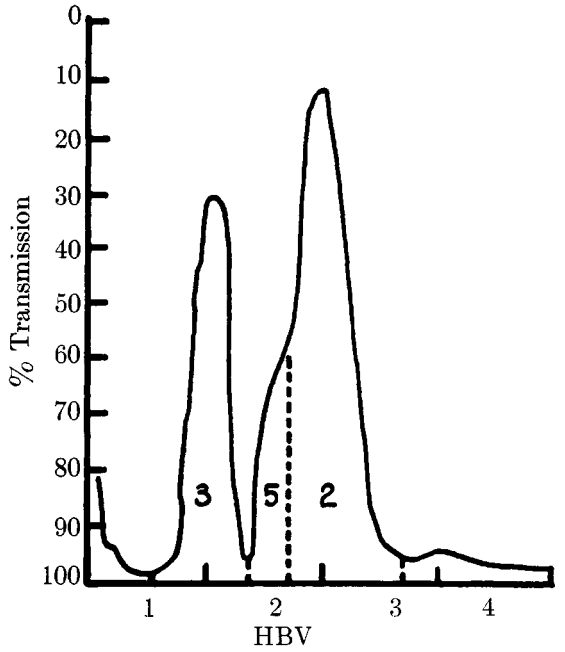


Figure 2

Anal. Calcd. for $C_{20}H_{25}O_2N$ (311.41): C, 77.13; H, 8.09; N, 4.50. Found: C, 76.78; H, 8.10; N, 4.44.

3-Methoxy-15α-carboxamido-estra-1,3,5(10)-trien-17β-ol (8a).—To a solution of benzene-solvated 15β-cyano-3-methoxyestra-1,3,5(10)-trien-17β-ol(**6e**, 0.800 g.) in ethanol (35 ml.) was added potassium hydroxide (2.5 g.) in water (7 ml.) and the solution was heated to reflux for 6 hr. A thin layer chromatographic analysis of the reaction mixture revealed that no hydrolysis had taken place. The ethanol was displaced with 1-propanol and the resulting solution was heated to reflux overnight. The reaction mixture was diluted with ethyl acetate, washed with dilute hydrochloric acid solution and with water, dried, and evaporated to 0.800 g. of a semicrystalline solid which was crystallized once from acetone–water and twice from acetone–petroleum ether to give 0.240 g., m.p. 208–210°, $[\alpha]_D$ +109° (methanol).

Anal. Calcd. for $C_{20}H_{27}O_3N$(329.42): C, 72.92; H, 8.26; N, 4.25. Found: C, 72.43, 72.40; H, 8.41, 8.18; N, 4.40.

A second crop, 0.170 g., m.p. 206–208°, was obtained from the mother liquors.

17β-Hydroxy-3-methoxyestra-1,3,5(10)-trien-15α-carboxylic acid (8b).—To a solution of 15β-cyano-3-methoxyestra-1,3,5(10)-trien-17β-ol(**6e**, 0.900 g.) in 40 ml. of ethylene glycol was added a solution of 3.0 g. of potassium hydroxide in 7 ml. of water. The resulting solution was refluxed for 22 hr., cooled, and acidified with dilute hydrochloric acid solution. The product was collected by filtration, washed with water, and dried to give 0.460 g., m.p. 181–184°. A sample for analysis was crystallized twice from methanol–water and twice from acetone and had m.p. 238–240°, $[\alpha]_D$ +130° (methanol).

Anal. Calcd. for $C_{20}H_{26}O_4$ (330.41): C, 72.70; H, 7.93. Found: C, 72.62; H, 8.15.

Attempted Addition of Methanol to 3-Methoxy-14β-estra-1,3,5(10),15-tetraen-17-one (2).[18]—To a solution of **2** (0.300 g.) in methanol (14 ml.) was added a 5% sodium hydroxide solution (0.7 ml.). The resulting solution was stirred 30 min. at room temperature, diluted with water, and the products were extracted with ethyl acetate. The extract was dried and evaporated to give 0.270 g. of an oil.

A pilot partition column on Celite 545[16] using an *n*-heptane–Methyl Cellosolve solvent system indicated the reaction mixture to contain 28.5% of **3**, 56.5% of **2**, and 15% of an unknown **5** occurring as a shoulder at HBV 1.5–1.8 on the peak corresponding to **2** (Fig. 2) A similar column run on a mixture obtained from a second run which was stirred for 24 hr. indicated the exact composition previously described. The remaining crude products of the two runs were combined (0.570 g.) and partitioned as described previously to give 0.100 g. of **3** and 0.235 g. of **2** (these compounds were identical by comparison of their thin layer chromatograms and their infrared spectra with the specimens described in ref. 18). In a larger run (0.900 g.) that peak corresponding to **5** was repartitioned twice using the same solvent system to give 0.060 g. of impure **5**. The latter was crystallized from methanol to give 0.028 g., m.p. 82–85°; the thin layer chromatogram indicated it to contain *ca.* 10% of **2**. The infrared spectrum of the crystallized sample showed only a 5-membered ring carbonyl maximum at 1725 cm.$^{-1}$ and its n.m.r. spectrum showed two O-methyl maxima at 6.16 (C-3) and 6.63 τ (C-15).

(18) 3-Methoxyestra-1,3,5(10),15-tetraen-17-one (**1**) was isomerized with *p*-toluenesulfonic acid for 15 min. in refluxing benzene according to the procedure of Johnson and Johns.[1] The resulting mixture was partitioned on Celite 545[16] using an *n*-heptane–Methyl Cellosolve solvent system. Holdback volumes 0.5–1.5 gave 3-methoxyestra-1,3,5(10),14-tetraen-17-one (**3**), m.p. 93–94°, $[\alpha]_D$ +293°. A HBV of 1.5–2.2 gave 3-methoxy-14β-estra-1,3,5(10),15-tetraen-17-one (**2**), m.p. 102–103°, $[\alpha]_D$ +477°.

Photodimerization of $\Delta^{4,6}$-Diene-3-keto Steroids

MORDECAI B. RUBIN, GEORGE E. HIPPS, AND DONALD GLOVER

Department of Chemistry, Carnegie Institute of Technology, Pittsburgh 13, Pennsylvania

Received August 8, 1963

Photoirradiation of heteroannular dienones such as $\Delta^{4,6}$-androstadien-3-on-17β-ol propionate and related steroids in homogeneous solution leads to formation of a single one of twenty possible dimeric products. This has been assigned the structure IIA or IID on the basis of physical properties and catalytic hydrogenation followed by thermal cleavage and identification of cleavage products. The dimerization can be reversed photochemically; the photostationary state has the composition 31% monomer and 69% dimer.

Although the photochemical reactions of conjugated and cross-conjugated dienones have been of considerable interest in recent years,[1] attention has been concentrated on homoannular systems where molecular rearrangement, valence-bond tautomerization, and ring cleavage are the predominant reaction paths. This paper describes the results obtained on reaction of a heteroannular dienone system where the more familiar photodimerization reaction of conjugated carbonyl compounds[2] is observed, albeit in an unexpected manner.[3]

Solutions of $\Delta^{4,6}$-androstadien-3-on-17β-ol propionate[4] (IA) in benzene–petroleum ether or benzene–

(1) For leading references see J. J. Hurst and G. H. Whitham, *J. Chem. Soc.*, 710 (1963); C. Ganter, E. C. Utzinger, K. Schaffner, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **45**, 2403 (1962); D. H. R. Barton, *ibid.*, **42**, 2604 (1959); P. de Mayo, "Advances in Organic Chemistry," Vol. II, Interscience Publishers, Inc., New York, N. Y., 1960, pp. 367–425.

