$$(DS_2H)^+ + RSH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} III + H^+ \quad (a)$$

$$III + RSH \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} (DTB) + RSSR \quad (b)$$

It is further postulated that III is an unstable intermediate, whose concentration remains small and nearly constant throughout the reaction, so that one can write to a good approximation

$$d[(III)]/dt = k_1[(DS_2H)^+][RSH] - k_{-1}[(III)][H^+] - k_2[(III)][RSH] \cong 0 \quad (4)$$

whence

$$[(III)] = \{k_1[(DS_2H)^+][RSH]\}/\{k_{-1}[H^+] + k_2[RSH]\} \quad (5)$$

Finally, it is postulated that $k_{-1}[H^+] >> k_2[RSH]$. Since, in the conditions, the reversal of eq. b is negligible, one can write

$$-d[(DS_2H)^+/dt = d[(DTB)]dt = k_2[(III)][RSH] = \{k_1k_2[(DS_2H)^+][RSH]^2\}/k_{-1}[H^+] \quad (6)$$

In the presence of a large excess of RSH and at constant pH, one can equate

$$k_1k_2[RSH]^2/k_{-1}[H^+] = k \quad (7)$$

The resulting expression can be integrated to give eq. 3. The specific rate constants reported in Tables I and II are related in the following ways

$$k_1k_2/k_{-1} = k'[H^+] = k[H^+]/[RSH]^2 \quad (8)$$

(in view of the approximate nature of the analysis, the distinction between hydrogen ion concentration and activity is not considered).

In other mercaptan–disulfide reactions it has been found that the equilibrium constants[2] for the reactions corresponding to eq. a and b are not very different from unity, from which one can conclude that the rate constants are usually of the same order of magnitude. Also, convincing evidence has been produced that the mechanism involves the reaction of disulfide with RS^-.[7] The mechanism proposed above for $(DS_2H)^+$ implies two principal points of difference. First, it is postulated that the rate of reversal of eq. a is greater than the forward rate of b; this can be rationalized on the grounds that, in the former case, the participating groups are held in close proximity at all times, the reaction being an intramolecular one. Secondly, $(DS_2H)^+$ must be more susceptible to S–S bond fission than ordinary disulfides, since the former can be attacked by RSH and the latter only by the more strongly nucleophilic RS^-. It should be noted that, in the pH range in question, $[RS^-]$ is very small; *i.e.*, it is not implied that $(DS_2H)^+$ cannot react with RS^-, only that the reaction is not important in the conditions employed. As a matter of fact, a likely explanation for the fact that the rate of reaction increases somewhat more rapidly with pH than predicted by eq. 6–8 is that RS^- makes an appreciable contribution to the over-all reactions at the higher pH values. The reaction with RS^- cannot be the principal one, however, as this would lead to a dependence of the rate on $1/[H^+]^2$, which is clearly not the case.

A degree of uncertainty attaches to the above analysis, because the spectrum of the mixed disulfide is not known. Owing to this, one cannot be sure that the mixed disulfide would not be produced in appreciable amounts, its presence escaping detection by a fortuitous compensation of the absorbances. However, this is not likely. The mechanism proposed, though speculative, provides a reasonable explanation for the experimental findings.

(7) O. Foss in "Organic Sulfur Compounds," Vol. I, N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, pp. 87–90.

The Solvolysis of 3-Hydroxyestr-5(10)-en-17-one Sulfonates

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Solvolyses of the sulfonates of 3α- and 3β-hydroxyestr-5(10)-en-17-one (**2a, 6a**) yield the cyclosteroids **4** and **8**, respectively. Other products of the solvolyses include the diene **11a** and the *inverted* alcohols. The mechanisms involved in the synthesis of these compounds are discussed.

i-Steroids, both in structural determination and the mechanism of formation, have been the basis of a fascinating story through several decades of organic chemistry.[1] Investigation in this area continues, in recent years concentrated largely on determination of the steric requirements necessary for the synthesis of these compounds[2] and on a more precise definition of the nonclassical cation intermediate in their formation.[3] Pertinent to both problems, the present work reports the results of experiments dealing with the C-3 sulfonates of $\Delta^{5(10)}$-steroids.[4] These compounds, containing both the participating double bond and the oxygen function in the *same* (unbridged) ring, represent a structural type whose solvolyses have not been investigated heretofore. Numerous examples exist of bridge 3-cyclohexenol sulfonate solvolyses.[5] How-

(1) L. F Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, p. 314; a recent list of *i*-steroid syntheses has been given by L. H. Knox, E. Velarde, S. Berger, D. Cuadriello, P. W. Landis, and A. D. Cross [*J. Am. Chem. Soc.*, **85**, 1851 (1963)].

(2) For leading references see the following: W. J. A. Vandenheuvel and E. S. Wallis, *J. Org. Chem.*, **27**, 1233 (1962); C. W. Shoppee and G. A. R. Johnston, *J. Chem. Soc.*, 3261 (1961); R. M. Moriarty and R. M. deSousa, *J. Org. Chem.*, **28**, 3072 (1963).

(3) (a) S. Winstein and E. M. Kosower, *J. Am. Chem. Soc.*, **81**, 4399 (1959) and references cited there; (b) G. H. Whitham, *Proc. Chem. Soc.*, 422 (1961).

(4) Portions of this work are included in U. S. Patents 2,944,067 (1960), 2,944,068 (1960), and 3,087,943 (1963). Work along similar lines has been recently reported by S. G. Levine, N. H. Eudy, and E. C. Farthing [*Tetrahedron Letters*, 1517 (1963)].

(5) J. A. Berson, "Molecular Rearrangements," P. DeMayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, p. 192, and references contained there.

ever, the corresponding reaction in the unbridged 3-cyclohexenol, Δ^9-octalol-2, or analogous polycyclic systems has escaped investigation.[6]

Although $\Delta^{5(10)}$-steroids are routinely obtained in the metal–ammonia reduction of compounds with an aromatic A-ring,[7] they are labile intermediates usually transformed to the corresponding conjugated ketone derivatives. Among the few reports dealing with the reactions of the 3-keto-$\Delta^{5(10)}$-steroids is Hartman's reduction of 17-hydroxyestr-5(10)-en-3-one,[8] this work attesting to the possibility of reduction of the carbonyl group without isomerization of the double bond. Following this precedent, the preparation of 3-hydroxyestr-5(10)-en-17-one was undertaken. The starting material, estr-5(10)-ene-3,17-dione,[9] was reduced carefully with sodium borohydride. The marked difference in the reactivity of the C-3 and C-17 carbonyl groups, previously described in the androstanes,[10] allowed reduction to occur selectively without appreciable attack at the C-17 carbonyl. In addition, no isomerization of the double bond was seen. The resultant product contained two hydroxy ketones (**2a** and **6a**) in a 5:1 ratio. A more stereoselective reduction was effected with lithium tri-*t*-butoxyaluminohydride[11] which afforded the same ketones in a 15:1 ratio.

