Kinetic Study of High Temperature Rearrangements.—Pure samples of the dimers were prepared as described above and distilled immediately prior to use.

Kinetic runs were performed according to the procedures described by Hammond and DeBoer,[14] and will not be described here. Control experiments showed the absence of surface effects and confirmed that no material was lost to polymerization. Occasionally, slight oxidation of the photodimer **4** accompanied rearrangement. This was attributed to the inferior degassing procedure (see ref. 14) necessitated by the small sample size and by the small sample tubes employed.

Analysis of samples was conducted with a Loenco 15 B flame ionization detector using a 150-ft. Apiezon J Golay column. The column temperature was 95–105°; the carrier gas pressure was 30 p.s.i. Samples of 0.01 μl. were delivered with a Hamilton 1-μl. syringe. This technique was the best found for this purpose and gave good separations of **2** and **4**. Compounds 1 and **3** were not entirely separated, however, and the analysis for rearrangement of **3** suffers imprecision for this reason.

All rates and activation parameters were obtained from slopes of least-squares plots of the data.

Acknowledgment.—This study was partially supported by both the Petroleum Research Fund of the American Chemical Society and the National Science Foundation. The authors wish to thank Mr. Kenneth L. Servis for helpful discussions of n.m.r. spectra. We are also indebted to Professor J. D. Roberts for helpful discussion and especially for invaluable service as an art critic, and to Dr. Philip E. Eaton for prepublication information concerning the dimers of cyclohexenone.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE, REHOVOTH, ISRAEL]

Photochemistry of Enolic Systems. I. Irradiation of Enol Acetates

BY AMNON YOGEV, MALKA GORODETSKY, AND YEHUDA MAZUR

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Irradiation of enol acetates with a low-pressure mercury lamp was studied. Irradiation of isopropenyl acetate (**1**) and cyclohexenyl acetate (**3**) resulted in an acetyl rearrangement and yielded, respectively, acetylacetone (**2**) and α-acetylcyclohexanone (**4**). Similarly, steroidal enol acetates **9**, 11, and **13** gave corresponding ketones **10**, **12**, and **14**. In all these irradiations considerable amounts of the starting materials were isolated. Enol acetate with a fully substituted double bond (**5**) gave, in addition to 2-acetyl-2-methylcyclohexanone (**7**), 2-methylcyclohexanone (**6**) and its dimer **8**. An analogous steroidal enol acetate **15** resulted mainly in the dimer **21** and also in the ketones **16**, **17**, and **18**. It was found that acetyl migration occurs by an intramolecular process, suggesting a cage mechanism. The stereochemistry of this photochemical acetyl rearrangement is also discussed.

The reactivity of the enol–acetate system in thermal reactions is well established. One of the main changes observed is the formation of β-diketones by acetyl migration from the oxygen to the vinylic carbon atom.[1]

We have undertaken an investigation of the behavior of these systems on ultraviolet irradiation, analogous acetyl migration being expected to occur. Our previous results of photolysis of enol benzoates[2] and the recently published observations of a photochemical Fries rearrangement[3] support the assumption that the O–acyl bond of the enol-acetate chromophore is most likely to cleave under the influence of the ultraviolet radiation.

The ultraviolet source chosen in the following experiments was a low pressure immersion mercury lamp (Hanau, NT 6/20) which emits almost entirely at 253.7 mμ, and the solvent chosen was cyclohexane. The enol acetates to be irradiated show absorption maxima in this solvent in the region 190–200 mμ (*ca.* ε 7000) and possess a finite, although small, absorption at 253.7 mμ (ε 30–50).[4] The light quantum absorbed at this higher wave length is sufficient to cause a photochemical change in the absorbing molecule.

When isopropenyl acetate (**1**) was irradiated, the product isolated was the expected acetylacetone (**2**) [λ_{max} 271 mμ (ε 9200) in cyclohexane].[5] This β-diketone could be obtained in pure form as the copper chelate after evaporation of the solvent and treatment of the residue with aqueous cupric acetate, and was found to be identical with an authentic sample of the chelate (**2**). The progress of the conversion of **1** to **2** was followed by the absorption intensity of **2** at 271 mμ in the irradiated solution. It was found that on irradiation of a 1% cyclohexane solution of **1**, the yield of **2** approached asymptotically the value of 29%[6] in 45 hr., and remains practically constant upon further irradiation. Working with more concentrated solution of **1**, the limit yield of **2** decreases, although it is reached after similar reaction periods. Thus, starting with a 10% solution of **1**, only a 9% conversion was observed after 45 hr. and further irradiation did not increase this yield appreciably. In all these cases the reaction mixtures were found to contain a considerable amount of the unrearranged starting material **1**. The product **2**, which exists in cyclohexane mainly in the enolic form,[5] does not undergo observable change when irradiated in cyclohexane solution under similar conditions, by itself or in admixture with isopropenyl acetate (**1**).[7]

(1) (a) P. E. Reiminger and P. D. Ritchie, *J. Chem. Soc.*, 2678 (1963); (b) W. M. Muir and P. D. Ritchie, *ibid.*, 2692 (1963); (c) R. J. P. Allan, R. L. Forman, and P. D. Ritchie, *ibid.*, 2717 (1955); (d) F. G. Young, F. C. Frostic, J. J. Sanderson, and C. H. Hauser, *J. Am. Chem. Soc.*, **72**, 3635 (1950).

