anions was virtually independent of concentration, so that the infrared and ultraviolet data were quantitatively comparable. Concentrations were determined from the known extinction coefficients of the diketo forms of the various compounds.[2,6]

For the infrared spectra in D_2O solution, path lengths varied from 15 to 50 μ. The cuvettes were calibrated by means of the known band extinction of the carbonyl group of acetone. Nonetheless the evaluations of molar extinctions (ϵ^A) from the measured path lengths were limited to an accuracy of ± 5–10%.

The shift in equilibrium point of the thymine monoanion equilibrium mixture as a function of temperature was measured in cuvettes fitted with ground stoppers in a specially constructed thermostated carriage fitted to the Hilger UVISPEK.

Acknowledgments. We are indebted to the World Health Organization for financial support of this work through the Department of Biophysics, University of Warsaw.

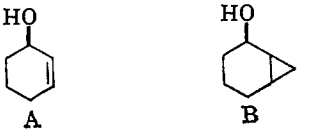
Steroids. CCLXXXIII.[1] Stereochemically Controlled Simmons–Smith Methylenation of Homoallylic Alcohols of Low Reactivity. A New Synthesis of 10α-Testosterone

R. Ginsig[2] and A. D. Cross

Contribution from the Research Laboratories, Syntex, S. A., Apartado 2679, Mexico, D. F. *Received June 28, 1965*

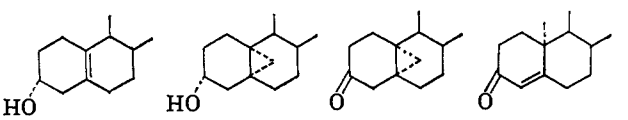
Employing published reaction conditions, no Simmons–Smith methylenation of steroid 5(10)-en-3α-ols occurred. A modification of the reaction method is reported which gave stereospecific α-face addition in up to 85% yields. Based on this new procedure a novel synthesis of 10α-testosterone (Ia) was achieved. With several reagents known to effect cleavage of cyclopropanes the 5α,10α-methylene steroids afforded principally 5α-substituted methyl derivatives, thus foiling attempts to prepare 19-substituted 10α-testosterone analogs.

In the few years which have elapsed since Simmons and Smith first described the over-all addition of methylene to double bonds by treatment of the olefin with methylene diiodide and a zinc–copper couple,[3] numerous syntheses of cyclopropanes by this method have been described.[4] Concurrently, Simmons and his co-workers studied the reaction mechanism observing the formation of ethers as reaction by-products and the operation of a large steric effect.[5] Also of interest were the observations by Winstein and others that the addition of methylene to the double bond of cyclic allylic and homoallylic alcohols takes place stereospecifically *cis* to the hydroxyl group (A → B), the stereochemical control being lost on acetylation of the alcohol.[6]



A B

As part of a broad program in these laboratories aimed at developing new synthetic routes to steroids of abnormal configuration,[7] we required an efficient chemical synthesis of 10α-androst-4-en-3-ones. A synthesis of 10α-testosterone (Ia) involving a photochemical transformation, then six chemical steps, had already been reported.[8] A purely chemical route to 10α-androstan-2-ones was subsequently described involving methyl Grignard addition to estr-1(10)-en-2-ones.[9] The recent findings that metal hydride reductions of steroid 5(10)-en-3-ones (readily available from estrone 3-ethers by Birch reduction) give predominantly 5(10)-en-3α-ols (C)[10,11] suggested a simple chemical synthesis of 10α-androst-4-en-3-ones according to the scheme C → F.



C D E F

Accomplishment of the synthesis depended on stereochemical control by the 3α-hydroxy group in the Sim-

(1) Steroids. CCLXXXII: J. A. Edwards, H. Carpio, A. Cruz, and M. J. Teran, *J. Org. Chem.*, in press.
(2) Syntex Postdoctoral Fellow, 1963–1964, Mexico.
(3) H. E. Simmons and R. D. Smith, *J. Am. Chem. Soc.*, 80, 5323 (1958); 81, 4256 (1959).
(4) See, for example, N. T. Castelluci and C. E. Griffin, *ibid.*, 82, 4107 (1960); E. F. Ullman and W. J. Fanshawe, *ibid.*, 83, 2379 (1961); A. C. Cope, S. Moon, and C. H. Park, *ibid.*, 84, 4843 (1962), and later papers in this series; R. S. Boikess and S. Winstein, *ibid.*, 85, 343 (1963); W. D. Kumler, R. Boikess, P. Bruck, and S. Winstein, *ibid.*, 86, 3126 (1964).
(5) E. P. Blanchard and H. E. Simmons, *ibid.*, 86, 1327 (1964); H. E. Simmons, E. P. Blanchard, and R. D. Smith, *ibid.*, 86, 1347 (1964); *cf.* also G. Wittig and F. Wingler, *Chem. Ber.*, 97, 2146 (1964).
(6) S. Winstein, J. Sonnenberg, and L. De Vries, *J. Am. Chem. Soc.*, 81, 6523 (1959); S. Winstein and J. Sonnenberg, *ibid.*, 83, 3235 (1961); E. J. Corey and R. L. Dawson, *ibid.*, 85, 1782 (1963); W. G. Dauben and G. H. Berezin, *ibid.*, 85, 468 (1963); W. G. Dauben and A. C. Ashcraft, *ibid.*, 85, 3673 (1963); P. Radlick and S. Winstein, *ibid.*, 86 1866 (1964).
(7) J. A. Edwards, P. Crabbé, and A. Bowers, *ibid.*, 85, 3313 (1963); J. A. Edwards, H. Carpio, and A. D. Cross, *Tetrahedron Letters*, 3299 (1964); A. D. Cross, J. A. Edwards, P. Crabbé, H. Carpio, and E. Denot, to be published.
(8) R. Wenger, H. Dutler, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, 45, 2420 (1960).
(9) M. Torigoe and J. Fishman, *Tetrahedron Letters*, 1251 (1963).
(10) S. G. Levine, N. H. Eudy, and E. C. Farthing, *ibid.*, 1517 (1963).
(11) A. D. Cross, E. Denot, R. Acevedo, R. Urquiza, and A. Bowers, *J. Org. Chem.*, 29, 2195 (1964).

mons–Smith methylenation of the 5(10)-double bond.[12] Isomerization of 5β,19-cyclosteroids to 10β-methyl steroids had already been realized using alumina[14] and acid[15] catalysis. For the 5α,19-cyclo-10α-steroid E, ring cleavage to the desired 10α-methyl derivative F leads to a less stable, fused-ring system. Realization of the synthesis is now reported together with novel solutions to problems encountered in the Simmons–Smith addition and the isomerization reactions.

