}$ = 316, *m/e* = 298, 283, 280. $C_{21}H_{32}O_2$: C, H.

Lithium acetylide—ethylenediamine complex. The reactions were performed under dry nitrogen atmosphere.

Reaction with 14β-hydroxy-androstan-17-one **8**. **11** was obtained with the same yield (34%).

Reaction with 14β-androstan-17-one **16**. 0.159 g of **16** in 4 cm^3 of THF were added slowly to a soln of 1 g of commercial lithium acetylide—ethylendiamine complex in 4 cm^3 of THF. The mixture was stirred 3 hr at room temp. Then 10 cm^3 of water were added carefully. After usual extraction with ether and TLC (pentane–ether: 3/1), 0.101 g of 17β-ethynyl-14β-androstan-17α-ol **17** were obtained (55% yield).

11 was hydrogenated in a classical way with palladium-charcoal catalyst to give **12**.

17α-ethyl-androstan-14β, 17β-diol **12**. M.p. = 158–160° (cyclohexane–$CHCl_3$), $\{\alpha\}_D^{24} = -17.6$ ($CHCl_3$, C = 1.2).

IR (CCl_4, 1 mm cell): 3612, 3596 cm^{-1} (free OH); 3510 cm^{-1} sharp (H bonded OH, intramolecular); 3400 cm^{-1} (broad) (OH, H bonded intramolecular). IR (CCl_4, 20 mm cell, C < 10^{-3} M): 3510 cm^{-1} sharp (H bonded OH, intramolecular) (no 3400 cm^{-1} absorption). ^1H NMR ($CDCl_3$): δ = 0.78 (s, 3H, 19-CH_3): δ = 1.00 (s, 3H, 18-CH_3); δ = 0.97 (t, 3H, 21-CH_3); δ = 1.47 (q, 2H, 20-CH_2). MS (EI): M^+ = 320, *m/e* = 302, 191, 187, 184. $C_{21}H_{36}O_2$: C, H.

Ethyl-lithium: reaction with 14β-hydroxy-androstan-17-one **8**. The reaction was performed under a dry nitrogen atmosphere. 10 cm^3 of commercial 1M suspension of ethyl-lithium in benzene were added to 0.191 g of ketone **8** in 5 cm^3 of dried THF. Stirring was continued for 1 hr, then the mixture was refluxed for 2 hr. After cooling, hydrolysis, extraction with CH_2Cl_2, TLC (cyclohexane–ether: 1/1, 2 elutions) afforded 0.023 g of starting material **8** and 0.035 g of **12** (17% yield).

Methyl-lithium: reaction with 14β-hydroxy-androstan-17-one **8**. The reaction was performed under dry nitrogen atm. 6 cm^3 of commercial 1,6M solution methyl-lithium in ether were added to 0.113 g of ketone **8** in 5 cm^3 of dried THF. Stirring was kept for 1 hr, then the mixture was refluxed for 2 hr. After cooling, hydrolysis, extraction with CH_2Cl_2, a mixture of ketone **8** and diol **13** was obtained. TLC separation was not effective. Treatment of the mixture in THF with $LiAlH_4$ gave a mixture of diol **15** and diol **13** which could be separated by TLC (pentane–ether: 1/3), 0.008 g of diol **15** and 0.020 g of diol **13** (17% yield) were obtained.

17α-methyl-androstan-14β, 17β-diol **13**. M.p. = 188–190° (ether), $\{\alpha\}_D^{24} = -18.6$ ($CHCl_3$, C = 1.2).

IR (CCl_4, 1 mm cell): 3610 cm^{-1} (free OH); 35110 cm^{-1} sharp (H bonded OH, intramolecular); 3400 cm^{-1} broad (H bonded OH, intermolecular). IR (CCl_4, 20 mm cell, C < 10^{-3} M): 3510 cm^{-1} sharp (OH, h bonded intramolecular) (no 3400 cm^{-1} absorption). ^1H NMR ($CDCl_3$): δ = 0.77 (s, 3H, 19-CH_3); δ = 0.98 (s, 3H, 18-CH_3); δ = 1.12 (s, 3H, 20-CH_3). MS (EI): no M^+; *m/e* = 288, 270, 255. $C_{20}H_{34}O_2$: C, H.

ACTION OF $LiAlH_4$, $LiBH_4$ ON KETONE 8

The reactions were performed under dry nitrogen atmosphere.

$LiAlH_4$. 0.100 g of $LiAlH_4$ were added to 0.112 g of ketone **9** in 15 cm^3 of dry THF. Stirring was continued for 2 hr at room temp. Usual workup yielded, after TLC separation (pentane–ether: 1/3), 0.082 g of diol **15** (73% yield). *Androstan-14β, 17α-diol* **15**. M.p. = 180–183° (cyclohexane–acetone) $\{\alpha\}_D^{24} = -15.8°$ ($CHCl_3$, C = 1.1).

IR (CCl_4, 1 mm cell, saturated sol.): 3645 cm^{-1} (free OH) (no H bonded OH absorption). ^1H NMR ($CDCl_3$): δ = 0.77 (s, 3H, 19-CH_3); δ = 1.02 (s, 3H, 18-CH_3); δ = 4.25 (m, 1H, 17-H). MS (3I): M^+ = 292, *m/e* = 274, 259, 256.

$LiBH_4$. 0.050 g of $LiBH_4$ were added to 0.050 g of **8** in 10 cm^3 of dry THF. Stirring was continued for 2 hr at room temp. Usual workup gave 0.036 g of **15** (72% yield).

$NaBH_4$. 0.080 g of $NaBH_4$ were added to 0.075 g of **8** in 10 cm^3 of methanol. Stirring was continued for 2 hr at room temp. Usual workup afforded 0.051 g of diol **15** (68% yield).

REACTION OF ALKYNES 9 AND 11 WITH SILVER CARBONATE ON CELITE

1.5 g of silver carbonate on Celite were added to 0.023 g of alkyne (**9** or **11**) in 20 cm^3 of benzene. The suspension was refluxed for 1.5 hr and then filtered. Evaporation of the solvent gave 0.019 g of a pure product identical to **8**.

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