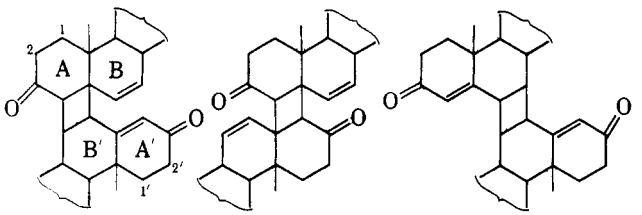
(2) A. Mustafa, *Chem. Rev.*, **51**, 1 (1952).

(3) After this work was completed, a report appeared [H. C. Throndsen, G. Cainelli, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **45**, 2342 (1962)] describing the determination of structure of the photodimer of $\Delta^{4,6}$-cholestadien-3-one. Our results confirm, by different methods, and extend the conclusions reached in this report.

(4) L. Ruzicka and W. Bosshard, *ibid.*, **20**, 328 (1937). The more convenient chloranil dehydrogenation procedure of E. J. Agnello and G. O. Laubach [*J. Am. Chem. Soc.*, **82**, 4293 (1960)] was used in this work.

dioxane remained homogeneous on exposure to light of wave length longer than 3000 Å. although occurrence of reaction was indicated by marked decrease in ultraviolet absorption. Chromatography of the reaction product on Florisil led to isolation of recovered starting material (64%) and a new crystalline compound (II), 34%, m.p. 168–169°, which regenerated IA quantitatively on heating for five minutes above its melting point. The dimeric nature of II was indicated by its molecular weight and the presence in its infrared spectrum of the original carbonyl bands of IA at 5.75 and 6.0 plus an additional band at 5.90 μ. In view of these facts and the well known tendency of conjugated carbonyl compounds to undergo photodimerization to derivatives of cyclobutane,[2] it seemed likely that II was a dimer of the cyclobutane type formed by interaction of one of the two double bonds of each monomer unit.

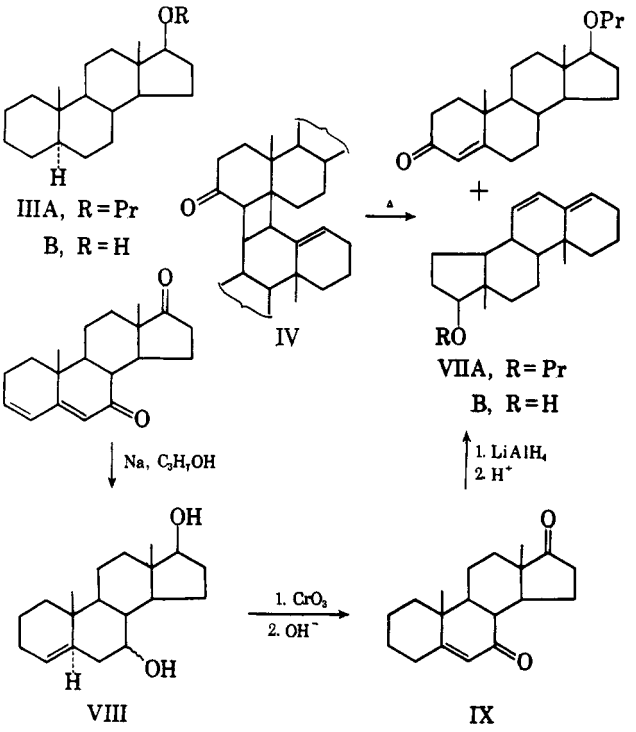
Neglecting finer details of stereochemistry at this point, the three structures IIA, B, C, and their head-to-head isomers need to be considered. Of these, only



IIA IIB IIC

IIA is in agreement with the infrared spectral data since it is the only one possessing both conjugated and unconjugated carbonyl[5] groups (as well as the side-chain ester group). The apparently anomalous ultraviolet absorption of II [254 mμ (ϵ 10,500)], representing a shift of 12 mμ from the usual position of the maximum in Δ^4-3-keto steroids, is explicable on the basis of the auxochromic effect of the cyclobutane ring[6] in IIA and also might be consistent with IIC but not with IIB. Further evidence in favor of IIA was provided by the n.m.r. spectrum of the dimer which showed three protons in the olefinic hydrogen region of the spectrum as singlets at 4.20 (1H) and 4.40 τ (2H),[7] consistent only with structure IIA or its head-to-head isomer.

Proof of the correctness of this structural assignment was provided by the results of catalytic hydrogenation of II and thermal cleavage of the reduction products. Barring the possibility of double bond isomerization during thermal cleavage, the positions of double bonds in the cleavage products should fix the points of attachment of the cyclobutane ring and allow an unequivocal choice between IIA, B, and C. Hydrogenation of II over pre-reduced platinum oxide in propionic acid[8] resulted in variable uptake of hydrogen which was explicable in terms of formation of varying proportions of a mixture of hexadecahydro (IIIA), hexahydro (IV), and tetrahydro (V) products, separable by chromatography on Florisil. In a typical run, 4.0 moles of hydrogen were absorbed per mole of IIA leading to 19% of IIIA, 61% of IV, and 10% of V.



The hexadecahydro product (IIIA) exhibited characteristic ester absorption at 5.79 and 8.39 μ and no absorption in the ultraviolet. It was identified as 5α-androstan-17β-ol propionate, the product of cyclobutane hydrogenolysis, by base-catalyzed hydrolysis to a solid, m.p. 138–152°, showing only hydroxyl absorption at 2.98 μ. Purification of this solid yielded 68% of 5α-androstan-17β-ol, m.p. 164–166° (IIIB), identical with an authentic sample.[9] None of the 5β isomer could be detected.

The hexahydro product (IV), m.p. 274–275°, contained only an unconjugated carbonyl group adjacent to a cyclobutane ring as shown by the maximum at 5.91 μ and the presence of only end absorption in the ultraviolet, 210 mμ (ϵ 8600). These observations plus the presence of a singlet at 4.37 τ (1H) in the n.m.r. suggested the structure shown. Confirmation was provided by the results of thermal cleavage of IV. Chromatography of the crude product obtained by heating IV for three hours at 270–280° in a sealed tube yielded, in addition to 33% of recovered starting material, 52% of testosterone propionate and 62% of a crystalline solid with ultraviolet absorption (230, 237, 246 mμ) characteristic of a heteroannular diene.[10] The spectrum did not allow a distinction between the two possible dienes, $\Delta^{3,5}$-androstadien-17β-ol propionate (VI) and $\Delta^{4,6}$-androstadien-17β-ol propionate (VIIA). However, the cleavage product was not identical with the 3,5-diene (VI) prepared by propionylation of the corresponding free alcohol[11] and was posi-

(5) The slight shift of the unconjugated carbonyl absorption to 5.90 μ has been observed in other cases where a cyclobutane ring is "conjugated" with a ketone; *cf.* A. Butenandt, L. Poschmann, G. Failer, U. Schiedt, and E. Biekert, *Ann.*, **676**, 123 (1951).