The general structure of each hydroxy ketone was shown by its infrared spectrum: absorption of both the secondary hydroxyl group and a five-membered ring carbonyl group was present. The n.m.r. spectra of these compounds showed no vinyl proton absorption indicating their respective double bonds had remained in a ditertiary position.

To prove the configuration of the C-3 hydroxyls in this pair of hydroxy ketones, the major component was converted by hydride reduction to the 3,17-diol (**2b**), identical with that prepared by Hartman.[8] Hydrogenation of this material under vigorous conditions afforded a good yield of 5α,10α-estrane-3α,17β-diol (**1**) and a minor amount of the corresponding 5β,10β-derivative.[12] Similarly, the minor component of the borohydride reduction product was converted to its diol (**6b**) and this in turn was hydrogenated to 5α,10α-estrane-3β,17β-diol (**9**). Since no change at C-3 can occur during hydrogenation, these experiments constitute a direct chemical proof of the configuration of **2a**: the major reduction product of the 3-keto-$\Delta^{5(10)}$-steroid has a C-3α hydroxyl group. This is contrary to the assignment made by analogy to the reduction of the C-3 carbonyl function in the normal steroids.[8,10,13]

The C-3 tosylate of the hydroxy ketone **2a**, prepared in good yield, was solvolyzed in buffered aqueous acetone following the classical procedure[14] and the products were separated readily by chromatography. The least polar material obtained (60% of the weight) was a mixture of dienes resulting from a simple elimination reaction. This same diene mixture could be formed by more conventional procedures such as passing the tosylate over activated alumina[15] or heating it in pyridine. Although the conjugated isomer **10**, having the extra stability conferred by resonance, was expected to predominate, it constituted less than 20% of the diene fraction as determined from the ultraviolet spectrum. The major component was a nonconjugated diene whose structure is most probably that shown in formula **11a**. The n.m.r. spectrum of the purified material showed vinyl proton absorption with an intensity equivalent to two protons, ruling out the several diene structures having three protons attached to olefinic bonds. A heteroannular relationship of these bonds was considerable improbable, not only because of the unnecessary complexity of the requisite reaction path, but also because of the ready oxidation of the diene to 3-desoxyestrone[16] with chromic acid–pyridine (among other reagents). The formation of the diene is presumably a kinetically controlled process; that isomerization of the double bonds does not occur during the reaction was shown by a separate demonstration of their marked stability to acid or base treatment. It should be noted however, that the nonconjugated isomer may have a thermodynamic stability very close to that of the conjugated isomer, for it possesses a strong stabilization provided by overlap of the π-electron clouds in 1,4-cyclohexadiene systems.[17] The steric factors involved in this reaction superficially favor neither direction of elimination, since both the C-2 and C-4 protons have similar steric accessibilities and both lie in the proper plane with the C-3 sulfonate for ready elimination. The conjugated diene component, although not isolated in pure form, almost certainly has the structure represented by structure **10**, the product of simple elimination of sulfonate and C-4 proton.

A normal component of the diene mixture was desoxyestrone (**12**), formed in the several reactions in which sulfonate elimination occurred. Especially large amounts of this material (30% of the product) were formed from the mesylate **3b** on activated alkaline alumina. Presumably this aromatic material was formed by autoxidation of the diene, although attempts to oxidize the diene mixture with oxygen in the presence of platinum catalyst effected no change in either diene component (**10** or **11a**).

Lithium–ammonia treatment of the crude diene effected reduction of the carbonyl function as well as of the conjugated double bonds of the contaminant **10**, providing the readily purified dienol **11b** (R′ = H) as the major product (see Chart I). Addition of acetylene proceeded normally to give the adduct **11b** (R′ = C≡CH). Hydrogenation of the ethynyl compound afforded smoothly the vinyl derivative **11b** (R′ =

(6) After the submission of this manuscript a solvolytic synthesis of bicyclo[3.1.0]hexan-2-ol appeared by M. Hanack and W. Keberle [*Chem. Ber.*, **96**, 2937 (1963)]. See also N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957), for other synthetic routes to this bicyclohexanol system. None of the corresponding bridged decalin analogs have been prepared.

(7) A. L. Wilds and N. A. Nelson, *J. Am. Chem. Soc.*, **75**, 5366 (1953).

(8) J. A. Hartman, *ibid.*, **77**, 5151 (1955).

(9) F. B. Colton, U. S. Patent 2,729,654 (1956).

(10) E. Elisberg, H. Vanderhaeghe, and T. F. Gallagher, *J. Am. Chem. Soc.*, **74**, 2814 (1952).

(11) O. H. Wheeler and J. L. Mateos, *Chem. Ind.* (London), 395 (1957); J. Fajkos, *Collection Czech. Chem. Commun.*, **24**, 2284 (1959).

(12) R. E. Counsell, *Tetrahedron*, **15**, 202 (1961). We wish to thank Dr. Counsell for providing several infrared spectra for comparison.

(13) Dr. S. G. Levine, Research Triangle Institute, has kindly pointed out this reversal of configurations contained in the patents on this subject (see ref. 4).