(2) M. Feldkimel-Gorodetsky and Y. Mazur, *Tetrahedron Letters*, 369 (1963).

(3) H. Kobsa, *J. Org. Chem.*, **27**, 2293 (1962); J. C. Anderson and C. B. Reese, *Proc. Chem. Soc.*, 217 (1960).

(4) *E.g.*, cholest-2-en-3β-ol acetate was found to have in cyclohexane λ_{max} 190 mμ (ε 6800) and ε-value of 4800 at 200 mμ. Compared with cholest-2-en [λ_{max} 190 mμ (ε 4700) and ε-value of 1500 at 200 mμ] it shows a bathochromic shift and an increase of the extinction coefficient. (*Cf.* J. H. Chapman and A. C. Parker, *J. Chem. Soc.*, 2075 (1961), and references cited therein.)

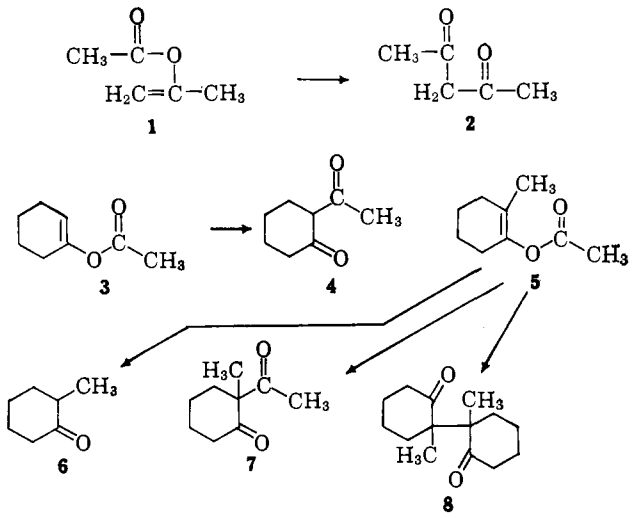
(5) Acetylacetone was found by us to exist in cyclohexane in the enolic form to the extent of 88%, as calculated from the n.m.r. spectrum in this solvent; *cf.* B. Eistert and W. Reiss, *Chem. Ber.*, **87**, 92 (1954).

(6) (a) These yields were calculated spectroscopically. The isolated compounds were obtained in somewhat smaller yields. (b) Similar values were obtained from the n.m.r. spectra of the total irradiated solution; see Experimental.

(7) No addition products between acetylacetone and isopropenyl acetate were observed in this irradiation; *cf.* P. de Mayo H. Takeshita, and A. B. M. A. Satter, *Proc. Chem. Soc.*, 119 (1962).

The absorption intensity of **2** at 253.7 mμ is roughly 200 times that of **1**, and therefore **2** must act as a strong filter in these experiments. This would explain the comparatively low final yields, but the dependence of these yields on the initial concentration points to the intervention of an additional factor. A likely explanation would be the quenching of the excited molecules of **1** by the product **2**.

When cyclohexen-1-yl acetate (**3**) was irradiated in 2% cyclohexane solution, the only product isolated was α-acetylcyclohexanone (**4**) [λ_{max} 286 mμ (ε 7600) in cyclohexane].[8] This substance was separated from



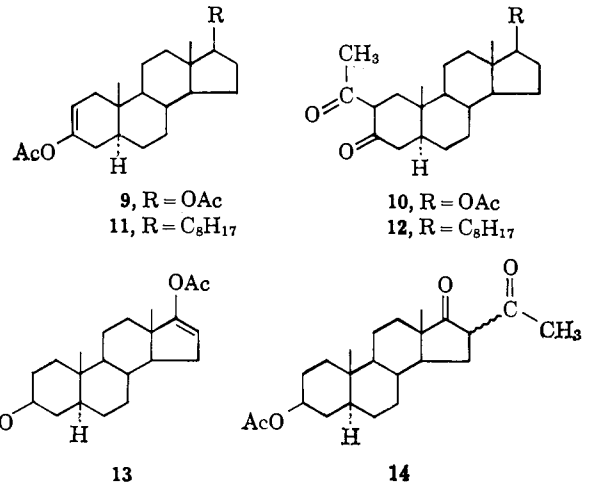
unchanged **3** by chromatography on silica gel or as the copper chelate. Both products were identified by comparison with authentic samples.[9] By measurement of the ultraviolet absorption intensity of the irradiated solution at 286 mμ, it was found that after 24 hr. a practically constant maximum was reached, corresponding to a 15% conversion.