(6) J. J. Wren, *J. Chem. Soc.*, 2208 (1956); *cf., inter alia*, G. Büchi and I. M. Goldman, *J. Am. Chem. Soc.*, **79**, 4741 (1957); P. D. Gardner, R. L. Brandon, and G. R. Haynes, *ibid.*, **79**, 6334 (1957).

(7) The poorly resolved triplet centered at 5.45 τ (due to the two C-17 protons) provided a convenient reference for determining the number of protons represented by each line in the spectrum in this and other cases.

(8) Milder reduction conditions afforded only small amounts of IIIA and recovered starting material.

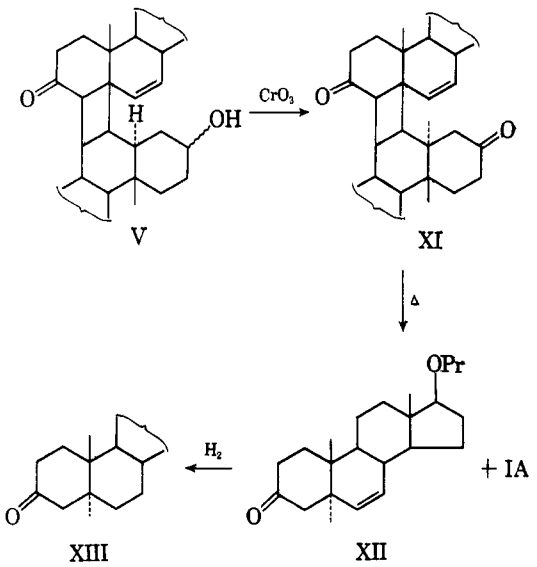
(9) C. W. Shoppee, D. G. Lewis, and J. Elks, *Chem. Ind.* (London), 454 (1950). The 5β isomer is reported to melt at 96°; F. Galinovsky, E. Kerschbaum, and H. Janisch, *Monatsh.*, **84**, 193 (1953).

(10) L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).

(11) G. Rosenkranz, St. Kaufmann, and J. Romo, *J. Am. Chem. Soc.*, **71**, 3689 (1949).

tively identified as the 4,6-diene (VIIA) by comparison with a sample obtained by the following synthesis modeled on the procedure used by Eck and Hollingsworth[12] for the preparation of $\Delta^{4,6}$-cholestadiene. Reduction of $\Delta^{3,5}$-androstadiene-7,17-dione[13] with sodium in propanol afforded the homoallylic diol (VIII) as a mixture of epimers which was oxidized with chromium trioxide in acetone[14] and treated with base to give Δ^{5}-androstene-7,17-dione (IX, 5.75 and 6.01 μ). Reduction of IX with lithium aluminum hydride yielded the allylic alcohol (X) as a mixture of epimers. Acid-catalyzed dehydration of X proceeded readily to give 94% of $\Delta^{4,6}$-androstadien-17β-ol (VIIB) which was propionylated to VIIA with propionic anhydride in pyridine. Both VI and VIIA were shown to be stable under the conditions of the thermal cleavage reaction and subsequent chromatographic purification.

The tetrahydro product (V) obtained in the catalytic hydrogenation also contained no conjugation as evidenced by the presence of only end absorption in the ultraviolet, 210 mμ (ϵ 2400). In addition to an unconjugated carbonyl group adjacent to a cyclobutane ring (5.92 μ), the presence of a hydroxyl group (2.74 μ) and of two olefinic hydrogens (doublets at 3.99 and 4.45 τ, J_{AB} = 12 c.p.s.) was indicated. Thermal cleavage of V followed by chromatography did not lead to crystalline products. On the basis of spectral analysis of individual fractions, the presence of IA, a hetero-

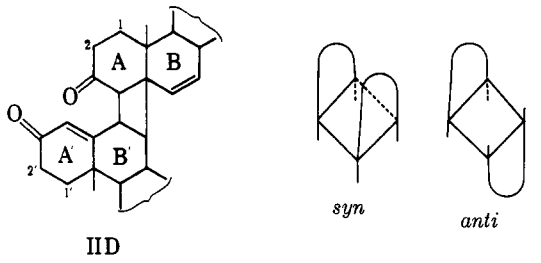


annular diene (or mixture of dienes), and recovered V was suggested. Since the difficulties encountered might have been due to dehydration of the alcohol function at the high temperature of the thermal cleavage, V was oxidized (in nearly quanitative yield) to the diketone XI which again showed no evidence for conjugation, 5.9 μ, 210 mμ (ϵ 2700). The olefinic hydrogens in XI also appeared as a pair of doublets at 4.05 and 4.52 τ (J_{AB} = 11 c.p.s.).

Cleavage of XI by heating at 270–280° for three hours proceeded satisfactorily. Chromatography of the crude product afforded 39% of recovered XI, 53% of IA, and 47% of 5α-Δ^{6}-androsten-3-on-17β-ol propionate (XII). The latter compound was characterized by the absence of ultraviolet absorption, infrared maxima at 5.77 (propionate) and 5.84 μ, and presence of a partially resolved multiplet centered at 4.64 τ (2H) in the n.m.r. Catalytic hydrogenation to known 5α-androstan-3-on-17β-ol propionate[15] (XIII) confirmed the structure assignment.

The spectral properties of the hydrogenation products IV, V, and XI and the identification of their thermal cleavage products are consistent only with assignment of structure IIA to the photodimer. The formation of IV and V apparently represents a competition between reduction of the conjugated carbonyl group at C-3′ and of the double bond ($\Delta^{4'}$) adjacent to it.[16] When reduction of the carbonyl group occurs first, the resultant allylic alcohol can undergo hydrogenolysis ultimately leading to IV (the major product). The results suggest that the $\Delta^{4'}$-double bond is subject to considerably more steric hindrance than the adjacent carbonyl group. A similar observation has been made by Ushakov and Kosheleva[17] and confirmed by Jeger, *et al.*,[3] who noted that hydrogenation of the photodimer (XVI) of $\Delta^{4,6}$-cholestadien-3-one led to a tetrahydro product in which complete reduction of the C-4′ ketone to methylene occurred without hydrogenation of either of the two olefinic bonds present.

The exclusion of IIB and IIC leaves eight possible structures to be considered for the photodimer assuming that the cyclohexane-to-cyclobutane ring fusions are *cis*.[18,19] Both the head-to-tail (IIA) and head-to-head structures (IID) might possess either *cis*- or *trans*-



IID

A/B ring fusions and, in addition, the relationship of the two steroid halves might be either *syn* or *anti* (as illustrated) about the cyclobutane ring allowing a total of four head-to-tail and four head-to-head possibilities.

These eight possibilities can be reduced to four on the basis of the catalytic hydrogenation of IIA to V which must, on the basis of its thermal cleavage to 5α-andro-

(12) J. C. Eck and E. W. Hollingsworth, *J. Am. Chem. Soc.*, **63**, 107 (1941).

(13) J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, **31**, 629 (1948).

(14) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).

(15) K. Miescher, H. Kagi, C. Scholz, A. Wettstein, and E. Tschopp, *Biochem. Z.*, **294**, 39 (1937).

(16) We have adopted the following notation for indicating position and stereochemistry in these dimers. The dimer, written with the upper half containing the ring A ketone "conjugated" with cyclobutane ring (this choice was made to conform with the structures presented by Jeger, *et al.*[3]), is considered to be composed of two independent steroid halves. For the upper half, positions and stereochemistry are designated in the usual manner; for the lower half, positions are designated as C-1′, C-2′, etc., and stereochemistry (α' or β') is related to the C-10′ methyl group of that half.