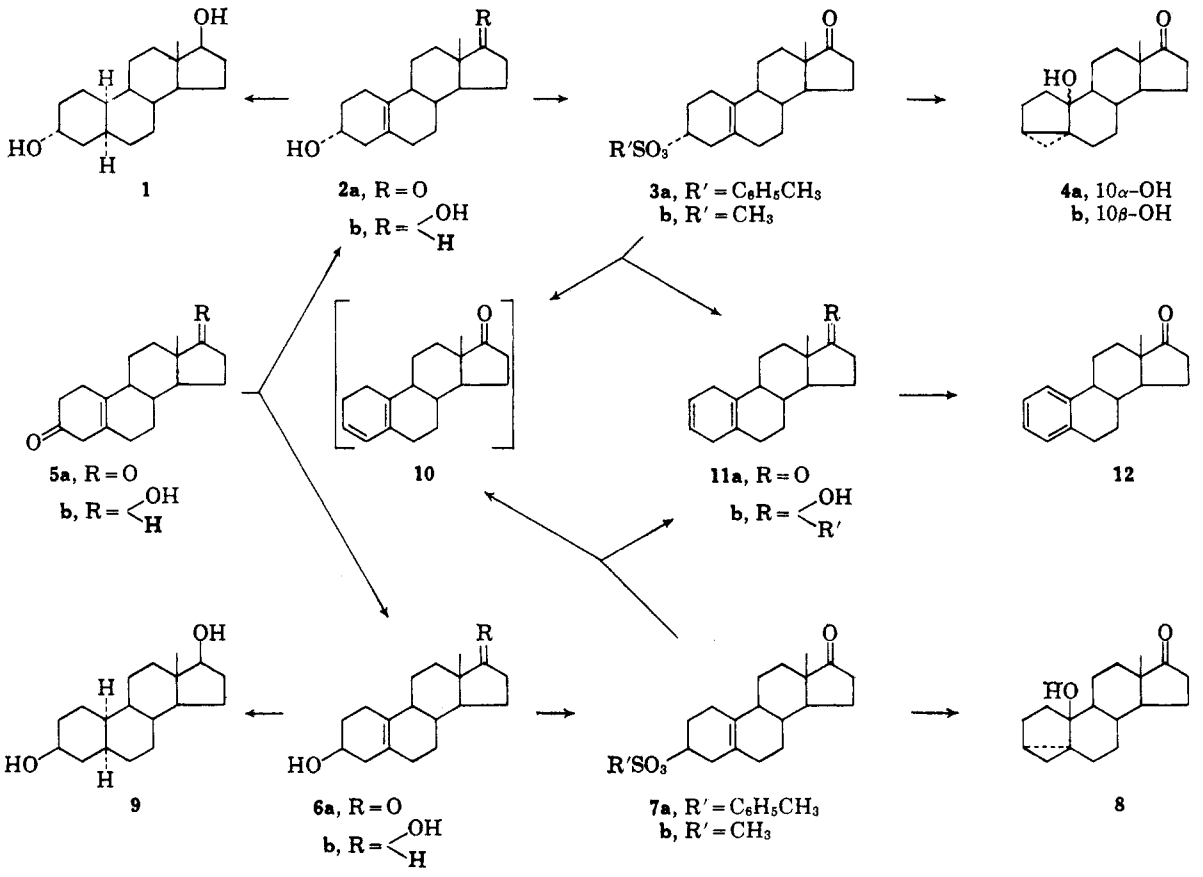
(14) E. M. Kosower and S. Winstein, *J. Am. Chem. Soc.*, **78**, 4347 (1956).

(15) F. C. Chang and R. T. Blickenstaff, *Chem. Ind.* (London), 590 (1958); G. H. Douglas, P. S. Ellington, G. D. Meakins, and R. Swindells, *J. Chem. Soc.*, 1720 (1959).

(16) This sample was kindly supplied by Dr. A. H. Goldkamp. See E. Caspi, E. Cullen, and P. K. Grover, *ibid.*, 212 (1963).

(17) R. B. Bates, R. H. Carnighan, and C. E. Staples, *J. Am. Chem. Soc.*, **85**, 3030 (1963).

CHART I



$CH{=}CH_2$). Further hydrogenation, however, was complicated by concomitant dehydrogenation of the A-ring.

The second product from solvolysis of the C-3α sulfonate exhibited signals in the n.m.r. spectrum at 7, 10, and 15 c.p.s. with an integrated area equivalent to three protons; these bands are most reasonably attributed to protons attached to a cyclopropyl ring.[18] The infrared spectrum of this compound showed the presence of a cyclopentanone carbonyl as well as a hydroxyl group. The latter group was determined to be tertiary by virtue of its stability to the usual acetylation or oxidation conditions. These facts are consistent with the formation of the *i*-steroid **4** expected from the positions of the double bond and hydroxyl group in the starting material. In agreement with this conclusion was the ready acid-catalyzed regeneration of the pure starting alcohol **2a**. The gross structural features of this compound are unique insofar as no cyclosteroids yet synthesized have either a tertiary hydroxyl group adjacent to the cyclopropane ring or a hydroxyl group as a substituent of the bridged cyclohexane ring. Solvolysis of the corresponding mesylate **3b** gave improved yields of the cyclosteroid **4** (30% instead of 20%). This may be due, in part, to a slower rate of the simple elimination reaction as suggested by a lower yield of accompanying dienes.

The cyclosteroid **4** was hydrogenated in an attempt to prove the configuration of its hydroxyl group.[19] The resulting noncrystalline mixture showed broadened methyl signals in the n.m.r. indicative of nonselective attack at the three cyclopropyl bonds. Under modified conditions, another hydrogenation attempt provided a product that was largely aromatic (**12**).

A hydroxy ketone fraction obtained from solvolysis of tosylate **3a** contained a third product, the inverted alcohol **6a**, in approximately 10% yield. This material is the result of a typical SN2 displacement of the sulfonate group (without rearrangement or participation of the double bond). Thus in the case of the estrenyl sulfonate, displacement and especially elimination reactions compete strongly with the rearrangement. In contrast, the hydrolysis of cholesteryl tosylate provides no products of simple displacement or elimination. This difference is readily ascribed to the difference in the geometry of the two systems.

Although the inverted alcohol **6a** was the main constituent of the hydroxy ketone fraction, the epimer **2a** was also present. The ratio of nucleophilic attack at C-3–C-10 of the nonclassical intermediate ion is expected to be a consequence of both steric and electronic factors. The small amounts of materials involved did not allow a good measure of this ratio or its comparison to the cholesteryl case (C-3–C-6 = 12:85).[3]

As a poorly crystalline, minor component of the borohydride reduction product, the 3β-alcohol **6a** could not be separated efficiently by chromatography and recrystallization. To obtain sufficient quantities of this compound for solvolysis studies, the mixture of alcohols was benzoylated; the desired benzoate was separated by fractional crystallization and saponified

(18) See D. J. Patel, M. E. H. Howden, and J. D. Roberts, *J. Am. Chem. Soc.*, **85**, 3218(1963), and references cited there.

(19) C. W. Shoppee and G. H. R. Summers [*J. Chem. Soc.*, 3361 (1952)] have reported the analogous hydrogenation of *i*-cholesterol.

to form the pure alcohol **6a**. In addition, the nucleophilic displacement of the C-3α tosylate in dimethylformamide[20] followed by saponification afforded the diene mixture (**10**, **11a**) and the inverted alcohol **6a**. Additional quantities of this compound were also realized from the chromatography of the mesylate **3b** on alkaline alumina.[15]

Solvolysis of the C-3β tosylate **7a** in buffered aqueous acetone provided three components in roughly the same relative proportions as formed in the reaction of the epimer **3**. The first product, formed by sulfonate elimination, consisted of a mixture of dienes (**10**, **11a**) and aromatic material (**12**). The second component in the solvolysis of the β-tosylate was a new *i*-steroid (**8**); supporting this assignment were the signals in the n.m.r. spectrum at 39, 42, and 47 c.p.s., the presence of a tertiary hydroxyl, and the acid-catalyzed conversion to starting material (**6a**). The final material obtained in the solvolysis of the β-tosylate was the product of inversion, the 3α-alcohol **2a**. The relative absence of starting alcohol (**6a**) again points to a preference of this system to undergo the SN2 displacement as compared to that found in the case of cholesterol.