When estr-5(10)-ene-3α,17β-diol (IIa) was treated with freshly prepared zinc–copper couple and methylene diiodide reagent[16] in refluxing ether, the steroid was recovered quantitatively. A nuclear magnetic resonance (n.m.r.) spectroscopic scan of mother liquors revealed no trace of characteristic, high-field cyclopropyl proton resonances.[17] Prolongation of the reaction time gave equally unsuccessful results and switching to tetrahydrofuran, dioxane, or diglyme solvents afforded no improvement. The inertness of the 5(10)-double bond to addition contrasted with the report by Blanchard and Simmons[5] of faster addition to more highly substituted double bonds but is in accord with their finding that steric effects are prominent. A mixture of the reagent and homoallylic diol IIa in ether was next sealed in a stainless steel tube and maintained at 92°[18] for 3 hr. Two oily fractions were obtained by column chromatography. N.m.r. spectral examination of the first oil revealed the presence of 5,10-methylene adducts (pair of doublets at 11.8, 16.2, 29.0, and 33.3 c.p.s. (J = 4.3 c.p.s.) for geminal cyclopropyl protons). However, the n.m.r. spectra also disclosed extensive concomitant etherification of the hydroxyls (a singlet at 198.5 c.p.s. for methoxy protons, and a quartet and a triplet characteristic of the methylene and methyl protons of ethoxy). The second oily product showed similar gross spectral properties but with the methoxyl resonance at 200.5 c.p.s. Etherification under the reaction conditions employed was not a surprise since the reagent reacts with alcohols to form hydrogen iodide. The latter reacts further with the reagent or solvent to release methyl and ethyl iodides, respectively. Formation of ethers can then proceed by well-known procedures. Detailed studies of the reaction mechanism[5] later provided a generous basis for these conclusions.

A dramatic improvement resulted when *the homoallylic diol IIa, an excess of methylene diiodide and zinc–copper couple, and ether were distilled to half-volume prior to sealing in the stainless steel tube.*[19] Reaction at 92°[18] (3 hr.) then afforded an 85% yield of 5α,19-cyclo-10α-androstane-3α,17β-diol (IIIa). Mother liquors showed mere traces of ethereal by-products on thin layer chromatography. The structure of the adduct IIIa was supported by the n.m.r. spectrum of the derived diacetate ester IIIb which showed a characteristic pair of doublets for geminal cyclopropyl protons at 14.7, 19.3, 30.6, and 35.2 c.p.s. (J = 4.6 c.p.s.). No methylene addition took place when the diacetate IIb was exposed to the reagent under standard of forcing conditions. Evidence for the 5α,10α-stereochemistry of the methylene bridge was found in the nonidentity of the dione IIIc (from two-phase chromic acid oxidation[20] of diol IIIa) with the known 5β,19-cycloandrostane-3,17-dione (IVa).[14,21,22] A minor product of the oxidation of the diol IIIa was 3α-hydroxy-5α,10α-methyleneestran-17-one (IIId) with a single carbonyl absorption in the infrared at 1740 cm.$^{-1}$. The new dione IIIc showed resonance for geminal cyclopropyl protons as a pair of doublets at 32.0 c.p.s., $\Delta\nu$ = 25 c.p.s., and J = 5.8 c.p.s., both protons being deshielded by the carbonyl at C-3 relative to the diol IIIa and diacetate IIIb. In comparison the geminal 19-methylene protons of the isomer IVa resonate as a pair of doublets at 30.5 c.p.s., $\Delta\nu$ = 3.5 c.p.s., and J = 5.8 c.p.s., the protons in this case having a much greater similarity of their chemical shifts.[22] Furthermore, the dione IIIc showed a positive Cotton effect curve with a peak of +3426° at 317 mμ, 853° higher than for the isomer IVa.

Exposure of the dione IIIc to hot concentrated hydrochloric or perchloric acid in ethanol led to opening of the cyclopropane ring. The major product, clearly a conjugated ketone ($\nu_{C=O}$ 1740 and 1675 cm.$^{-1}$), showed λ_{max} 234 mμ (log ε 3.92) and resonance at 364.5 (2 H) and 416 c.p.s. (1 H) for two olefinic protons of an ABX system. This rearrangement product was therefore assigned structure Va. Observed coupling constants $J_{1,2}$ = 10.2 c.p.s., $J_{1,10}$ = 1.5 c.p.s., and $J_{2,10}$ = 2.8 c.p.s. were in accord with expectations since examination of a model[13] showed the 10β-CH bond to be virtually at right angles to the plane of the double bond, a condition highly favorable to strong allylic coupling[23] but to only weak coupling of the adjacent 1- and 10β-protons.[24] The minor reaction products were devoid of strong ultraviolet absorption and showed an extra methyl group three-proton resonance in the n.m.r. spectrum. One of these minor products was isolated and showed n.m.r. peaks in agreement with structure VIa. Products Va and

(12) Addition of nucleophilic reagents to the 5(10)-double bond normally proceeds by attack at the β-face; see ref. 10 and J. P. Ruelas, J. Iriarte, F. A. Kincl, and C. Djerassi, *J. Org. Chem.*, **23**, 1744 (1958). However, it was reasoned that providing the equatorial[10] 3α-hydroxyl can adopt the axial configuration by a change of ring A to its alternative half-chair conformation the Simmons–Smith reaction intermediate complex should be able to deliver "methylene" α to the 5(10)-double bond. The 3α-acetate in a structurally related 5β,10β-epoxide (ring A of similar conformation to the estr-5(10)-en-3α-ol C as judged from molecular models[13]) had been shown already to be capable of delivering acetate across the α-face to C-5.[11] Therefore, methylenation in the desired manner appeared possible.

(13) A. S. Dreiding, *Helv. Chim. Acta*, **42**, 1339 (1959).

(14) J. J. Bonet, H. Wehrli, and K. Schaffner, *ibid.*, **45**, 2615 (1962).

(15) A. J. Birch, J. M. Brown, and G. S. R. Subba Rao, *J. Chem. Soc.*, 3309 (1964); L. H. Knox, E. Velarde, and A. D. Cross, *J. Am. Chem. Soc.*, **87**, 3727 (1965).