The next substance irradiated was 2-methylcyclohexenyl acetate (**5**), an enol acetate with a fully substituted double bond. The progress of the irradiation was followed by the disappearance of the infrared bands at 5.68, 8.15, and 8.28 μ corresponding to the vinyl acetate chromophore. After 15 hr., when the quantity of **5** had dropped to 30%, the reaction was discontinued[10] and the products were separated by chromatography. Three transformation products were identified, all of them ketones. The first one was found to be 2-methylcyclohexanone (**6**, 5% yield). The second one proved to be 2-acetyl-2-methylcyclohexan-1-one (**7**, 17% yield), which showed two carbonyl peaks in the infrared (at 5.80 and 5.87 μ) and the expected nuclear magnetic resonance (n.m.r.) spectrum and was identical with a sample prepared by methylation of α-acetylcyclohexanone (**4**) with methyl iodide and potassium *t*-butoxide.[11] The third ketonic product was obtained in 7% yield; it showed one carbonyl peak in the infrared at 5.85 μ and one sharp signal in the n.m.r.[12] at 71 c.p.s. We assigned to it the formula of 2-methylcyclohexanone dimer **8**.

In order to establish the scope and the steric course of this type of irradiation we applied it to steroidal enol acetates.

5α-Androst-2-ene-3,17β-diol diacetate (**9**) was irradiated to give 2-acetyl-5α-androstan-3-on-17β-ol acetate (**10**), m.p. 178–179° [$\lambda_{max}^{C_6H_{12}}$ 283 mμ (ε 8900)],[8] identified by comparison with an authentic sample.[13,14] In a 0.9% solution the yield of **10** reached the limiting value of 12% in 16 hr.[6a] Most of the starting material **9** was recovered unchanged. Similarly, cholest-2-en-3-ol acetate (**11**) gave the corresponding 2-acetylcholestan-3-one (**12**)[13,14] in 15% yield[6a] after a 16-hr. irradiation.

Irradiation of 5α-androst-16-ene-3β,17-diol diacetate (**13**) yielded the 16-acetyl derivative **14** which exhibited an ultraviolet absorption maximum at 282.5 mμ (ε 5000) in cyclohexane. The n.m.r. spectrum of **14**



indicated that it exists as a mixture of enol and ketone tautomers, in about equal amounts as estimated from the n.m.r. spectra. This acetyl compound **14** was characterized as the copper chelate, m.p. 300–302°, λ_{max}^{EtOH} 260 and 308 mμ (ε 12,300 and 20,400).[13] On acid decomposition, the chelate gave the same equilibrium mixture of the enol and ketone forms of **14**. The limiting yield of **14** was 37%[6a] after a 24-hr. irradiation. The comparatively higher yield in the irradiation of **13** could be explained by the lower concentration of the enolic form of the product **14**, since this form alone acts as a filter.

Different results were obtained when 2-methyl-5α-androst-2-ene-3,17β-diol diacetate (**15**) was irradiated. The reaction was interrupted when the percentage of **15** had dropped to *ca.* 40%,[10] as estimated from the infrared bands of the enol acetate chromophore at 5.75, 8.18, and 8.28 μ. The total material after irradiation showed an absorption maximum at 230 mμ (ε 3000). The chromatographic separation of the total mixture yielded four ketonic transformation

(8) The n.m.r. spectrum of this compound in cyclohexane indicates its being completely enolic.

(9) H. Meerwein and D. Vossen, *J. prakt. chem.*, **141**, 149 (1934); M. E. McEntee and A. P. Pinder, *J. Chem. Soc.*, 4419 (1957).

(10) Prolonged irradiation results in complete disappearance of starting material. No meaningful conclusion could be obtained in these prolonged experiments, probably owing to decomposition of the products by the excessive light action.

(11) G. B. Payne, *J. Org. Chem.*, **26**, 4793 (1961).

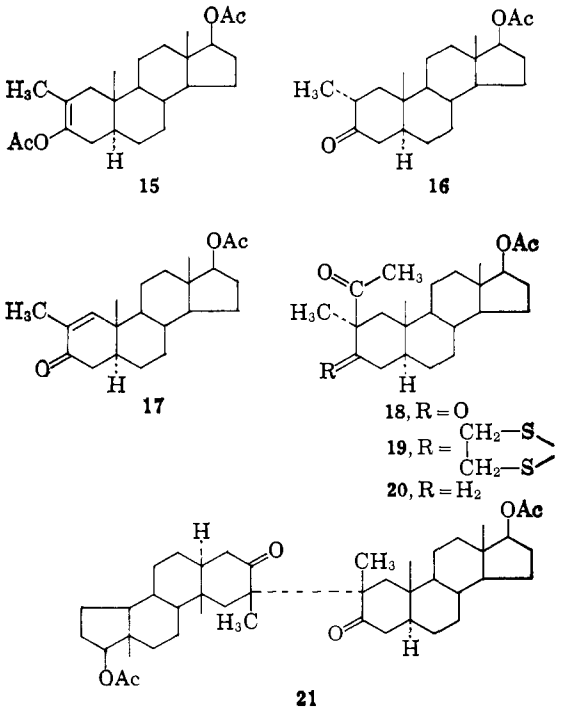
(12) The n.m.r. spectra were taken in deuteriochloroform (unless otherwise stated) on a A-60 Varian spectrometer (60 Mc./sec.), tetramethylsilane serving as the internal reference. Peak positions are reported in c.p.s. downfield from tetramethylsilane.