Whereas the gross structural features of the cyclosteroids **4** and **8** are dictated by the positions of the double bond and hydroxyl group of the starting materials, at present the configurations of the carbon–carbon bridge and the C-10 hydroxyl groups can only be inferred by consideration of mechanism and several pertinent facts. In cholesteryl derivatives, the equatorial leaving group (3β) can undergo the *i*-steroid rearrangement, but the axial (3α) epimer fails completely.[21] This is ascribed, for the equatorial isomer, to the geometrically favorable overlap of the π-electrons of the double bond with the carbonium ion, affording anchimeric assistance in the solvolysis.[3] The axial epimer, lacking this π-electron overlap, undergoes a different course of reaction and forms no *i*-steroid. In sharp contrast to this more rigid system is the flexibility of the cyclohexene system in the $\Delta^{5(10)}$-steroids; here *both* epimers (C-3α and C-3β sulfonates) can assume readily an equatorial conformation. Thus, for both epimers the rearrangement occurs starting with an equatorial sulfonate, the conformer which meets the steric requirements of the reaction.

The departure of the sulfonate group in cholesteryl derivatives is assisted by the electron pair of the double bond, in effect causing an inversion at C-3 and producing the incipient cyclopropyl bond.[3] Precisely the same situation is present in the 3β-derivative **7** and no change in the stereochemistry of the bridge need be considered. However, in the case of the 3α-sulfonate **3**, the opposite situation exists; inversion at C-3 by the electron pair of the double bond should produce a C-3β–C-5 bridge.[22] That the difference in these 10-hydroxy *i*-steroids (**4**, **8**) is due to the configuration of the bridge rather than that of the 10-hydroxyl is clear from the acid-catalyzed reversal of these compounds: each forms only its starting alcohol. If the difference were due solely to the configuration of the hydroxyl, the intermediate carbonium ion in this reaction would be one common to both compounds and a single alcohol would result. This is demonstrated in the acid-catalyzed formation of cholesterol from both *i*-cholesterol and *epi-i*-cholesterol.[23]

The configuration of the C-10 hydroxyl is a more complex question. In the normal *i*-steroid rearrangement the β-configuration of the C-6 hydroxyl is a result of an axial attack at the point of maximum overlap of the π-orbitals with the incoming anion. The reaction of the 3β-derivative **7** is closely analogous, axial attack at C-10 occurring from the β-face yielding a C-10β hydroxyl group. Again by analogy, the solvolysis of the C-3α tosylate **3a** should form a C-10α hydroxyl group. However, inspection of the molecular models shows that the B-ring of a C-10α hydroxy cyclosteroid is required to assume an energetically disfavored boat conformation. Even with conformational modification by twisting,[24] the molecule remains in a form presumably more strained than the 10β-hydroxy cyclosteroid. The formation of this molecule from its sulfonate should occur in lower yields than the analogous formation of the 10β-hydroxy cyclosteroid **8**; consequent enhanced yields of the products of the competing substitution and elimination reactions should be realized. That no appreciable difference in yields of the cyclosteroids is seen leads to the surprising implication that no appreciable energy difference exists in the formation of cyclosteroids **4** and **8**.

An interpretation of the reaction course which circumvents this unusual conclusion can be delineated. In the *i*-steroids previously synthesized, the rigidity of the systems involved allows only one possible direction of axial attack by the incoming anion. An inference which might be drawn from these examples is that the entering and leaving groups in the cyclosteroid rearrangement must be *cis*. However, no compelling mechanistic argument supports this thesis. Axial attack of the homoallylic double bond should cause expulsion of an equatorial leaving group from either face of the molecule despite the *cis* or *trans* relationships of the two groups involved. In the present case, due to the intracyclic position of the double bond, axial attack at the double bond can be *trans* (β-face approach) to the C-3α leaving group, considering the B-ring as plane of reference. This route would provide the C-10β hydroxyl derivative **4b** in which the B-ring can readily assume the energetically favored chair conformation. Thus the hydroxyl group can be produced theoretically in either the 10α- or 10β-position. In the absence of concrete evidence to this point this configuration is left unassigned.

(20) F. C. Chang and R. T. Blickenstaff, *J. Am. Chem. Soc.*, **80**, 2906 (1958).

(21) D. N. Jones, J. R. Lewis, C. W. Shoppee, and G. H. R. Summers, *J. Chem. Soc.*, 2876 (1955); E. J. Becker and E. S. Wallis, *J. Org. Chem.*, **20**, 353 (1955).

(22) This structural type has been recently demonstrated in steroids as the result of a photochemical reaction [*cf.* W. G. Dauben and F. G. Wiley, *Tetrahedron Letters*, 893 (1962); W. G. Dauben and J. A. Ross, *J. Am. Chem. Soc.*, **81**, 6521 (1959)].

(23) A. F. Wagner and E. S. Wallis, *ibid.*, **72**, 1047 (1950). Since the configuration of the alcohol in the reverse rearrangement normally derives from the nucleophile attacking the C-3–C-5 bond to produce over-all inversion at C-3, it is not unreasonable to expect that the product derived from a C-3β–C-5 bridge would have a C-3α hydroxyl group. However, Dauben (ref. 22) observed an A-nor product on acid treatment of his 3β,5-cyclosteroid. One interpretation of this difference in products is due to the possible configurational differences in the oxygen functions in Dauben's cyclosteroid (β) and that reported here (α?). We wish to thank the referee for offering this explanation as well as several other valuable comments.

(24) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger, and W. N. Hubbard, *ibid.*, **83**, 607 (1961).

Experimental[25]

3α-Hydroxyestr-5(10)-en-17-one (2a). A. Sodium Borohydride Reduction.—To an efficiently stirred solution of 86 g. of estr-5(10)-ene-3,17-dione (**5a**) in 2 l. of methanol at 10° was added a cooled solution of 3.18 g. of sodium borohydride in 65 ml. of water over a 10-min. period. After an additional 5 min. the solution was poured into 4 l. of water containing 20 ml. of acetic acid. The resulting precipitate was collected on a filter and washed with water. This material (75 g.) was adsorbed on 1.7 kg. of silica (60–200 mesh). Elution with 10% ethyl acetate in benzene afforded 7.7 g. of the starting diketone. The following fractions contained 58 g. of the two epimeric alcohols, the α-isomer (**2a**) being in pure form in the earlier fractions. Analysis by paper chromatography[26] showed the isomers to be present in a 5:1 ratio (α–β). Recrystallization from methanol gave 31.2 g. of dense prisms, m.p. 183–188°, which were recrystallized from acetone–ether to give the pure compound, m.p. 192–194°, λ_{max} 2.74 and 5.74 μ, $[\alpha]_D$ 263°.[27]

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.54; H, 9.82.

Careful fractional recrystallization of the later hydroxy ketone fractions from cyclohexane and from acetonitrile provided a sample of the epimeric C-3β derivative **6a**, identical with the material described below.