(16) R. S. Shank and H. Schechter, *ibid.*, **24**, 1825 (1959).

(17) N.m.r. spectra were obtained for 5–10% solutions in deuteriochloroform containing a little tetramethylsilane (TMS) as an internal reference. Chemical shifts are quoted as c.p.s. downfield from the TMS reference (0.0 c.p.s.) and are accurate to ±0.5 c.p.s. Coupling constants, also quoted in c.p.s. units, are accurate to ±0.5 c.p.s. Spectra were recorded on a Varian A-60 spectrometer through the kind cooperation of Mr. E. Diaz and the Universidad Nacional Autónoma de México.

(18) Steam bath temperature, Mexico City.

(19) It was reasoned that since addition required forcing conditions the reaction between the steroid alcoholic functions and the reagent could be brought about at ether reflux temperature and the resulting undesirable alkyl iodides removed simply by distillation, thereby avoiding steroid ether formation at higher temperatures.

(20) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, **83**, 2952 (1961).

(21) L. H. Knox, E. Velarde, and A. D. Cross, *ibid.*, **85**, 2533 (1963).

(22) O. Halpern, P. Crabbé, A. D. Cross, I. Delfin, L. Cervantes, and A. Bowers, *Steroids*, **4**, 1 (1964).

(23) T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Am. Chem. Soc.*, **85**, 1699 (1963); D. J. Collins, J. J. Hobbs, and S. Sternhell, *Tetrahedron Letters*, 197 (1963).

(24) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959); *J. Am. Chem. Soc.*, **85**, 2870 (1963).

VIa presumably arise by proton loss at C-1 and C-9, respectively, from the intermediate tertiary carbonium ion, the 1,10-double bond in the former case moving into conjugation with the 3-ketone, as in Va. It was apparent, therefore, that, in acid-catalyzed cleavage of the cyclopropyl ring, formation of products with a 5α-methyl stereochemistry is a more favored process than that leading to 10α-methyl compounds, even though the latter mechanism leads to a conjugated 4-en-3-one system as direct end product. Lithium aluminum hydride reduction of the conjugated dione Va followed by back oxidation of the allylic hydroxyl with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ)[25] afforded 17β-hydroxy-5α-methylestr-1-en-3-one (Vb).

Similar results were obtained when the 5α,10α-methylene-3α,17β-diol IIIa was treated with hot ethanolic hydrochloric acid. The principal product lacked vinyl proton resonance in the n.m.r. spectrum but the presence of a new methyl group was indicated in agreement with probable structure VIb for this compound. Again, cyclopropane ring opening in the undesired manner occurred. Low-temperature bromination (Br_2CHCl_3) of the cyclopropane ring of the diacetate IIIb, followed by treatment of the crude product with lithium carbonate–dimethylformamide, then acid hydrolysis, furnished the 5α-bromomethyl derivative VIIa, two-phase oxidation[20] of which gave the corresponding diketone VIIb. This diketone showed no ultraviolet absorption with n.m.r. resonance for only one vinylic proton at 337 c.p.s., and a pair of doublets at 210 c.p.s. for CH_2Br. The circular dichroism curve (see Experimental Section) for this dione was in good agreement for the 5α-bromomethyl structure VIIb and was incompatible with the isomeric 10α-bromomethyl-Δ^5 structure. An ethanolic solution of the diketone VIIb on addition of hydrochloric acid developed an ultraviolet maximum at 230 mμ, consistent with isomerization to the conjugated ketone Vc. Conversely, addition of aqueous sodium carbonate, instead of acid, generated an ultraviolet maximum at 275 mμ, indicative of the norcarenone VIII.[26] An attempt to cleave the cyclopropane ring by treatment of the diacetate IIIb with lead tetraacetate and acetic acid[27] gave only starting material from the reaction.

Since it was apparent therefore that cleavage of the 5α,10α-methylene compounds to 10α-methyl analogs could not be achieved readily by addition of a cationic species to the cyclopropane ring, the influence of bases was investigated.[28] It was found that sodium hydroxide in dioxane, potassium methoxide–methanol, and potassium *t*-butoxide in *t*-butyl alcohol all failed to isomerize the dione IIIc to the corresponding Δ^4-3-ketone. Using potassium *t*-butoxide and dimethyl sulfoxide, solvent rearrangement occurred, although the product appeared to be polymeric in nature. An ultraviolet absorption maximum at 244 mμ and n.m.r. signals for the C-4 olefinic proton (348 c.p.s.) and a new angular methyl group (singlet at 75 c.p.s.) were collectively indicative of the 10α-methylestr-4-en-3-one system. However, a complicated pattern of resonance at 45–60 c.p.s. totaling three protons, instead of a clean singlet, for H-18, suggested base-catalyzed condensation or addition at C-16 and/or C-17. Accordingly, the sequence C → F was repeated with the C-17 position in the nonketonic form.

17β-Hydroxyestr-5(10)-en-3-one (IIc)[11] was protected as the tetrahydropyran-2-yl ether IId and then reduced with sodium borohydride to the 3α-alcohol IIe contaminated with some of the 3β-isomer IIf. Treatment of this mixture with zinc–copper couple and methylene diiodide in ether at 92° under the modified conditions afforded mainly the diol IIIa. To avoid loss of the tetrahydropyranyl protecting group the Simmons–Smith reaction was checked with normal ether reflux. The resultant crude oily adduct was oxidized directly with chromium trioxide–pyridine complex,[29] and the tetrahydropyranyl protecting group was removed by mild acid hydrolysis. Chromatography of the products gave estr-5(10)-en-3α,17β-diol (IIa)[30] and 17β-hydroxy-5β,19-cycloandrostan-3-one (IVb). The latter showed an n.m.r. singlet at 29 c.p.s. for two chemically equivalent geminal cyclopropyl protons and was isomerized by *t*-butoxide–dimethyl sulfoxide to testosterone. It was apparent that under standard reflux conditions Simmons–Smith methylenation occurred for only the minor borohydride reduction product (IIf) giving β-face addition.