(17) M. I. Ushakov and N. F. Kosheleva, *J. Gen. Chem. USSR*, **14**, 1138 (1944); *Chem. Abstr.*, **40**, 4071 (1946).

(18) Preliminary reports have appeared describing the formation of the *trans*-bicyclo[4.2.0]octane system as minor product of the photoaddition of maleic anhydride to cyclohexene: P. de Mayo, R. W. Yip, and S. T. Reid, *Proc. Chem. Soc.*, 54 (1963); J. A. Barltrop and R. Robson, *Tetrahedron Letters*, 597 (1963).

(19) The photodimerization of dimethyl 3-keto-1,4-pentadiene-1,5-dicarboxylate has also been reported to lead to product in which *trans* fusion of cyclobutane and cyclohexane rings occurs: J. Corse, B. J. Finkle, and R. E. Lundin, *ibid.*, **No. 1**, 1 (1961).

stan-3-on-17β-ol propionate, possesses the 5′α′ configuration. From examination of models it seems extremely unlikely that hydrogenation from the α side of the lower steroid half of the dimer could occur if the cyclobutane ring were attached at the 6′α′,7′α′-positions since the upper half of the dimer would provide considerable hindrance to reaction at the 5′α′-position. The fact that 5α-androstan-17β-ol propionate (IIIA) also is formed in the catalytic hydrogenation to the exclusion of the 5β isomer is not necessarily significant since it is not clear at what stage in the reduction insertion of the 5α-hydrogen occurs.[20]

We have observed slow reversal of II to $\Delta^{4,6}$-androstadien-3-on-17β-ol (IC)[21] under mild acidic conditions as had been reported by Jeger, *et al.*,[3] for the dimer of $\Delta^{4,6}$-cholestadien-3-one. These authors suggested that this result supports the head-to-tail structure for the dimer. This interpretation appears to us to be based on the assumption of an initial protonation of either carbonyl group of the dimer followed by a stepwise fragmentation involving a series of carbonium ions. Such a mechanism applied to the head-to-head isomer would require a carbonium ion adjacent (or vinylogously adjacent) to a carbonyl group which would not be the case for the head-to-tail isomer where only isolated or allylic carbonium ions would be required. Unfortunately, the absence of detailed information on the mechanism of the acid-catalyzed cleavage and the lack of a standard (such as a second isomer) with which to compare the rate of cleavage make such an inference of limited value. Complete details of the structure of these photodimers await further investigation.

As has been noted, the nature of absorption in the olefinic hydrogen region of n.m.r. spectra has been of considerable value in elucidation of the structures of II and its degradation products. The usual broad envelope with occasional protruding sharp lines characteristic of the aliphatic hydrogen region of steroids[22] also was observed. All of the compounds which bore a 17-propionate exhibited a quartet centered at about 7.66 τ (J = 8 c.p.s.) due to the methylene protons adjacent to the ester carbonyl and a triplet centered at 8.86 τ (J = 8 c.p.s.) due to the propionate methyl group. In addition, the following lines due to angular methyl groups were observed: monomer (IA), 8.85 (C-19 protons) and 9.10 (C-18); dimer (II), 8.70, 9.15, 9.19, 9.25; hexahydro product (IV), 8.78, 9.20 (this line was approximately twice as intense as the lower field line); tetrahydro product (V), 8.93, 9.16 (broad), 9.31; XI, 8.74, 8.98, 9.15, 9.22, 9.32 τ. This apparently capricious pattern of absorption is presumably due to the operation of long-range shielding effects and might provide some clues to the detailed structure of the dimer.

Irradiation performed under conditions similar to those used with IA led to conversion of $\Delta^{4,6}$-androstadien-3-one (IB) to dimer XIV, $\Delta^{4,6}$-androstadien-3-on-17β-ol (IC) to XV, and $\Delta^{4,6}$-cholestadien-3-one (ID) to XVI (solutions remained homogeneous throughout irradiation). These dimers were all assigned partial structure IIA (or IID), differing only in substitution at C-17, on the basis of their spectral properties (see Experimental). In the case of XV the structure was confirmed by esterification with propionic anhydride and pyridine at room temperature to give material identical with the dimer of IA. The identical dimer (XVI) was obtained from ID by irradiation of petroleum ether solutions where the product crystallized during the course of the reaction or by irradiation of benzene–dioxane solutions which remained homogeneous through out the course of the reaction. In the latter case XVI was isolated by chromatography on Florisil. The physical properties of XVI were in good agreement with those reported by Jeger, *et al.*, for the dimer formed by irradiation of ethanol solutions of ID where the product crystallized during the course of the reaction.

Probably the most striking aspect of these dimerizations is the complete specificity observed. As noted previously, four isomers of IIA and four of IID are possible; consideration of the number of isomers which could result from dimerizations involving two α,β double bonds or two γ,δ double bonds leads to a total of twenty possible dimers from irradiation of IA. However, 98% of the original material was recovered either as unchanged starting material or as the single homogeneous product. Careful examination of individual fractions from column chromatography by infrared spectral comparison and thin layer chromatography did not indicate the presence of any other reaction product, nor did protracted irradiation result in any detectable by-products. In contrast, the dimerization of cyclopentenone in homogeneous solution[23] results in the formation of approximately equal amounts of *anti* head-to-head and *anti* head-to-tail dimers, two of the four possible products. The specificity of these steroid dimerizations is particularly remarkable since it was demonstrated that the dimerizations can be reversed photochemically. The composition of the photostationary state resulting from irradiation of IA or II in benzene–dioxane solution was 31% monomer and 69% dimer at 27–28°. Examination of molecular models provides no clue to preference for a single one of twenty possible products in a reversible reaction taking place in homogeneous solution. In fact, the products which involve the least steric hindrance are those formed by interaction of two α,β double bonds (IIB) and possessing the head-to-tail, *anti* configuration. Such isomers also might be predicted to accumulate upon irradiation, since they would have extremely weak light absorption at wave lengths above 3000 Å. Work in progress is concerned with the factors determining product structure in dimerizations of this type.

Experimental[24]

Photoirradiation of $\Delta^{4,6}$-Androstadien-3-on-17β-ol Propionate (IA). A. In Homogeneous Solution.—A solution of 7.25 g. of compound IA[4] [m.p. 135–136°, λ_{max} 284 mμ (ϵ 27,500)] in 35 ml. of 1:1 benzene–petroleum ether was irradiated for 7 hr.

(20) Treatment of II with reduced platinum oxide in propionic acid resulted in recovery of unchanged starting material.

(21) Hydrolysis of the ester group occurred under the conditions of the cleavage.

(22) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958); G. Slomp and B. R. McGarvey, *ibid.*, **81**, 2200 (1959); J. S. G. Cox, E. O. Bishop, and R. E. Richards, *J. Chem. Soc.*, 5118 (1960).

(23) P. E. Eaton, *J. Am. Chem. Soc.*, **84**, 2344, 2454 (1962).