Elution of the column with ethyl acetate yielded 8 g. of the crude diol (**2b**, **6b**), recrystallized to give a pure sample of estr-5(10)-ene-3α,17β-diol, m.p. 206–213°, identical with an authentic sample.[28]

B. Lithium Tri-*t*-butoxyaluminohydride Reduction.[29]—To a solution of 86 g. of the dione **5a** in 1 l. of tetrahydrofuran at 5° was added a solution of 176 g. of lithium tri-*t*-butoxyaluminohydride in 1 l. of tetrahydrofuran over a 1-hr. period. The cooling bath was removed and the reaction mixture was stirred for an additional 4 hr. at ambient temperature. The product was precipitated by pouring the solution slowly with stirring into 16 l. of water containing 100 ml. of acetic acid. This material was washed with water and dissolved in benzene. The resulting solution was washed with water, dried, and evaporated. The crystalline residue was shown by paper chromatography to consist of the 3α-hydroxy derivative **2a** contaminated with 5–8% of the 3β-hydroxy ketone **6a** and 3–4% of the 17-hydroxy derivatives **2b** and **6b**. Recrystallization from acetone gave 44 g., m.p. 175–181°, and 15 g., m.p. 172–175°, of the hydroxy ketone **2a**.

Lower yields obtained in other runs were probably due to pre-reduction isomerization of the double bond.

3α-Acetoxyestr-5(10)-en-17-one.—The hydroxy ketone **2a** (50 mg.) was heated in 2 ml. of pyridine and 1 ml. of acetic anhydride at 100° for 10 min. The cooled reaction was diluted with water. The resulting precipitate was separated by filtration and recrystallized from methanol, giving the pure acetate, m.p. 156–158°, λ_{max} 5.77 μ, $[\alpha]_D$ 240°.

Anal. Calcd. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 76.20; H, 8.88.

3α-Benzoyloxyestr-5(10)-en-17-one.—The hydroxy ketone **2a** (0.30 g.) was heated in 10 ml. of pyridine containing 1 ml. of benzoyl chloride at 100° for 15 min., was cooled and diluted with water, and then was heated again at 100° for 20 min. The mixture was cooled and filtered. Recrystallization of the product from methanol gave 0.23 g. of the pure material, m.p. 176–180°, λ_{max} 5.72 and 5.80 μ, $[\alpha]_D$ 196°. The C-3β proton had a half-height width of 14 c.p.s., centered at 307 c.p.s.

Anal. Calcd. for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.24; H, 8.13.

5(10)-Estrene-3α,17β-diol (2b).—A solution of the hydroxy ketone **2a** (0.20 g.) and lithium tri-*t*-butoxyaluminohydride (1 g.) in 30 ml. of tetrahydrofuran was allowed to stand at room temperature for 18 hr. The solution was poured into 300 ml. of water containing 20 ml. of acetic acid. The precipitate which formed was collected on a filter and recrystallized from acetone–ethyl acetate providing 0.12 g. of material (**2b**), m.p. 210–213°, $[\alpha]_D$ 187°, identical with an authentic sample.[28]

Sodium borohydride reduction of **5b** also gave a good yield of the same diol (**2b**).

Hydrogenation of Estr-5(10)-ene-3α,17β-diol (2b).—The estradiol **2b** (2.0 g.) and ruthenium oxide (2.0 g.) in 50 ml. of ethanol (3A) was stirred at 100° and 1600 p.s.i. for 8 hr. The uptake of hydrogen could not be accurately measured because of the small size of the sample relative to the volume of the apparatus. The solution, after filtration of the catalyst, was concentrated to dryness under reduced pressure.[30] The residue was crystallized from acetone–ethyl acetate to yield 1.05 g. of material, m.p. 219–222°, identical in the infrared with an authentic sample of 5α,10α-estrane-3α,17β-diol (**1**, lit.[12] m.p. 223–225°). The mother liquors of the reaction (0.9 g.) were submitted to chromatography on 100 g. of silica. Elution with 10% ethyl acetate in benzene provided an additional 0.59 g. of crude *cis*-α-diol **1**, recrystallized to yield 0.30 g. of the pure compound, m.p. 209–215° (identical in the infrared with the above sample). Elution with more polar solvents gave 0.13 g. of crude crystalline material recrystallized from acetone to yield 20 mg. of product, m.p. 209–211°, identical in the infrared with an authentic sample of 5β,10β-estrane-3α,17β-diol.[12]

Rhodium–alumina catalyst (5%, 5 g.) also effected hydrogenation of the diol (1.0 g.) in acetic acid (1600 p.s.i., 67°, 8 hr.), affording, after saponification, 0.42 g. of the *cis*-diol **1**, m.p. 225–226°.

3α-Tosyloxyestr-5(10)-en-17-one (3a).—To a solution of 8.65 g. of the hydroxy ketone **2a** in 500 ml. of pyridine at 0° was added 15 g. of *p*-toluenesulfonyl chloride. The solution was removed from the cooling bath and allowed to stand at room temperature for 16 hr. Aqueous potassium bicarbonate was added and the mixture was stirred for 10 min. The solution was partitioned between water and benzene. The organic layer was separated and washed with water and twice with excess 10% hydrochloric acid. A routine extraction procedure[31] yielded an oil which was crystallized from ether–methanol, providing 7.55 g., m.p. 128–134°, and 2.50 g., m.p. 132–134°, of the tosylate **3a**. Recrystallization from methylene chloride–methanol gave the analytically pure material, m.p. 134–136°, λ_{max} 5.76 μ, $[\alpha]_D$ 182°.

Anal. Calcd. for $C_{25}H_{32}O_4S$: C, 70.06; H, 7.53. Found: C, 69.96; H, 7.38.

Chromatography on silica caused considerable decomposition of the tosylate, leading to noncrystalline mixtures.

3α-Mesyloxyestr-5(10)-en-17-one (3b).—To a stirred solution of 40 g. of the hydroxy ketone **2a** in 500 ml. of pyridine at −10° was added dropwise 20 ml. of methanesulfonyl chloride over a 5-min. period. The reaction mixture was allowed to warm slowly. After 2 hr. (final temperature, 10°), the reaction mixture was poured into aqueous potassium bicarbonate. The resulting product was collected on a filter, yielding 43 g. of mesylate, m.p. 127–128°. Recrystallization from ether gave 34.0 g. of the pure mesylate, m.p. 129–130°; λ_{max} 5.75, 7.37, 7.49, and 8.51 μ; Δν 183 c.p.s. (SO_2CH_3).

Anal. Calcd. for $C_{19}H_{28}O_4S$: C, 64.74; H, 8.00. Found: C, 64.52; H, 8.10.

The mesylate, like the tosylate, was unstable to chromatography on silica.