Finally, the modified methylenation reaction was carried out on a purer sample of the 3α-alcohol IIc (from reduction of IId with lithium tri-*t*-butoxyaluminum hydride) in a steel tube at 50°. Using this compromise the tetrahydropyranyl group was not lost and α-face addition did take place. Subsequent oxidation of the adduct IIIe and hydrolysis of the crude ketone IIIf furnished 17β-hydroxy-5α,19-cyclo-10α-androstan-3-one (IIIg), for which the geminal cyclopropyl protons resonated at 31.5 c.p.s. as a pair of doublets, J = 5 c.p.s. and $\Delta\nu$ = 24 c.p.s., in marked contrast to the pattern recorded for the 5β,10β-isomer IVb (*vide supra*). The stereochemical difference between this pair of stereoisomeric ketones was further confirmed by circular dichroism (C.D.) measurements in which the α-methylene adduct showed a positive Cotton effect and the β-adduct a negative Cotton effect.

Isomerization of the α-adduct IIIg proceeded smoothly, with no complications in ring D, in the presence of *t*-butoxide–dimethyl sulfoxide to furnish 17β-hydroxy-10α-androst-5-en-3-one (IX) [ν_{19-H} 77.5, ν_{6-H} 328, ν_{4-H} 185.5 (pair of doublets, J = 15 c.p.s.)] and 10α-testosterone (Ia). By acetylation there was obtained 10α-testosterone acetate (Ib) with physical constants (see Experimental Section) in agreement with those determined by Jeger and his co-workers,[8] except for the optical rotatory dispersion (O.R.D.) data. The O.R.D. values recorded in the present work were nevertheless very similar to those reported recently by Snatzke and his collaborators who corrected the earlier published data for 10α-testosterone.[31] Isolation of the β,γ-unsaturated ketone IX under the reaction condi-

(25) D. Burn, V. Petrow, and G. O. Weston, *Tetrahedron Letters*, 14 (1960).

(26) The stereoisomeric 5β,10β-norcarenone shows λ_{max} 272 mμ.[15]

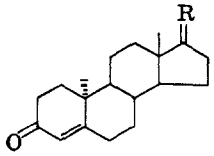
(27) R. J. Ouellette and D. L. Shaw, *J. Am. Chem. Soc.*, **86**, 1651 (1964).

(28) S. Rakhit and M. Gut, *ibid.*, **86**,1432 (1964), recently reported base-catalyzed isomerization of IVa to androst-4-ene-3,17-dione.

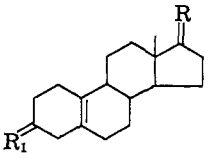
(29) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

(30) The 3α-hydroxyl group in the diol IIa is oxidized only slowly by chromium trioxide–pyridine reagent as was determined in a separate experiment.

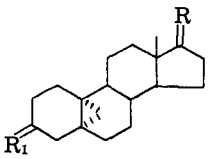
(31) R. Tschesche, I. Morner, and G. Snatzke, *Ann.*, **670**, 103 (1963).



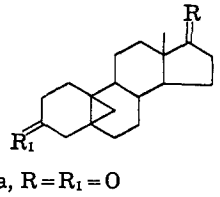
Ia, R = α-H, β-OH
b, R = α-H, β-OAc



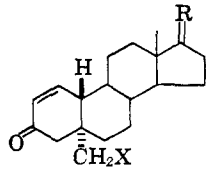
IIa, R = α-H, β-OH; R₁ = α-OH, β-H
b, R = α-H, β-OAc; R₁ = α-OAc, β-H
c, R = α-H, β-OH; R₁ = O
d, R = α-H, β-O-(THP); R₁ = O
e, R = α-H, β-O-(THP); R₁ = α-OH, β-H
f, R = α-H, β-O-(THP); R₁ = α-H, β-OH



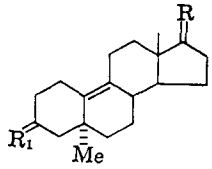
IIIa, R = α-H, β-OH; R₁ = α-OH, β-H
b, R = α-H, β-OAc; R₁ = α-OAc, β-H
c, R = R₁ = O
d, R = O; R₁ = α-OH, β-H
e, R = α-H, β-O-(THP); R₁ = α-OH, β-H
f, R = α-H, β-O-(THP); R₁ = O
g, R = α-H, β-OH; R₁ = O



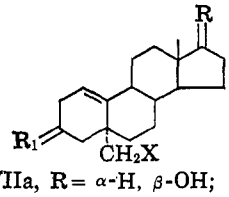
IVa, R = R₁ = O
b, R = α-H, β-OH; R₁ = O



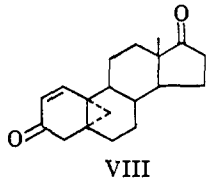
Va, R = O; X = H
b, R = α-H, β-OH; X = H,
c, R = O; X = Br



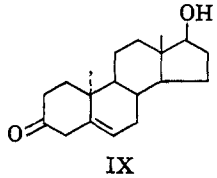
VIa, R = R₁ = O
b, R = α-H, β-OH; R₁ = α-OH, β-H



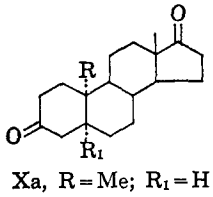
VIIa, R = α-H, β-OH;
R₁ = α-OH, β-H; X = Br
b, R = R₁ = O; X = Br



VIII



IX



Xa, R = Me; R₁ = H
b, R = H; R₁ = Me

tions employed suggests that the base-catalyzed equilibrium Δ^4-3-ketone $\leftrightarrow$ Δ^5-3-ketone lies appreciably more towards the unconjugated ketone in the 10α-series than in the 10β-series.[32]

Prior to the discovery of base catalysis for isomerization to 10α-methyl steroids, the diacetate IIIb in acetic acid solution was hydrogenated over platinum catalyst under pressure. The product, homogeneous on a chromatoplate, was saponified and then oxidized[20] to a mixture of inseparable diketones, Xa and Xb, both containing one new angular methyl on the basis of n.m.r. spectroscopy (singlets at 67 and 77 c.p.s. totalling three protons by area measurement). An O.R.D. curve for the mixture was consistent with 5α,10α stereochemistry. Dehydrogenation of the mixture led to an inseparable mixture of estr-1-en-3-ones (λ_{max} 234 mμ) which was not investigated further.