(24) Photoirradiations were performed in nitrogen atmosphere in Pyrex vessels using a Pyrex-jacketed, water-cooled, 1000-w. General Electric high-pressure mercury lamp (AH-6). Melting points are corrected. The solvent for optical rotations was chloroform (1% solutions) and for ultraviolet measurements was 95% alcohol. Molecular weights were determined in benzene solution with a Mechrolab osmometer. N.m.r. spectra were determined at 60 Mc. with a Varian Associates HR-60 spectrometer using tetramethysilane as internal standard in deuteriochloroform solution.

and the clear solution then adsorbed on 350 g. of Florisil. Elution with five 1-l. portions of 7% ethyl acetate–benzene gave 4.65 g. (64%) of IA, m.p. 131–136° (infrared spectra of all fractions were identical with authentic IA; thin layer chromatograms[25] of all fractions showed the presence of only a single component, identical in R_f value with IA). The combined fractions after recrystallization from methylene chloride–petroleum ether gave 4.42 g. of white crystals, m.p. 135–136°.

Further elution with five 1-l. portions of 30% ethyl acetate–benzene and two of 50% ethyl acetate–benzene gave a total of 2.45 g. (34%) of photodimer II, m.p. 166–168° (infrared spectra of all fractions were identical; examination of thin layer chromatograms under ultraviolet light and by treatment with concentrated sulfuric acid revealed the presence of only a single component identical in R_f value with pure II). One crystallization of the combined fractions from methylene chloride–petroleum ether gave 1.52 g., m.p. 168–169°. A portion, recrystallized from the same solvent mixture, yielded the analytical sample, m.p.[26] 167–168°, 256 mμ (ε 10,800); λ_{max}^{KBr} 5.71, 5.86, 5.98, 6.21, 8.40 μ; $\lambda_{max}^{CHCl_3}$ 5.78, 5.90, 5.99, 6.24, 8.39 μ; $[\alpha]^{26}D$ +16 ± 2°.

Anal. Calcd. for $C_{44}H_{60}O_6$: C, 77.15; H, 8.83; mol. wt., 685. Found: C, 77.39; H, 8.78; mol. wt., 689.

B. In the Solid State.—A thin layer of 549 mg. of IA between two glass plates was irradiated on alternate sides for a total of 43 hr. The product after irradiation had λ_{max} 285 mμ (ε 26,200). Examination of the thin layer chromatogram indicated only a single component identical in R_f value with starting material.

Thermal Cleavage of Photodimer II.—Heating 18 mg. of II at 175° in a sealed, evacuated capillary for 5 min. produced a light yellow oil identical in infrared spectrum with IA, λ_{max} 283 mμ (ε 25,200).

Catalytic Hydrogenation of Photodimer II.—A solution of 3.145 g. (4.6 mmoles) of II in 50 ml. of anhydrous propionic acid was added to 315 mg. of pre-reduced platinum oxide in 50 ml. of anhydrous propionic acid at 32° (741 mm.). After 7 hr., 473 ml. (4.0 equiv.) of hydrogen had been absorbed. The catalyst was filtered, washed with ethyl acetate, and the combined solutions evaporated to dryness under reduced pressure on the steam bath. The resulting oil was chromatographed on 177 g. of Florisil.

Elution of 1 l. of benzene gave 595 mg. (19%) of oil which was crystallized from methanol to give 444 mg. of 5α-androstan-17β-ol propionate (IIIA), m.p. 54–56°; λ_{max} (CH_2Cl_2) 5.79, 8.39, no absorption 2.5–3.1 μ.

Elution with four 1-l. portions of 3% ethyl acetate–benzene gave 1.886 g. (61%) of the hexahydro product (IV). The analytical sample was obtained by crystallization from methanol, m.p. (sealed, evacuated capillary) 274–275°; end absorption, 210 mμ (ε 8700); λ_{max}^{KBr} 5.77, 5.91, 8.42 μ; $[\alpha]^{28}D$ +38 ± 2°.

Anal. Calcd. for $C_{44}H_{64}O_5$: C, 78.53; H, 9.59; mol. wt., 677. Found: C, 78.52; H, 9.62; mol. wt., 673.

Further elution with two 1-l. portions of 20% and three of 30% ethyl acetate–benzene yielded 331 mg. (10%) of tetrahydro product (V). The analytical sample was obtained by crystallization from methylene chloride–petroleum ether, m.p. (sealed, evacuated capillary) 276–278°; end absorption, 210 mμ (ε 2400); $\lambda_{max}^{CH_2Cl_2}$ 2.74, 5.78, 5.92, 8.39 μ; $[\alpha]^{27}D$ +62 ± 2°.

Anal. Calcd. for $C_{44}H_{64}O_6$: C, 76.70; H, 9.36; mol. wt., 689. Found: C, 76.44; H, 9.48; mol. wt., 704.

Hydrolysis of 5α-Androstan-17β-ol Propionate (IIIA).—A solution of 200 mg. of IIIA in 10 ml. of methanol containing 0.8 ml. of 10% aqueous potassium hydroxide was allowed to stand overnight at room temperature. After neutralization with acetic acid, the solution was concentrated on the steam bath under reduced pressure. The residue was taken up in ethyl acetate which was washed with water, dried over anhydrous sodium sulfate, and concentrated to give 167 mg. (100%) of white solid, m.p. 138–152°. Recrystallization from methanol gave 85 mg. (51%) of 5α-androstan-17β-ol (IIIB), m.p. 164–166°; lit.[9] m.p. 164°; λ_{max}^{KBr} 2.98, no absorption at 5.5–6.5 μ. The residue was a light yellow solid, m.p. 95–108° (lit.[9] m.p. 96° for 5β-androstan-17β-ol). An additional 28 mg. (17%) of IIIB was obtained by chromatography of the residue on Florisil.

Thermal Cleavage of Hexahydro Product IV.—Heating 380 mg. of IV at 270–280° in a sealed, evacuated tube for 3.5 hr. gave a light yellow oily product, λ_{max} 238 mμ (ε 12,000). This was dissolved in benzene and chromatographed on 19 g. of Florisil collecting 200-ml. fractions.

Elution with 50% benzene–petroleum ether gave 117 mg. (31%) of $\Delta^{4,6}$-androstadien-17β-ol propionate (VIIA), m.p. 99–102°, which was recrystallized from methanol to yield 96 mg., m.p. 103–104°, identical with the synthetic sample described subsequently.

Elution with 1, 2, 3, and 4% ethyl acetate–benzene gave a mixture which was rechromatographed on 12 g. of Florisil (100-ml. fractions). Six fractions of 0.5% ethyl acetate–benzene gave 127 mg. (33%) of solid, identical by infrared analysis with IV.

Further elution with two portions of 1% and four of 2% ethyl acetate–benzene gave a total of 101 mg. (26%) of solid identical by infrared with testosterone propionate. Crystallization from methanol afforded white crystals, m.p. 120–122°, undepressed on mixture with authentic material.

$\Delta^{3,5}$-Androstadien-17β-ol Propionate (VI).—$\Delta^{3,5}$-Androstadien-17β-ol was prepared by the procedure of Rosenkranz, *et al.*,[11] m.p. 155–157°; λ_{max} 228 mμ (ε 19,000), 234 (20,400), 243 (12,900). A solution of 600 mg. of this alcohol in 3 ml. of propionic anhydride and 6 ml. of pyridine was allowed to stand overnight in the dark at room temperature. The light yellow solution was taken to dryness on a rotary evaporator to give 526 mg. (73%) of solid, m.p. 134–140°. Several crystallizations from petroleum ether gave white crystals, m.p. 135–138°. When 282 mg. of the product was washed through 15 g. of Florisil with 50% petroleum ether–benzene, there was obtained 268 mg. of white solid, m.p. 136–138°. The infrared spectra in methylene chloride were identical before and after chromatography. One crystallization of the chromatographed material from petroleum ether gave the analytical sample, m.p. 138–139°; λ_{max} 228 mμ (ε 21,300), 234 (23,000), 243 (14,500); λ_{max}^{KBr} 5.78, 6.09, 8.40 μ; $[\alpha]^{27}D$ −177 ± 2°; n.m.r., 5.37 (triplet, J = 7 c.p.s.), 7.68 (quartet, J = 8 c.p.s.), 8.87 (triplet, J = 8 c.p.s.), 9.04, 9.17 τ; also lines at 364, 354, 343, 338, 326 (broad) c.p.s. downfield from tetramethylsilane.