(13) Also prepared by acylation of the respective ketone with acetic anhydride and boron trifluoride etherate (to be published later).

(14) (a) C. A. Manson, *et al.*, *J. Med. Chem.*, **6**, 1 (1963); (b) R. Youssefyeh, *J. Am. Chem. Soc.*, **85**, 3901 (1963); (c) R. Leedon and G. I. Fujimoto, Abstracts, 139th National Meeting of the American Chemical Society, March, 1961, p. 22N.

products. The first (1% yield) was identified as 2α-methyl-5α-androstan-3-on-17β-ol acetate (**16**). The second [m.p. 144–147°, $\lambda_{max}^{C_6H_{12}}$ 230 mμ (ε 1800)], obtained in 5% yield, was proved to be a crystalline mixture of the methyl ketone **16** and 2-methyl-5α-androst-1-en-3-on-17β-ol acetate (**17**) by the n.m.r. spectrum. This mixture could not be separated by repeated chromatography or by recrystallizations. Separation could be achieved only after lithium aluminum hydride reduction and subsequent oxidation with 2,3-dichloro-5,6-dicyano-1,4-quinone, whereby 2-methyl-5α-androst-1-en-3-on-17β-ol and 2α-methyl-5α-androstan-3β,17β-diol were isolated and identified.

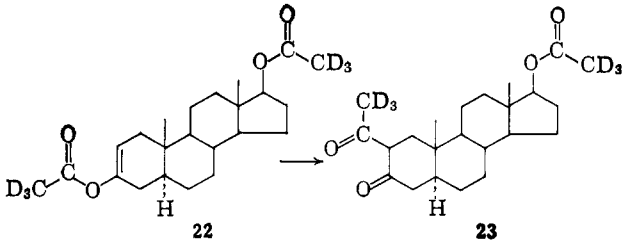
The third ketonic material, obtained in 2% yield, was found to be 2β-acetyl-2α-methyl-5α-androstan-3-on-17β-ol acetate (**18**),[14c] m.p. 189–190°. It was identical with a product synthesized by methylation of 2-acetyl-5α-androstan-3-on-17β-ol acetate (**10**) with methyl iodide and potassium *t*-butoxide. In order to establish the configuration at C-2 of **18**, the ketone at C-3 was removed through conversion to the thioketal **19** and desulfurization with Raney nickel to yield 2β-acetyl-2α-methyl-5α-androstan-17β-ol acetate (**20**). The n.m.r. spectrum of **20** showed a signal at 38 c.p.s. assigned to the C_{19}-methyl, which is shifted to higher field by 9 c.p.s. as compared to the C_{19} signal at 47 c.p.s. of 5α-androstan-17β-ol acetate. This diamagnetic displacement is most probably the result of the shielding of the C_{19}-methyl by the carbonyl of the 2-acetyl group. In order for such a shielding effect to take place, this carbonyl must assume the conformation indicated in Fig. 1 (or alternatively the one obtained by rotation of the C=O by 180°). When the acetyl group is in the 2α-position, no conformation which will result in the shielding of C_{19}-methyl can be conceived. Hence the acetyl group in the ketone **20** possesses the β-configuration, and therefore also in the diketone **18**.



The last compound (5% yield) isolated from the irradiation of **15** was the diketone **21**, m.p. 260–261°. The infrared spectrum showed bands at 5.78 (acetate) and 5.91 μ (carbonyl), and the mass spectrum revealed a molecular peak at 690 *m/e* in accordance with the proposed formula.[15] The most sterically feasible conformation of the diketones **21** is one having rings A in a chair or slightly distorted chair conformation in which the bond between the two C-2 carbons is α and equatorial in respect to both A-rings. The proposed structure and conformation of the diketone **21** is compatible with the n.m.r. spectrum, which reveals sharp signals at 47, 65, and 71 c.p.s. with equal intensity area, assigned, respectively, to the C_{18}-, C_{19}-, and C_2-methyl hydrogens. The position of the chemical shift at 65 c.p.s. is the expected one for C_{19}-methyl in 2β-methyl-3-keto-5α-steroids in which the ring A is in a chair conformation.[16]

When the dimeric ketone **21** was heated for a short time at 250° under vacuum, the resulting oil was found by n.m.r. and ultraviolet spectroscopy to consist of about equal parts of the saturated and unsaturated 2-methyl ketones **16** and **17**. It is of interest to note that in the mass spectrum of the diketone **21**, four peaks of equal intensity at 344, 345, 346, and 347 *m/e* were observed (among others), which are probably attributed to the cleavage of this dimeric molecule into saturated and unsaturated moieties.

In order to establish the mechanism of this photochemical acetyl migration, experiments were devised to decide between an intermolecular or intramolecular process. Mixtures containing two different enol acetates were photolyzed, namely cholest-2-en-3-ol acetate (**11**) and 5α-androst-2-ene-3,17β-diol d_6-diacetate (**22**).