Experimental Section[33]

5α,19-Cyclo-10α-androstane-3α,17β-diol (IIIa). Estr-5(10)-ene-3α,17β-diol (IIa, 10 g.)[10] was added during 1 hr. to a refluxing ethereal solution of zinc–copper couple and methylene diiodide (prepared from 350 ml. of ether, 180 g. of methylene diiodide, and 60 g. of zinc–copper couple[14]). After addition was completed, half of the solvent was removed by distillation and more dry ether (200 ml.) was added. The whole reaction mixture was then kept for 3 hr. in a sealed stainless steel tube at 92°[18] before being cooled in an ice bath and poured into saturated aqueous sodium bicarbonate solution (500 ml.). Three extractions with ether and evaporation of the combined dried (Na_2SO_4) extracts yielded a solid residue which was recrystallized from acetone to give 5α,19-cyclo-10α-androstane-3α,17β-diol (IIIa): 8.45 g., m.p. 162–163°, $[\alpha]D + 40°$, λ_{max} 3310 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41; O, 11.02. Found: C, 78.87; H, 10.55; O, 11.00.

A prior attempt to achieve the same transformation by refluxing the ethereal reaction mixture for from 1 to 72 hr. (standard conditions)[3] and work-up as above led to recovered starting material only. When ether solvent was replaced by refluxing tetrahydrofuran (24 hr.), dioxane (15 hr.), and diglyme (7 hr.), no cyclopropane product IIIa could be isolated.

A similar reaction to the successful one described above, on one-tenth scale, but omitting the distillation to half-volume, gave an oily product. The latter was separated by chromatography over silica gel (40 g.) and elution with hexane–ethyl acetate (7:3) into two oily fractions, A (120 mg.) and B (500 mg.), both less polar than starting material (IIa). Oil A showed n.m.r. signals at 11.5, 16, 29, and 33.5 (cyclopropyl geminal protons, pair of doublet, J = 4.3 c.p.s.), 47 (18 H, singlet), 198.5 (OMe, singlet), 281 (OH,

(32) Earlier experiments conducted in the organic chemistry laboratories, E. T. H., Zurich, led to the same conclusion; personal communication from Dr. K. Schaffner.

(33) Melting points were recorded on the Fisher-Johns block and are corrected. Except where stated otherwise, solutions were for chloroform solutions, ultraviolet spectra were for solutions in ethanol, circular dichroism measurements were recorded with dioxane solutions, and infrared spectra were measured with potassium bromide disks and a Perkin-Elmer Model 21 spectrophotometer. Microanalyses were performed by Midwest Micro Labs, Indianapolis, Ind., or by A. Bernhardt, Mülheim (Ruhr), W. Germany.

singlet), 216.5 (OCH_2CH_3, quartet, J = 7 c.p.s.), and 72.5 c.p.s. (OCH_2CH_3, triplet, J = 7 c.p.s.). Oil B gave n.m.r. signals at 12, 16.5, 29, and 33.5 (cyclopropyl geminal protons, pair of doublet, J = 4.5 c.p.s.), 46.5 (18 H, singlet), 200.5 (OMe, singlet), 281 (OH, singlet), 216.5 (OCH_2CH_3, quartet, J = 7 c.p.s.), and 72.5 (OCH_2CH_3, triplet, J = 7 c.p.s.). Each oil contained the second as a contaminant and, additionally, showed weak proton resonance singlet at 24 c.p.s. attributable to some 5β,19-cycloandrostane-3β,17β-diol arising from estr-5(10)-ene-3β,17β-diol impurity in starting material.

Exposure of estr-5(10)-ene-3α,17β-diol diacetate (IIb, 1 g.) to the forcing reaction conditions described above gave, as the only isolable compound, recovered starting material (750 mg.).

5α,19-Cyclo-10α-androstane-3α,17β-diol Diacetate (IIIb). The above diol IIIa (2.0 g.) was kept on the steam bath for 1 hr. and admixed with acetic anhydride (20 ml.) and pyridine (20 ml.). Distillation to dryness *in vacuo* left a residue of the diacetate IIIb (2.4 g.) which, after recrystallization from hexane, showed m.p. 97°; $[\alpha]_D$ +4°; ν_{max} 1730 and 1250 cm.$^{-1}$; n.m.r. 14.7, 19.3, 30.6, and 35.2 (cyclopropyl CH_2, pair of doublet, J = 4.6 c.p.s.), 49 (18 H, singlet), 118.7 (3α OAc, singlet), 121.2 (17β OAc, singlet), and 255–295 c.p.s. (3β H and 17α H, multiplet).

Anal. Calcd. for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64; O, 11.00. Found: C, 73.30; H, 9.34; O, 16.98.

5α,19-Cyclo-10α-androstane-3,17-dione (IIIc) and 3α-Hydroxy-5α,19-cycloandrostan-17-one (IId). A solution of the diol IIIa (1.0 g.) in ether (280 ml.) was stirred for 15 hr. with aqueous chromic acid (prepared from 8 g. of sodium dichromate, 6 ml. of concentrated sulfuric acid, and 140 ml. of water) and the two-phase system then was separated. The ethereal solution was washed with aqueous sodium bicarbonate and sodium chloride solutions, dried (Na_2SO_4), and evaporated. Recrystallization of the residue from ether furnished the dione IIIc (0.880 g.) as prisms: m.p. 138–140°; $[\alpha]_D$ +164°; rotary dispersion (R.D.) (*c* 0.1, dioxane) $[\phi]_{310}$ + 7700°, $[\phi]_{317.5}$ +9900°, and $[\phi]_{700}$ +423°; ν_{max} 1705 and 1740 cm.$^{-1}$; n.m.r. 17.6, 23.2, 42.8, and 48.6 (geminal cyclopropyl methylene, pair of doublet, J = 5.8 c.p.s.), 53.8 (18 H, singlet), and 152 c.p.s. (C_4-methylene protons, singlet).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15; O, 11.17. Found: C, 79.39; H, 8.90; O, 11.17.

In a second experiment the oxidation of the diol IIIa (2 g.) was worked up after 2 hr. Chromatography of the residue over silica gel (60 g.) and eluting with ethyl acetate–hexane (3:7) gave the diketone IIIc (985 mg.), the monoketone IIId (310 mg.), and unreacted diol IIIa (50 mg.). The monoketone IIId was purified by recrystallization from ether–hexane: m.p. 115–116°, $[\alpha]_D$ +100°, ν_{max} 1740 and 3610 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 791.2; H, 9.79; O, 11.10. Found: C, 79.35; H, 9.78; O, 11.10.