Anal. Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83. Found: C, 80.17; H, 9.86.

A sample, heated for 3.5 hr. at 270–280° in a sealed, evacuated tube, was recovered unchanged as shown by infrared and ultraviolet analysis, m.p. 135–138°.

Δ^4-Androstene-7,17β-diols (VIII).—Eight and one-half grams of sodium was added in portions to a refluxing solution of 3.0 g. of $\Delta^{3,5}$-androstadiene-7,17-dione[13] in 200 ml. of 1-propanol. After all the sodium had reacted, the solution was cooled, poured into ice and water, and neutralized by addition of 22.2 ml. of glacial acetic acid. Methanol was removed by evaporation under reduced pressure on the steam bath and the residue extracted twice with ethyl acetate. The extracts were washed twice with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure on the steam bath to give 3.28 g. of tacky solid which showed only end absorption in the ultraviolet. One crystallization from aqueous methanol gave 2.41 g. (80%) of VIII, m.p. 155–170°. Further crystallization from aqueous methanol gave an analytical sample of mixed C-7 epimers, m.p. 175–183°; λ_{max}^{KBr} 2.93 μ; $[\alpha]^{30}D$ +61 ± 2° (*c* 0.5).

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 79.23; H, 10.70.

Δ^5-Androstene-7,17-dione (IX).—A solution of 2.12 g. of diols VIII in 250 ml. of acetone maintained at 10–15° in an atmosphere of nitrogen was treated dropwise with stirring with 7 ml. of solution prepared from 2.137 g. of chromium trioxide and 1.84 ml. of concentrated sulfuric acid made up to 8 ml. with water.[14] After addition was complete, the solution was stirred for 15 min. and then poured into 1 l. of water. Acetone was removed under reduced pressure and the residual oily solution was extracted with ethyl acetate. The extracts were washed with water, dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure on the steam bath.

The residue was dissolved in 200 ml. of warm methanol, 1 ml. of 10% aqueous potassium hydroxide solution added, and the solution refluxed for 5 min. After neutralization with acetic acid, the solution was concentrated under reduced pressure on the steam bath. The residue was dissolved in ethyl acetate, washed twice with water, dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure on the steam bath

(25) V. Cerny, J. Joska, and L. Labler, *Collection Czech. Chem. Commun.*, **26**, 1658 (1961).

(26) The melting point varied with rate of heating due to thermal cleavage of II. The melting points reported here were obtained by placing the capillary in a bath at 160° and raising the temperature at the rate of 1°/per minute.

to give 2.08 g. of light yellow crystals, m.p. 96–164°; λ_{max} 238 mμ (ε 5400). One crystallization from methanol gave 530 mg. (25%) of IX, m.p. 164–173°. Further crystallization from methanol furnished the analytical sample, m.p. 180–181°; 238 mμ (ε 13,100); λ_{max}^{KBr} 5.75, 6.01, 6.16 μ; $[\alpha]^{27}D$ −116 ± 2°.

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.84; H, 9.32.

Δ^5-Androstene-7,17β-diols (X).—Reduction of 520 mg. of IX with 653 mg. of lithium aluminum hydride in 75 ml. of ether afforded, after addition of water, filtration, and evaporation of solvent, 548 mg. of X, m.p. 107–170°; end absorption, 210 mμ (ε 9900); $\lambda_{max}^{CH_2Cl_2}$ 2.7 μ.

Reaction of 15 mg. of crude X with 150 mg. of activated manganese dioxide[27] in 3 ml. of chloroform at room temperature for 18 hr. afforded, after filtration and evaporation of solvent, 16 mg. of oil, 239 mμ (ε 6700); $\lambda_{max}^{CH_2Cl_2}$ 2.73, 6.02, 6.16 μ.

$\Delta^{4,6}$-Androstadien-17β-ol Propionate (VIIA).—A solution of 25 mg. of crude diol X in 5 ml. of 95% ethanol containing one drop of concentrated hydrochloric acid was refluxed for 2 hr. After cooling, the solution was neutralized with excess solid sodium carbonate, concentrated under reduced pressure, and the resulting white solid taken up in ethyl acetate and water. The layers were separated, the organic layer washed twice with water, dried over anhydrous sodium sulfate, and evaporated to dryness under reduced pressure on the steam bath. The crude alcohol, 24 mg. (94%), exhibited m.p. 137–157°; λ_{max} 230 mμ (ε 18,300), 238 (20,400), 246 (13,000); $\lambda_{max}^{CH_2Cl_2}$ 2.73 μ.

The crude product, 376 mg. from the reaction of 400 mg. of X as described, was esterified with 5 ml. of propionic anhydride and 10 ml. of pyridine overnight at room temperature. After removal of solvent on a rotary evaporator the residue was chromatographed on 18.5 g. of Florisil. Elution with one 200-ml. portion of petroleum ether and two of 10% benzene–petroleum ether gave a total of 360 mg. of VIIA, m.p. 91–103°. Crystallization from methanol and then petroleum ether gave the analytical sample, m.p. 103–104°; λ_{max} 230 mμ (ε 21,000), 238 (22,400), 246 (13,700); λ_{max}^{KBr} 5.74, 6.12, 8.40 μ; $[\alpha]^{28}D$ −3 ± 2°; n.m.r., 5.30 (multiplet), 7.64 (quartet, J = 8 c.p.s.), 8.86 (triplet, J = 8 c.p.s.), 9.04, 9.12 τ; also lines at 364, 355, 335, 329, 326 c.p.s. downfield from tetramethylsilane.

Anal. Calcd. for $C_{22}H_{32}O_2$: C, 80.44; H, 9.83. Found: C, 80.54; H, 9.84.

A sample, heated for 3 hr. at 270–280° in a sealed, evacuated tube, was recovered unchanged as shown by infrared and ultraviolet analysis, m.p. 98–104°.

Oxidation of Tetrahydro Product V to XI.—To a stirred solution of 352 mg. of V in 40 ml. of acetone maintained at 10–15° under nitrogen was added 0.145 ml. of a solution containing 2.137 g. of chromium trioxide and 1.84 ml. of concentrated sulfuric acid made up to 8 ml. with water.[14] After the dropwise addition was completed, the solution was stirred for 5 min. and then poured into water. The solution containing white solid was concentrated to remove acetone, the solid filtered and washed with water to give 348 mg. (99%) of XI, m.p. 268–271°, no absorption at 2.5–3.1 μ in methylene chloride solution. The sample for analysis was crystallized from methylene chloride–petroleum ether, m.p. 273–275° (sealed capillary); end absorption, 210 mμ (ε 2700); λ_{max}^{KBr} 5.76, 5.91, 8.44 μ; $[\alpha]^{28}D$ +60 ± 2°.