In the first experiment a mixture containing an excess of the nondeuterated enol acetate **11** and the deuterated enol acetate **22** (3:1) were irradiated. The resulting mixture was separated, and the 2-acetyl ketone derived from **22** was found to be the 2-(d_3-acetyl)-5α-androstan-3-on-17β-ol d_3-acetate (**23**) of at least 97% isotopic purity as determined by the n.m.r. spectrum. In this spectrum the signal attributed to the three protons of the 2-acetyl group at 129 c.p.s. was completely absent.

In the second experiment the same two compounds were photolyzed, but an excess of the deuterated enol acetate **22** was used (3 parts **22** to 1 part **11**). The isolated 2-acetyl ketone derived from the nondeuterated enol acetate **11** was 2-acetylcholestan-3-one (**12**) in which no deuteration could be detected; in the n.m.r. spectrum the signal at 129 c.p.s. assigned to the 2-acetyl hydrogens was found by integration to correspond exactly to three protons. Both enol acetates **11** and **22** reisolated after the irradiations were

(15) We are indebted to Prof. C. Djerassi for his kind help in determination of the mass spectrum of this compound.

(16) The chemical shift of the C_{19}-methyl group in 5α-androstan-3-on-17β-ol acetate, 2α-methyl, and 2,2-dimethyl analogs are observed at 62, 63, and 65 c.p.s., respectively.

also found to be completely unchanged, as determined by the n.m.r. spectra.

This intramolecular acyl migration may involve a primary cleavage of the O–acetyl bond and the formation of acetyl radicals. Alternatively a 4-centered transition-state reaction involving a concerted bond fission and bond formation could be envisaged. The latter was postulated for the intramolecular thermic decomposition of vinylic esters.[1] On the other hand, the related photochemical Fries rearrangement involves acetyl migration both to the *ortho* and the *para* positions, excluding the 4-centered mechanism.[3] Furthermore, the fact that the acetyl migration occurs in enol acetates, where the double bond is fully substituted as in **5** and in **15**, points to the formation of acetyl radicals. The vinylic methyl group hinders the ester group from assuming the orientation required for a 4-center reaction.

The formation of the acetyl radicals involves first an excited state; subsequently, after electron demotion, this cleaves to give two excited radicals, which are probably enclosed in a solvent cage. The last step involves recombination of these two radicals.

The preferential attack of the migrating acetyl from the more hindered β-axial side to give the thermodynamically less stable 2β-acetyl-2α-methyl-5α-androstan-3-on-17β-ol acetate (**18**) may be explained by stereoelectronic factors. The transition state in the photochemical reaction would be somehow analogous to that postulated in ketonizations of enols and related reactions.[17] The orbital occupied by the single electron at the α-carbon atom would be stabilized by interaction with the exocyclic π-electron orbital only if the former is axially oriented. When the acetyl radical is removed and the recombination in the cage cannot take place, the lone steroid radical can lead to other products. One of them is the dimer **21** in which both methyl groups are axially oriented. This results from the only sterically possible dimerization.

The accompanying saturated and unsaturated 2-methyl ketones **16** and **17** formed in the irradiation of enol acetate **15** could result by an addition or an abstraction of hydrogen from the steroid radical. The other possibility for the formation of the two ketones **16** and **17** is the decomposition of the dimeric diketone **21**, which is probably produced in a vibrationally excited ground state. The latter would then be similar to the thermal decomposition of this dimeric diketone.

Experimental

All melting points were taken in capillaries and were uncorrected. Ultraviolet spectra were determined on a Cary 14 spectrophotometer and the infrared spectra on a Perkin–Elmer Infracord. The rotations were done in chloroform. All the irradiations were performed with an immersion Hanau low pressure NT 6/20 ultraviolet mercury lamp in an externally cooled tube of 40-mm. diameter and *ca.* 150-cc. volume.

Irradiation of Isopropenyl Acetate (1).—(a) A solution of 1 g. of isopropenyl acetate in 100 cc. of cyclohexane was irradiated for 45 hr. Aliquots were taken out during the irradiation and their absorbance established. The molar extinction coefficient of the irradiated solution and the percentage of the conversion are plotted as the function of the irradiation time (Fig. 4).

The solvent was evaporated and the residue was dissolved in 5 cc. of methanol and treated with 5 cc. of saturated aqueous cupric acetate solution on water bath. After being left at the same temperature for 5 min., the mixture was extracted with ether and the isolated compound was crystallized from benzene to give 0.2 g. of copper chelate of acetylacetone, m.p. 330° dec., λ_{max}^{EtOH} 254 and 304 mμ (ϵ 18,000 and 26,000), identical with an authentic sample.[18] Decomposition of ether solution of the copper chelate with 5% hydrochloric acid solution gave acetylacetone (**2**) identical with an authentic sample.

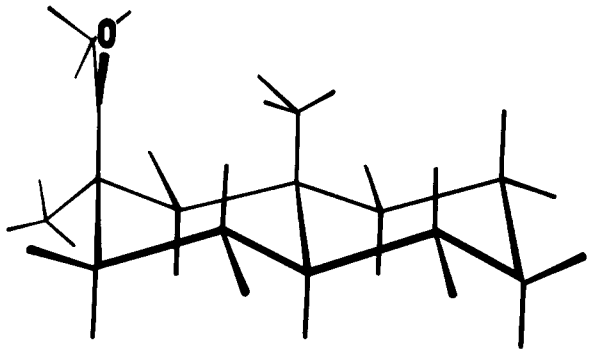


Fig. 1.—Conformation of 2β-acetyl-2α-methyl-5α-androstan-17β-ol acetate (**18**).