Action of Acids on the Dione IIIc. A solution of 5α,-19-cyclo-10α-androstane-3,17-dione (IIIc, 1.5 g.) in ethanol (60 ml.) and concentrated hydrochloric acid (20 ml. of 36%) was kept under reflux for 1 hr. and then poured into ice water (300 ml.). The solid product which separated out was collected at the filter and crystallized twice from acetone thus yielding 5α-methylestr-1-ene-3,17-dione (Va): 320 mg.; m.p. 210–213°; $[\alpha]_D$ −69°; λ_{max} 234 mμ (log ε 3.92) and 300 mμ (log ε 1.85); ν_{max} 1740 and 1675 cm.$^{-1}$; circular dichroism (C.D.) (*c* 0.144)[33] $[\theta]_{390}$ 0°, $[\theta]_{369}$ −1042°, $[\theta]_{350}$ −2588°, $[\theta]_{338}$ −2979°, $[\theta]_{324}$ 0°, $[\theta]_{301}$ +10,320°, and $[\theta]_{250}$ 0°; n.m.r. 53.5 (18 H, singlet), 70 (5α Me, singlet), 364.6 (2 H, pair of doublet, $J_{1,2}$ = 10.2 and $J_{2,10}$ = 2.8 c.p.s.), and 416 c.p.s. (1 H, pair of doublet, $J_{1,2}$ = 10.2 and $J_{1,10}$ = 1.5 c.p.s.).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.12; O, 11.17. Found: C, 80.00; H, 9.21; O, 11.45.

Chromatography of the mother liquors over silica gel and elution with hexane–ethyl acetate (7:3) gave first some minor reaction products (120 mg.) showing no strong ultraviolet absorption, and then more conjugated ketone Va (170 mg.).

In a separate experiment, chromatography of the mother liquors led to isolation of a small quantity of one of the minor products, considered to be VIa on the basis of physical data: m.p. 133–135°; $[\alpha]_D$ +69.5°; no strong ultraviolet absorption; n.m.r. 60 (18 H, singlet) and 65.5 (5α Me, singlet), and no resonance for olefinic protons; insufficient for analysis.

Perchloric acid catalyzed cyclopropane ring cleavages proceeded similarly.

17β-Hydroxy-5α-methylestr-1-en-3-one (Vb). Lithium aluminum hydride (700 mg.) was added to a solution of 5α-methylestr-1-ene-3,17-dione (IIIc, 500 mg.) in dry tetrahydrofuran (50 ml.) and the mixture was maintained under reflux for 3 hr. The reaction was then worked up in the normal manner (acid procedure) and the crude allyl alcohol product was dissolved in dioxane (5 ml.) and added to a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (500 mg.) in the same solvent (5 ml.). After being kept for 3 hr. at room temperature, the reaction mixture was filtered and the filtrate was evaporated to dryness. Chromatography of the residue over silica gel (30 g.) gave, in the hexane–ethyl acetate (1:1) eluates, 17β-hydroxy-5α-methylestr-1-en-3-one (Vb, 275 mg.) which, after recrystallization from acetone, showed m.p. 200–202°, $[\alpha]_D$ −216°, λ_{max} 234 mμ (log ε 3.98), ν_{max} 1655 and 3450 cm.$^{-1}$.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79; O, 11.10. Found: C, 79.31; H, 10.08; O, 10.83.

Acid-Catalyzed Isomerization of 5α,19-Cyclo-10α-androstane-3α,17β-diol (IIIa). A solution of the diol IIIa (450 mg.) in ethanol (20 ml.) containing hydrochloric acid (7 ml. of 36%) was maintained under reflux for 90 min. The precipitate which separated on addition to cold water (100 ml.) was collected at the filter and then crystallized from chloroform–hexane to afford an isomer (210 mg.), m.p. 144–145°, a recrystallized sample of which showed physical properties consonant with structure VIb: m.p. 146–147°; $[\alpha]_D$ −60°; ν_{max} 1105 and 3270 cm.$^{-1}$; n.m.r. 44.5 (18 H, singlet), 66.5 (5α Me, singlet), and *ca.* 225 c.p.s. (3β H and 17α H, multiplet).

5α-Bromomethylestr-1(10)-ene-3,17-dione (VIIb). To a solution of 5α,19-cyclo-10α-androstane-3α,17β-diol diacetate (IIIb, 2.0 g.) in chloroform (100 ml.) at 0° there was added over 30 min. a solution of bromine (2.2 g.) in chloroform (55 ml.). After addition of lithium carbonate (4.0 g.) chloroform was removed by distillation *in vacuo* at room temperature and dimethylform-

amide (30 ml.) then was added. The resulting reaction mixture was boiled under reflux for 15 min. and then reduced to dryness by vacuum distillation. There remained an oily residue, a methanol (50 ml.) solution of which was treated with concentrated hydrochloric acid (1 ml. of 36%), and the mixture was kept at room temperature overnight. Saturated aqueous sodium chloride solution was added next and the mixture extracted three times with ether. Evaporation of the aqueous sodium bicarbonate and sodium chloride washed and dried (Na_2SO_4) ether extracts yielded crystalline material. Recrystallization from acetone afforded 5α-bromomethylestr-1(10)-ene-3α,17β-diol (VIIa): 970 mg., m.p. 160–161°, $[\alpha]_D$ −30°; ν_{max} 3330 cm.$^{-1}$.

The diol VIIa (300 mg.) was oxidized in a two-phase system consisting of ether (150 ml.), concentrated sulfuric acid (1.8 ml.), and aqueous potassium dichromate (2.7 g. in 42 ml.) over 15 hr. The ether layer was separated and washed with aqueous sodium bicarbonate and water, dried (Na_2SO_4), and evaporated. Crystallization of the residue from ether furnished the dione VIIb (20 mg.), m.p. 126–135° dec. A recrystallized sample showed m.p. 135–144° dec.; $[\alpha]_D$ +116°; C.D. (*c* 0.047) $[\theta]_{330}$ 0°, $[\theta]_{304}$ +14,600°, $[\theta]_{296}$ +14,670°, and $[\theta]_{250}$ 0°; λ_{max} (EtOH–HCl) 230 mμ (Vc), λ_{max} (EtOH neutral) no strong absorption, λ_{max} (EtOH–Na_2CO_3) 275 mμ (VIII); ν_{max} 1735 and 1720 cm.$^{-1}$; n.m.r. 54.5 (18 H, singlet), 210 (CH_2Br, ill-resolved pair of doublet), and 337 c.p.s. (1 H, multiplet).

