pentanoic acid lactone). Recrystallization from carbon tetrachloride gave analytically pure *dl*-**3**: 0.21 g; mp 95-96°; ir ($CHCl_3$) 1735 cm^{-1}; nmr ($CDCl_3$) 4.90-4.31 (m, methine H) and 2.72-1.5 ppm (m). *Anal.* Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.25; H, 7.62.

Conversion of the 60° Melting Isomer of 2 to *dl*-6.—The crude dilactone was prepared from the 60° melting isomer of **2**, and without subsequent purification it was converted (>80%) *via* the above sequence to a single[14] dioxane *dl*-**6**: bp 129-134° (0.3 mm); ir (neat) 1725 cm^{-1}; nmr (CCl_4) 1.27 (s, 6 H, $\overset{\text{O}}{\underset{\text{O}}{>}}\text{CMe}_2$), 3.65 (s, 6 H, CO_2CH_3), 2.28 (dd, J = 6 Hz each, 4 H, $CH_2CO_2CH_3$), and 3.5-3.9 ppm (m, 2 H, CHO); mol wt (mass spectrum), calcd 329.196 (found 329.194).

The crude intermediary dilactone can be easily purified by chromatography on silica gel by eluting with 25% ethyl acetate-petroleum ether. After the solution of traces of benzoic acid, the 6,6′-methylenebis(6-hydroxyhexanoic acid lactone) was isolated. Recrystallization from petroleum ether gave pure *dl*-**4**, mp 107° (lit.[5] mp 108-109.5°).

Analysis of the 38° Melting Isomer of 1.—The conversion of this 38° melting component of **1** to the dilactone and then to the substituted dioxane **5** followed the above sequence. The glc analysis[14] indicated a mixture of 39% of *dl*-**5** and 61% of the isomeric dioxane *meso*-**5**: ir (neat) 1725 cm^{-1}; nmr (CCl_4) 1.29 (s, 3 H, $\overset{\text{O}}{\underset{\text{O}}{>}}\text{CCH}_{3\,\text{equatorial}}$), 1.38 (s, 3 H, $\overset{\text{O}}{\underset{\text{O}}{>}}\text{CCH}_{3\,\text{axial}}$), 3.61 (s, 6 H, CO_2CH_3), 2.25 (dd, J = 6 Hz each, 4 H, $CH_2CO_2CH_3$), 3.5-4.0 ppm (m, 2 H, CHO); mol wt (mass spectrum), calcd 301.1651 (found 301.165).

Registry No.—*dl*-**1**, 30469-91-1; *meso*-**1**, 30469-92-2; *dl*-**2**, 30469-93-3; *dl*-**3**, 30469-94-4; *dl*-**5**, 30469-95-5; *meso*-**5**, 30469-96-6; *dl*-**6**, 30469-97-7.

Acknowledgment.—We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research, the Research Corporation, and the National Science Foundation for the Science Faculty Fellowship (1969-1970) for research (C. J. A.).

Stereospecific Reduction of Steroidal 4-Ene-3β-ols with Hydrazine

YUSUF J. ABUL-HAJJ

College of Pharmacy, University of Minnesota,
Minneapolis, Minnesota 55455

Received March 9, 1971

In connection with a related problem under investigation in our laboratory, it became desirable to prepare 5α-androstane-3β,17β-diol labeled stereospecifically with isotopic hydrogen in the 4α position. We now wish to report a convenient method for the reduction of the 4,5 double bond to the 5α isomer.

The reduction of olefins with hydrazine has been shown to occur by a stereospecific cis addition of hydrogen.[1] Thus, reduction of androst-4-ene-3β,17β-diol with hydrazine gave 5α-androstane-3β,17β-diol in yields ranging from 85 to 95% with no detectable amounts of the 5β isomer.

Heretofore, heterogeneous catalytic hydrogenation of 4-ene-3β-ol using various catalysts and conditions[2] has been the preferred method for the reduction of the 4,5 double bond. This method not only results in a mixture of the 5α and 5β isomers but also involves isotope exchange at an allylic position when deuterium or tritium gas is employed.[3-5]

The use of hydrazine has the distinct advantage of convenience and speed in the preparation of the 5α isomer and offers a useful alternative to the catalytic hydrogenation that gives a mixture of the 5α and 5β isomers which often is tedious and time consuming to separate. The reaction gives also exclusively the 5α isomer when cholest-4-ene-3β-ol and pregn-4-ene-3β,20β-diol are used.

Experimental Section

To a solution of androst-4-ene-3β,17β-diol (612 mg)[6] in methanol (15 ml) was added hydrazine hydrate (7 g)[7] and cupric acetate (1.9 mg). The reaction mixture was stirred at room temperature for 7 hr[8] in an atmosphere of dry air, poured into dilute HCl solution, and extracted with ether. The combined ether extracts were washed with water, allowed to stand for 10 min over sodium sulfate, filtered, and evaporated to dryness. The crystalline residue weighed 550 mg (90%), mp 160-163°. Recrystallization from ethanol gave 5α-androstane-3β,17β-diol melting at 163-164° (mixture melting point, ir).

Registry No.—Hydrazine, 302-01-2; androst-4-ene-3β,17β-diol, 1156-92-9.

---

[1] E. J. Corey, D. J. Pasto, and W. L. Mock, *J. Amer. Chem. Soc.*, **83**, 2957 (1961).

[2] C. W. Shoppee, B. D. Agashae, and G. H. R. Summers, *J. Chem. Soc.*, 3107 (1957).

[3] D. K. Fukushima and T. F. Gallagher, *J. Amer. Chem. Soc.*, **77**, 139 (1955).

[4] H. J. Brodie, S. Baba, M. Gut, and M. Hyano, *Steroids*, **6**, 569 (1965).

[5] Y. J. Abul-Hajj, *J. Label Compounds*, **7**, 33 (1971).

[6] Prepared by sodium borohydride reduction of testosterone in isopropyl alcohol.

[7] Supplier: K & K Laboratories, Inc., Plainview, N. Y.

[8] In more recent experiments the stirring time was reduced to 3 hr with equally good results.