Anal. Calcd. for $C_{44}H_{64}O_6$: C, 76.70; H, 9.36. Found: C, 76.03; H, 9.48.

Thermal Cleavage of XI.—Heating 166 mg. of XI in a sealed, evacuated tube at 275° for 3 hr. gave an amber oil which failed to crystallize, λ_{max} 284 mμ (ε 7000). Fourteen milligrams of this was set aside and the remainder, dissolved in the minimum volume of benzene, was chromatographed on 8 g. of Florisil. Elution with 150 ml. of 2% ethyl acetate in benzene yielded 36 mg. (47%) of 5α-Δ^6-androsten-3-on-17β-ol propionate (XII), m.p. 125–136°; $\lambda_{max}^{CH_2Cl_2}$ 5.80–5.85, 8.4 μ; n.m.r., 4.64 (2H, broad), 5.33 (1H), 7.67 (quartet, J = 8 c.p.s.), 8.85 (triplet, J = 8 c.p.s.), 8.97, 9.09 τ. The material recovered from the n.m.r. determination was rechromatographed on Florisil and crystallized once to give the analytical sample of XII, m.p. 136–138°; λ_{max}^{KBr} 5.77, 5.84, 8.44 μ.

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 75.78; H, 9.34.

Further elution with 240 ml. of 3% and 150 ml. of 5% ethyl acetate in benzene gave 40 mg. (53%) of material exhibiting an infrared spectrum identical with that of IA. Elution with 240 ml. of 10% and 150 ml. of 20% ethyl acetate in benzene afforded 60 mg. (39%) of recovered XI, identified by infrared analysis.

Androstan-3-on-17β-ol Propionate (XIII).—Hydrogenation of 17.2 mg. of XII in 5 ml. of ethyl acetate containing 3 mg. of 10% palladium on charcoal yielded, after filtration and concentration, 21.8 mg. of white solid, m.p. 110–119°, which was chromatographed on 1 g. of Florisil. Elution with 20 ml. of 5% ethyl acetate in benzene gave 11.8 mg. (69%) of XIII, m.p. 118–124°. One crystallization from hexane raised the melting point to 124–126°, lit.[15] m.p. 121–122°. This material exhibited an infrared spectrum identical with that of an authentic sample of XIII.[15]

Acid-Catalyzed Cleavage of Photodimer II.—A suspension of 100 mg. of II in 25 ml. of 5% *p*-toluenesulfonic acid in methanol was allowed to stand in the dark at room temperature. After 3.5 hr. the solid had completely dissolved; after an additional 17.5 hr. the solution was neutralized with 5% sodium hydroxide solution and methanol was removed under reduced pressure without heating. The residue was extracted with ethyl acetate, the extracts washed twice with water, dried over anhydrous sodium sulfate, and concentrated under reduced pressure to give 88 mg. of light yellow solid, m.p. 192–195°. The infrared spectrum was identical with that of an authentic sample of $\Delta^{4,6}$-androstadien-3-on-17β-ol.[28] One crystallization from ethyl acetate gave 41 mg., m.p. 199–202°, lit.[28] m.p. 204–205°.

Similar results were obtained by reaction with 5% hydrochloric acid in methanol for 33 hr. at room temperature in the dark.

$\Delta^{4,6}$-Androstadien-3-one (IB).—A suspension of 9.44 g. of Δ^4-androsten-3-one[5] and 18.87 g. of chloranil in 500 ml. of *t*-butyl alcohol[29] was refluxed for 3 hr. Excess chloranil was filtered after cooling, washed with *t*-butyl alcohol, and the combined solutions evaporated to dryness. The black residue was dissolved in ethyl acetate, washed with water and then with 5% sodium hydroxide solution until the washings were almost colorless, then with water and saturated salt solution. The organic layer was dried over anhydrous sodium sulfate and concentrated under reduced pressure on the steam bath to give 15.75 g. of black tar. This was dissolved in benzene and washed through 200 g. of alkaline alumina with 1 l. of 1:1 benzene–petroleum ether and 1 l. of benzene to give, after concentration, 5.59 g. (59%) of light yellow solid, m.p. 146–147°. The analytical sample was obtained by crystallization from petroleum ether, m.p. 146–147° (transition from granules to cubes at 135–145° on the hot stage); λ_{max} 285 mμ (ε 25,500); λ_{max}^{KBr} 5.98, 6.15, 6.29 μ; $[\alpha]^{26}D$ +67 ± 3°.

Anal. Calcd. for $C_{19}H_{26}O$: C, 84.39; H, 9.65. Found: C, 84.45; H, 9.47.

Photoirradiation of $\Delta^{4,6}$-Androstadien-3-one. Photodimer XIV.—A solution of 1.59 g. of IB in 20 ml. of 1:1 benzene–petroleum ether was irradiated for 24 hr. and the clear solution then adsorbed on 75 g. of Florisil. Elution with 3 l. of 1% ethyl acetate–benzene gave 767 mg. (48%) of IB, m.p. 140–147°. Further elution with 2 l. of 2% and two of 3% ethyl acetate–benzene gave 595 mg. (37%) of photodimer XIV, m.p. 152–155°. Three crystallizations from chloroform–petroleum ether and two from methanol gave the analytical sample, m.p. 155°; λ_{max} 256 mμ (ε 10,300); λ_{max}^{KBr} 5.90, 5.98, 6.22 μ; $[\alpha]^{27}D$ +12 ± 3°.

Anal. Calcd. for $C_{38}H_{52}O_2$: C, 84.39; H, 9.69; mol. wt., 540. Found: C, 84.50, 84.60; H, 9.59, 9.76; mol. wt., 500.

Heating 10 mg. of XIV in a sealed capillary at 165° for 5 min. afforded a yellow oil, λ_{max} 284 mμ (ε 21,200), which was identical with IB by infrared analysis.

Photoirradiation of $\Delta^{4,6}$-Androstadien-3-on-17β-ol (IC). Photodimer XV.—A solution of 580 mg. of IC[28] in 20 ml. of 1:1 benzene–dioxane was irradiated for 6 hr. After removal of solvent in an air stream without heating, a portion (123 mg.) of the crude product was crystallized from chloroform–ethyl acetate to give 60 mg. (49%) of XV, m.p. 199–201°. Three crystallizations from the same solvent mixture gave the analytical sample, m.p. 200–201.5°; λ_{max} 257 mμ (ε 10,000); λ_{max}^{KBr} 5.90, 6.05, 6.27 μ; $[\alpha]^{30}D$ +33°.

Anal. Calcd. for $C_{38}H_{52}O_4$: C, 79.68; H, 9.15. Found: C, 79.68; H, 8.72.

Esterification of 55 mg. of XV by reaction with 0.5 ml. of propionic anhydride in 1 ml. of pyridine at room temperature overnight gave a crude product which was chromatographed on 3

(27) Beacon Chemical Industries, Inc., Cambridge 40, Mass.

(28) C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann, and J. Pataki, *J. Am. Chem. Soc.*, **72**, 4534 (1950).

(29) E. J. Agnello and G. O. Laubach, *ibid.*, **82**, 4293 (1960).

g. of Florisil. Elution with 100 ml. of 20% and 30 ml. of 50% ethyl acetate–benzene gave 49 mg. (74%) of II which, after one crystallization from methylene chloride–petroleum ether, gave 39 mg., m.p. 168.5–170°, identical by infrared spectrum and mixture melting point with II obtained by photoirradiation of IA.