Estra-2,5(10)-dien-17-one (11a).—A solution of 1.0 g. of the tosylate **3a** in 50 ml. of 1:1 benzene–petroleum ether was adsorbed on a column of Woelm cationotropic alumina, causing the immediate appearance of a bright yellow band. Elution with benzene yielded 0.48 g. of material which was recrystallized from methanol to yield 0.21 g. of the diene **11a**, m.p. 133–134°, and 0.20 g., m.p. 130–133°, λ_{max} 5.75 μ, $[\alpha]_D$ 238°. The n.m.r. showed a strong peak at 344 c.p.s. with a weaker absorption at 346 c.p.s. (total width at half-height, 3 c.p.s.).

(25) Infrared spectra and rotations (1%) were determined in chloroform and ultraviolet spectra in methanol. N.m.r. spectra were determined in deuteriochloroform on a Model A-60 spectrometer, Varian Associates, Inc., at 60 Mc., using tetramethylsilane as in internal standard (Δν = 0 c.p.s.). Petroleum ether refers to the fraction with b.p. 63–68°. Melting points are uncorrected.

(26) Effective product analysis throughout this work was accomplished routinely by paper chromatography. We wish to thank Dr. E. G. Duskalakis and staff for these separations as well as for all the column chromatography described here.

(27) We are indebted to Dr. R. T. Dillon and staff for the spectra and analyses reported here.

(28) We wish to thank Mr. L. N. Nysted for this comparison; see U. S. Patent 2,705,721 (1955) and ref. 8.

(29) We wish to acknowledge the assistance of Mr. R. Mayne who conducted the experiments with this reagent.

(30) We are grateful to Mr. W. M. Selby and staff for performing the hydrogenations and the autoxidation described in this paper.

(31) This procedure generally involved washing a benzene solution of the crude reaction product with water, aqueous potassium bicarbonate, and water, drying the solution over anhydrous magnesium sulfate, and distilling the solvent under reduced pressure (temperature less than 50°).

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found: C, 84.43; H, 9.12.

The conjugated diene **10** was a contaminant of the diene **11a**, as was seen in the ultraviolet spectrum of the crude product [λ_{max} 265 mμ (ϵ 1600)].[32] In addition the crude diene contained 5–10% of **12** as indicated by n.m.r. and paper chromatography.

The same elimination reaction was effected by boiling the tosylate for 6 hr. in pyridine.

The mesylate **3b** also underwent an elimination on Woelm basic alumina (activity grade 1) although in this case 30% of the product had aromatized as evidenced by the typical n.m.r. signals in the 420–440 c.p.s. region. With Merck alumina, 1.0 g. of mesylate **3b** afforded 0.56 g. of the diene (**10**, **11a**), λ_{max} 264 mμ (ϵ 1100), containing no discernible amounts of the aromatic compound. Also obtained in this case was 0.11 g. of hydroxy compound **6a**, shown to contain none of the isomeric alcohol **2a** by paper chromatography.

The stability of the double bonds in the unconjugated position was demonstrated by treating a sample of the diene **11a** in refluxing methanol containing aqueous hydrochloric acid for 20 hr. The product was largely unchanged, exhibiting less than 20% of the strong ultraviolet spectrum typical of the 3,5-diene system. The diene showed no change after being boiled for 2 hr. in methanol containing aqueous potassium hydroxide.

Oxidation of the Diene.—A solution of 14.8 g. of the diene mixture (**10**, **11a**) in 300 ml. of pyridine was added to 15 g. of chromic acid slurried[33] in 300 ml. of pyridine at 10°. After 90 min., the solution was diluted with water, and the product was separated by extraction with ether in the usual way.[31] The residue was recrystallized from methylene chloride–methanol to yield 10.8 g. of estra-1,3,5(10)-trien-17-one (**12**), m.p. 144–145°, identical with an authentic sample[16] by comparison of the usual criteria. An additional 1.56 g. of the same material, m.p. 137–144°, was obtained by chromatography of the mother liquors.

Dehydrogenation was effected also when the diene **11a** was mixed with 5% palladium–charcoal catalyst and heated to 180° for 5 min.; this procedure tended to produce more highly aromatized materials as by-products than did direct oxidation. N-Bromosuccinimide in carbon tetrachloride reacted readily with the diene giving the aromatic compound and an unstable brominated product, the mixture being converted by treatment in refluxing pyridine to a total of 50% of desoxyestrone.

The diene **11a** in ethyl acetate underwent no change when stirred with oxygen in presence of palladium or platinum catalyst at atmospheric pressures.[30]

Estra-2,5(10)-dien-17β-ol.—A solution of 1.40 g. of the crude diene (**10**, **11a**) in 20 ml. of ethanol was added dropwise to a solution of 1 g. of lithium wire in 600 ml. of ammonia and 30 ml. of ethanol. An additional 4 g. of lithium wire was added in three portions over a 1-hr. period. The ammonia was distilled from the colorless solution and replaced with ether–benzene. Water was added (carefully at first) and the product was isolated by benzene extraction.[31] The product was crystallized from acetone, 0.30 g., m.p. 139–141°; a second crop was obtained from petroleum ether, 0.64 g., m.p. 139–141°. The analytical sample of **11b** (R′ = H) was obtained by recrystallization from acetone, m.p. 139–141°.

Anal. Calcd. for $C_{18}H_{26}O$: C, 83.66; H, 10.14. Found: C, 83.77; H, 10.25.

Estra-2,5(10)-dien-17β-ol propionate was prepared by treating the hydroxydiene with propionic anhydride–pyridine at 100° and had m.p. 88–90° on recrystallization from ethanol.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Found: C, 80.11; H, 9.72.

The diene was also preparable by selective tosylation of the diol **2b** (1 mole equiv. of *p*-toluenesulfonyl chloride, 5°). The product was passed over Woelm basic alumina (activity grade I) forming a mixture which consisted of roughly equal parts of a diene C-17-tosylate, the desired product **11b** (R′ = H), and starting material.

17α-Ethynylestra-2,5(10)-dien-17-ol.—Through a stirred solution of 3.0 g. of potassium metal in 40 ml. of *t*-amyl alcohol at 5° was passed a stream of acetylene gas (passed through water and concentrated sulfuric acid washing towers). After saturation of the solution with acetylene, 2.0 g. of the diene **11a** (no solvent) was added to the reaction mixture. A slow stream of acetylene was passed over the reaction at 5° for 6 hr. The mixture was stoppered and stored at 0°. After 18 hr. the solution was diluted with 100 ml. of water containing 20 g. of ammonium chloride. The product was extracted with benzene in the usual way,[31] affording 2.55 g. of an oil that was chromatographed on 60 g. of silica. The material eluted with 70% benzene–petroleum ether afforded, on recrystallization from petroleum ether, 0.24 g. of the pure product, m.p. 98.0–98.5°; λ_{max}^{KBr} 2.81, 2.95, and 3.03 μ; [α]D 1.3.