(b) A solution of 10 g. of isopropenyl acetate in 100 cc. of cyclohexane was irradiated in a similar manner. The aliquots were taken out during the irradiation and their absorbance established (Fig. 4). The n.m.r. spectrum of the cyclohexane solution after a 45-hr. irradiation shows peaks attributed to both isopropenyl acetate and acetylacetone. The intensity of the signal at 308 c.p.s. (assigned to the vinylic hydrogen of the enolic form of acetylacetone) and of the signal at 258 c.p.s. (attributed to the two hydrogens of the terminal methylene group) was compared to the respective signals of a calibrated solution of acetylacetone and isopropenyl acetate. It was found that the irradiated solution contains *ca.* 8–10% of acetylacetone and 55–60% of isopropenyl acetate.

Irradiation of Cyclohexen-1-yl Acetate (**3**).—(a) A solution of 1.5 g. of **3** in 80 cc. of cyclohexane was irradiated for 4 hr. Evaporation of the solvent gave an oil [$\lambda_{max}^{C_6H_{12}}$ 286 mμ (ϵ 1150)] which was chromatographed on silica gel (45 g.). The fractions (0.15 g.) eluted with a mixture of pentane–ether (97:3) which gave a positive ferric chloride test were combined and purified by distillation. Most of the material distilled at 92° (10 mm.) [$\lambda_{max}^{C_6H_{12}}$ 286 mμ (ϵ 7600)], and was identical with an authentic sample.[9]

(b) Irradiation of 1.5 g. of **3** under similar conditions and subsequent evaporation of the solvent gave a residue which was dissolved in 50 cc. of methanol, heated on a steam bath, and treated with 5 cc. of a hot saturated solution of cupric acetate. The mixture was heated on a steam bath for another 10 min. It was then extracted with ether, washed with saturated sodium chloride solution, and the ether residue was crystallized from ether–hexane to give 0.05 g. of green crystals, m.p. 160–162°, of the copper chelate of **4**. It was identical with the copper chelate of 2-acetylcyclohexanone (**4**).[9] The n.m.r. of **4** revealed a singlet at 130 c.p.s. (relative intensity 3 protons, assigned to the protons of the acetyl group) and two multiplets (4 protons each) centered at 135 (protons at C-3 and C-5) and 105 c.p.s. (protons at C-4 and C-6).

Irradiation of 2-Methylcyclohexen-1-yl Acetate (**5**).—A solution of 3 g. of **5** in 120 cc. of cyclohexane was irradiated for 15 hr. The total material obtained after evaporation of solvent was chromatographed on silica gel (100 g.). The material (0.9 g.) eluted with pentane–ether (80:20) was identical with the starting material. The second fraction (0.11 g.) eluted with pentane–ether (75:25) was identical with the 2-methylcyclohexanone (**6**). The third fraction (0.5 g.) eluted with the same solvent had n_D 1.4657, b.p. 61.5° (0.5 mm.). It was identical with a sample of 2-acetyl-2-methylcyclohexanone (**7**) prepared by methylation of 2-acetylcyclohexanone (**4**).[11] In the n.m.r. spectrum it showed signals at 76 (methyl protons) and 128 c.p.s. (acetyl protons).

The fourth fraction (0.2 g.) eluted with pentane–ether (70:30) was purified by repeated chromatography on 50 g. of silica gel. The fractions eluted with pentane–ether (50:50) which gave one spot of the same R_f value on thin-layer Kieselgel plate were

(17) E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.*, **78**, 6269 (1956); H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956).

(18) R. L. Belford, A. E. Martell, and M. Calvin, *J. Inorg. Nucl. Chem.*, **2**, 11 (1956).

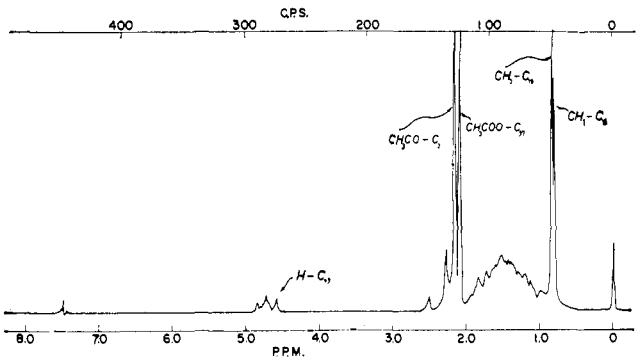


Fig. 2.—Nuclear magnetic resonance spectrum of 2-acetyl-5α-androstan-3-on-17β-ol acetate (**10**) in $CDCl_3$.