Anal. Calcd. for $C_{19}H_{25}BrO_2$: C, 62.50; H, 6.91; Br, 21.88; O, 8.77. Found: C, 62.36; H, 6.92; Br, 21.90; O, 8.90.

Base-Catalyzed Isomerization of 5α,19-Cyclo-10α-androstane-3,20-dione (IIIc). The dione IIIc (200 mg.) was dissolved in dimethyl sulfoxide (100 ml.), dry potassium *t*-butoxide (3.3 g.) was added, and the whole was heated at 80° for 45 min. Precipitation into water (200 ml.), then filtration, gave an amorphous solid (120 mg.). Chromatography of the latter over silica gel (30 g.) and elution with ethyl acetate–hexane (3:7) furnished an inhomogeneous product showing m.p. 132–158°; λ_{max} 244 mμ; ν_{max} 1677 and 1750 cm.$^{-1}$; n.m.r. 75 (19 H, singlet), 348 (4 H, singlet), and 45–60 c.p.s. (18 H, a collection of singlets totaling three protons).

Similar attempted rearrangements employing sodium hydroxide in anhydrous dioxane, potassium methoxide–methanol, and potassium *t*-butoxide in *t*-butyl alcohol all gave unchanged starting material.

17β-(Tetrahydropyran-2-yl)oxyestr-5(10)-en-3α-ol (IIe). A solution of 17β-hydroxy-estr-5(10)-en-3-one (IIc, 9.0 g.) and dihydropyran (20.0 g.) in benzene (400 ml.) was dried by azeotropic distillation of a fifth of the solvent and then added to a similarly dried solution of *p*-toluenesulfonic acid (20 mg.) in benzene (20 ml.). After 45 min. at room temperature the solution was washed with aqueous sodium bicarbonate solution, dried, and evaporated to furnish the tetrahydropyranyl ether IId.

The crude ether IId was added to a solution of sodium borohydride (10.0 g.) in methanol (600 ml.) and kept overnight at room temperature, and the mixture was then poured into water (2 l.). Methylene chloride extracts were washed with aqueous sodium chloride solution, dried, and evaporated. Crystallization of the residue from benzene–hexane gave 17β-(tetrahydropyran-2-yl)oxyestr-5(10)-en-3α-ol (IIe, 5.25 g.) contaminated with some of the corresponding 3β-alcohol IIf. The mixture showed m.p. 140–142°, $[\alpha]_D$ +146°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07; O, 13.31. Found: C, 76.99; H, 10.14; O, 13.33.

Hydrolysis of a small sample of this mixture by treatment with methanolic oxalic acid furnished the free diol IIa, contaminated with some of the stereoisomeric 3β,17-diol as revealed by the melting point, 195–200° (pure IIa shows m.p. 210–212°).

17β-Hydroxy-5β,19-cycloandrostan-3-one (IVb). The crude mixture of 3α- and 3β-alcohols IIe and IIf (4.0 g.) was dissolved in ether (120 ml.) and added to Simmons–Smith reagent (prepared from 15 g. of zinc–copper couple, 36 g. of methylene diiodide, and 120 ml. of ether), and the solution was then maintained under reflux for 4 hr. Usual work-up afforded an oily product which was oxidized with chromium trioxide (4 g.) in pyridine (200 ml.) at room temperature for 17 hr. After the addition of water, the reaction mixture was extracted several times with ether and the combined extracts were washed with aqueous sodium chloride solution, dried, and evaporated. The solid which remained was taken up into a mixture of methanol (150 ml.), water (10 ml.), and oxalic acid (200 mg.), and the solution was refluxed for 0.5 hr., then poured into water (500 ml.), and extracted with methylene chloride. The oily extracts obtained by evaporation of the washed (H_2O) and dried (Na_2SO_4) solution were subjected to chromatography over silica gel (150 g.). Ethyl acetate–hexane (3:7) eluted first 17β-hydroxy-5β,19-cycloandrostan-3-one (IVb, 510 mg.) which, after recrystallization from ether had m.p. 134–136°; $[\alpha]_D$ +46°; ν_{max} 1698 and 3400 cm.$^{-1}$; n.m.r. 29 (cyclopropyl geminal methylene protons, singlet), 45.5 (18 H, singlet), 127 (C_4-methylene, apparent singlet), and 221 c.p.s. (17α H, triplet); C.D. (*c* 0.08) $[\theta]_{332}$ 0°, $[\theta]_{323}$ −715°, $[\theta]_{311}$ −1190°, $[\theta]_{300}$ −1430°, $[\theta]_{291}$ −1280°, and $[\theta]_{250}$ 0°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79; O, 11.10. Found: C, 78.87; H, 9.69; O, 11.60.

Further elution of the column with the same solvent mixture afforded the 3α,17β-diol IIa (610 mg.), m.p. 208–210, identical with a pure sample by infrared analysis and mixture melting point.

A Simmons–Smith reaction on the same mixture of 3α- and 3β-alcohols IIe and IIf using the forcing conditions (100°, sealed steel tube) gave, by chromatography of the reaction product, mainly the 5α,10α-methylenated product IIIa, with loss of the 17β-ether protecting group.

Base-Catalyzed Isomerization of 17β-Hydroxy-5β,19-cycloandrostan-3-one (IVb). The 5β,19-cyclosteroid IVb (200 mg.) was added to a solution of potassium *t*-butoxide (3.5 g.) and dimethyl sulfoxide (200 ml.), the mixture kept at 80° for 40 min., then poured into ice water (500 ml.), and extracted with ether. After being washed with water the combined extracts were dried and evaporated to produce testosterone (130 mg.), m.p. 140–141°. Recrystallization from ether yielded a purer sample, m.p. 149–150° alone or on admixture with an authentic specimen of testosterone.

17β-Hydroxy-5α,19-cyclo-10α-androstan-3-one (IIIg). Crude ether IId (5.0 g.), prepared as described above,

was reduced in the normal manner with lithium tri-*t*-butoxyaluminum hydride (8.0 g.) in ether (500 ml.). The resultant 3α-alcohol IIe (4.0 g.) appeared by chromatoplate to be almost free of the 3β-isomeric alcohol IIf.