Anal. Calcd. for $C_{20}H_{26}O$: C, 85.05; H, 9.28. Found: C, 85.34; H, 9.08.

A second crop (0.95 g., m.p. 97–99°) was also obtained.

17α-Vinylestra-2,5(10)-dien-17-ol.—A solution of 0.56 g. of the ethynyl derivative (**11b**, R′ = C≡CH) in 30 ml. of pyridine and 0.28 g. of 5% palladium–calcium carbonate catalyst were stirred in an atmosphere of hydrogen for 25 min. The mixture, filtered and concentrated, yielded a residue (0.56 g.) which was chromatographed on 40 g. of silica. The fractions obtained with 70% benzene–petroleum ether were combined to yield 0.50 g. of material, recrystallized from aqueous methanol to give the analytical sample of **11b** (R′ = CH=CH$_2$), m.p. 106–108°, λ_{max}^{KBr} 2.97 and 6.08 μ, [α]D 117°.

Anal. Calcd. for $C_{20}H_{28}O$: C, 84.45; H, 9.92. Found: C, 84.17; H, 9.81.

Attempts to reduce the vinyl double bond in the presence of palladium–carbon catalyst led to a mixture from which ring-A aromatic derivatives were isolated and identified by infrared and n.m.r. spectra.

3β-Hydroxyestr-5(10)-en-17-one (6a).—A solution of 5.0 g. of the tosylate **3a** in 50 ml. of dimethylformamide was heated at 65° for 68 hr. The product (3.3 g.), isolated by dilution with water and benzene extraction,[31] was saponified by boiling in 50 ml. of methanol containing 15 ml. of 10% aqueous potassium hydroxide in a nitrogen atmosphere for 2 hr. The reaction mixture was diluted with water, and the product was isolated by benzene extraction.[31] The residue (3.1 g.) was chromatographed on 300 g. of silica. The initial eluates (5% ethyl acetate in benzene) provided 0.60 g. of a mixture of dienes (**11a** and **10**) containing 20% of aromatic material **12** (n.m.r. analysis). Elution with 8% ethyl acetate in benzene gave a total of 1.0 g. of material, shown by paper chromatography to contain 15% of the epimer **2a**. The product was recrystallized from cyclohexane (Darco) to yield 0.68 g. of the 3β-hydroxy ketone **6a**, m.p. 137–140°, λ_{max} 2.75 and 5.72 μ, [α]D 202°.

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.97; H, 9.47.

Treatment of the mesylate **3b** with dimethylformamide under these conditions caused reaction of only 70% of the starting material in 68 hr. by n.m.r. assay. Added sodium benzoate helped little.[34]

3β-Benzoyloxyestr-5(10)-en-17-one.—The benzoate was prepared in the same manner as its epimer. Recrystallization of the crude product from methylene chloride–methanol gave the pure benzoate, m.p. 136–138°, λ_{max} 5.75 and 5.82 μ, [α]D 135°. The C-3α proton had an n.m.r. signal centered at 322 c.p.s. (half-height width, 18 c.p.s.).

Anal. Calcd. for $C_{25}H_{30}O_3$: C, 79.33; H, 7.99. Found: C, 79.24; H, 8.13.

The same compound could be obtained from a mixture of the 3α- and 3β-benzoates, obtained by benzoylation of the crude borohydride product. Chromatography of the mixture on silica was followed by fractional crystallization of the material eluted at 1% ethyl acetate in benzene, giving the pure 3β-isomer, m.p. 136–138°.

Estr-5(10)-ene-3β,17β-diol (6b).—A solution of 1.05 g. of the hydroxy ketone **6a** in 50 ml. of tetrahydrofuran containing 3.0 g. of lithium tri-*t*-butoxyaluminohydride was allowed to stand at room temperature for 18 hr. The solution then was poured into aqueous acetic acid, and the resultant precipitate was collected on a filter. Recrystallization of the product from acetonitrile and

(32) Preparation of this diene system (**11**) has not been described in the literature. Near analogs are estra-2,4-dien-17-ol acetate, λ_{max} 268 mμ (ϵ 5270) [P. N. Rao and H. R. Goldberg, *Chem. Ind.* (London), 1317 (1961)], and several androsta-2,4-dienes, λ_{max} 266 mμ (ϵ 6500) [B. Berkoz, A. D. Cross, M. E. Adame, H. Carpio, and A. Bowers, *J. Org. Chem.*, **28**, 1976 (1963)].

(33) For precautions, see G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(34) *Cf.* E. J. Reist, R. R. Spencer, and B. R. Baker, *J. Org. Chem.*, **24**, 1618 (1959).

from aqueous methanol gave 0.44 g. of the pure diol **6b**, m.p. 137–138° as a monohydrate, λ_{max}^{KBr} 3.05 μ.

Anal. Calcd. for $C_{18}H_{28}O_2 \cdot H_2O$: C, 73.43; H, 10.27. Found: C, 73.29; H, 10.13.

Hydrogenation of Estr-5(10)-ene-3β,17β-diol (6b).—A solution of 0.43 g. of the diol **6b** in ethanol (50 ml.) and ruthenium oxide catalyst (1.0 g.) were heated in an atmosphere of hydrogen at 100°, 1600 p.s.i. for 8 hr. The solution was filtered and concentrated, yielding a residue which was recrystallized from aqueous methanol to yield 0.22 g. of 5α,10α-estrane-3β,17β-diol (**9**), m.p. 171–175°, identical with an authentic sample in the infrared.[12]

10ξ-Hydroxy-3β,5-cycloestran-17-one (4). A. Tosylate Solvolysis.—A solution of 9.2 g. of the tosylate **3a** in 300 ml. of acetone and 100 g. of potassium acetate in 500 ml. of water were stirred together at the boiling point for 18 hr. (Later experiments showed this time could be reduced to 3 hr.) The solution was concentrated to half volume and the product was extracted with benzene.[31] The semicrystalline residue (7.0 g.) was adsorbed onto 300 g. of Merck chromatographic alumina (alkaline). Elution with benzene gave 3.4 g. of crystalline material, recrystallized from methanol to provide the diene **11a**, m.p. 133–134°. Elution of the column with 1 and 2% ethyl acetate in benzene gave 1.3 g. (19%) of material, recrystallized from acetone–petroleum ether to yield 1.15 g. of the pure *i*-steroid **4**, m.p. 193–195°; $\lambda_{max}^{CCl_4}$ 2.78 and 5.75 μ; $\Delta\nu$ 7, 10, and 15 c.p.s. (cyclopropane protons); $[\alpha]_D$ 115°.

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.92; H, 9.42.

Acetylation of this material failed to occur with pyridine–acetic anhydride at 100° for 10 min. Treatment with 4 *N* chromic acid in acetone at room temperature effected no reaction.