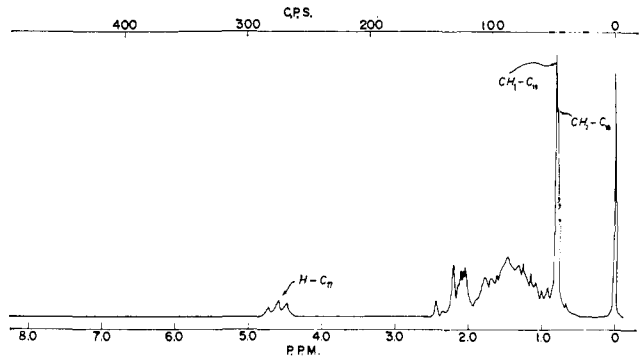


Fig. 3.—Nuclear magnetic resonance spectrum of 2-(d_3-acetyl)-5α-androstan-3-on-17β-ol d_3-acetate (**23**) in $CDCl_3$.

combined. This material showed one carbonyl peak in the infrared at 5.85 μ and in the ultraviolet it had λ_{max}^{EtOH} 290 mμ (ε 40). The structure **8** was assigned to this compound.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.82; H, 10.02.

Irradiation of 5α-Androst-2-ene-3,17β-diol Diacetate (9).—A solution of 0.9 g. of **9** in 100 cc. of cyclohexane was irradiated for 16 hr. The solvent was evaporated *in vacuo* and the residue [$\lambda_{max}^{C_6H_{12}}$ 283 mμ (ε 1350)] was chromatographed on 30 g. of silica gel. Elution with pentane–ether (95:5) gave a crystalline material (0.7 g.), m.p. 173–174°, identical with the starting material. Further elution with the same solvent mixture yielded material which, after crystallization from ether–pentane, gave 0.1 g. of 2-acetyl-5α-androstan-3-on-17β-ol acetate (**10**), m.p. 178–179°, $[\alpha]_D$ +41°, λ_{max}^{EtOH} 289 mμ (ε 9000); λ^{KBr} 5.75, 6.12, and 8.04 μ. The n.m.r. spectrum of **10** showed sharp signals with equal intensity at 48.5, 49.5, 123.5, and 129.0 c.p.s. assigned, respectively, to the protons of C_{18}-, C_{19}-methyl groups, and the protons of the 17-acetoxy and of the 2-acetyl groups. In addition a sharp one-hydrogen signal was observed at 575 c.p.s.—assigned to the enolic hydrogen.

Irradiation of Cholest-2-ene-3,17β-diol Diacetate (11).—A solution of 1 g. of enol acetate **11** in 120 cc. of cyclohexane was irradiated for 14 hr. The solvent was then evaporated to dryness, the residue [$\lambda_{max}^{C_6H_{12}}$ 283 (ε 1400)] dissolved in pentane and chromatographed on silica gel. The first fraction eluted with pentane gave 0.68 g. of the starting material. Further elution with pentane gave crystalline material which after recrystallization from pentane yielded 0.095 g. of 2-acetylcholestan-3-one (**12**),[13,14] m.p. 101–102°, λ_{max}^{EtOH} 289 mμ (ε 9500).

Irradiation of 5α-Androst-16-ene-3β,17-diol Diacetate (13).—A solution of 1 g. of **13** in 120 cc. of cyclohexane was irradiated for 21 hr. It was evaporated to dryness and the residue chromatographed on 30 g. of silica gel. The fractions (0.3 g.) eluted with pentane–ether (80:20) which gave a strong coloration with ferric chloride solution were combined. The n.m.r. of this fraction was composed of signals corresponding to the separate tautomers of **14.** The signals assigned solely to the enol tautomer were observed at 119 (C-16 acetyl) and 48 c.p.s. (C-18 methyl) and those attributed to the ketone at 143 (C-16 acetyl) and 56 c.p.s. (C-18 methyl). In addition, single peaks of both forms were found at 123 c.p.s. (C-3 acetoxy) and 52.5 c.p.s. (C-19 methyl). This mixture of tautomers **14** was dissolved in 5 cc. of methanol, treated with 5 cc. of a saturated solution of cupric acetate, heated on a water bath for 10 min., and then extracted with ether and washed with water. The ether residue was crystallized from benzene–ether to give 0.08 g. of deep green crystals of the copper chelate of **14**, m.p. 300–302°, λ_{max}^{EtOH} 260 and 308 mμ (ε 12,300 and 20,400); λ^{KBr} 5.76, 6.27, 6.71, and 8.04 μ.

Anal. Calcd. for $C_{46}H_{66}O_8Cu$: C, 68.14; H, 8.14. Found: C, 68.27; H, 8.15.

The copper chelate of **14** (0.05 g.) dissolved in 20 cc. of ether was shaken with cold hydrochloric acid solution (10%) until the ether solution became colorless. Evaporation of ether gave an oily compound [$\lambda_{max}^{C_6H_{12}}$ 282.5 mμ (ε 5000)] which had an n.m.r. spectrum identical with that of the mixture of tautomers **14** from above.