Heating 13 mg. of XV in a sealed, evacuated capillary for 15 min. at 215° gave material exhibiting infrared and ultraviolet spectra identical with those of IC.

Photoirradiation of $\Delta^{4,6}$-Cholestadien-3-one (ID). Photodimer XVI. A. In Petroleum Ether.—A solution of 518 mg. of $\Delta^{4,6}$-cholestadien-3-one[30] (ID) in 15 ml. of petroleum ether was irradiated for 1.75 hr. at 3–4°. The solid which precipitated was filtered to give 247 mg. (48%) of dimer XVI, m.p. 175–177°. The yield could be raised to 79% by successive crop taking and reirradiation. The analytical sample was obtained by crystallization from ethyl acetate, m.p. 174.5–175°; $\lambda_{max}^{cyclohexane}$ 243 mμ (ε 10,600); λ_{max}^{KBr} 5.93, 5.98, 6.25 μ; $[\alpha]^{26}D$ +37°; lit.[3] λ_{max}^{alc} 258 mμ (ε 9100); $\lambda_{max}^{CHCl_3}$ 5.91, 6.02, 6.21 μ; $\lambda_{max}^{CCl_4}$ 5.89, 5.97, 6.23 μ; lit.[17] m.p. 173–174°, 179–180°; $[\alpha]D$ +37°.

Anal. Calcd. for $C_{54}H_{84}O_2$: C, 84.75; H, 11.07; mol. wt., 765. Found: C, 84.55; H, 10.93; mol. wt., 730.

Heating 16 mg. of XVI in a sealed capillary at 215° for 15 min. gave an oil, λ_{max} 284 mμ (ε 25,200), identical with ID by comparison of infrared spectra.

B. In Benzene–Dioxane Solution.—A solution of 206 mg. of ID in 5.4 ml. of 1:1 benzene–dioxane was irradiated for 5.5 hr. The solution remained clear. After removal of solvent under reduced pressure, the residue was chromatographed on 10 g. of Florisil. Elution with 800 ml. of 1% ethyl acetate–benzene yielded 87 mg. of starting material. Elution with 600 ml. of 3% ethyl acetate–benzene afforded 36 mg. (18%) of XVI. One crystallization from methylene chloride–ethyl acetate gave 18 mg., m.p. 172.5–173°; mixture melting point with product from the petroleum ether reaction, 172.5–173°. Infrared spectra were identical.

Reversibility of Photodimerization of IA.—A solution of 480 mg. of dimer II in 14 ml. of 1:1 benzene–dioxane was irradiated for 12.5 hr. The clear solution was concentrated under reduced pressure and the residue, λ_{max} 284 mμ (ε 11,800), chromatographed on 21 g. of Florisil as described for the photoirradiation of IA to give 46% of IA, m.p. 135–136°, and 38% of II, m.p. 167–169°. Identity was further established by comparisons of infrared spectra.

Photostationary States.—Solutions of IA (0.1 *M*) or II (0.05 *M*) in 1:1 benzene–dioxane were immersed in a water bath having a Pyrex window and irradiated until ultraviolet spectra of samples from each solution were identical. Compositions were calculated from the extinction coefficients of the monomer at 280 mμ (ε 26,900) correcting for the relatively weak absorption (ε 5200) of dimer at this wave length. At 3–4°, 15 hr. were required to attain equilibrium; the product of irradiation of IA contained 29% IA and 71% II, the product from II contained 28% IA and 72% II. At 27–28° equilibrium was attained in 3 hr.,[31] the compositions were 31% IA and 69% II in both cases.

Acknowledgment.—Financial support from the Squibb Institute for Medical Research is gratefully acknowledged. N.m.r. spectra were determined by Miss P. Zwitkowitz.

(30) A. L. Wilds and C. Djerassi, *J. Am. Chem. Soc.*, **68**, 1712 (1946). Use of the chloranil oxidation procedure as described for IB afforded ID in 65% yield.

(31) The considerable differences in duration of reaction may have been due to relative age of the lamp in the two sets of experiments.

Perhydroindanone Derivatives. IV. The 1,1a,4,4a-Tetrahydrofluoren-9-one System[1a]

HERBERT O. HOUSE AND ROBERT G. CARLSON[1b]

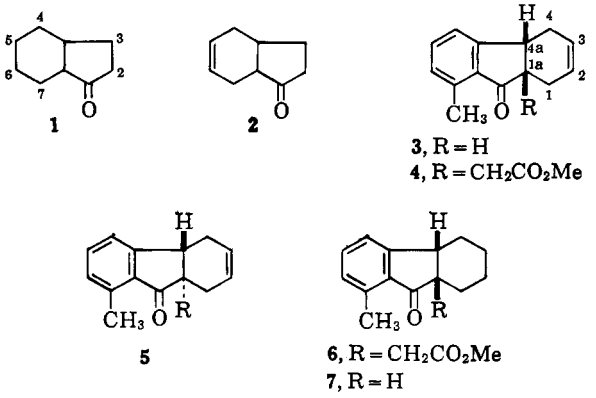
Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts

Received July 24, 1963

The *cis*-fused isomer (the more stable) of 8-methyl-1,1a,4,4a-tetrahydrofluoren-9-one (**3**) has been synthesized and found to give primarily the *cis*-fused product **4** on alkylation. Several possible routes to the 2-keto hexahydrofluorenone system **20** have been explored and a satisfactory preparative route is described.

Upon finding[2] that the relative stability of the *cis* isomer of perhydroindan-1-one (**1**, 75% *cis* at equilibrium) could be diminished by the introduction of a double bond at the 5–6-position (as in **2**, 53% *cis* at equilibrium), it became of interest to learn whether the alkylation of the tetrahydrofluorenone system **3** would lead to a mixture of the *cis* and *trans* ring-fused products **4** and **5** rather than only (or at least very largely) a *cis*-fused product such as **6** obtained from alkylation of the hexahydrofluorenone **7**.[3] The realization of such a nonstereoselective alkylation appeared to offer a possible route to intermediates useful for the synthesis of both allogibberic acid (*trans* B–C ring fusion) and epiallogibberic acid (*cis* B–C ring fusion) without requiring inversion of a center at some later stage.[4]

To examine this question the tetrahydrofluorenone **3** was prepared as indicated in Chart I following a sequence previously applied to 1-indanone.[5] Since a preliminary attempt to prepare the Diels–Alder adduct **10** led to a complex mixture (*cf.* ref. 5), we modified the procedure to generate the very reactive indenone **11** in the presence of excess butadiene. A single crystalline adduct **3** was isolated from this Diels–Alder reaction. This material was stable to refluxing methanolic sodium methoxide although these



(1) (a) Supported in part by Grant No. G-25214 from the National Science Foundation; (b) National Institutes of Health Predoctoral Fellow, 1960–1963.

(2) H. O. House and G. Rasmusson, *J. Org. Chem.*, **28**, 31 (1963).

(3) H. O. House, V. Paragamian, and D. J. Wluka, *J. Am. Chem. Soc.*, **82**, 2561 (1960); **83**, 2714 (1961).

(4) For one method, albeit a circuitous one, of effecting this inversion in the system **4**, see H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *ibid.*, **84**, 2614 (1962).

(5) H. O. House, V. Paragamian, R. S. Ro, and D. J. Wluka, *ibid.*, **82**, 1452, 1457 (1960).