Further elution of the column with 10 and 20% ethyl acetate in benzene gave a crude product containing about 5% of the 3α-alcohol (by paper chromatogram); recrystallization from cyclohexane afforded 0.60 g. of the major constituent, the 3β-alcohol, m.p. 133–136°.

B. Mesylate Solvolysis.—A slurry of the mesylate **3b** (7.0 g.) in 250 ml. of acetone and 250 ml. of water containing 18 g. of potassium acetate was stirred at the reflux temperature. The initially present crystals dissolved slowly giving way to an oily precipitate. After 2.5 hr. the solution was concentrated *in vacuo*, producing a crystalline solid (4.85 g.) which was collected on a filter. Extraction of the filtrate with benzene afforded an additional 0.6 g. of material. Neither product contained mesylate as seen clearly from the n.m.r. spectra. Chromatography showed the product to consist of 2.0 g. (40%) of the diene [λ_{max} 260 mμ (ϵ 1000)] containing 3–6% of aromatic material (n.m.r. analysis). Also obtained was 1.8 g. (33%) of the crude cyclosteroid **4**, recrystallized to give 1.0 g., m.p. 187–191°, and 0.35 g., m.p. 178–182°, of **4**. Later fractions contained 0.57 g. (12%) of the hydroxy ketone **6a**.

Acid-Catalyzed Rearrangement of the Cyclosteroid 4.—A solution of 50 mg. of the cyclosteroid **4** in 20 ml. of 98% formic acid containing 0.2 ml. of triethylamine was allowed to stand at room temperature for 18 hr. The solution was diluted with water and the precipitate was collected on a filter. The product (42 mg). was dissolved in 10 ml. of methanol containing 0.5 ml. of 5% aqueous potassium hydroxide, and the solution was heated at reflux for 30 min. The methanol was distilled and replaced with water, yielding a crystalline material which was collected and washed on a filter. The product, 40 mg. of **2a**, m.p. 186–190°, was identical in the infrared with an authentic sample. A paper chromatogram of this material showed it to be free of any contaminant including the 3β-hydroxy compound **6a**.

Hydrogenation of the Cyclosteroid 4.—A solution of 0.20 g. of the cyclosteroid **4** in 15 ml. of dioxane and 0.8 ml. of acetic acid was stirred at room temperature under hydrogen for 27 hr.[19] The mixture absorbed *ca.* 1 mole equiv. of gas. The product, isolated by filtration of the catalyst and evaporation of the solvent, was chromatographed on 4 g. of silica. The fractions, all amorphous, were combined into three groups and each was examined by n.m.r.; the spectra showed marked broadening of the methyl group signals, implying that the hydrogenation had produced new methyl groups.

In a subsequent run, the same procedure was followed except the acid was omitted. The product from 0.90 g. of cyclosteroid **4** was chromatographed on alumina and afforded 0.58 g. of a semicrystalline material. Crystallization from petroleum ether yielded 60 mg., m.p. 105–115°, and 50 mg., m.p. 123–125°, of desoxyestrone **12**, as seen from comparison of n.m.r. and infrared spectra. No other crystalline products were obtained. In another experiment, palladium-on-carbon catalyst caused increased pressure in the system due to release of hydrogen.

3β-Tosyloxyestr-5(10)-en-17-one (7a).—A solution of 0.95 g. of the 3β-hydroxy compound **6a** and 1.5 g. of *p*-toluenesulfonyl chloride was allowed to stand at 15° for 18 hr. The solution was diluted with aqueous potassium bicarbonate and the resulting precipitate was separated by filtration and washed with water, yielding 1.0 g. of product, m.p. 135–138°. Recrystallization of this material from acetone–petroleum ether gave the pure sample, m.p. 140–142°, λ_{max} 5.75 μ, $[\alpha]_D$ 138°.

Anal. Calcd. for $C_{25}H_{32}O_4S$: C, 70.06; H, 7.53. Found: C, 69.91; H, 7.32.

The same compound was isolated readily as a second crop from a mixture of 3α- and 3β-tosylates. This afforded an additional method of separating reasonably pure 3β-derivatives.

Passage of the tosylate **7a** (0.20 g.) over 6 g. of Woelm basic alumina gave 0.13 g. of crude diene **11a** [λ_{max} 266 mμ (ϵ 1200)].

10β-Hydroxy-3α,5-cycloestran-17-one (8).—A solution of 2.0 g. of the tosylate **7a** in 100 ml. of acetone and 10 g. of potassium acetate in 80 ml. of water was stirred at room temperature for 6 hr. The solution then was heated at reflux for 24 hr., cooled, and diluted with water. The product, isolated by benzene extraction,[31] amounted to 1.40 g. of an oil which was chromatographed on 40 g. of silica. The early fractions, eluted with 2% ethyl acetate in benzene, amounted to 0.42 g. of the crude diene (infrared correlation). Elution with 10% ethyl acetate in benzene provided 0.21 g. of the crude *i*-steroid, recrystallized from acetone–petroleum ether to provide the analytical sample, m.p. 173–176°; $\lambda_{max}^{CCl_4}$ 2.78 and 5.75 μ; $\Delta\nu$ 39, 42, and 47 c.p.s.; $[\alpha]_D$ 138°.

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.94; H, 9.43.

Later eluents provided 0.23 g. of the 3α-alcohol **2a** contaminated with 10–15% of the 3β-alcohol **6a**; the latter epimer probably was derived largely from the epimeric tosylate **3a** present in the starting material.

The mesylate **7b**, an amorphous material prepared in the same manner as the epimer **3b**, was solvolyzed under the same conditions as described for **3b**. The product from 1.4 g. of **7b** was chromatographed to yield the following crude fractions: 0.31 g. of the diene **11a** [λ_{max} 266 mμ (ϵ 1060)], 0.39 g. of the cyclosteroid **8** (37%), and 0.20 g. of the alcohol **2a** (containing 8–10% of the epimer **6a**).

Acid-Catalyzed Rearrangement of the Cyclosteroid 8.—A solution of 30 mg. of the cyclosteroid **8** in 5 ml. of formic acid and 0.05 ml. of triethylamine was allowed to stand at room temperature for 16 hr. The solution was diluted with water, and the product was isolated by extraction with benzene.[31] The residue, 32 mg. of an oil, was boiled in 10 ml. of methanol containing 2 ml. of 10% aqueous potassium hydroxide for 30 min. The product was isolated by dilution with water and extraction with benzene. The resulting material, 34 mg., was adsorbed on 3 g. of silica. Elution with 10% ethyl acetate in benzene provided 30 mg. of material which was crystallized from petroleum ether to yield the 3β-isomer **6a**, m.p. 134–138°. Analysis of total product by paper chromatography showed the presence of 85% of the 3β-epimer and 10% of the 3α-epimer. The latter compound arose from the epimeric cyclosteroid **4a** shown by paper chromatography to be present in the starting material.

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