This 3α-alcohol IIe was then added to a solution of Simmons–Smith reagent (prepared from 15 g. of zinc–copper couple, 36 g. of methylene diiodide, and 120 ml. of ether) and approximately 50% of the solvent was removed by distillation and replaced with dry ether (50 ml.). The remaining solution was sealed in a stainless steel pressure tube and kept at 50° for 17 hr., then worked up as usual. Oxidation of the crude product (3.8 g.) with chromium trioxide (4.0 g.) in pyridine (300 ml.) and cleavage of the tetrahydropyranyl protecting group with 0.1% methanolic oxalic acid was then effected as described above leading to a solid product (2.81 g.). Chromatography of the latter over silica gel (300 g.) and elution with ethyl acetate–hexane (3:7) furnished 17β-hydroxy-5α,19-cyclo-10α-androstan-3-one (IIIg., 990 mg.) which, after recrystallization from ether, had m.p. 132–134° (depressed to m.p. 124–129° on admixture with a sample of the 5β,-19-cyclo isomer IVb); $[\alpha]_D$ + 76°; ν_{max} 1715 and 3210 cm.$^{-1}$; n.m.r. 46.5 (18 H, singlet), 16.5 and 21.5, 40.5, and *ca.* 45.5 (geminal cyclopropyl protons, pair of doublet, J = 5 c.p.s.), 218 (17α H, triplet), and 151 c.p.s. (OH, singlet); C.D. (*c* 0.1), $[\theta]_{330}$ 0°, $[\theta]_{310}$ +2060°, $[\theta]_{299}$ +2820°, $[\theta]_{290}$ +2560°, and $[\theta]_{225}$ 0°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.70. Found: C, 79.03; H, 10.08.

Base-Catalyzed Isomerization of 17β-Hydroxy-5α,19-cyclo-10α-androstan-3-one (IIIg). A mixture of potassium *t*-butoxide (3.5 g.), dimethyl sulfoxide (500 ml.), and 17β-hydroxy-5α,19-cyclo-10α-androstan-3-one (IIIg, 500 mg.) was heated to 80° for 1.5 hr. then poured into ice water (1 l.) and extracted with ether. The washed (H_2O) and dried (Na_2SO_4) extracts were evaporated to dryness leaving an oily product which was chromatographed over silica gel (40 g.). Elution with ethyl acetate–hexane (1:1) furnished 17β-hydroxy-10α-androst-5-en-3-one (IX, 120 mg.), an analytical sample of which was prepared by recrystallization from ether, and showed m.p. 173–175°; $[\alpha]_D$ −143°; ν_{max} 1705 and 3390 cm.$^{-1}$; n.m.r. 45.5 (18 H, singlet), 77.5 (19 H, singlet), 328 (6 H, multiplet), 219 (17α H, triplet), 159 and 174, 197, and 212 c.p.s. (C_4-methylene protons, pair of doublet, J = 15 c.p.s.); C.D. (*c* 0.12) $[\theta]_{330}$ 0°, $[\theta]_{296}$ −14,100°, and $[\theta]_{250}$ 0°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79; O, 11.10. Found: C, 79.03; H, 10.08; O, 10.95.

Later fractions eluted with the same solvent mixture consisted of 10α-testosterone (Ia, 60 mg.). This product was treated with acetic anhydride (5 ml.) and pyridine (5 ml.) for 1 hr. on the steam bath and all volatile material was removed by distillation *in vacuo*. Thereby was obtained 10α-testosterone acetate (Ib, 60 mg.). Recrystallization from ether–hexane gave an analytical specimen, m.p. 137°; $[\alpha]_D$ −201°; λ_{max} 244 mμ (log ϵ 4.19); ν_{max} 1735, 1663, 1625, and 1255 cm.$^{-1}$; n.m.r. 45.5 (18 H, singlet), 74 (19 H, singlet), 122 (OAc, singlet), 276.5 (17α H, multiplet), and 34.6 c.p.s. (4 H, singlet, half-band width 4 c.p.s.); R.D. (*c* 0.1, MeOH), $[\phi]_{350}$ −5350°, $[\phi]_{320}$ 0°, and $[\phi]_{312}$ +900° (Wenger, *et al.*,[8] report m.p. 136°; $[\alpha]_D$ −222°; $\nu_{max}^{CHCl_3}$ 1720, 1660, 1625, and 1255 cm.$^{-1}$; λ_{max} 245 mμ (log ϵ 4.20); n.m.r. 46 (18 H), 74 (19 H), 123 (OAc), *ca.* 270 (17α H), and 347 c.p.s. (4 H)).

Hydrogenolytic Cleavage of 5α,19-Cyclo-10α-androstane-3α,17β-diol Diacetate (IIIb). A solution of the diacetate IIIb (1.0 g.) in acetic acid (20 ml.) was shaken with hydrogen gas at 40 atm. in the presence of prereduced Adams platinum oxide catalyst (1 g.). The product resulting from filtration and evaporation was homogeneous on a thin layer chromatoplate. Hydrolysis with sodium hydroxide (2.0 g.) in methanol (50 ml.) for 1 hr. on the steam bath was then carried out, and the free diols were isolated from the reaction mixture by precipitation, following water dilution and collection at the filter. This product was added to a mixture of ether (250 ml.), water (140 ml.), concentrated sulfuric acid (6 ml.), and sodium dichromate (8 g.) and the two-phase reaction mixture was stirred vigorously for 5 hr. at room temperature. The ether layer was then separated, washed with water to neutrality, dried (Na_2SO_4), and evaporated. A mixture of the two diketones Xa and Xb (350 mg.) was obtained. Three crystallizations from ether gave a sharp melting 1:1 mixture showing m.p. 127–128°; $[\alpha]_D$ + 64°; ν_{max} 1717 and 1747 cm.$^{-1}$; R.D. (*c* 0.1, MeOH) $[\phi]_{302}$ + 4730°, $[\phi]_{312.5}$ + 7080°, and $[\phi]_{350}$ 0°; n.m.r. 52 (18 H, singlet), 67.5 and 78 c.p.s. (5α Me and 10α Me, totaling three protons, two singlets).

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79; O, 11.10. Found: C, 79.43; H, 9.79; O, 11.19.

A mixture of the diketones Xa and Xb (100 mg.) was added to a dioxane (5 ml.) solution of 2,3-dichloro-5,6-dicyanobenzoquinone (200 mg.) and the mixture was boiled under reflux for 2 hr. The filtered mixture was then passed through a column of alumina (10 g.) and eluted with methylene chloride. There resulted a mixture of Δ^1-3-ketones (20 mg.), m.p. 173–195°, λ_{max} 234 mμ.