Irradiation of 2-Methyl-5α-androst-2-ene-3,17β-diol Diacetate (15).—A solution of 2.85 g. of enol acetate **15** was dissolved in 100 cc. of cyclohexane and was irradiated for 20 hr. The solvent was evaporated and the residue chromatographed on 100 g. of acid-washed alumina. Elution with benzene–pentane (70:30) yielded 1 g. of the starting material **15**. The second fraction (0.03 g.) eluted with benzene–pentane (50:50) was crystallized from ether–methanol to give 2α-methyl-5α-androstan-3-on-17β-ol acetate (**16**), m.p. 160–162°, identical with an authentic sample. The third fraction (0.13 g.) eluted with the same solvent mixture was crystallized from ether–methanol and had m.p. 144–147°. This material was dissolved in 5 cc. of dry tetrahydrofuran and added dropwise to a mixture of 0.1 g. of lithium aluminum hydride and 5 cc. of tetrahydrofuran. After reflux for 24 hr. the excess of lithium aluminum hydride was decomposed with saturated sodium sulfate solution and the material was extracted with ethyl acetate. The residue dissolved in 100 cc. of dioxane was treated with 0.035 g. of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and left for 4 days at room temperature. Methylene chloride (100 cc.) was then added and the solution was filtered through a column of alumina (4 g.). The total material was then chromatographed on alumina. The fraction eluted with benzene–ether (70:30) gave 0.008 g. of crystals, m.p. 152–154°, $[\alpha]_D$ +51.5°, λ_{max}^{EtOH} 241 mμ (ε 10,600), identical with an authentic sample of 2-methyl-5α-androst-1-en-3-on-17β-ol.[19] The material eluted with ether (0.005 g.) had m.p. 163–164° and was identified as 2α-methyl-5α-androstane-3β,17β-diol.[20] The fourth fraction (0.057 g.) from the irradiated material eluted with pentane–benzene (20:80) was recrsytallized from ether–hexane to give crystals (0.03 g.), m.p. 189–190°, $[\alpha]_D$ +77°.

Anal. Calcd. for $C_{24}H_{36}O_4$: C, 74.19; H, 9.34. Found: C, 74.01; H, 9.39.

This material was identical with 2β-acetyl-2α-methyl-5α-androstan-3-on-17β-ol acetate (**18**) obtained by methylation of 2-acetyl-5α-androstan-3-on-17β-ol acetate (**9**). In the n.m.r. this compound showed signals at 48 (C-18 methyl), 53 (C-19 methyl), 72 (C-2 methyl), 122 (C-17 acetoxy), and 130 c.p.s. (C-2 acetyl), all sharp with the same integration area.

The last fraction (0.35 g.) eluted with benzene–ether (90.10) was recrystallized from ether–hexane to give 0.14 g. of needles, m.p. 260–261°, $[\alpha]_D$ +109°. The structure **21** was assigned to this compound.

Anal. Calcd. for $C_{44}H_{66}O_6$: C, 76.48, H, 9.63. Found: C, 76.38; H, 9.52.

2β-Acetyl-2α-methyl-5α-androstan-3-on-17β-ol Acetate (18).—Potassium (1.2 g.) was dissolved in 100 cc. of *tert*-butyl alcohol; then 3.74 g. of 2-acetyl-5α-androstan-3-on-17β-ol acetate (**10**) was added and the yellow solution was treated with 10 cc. of methyl iodide and left overnight at room temperature under nitrogen. The solvent was evaporated and the residue acetylated with acetic anhydride (4 cc.) and pyridine (4 cc.) overnight at room temperature. Crystallization from ether yielded 1.86 g. of the product **18**, m.p. 189–190°, $[\alpha]_D$ +77°, identical with the compound obtained by irradiation of the enol acetate **15**.

2β-Acetyl-2α-methyl-5α-androstan-17β-ol Acetate (20).—The diketone **18** (1.86 g.) was treated with 10 cc. of ethanedithiol and 4 cc. of boron trifluoride etherate for 4 hr. at room temperature. It was extracted with ether and washed with a cold sodium hydroxide solution (10%). The crystals obtained were recrystallized from ether to give the thioketal **19** (1.2 g.), m.p. 239–240°, $[\alpha]_D$ +82°, λ^{KBr} 5.75 and 5.89 μ. In the n.m.r., peaks were observed at 43 (C-19 methyl), 48 (C-18 methyl), 85 (C-2 methyl),

(19) R. Mauli, H. J. Ringold, and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 5494 (1960); *cf.* J. A. Edwards, M. C. Calzada, and A. Bowers, *J. Med. Chem.*, **6**, 178 (1963).

(20) L. Ruzicka, M. W. Goldberg, and H. R. Rosenberg, *Helv. Chim. Acta*, **18**, 1487 (1935).

122 (C-17 acetoxy), and 132 c.p.s. (C-2 acetyl), all with integration area of three protons. In addition, a multiplet at 190 c.p.s. was observed and assigned to the hydrogens of the thioketal group.

Anal. Calcd. for $C_{26}H_{40}O_3S_2$: C, 67.21; H, 8.68. Found: C, 67.34; H, 8.72.

A solution of 1.2 g. of the thioketal **19** in 100 cc. of ethanol was treated with Raney nickel (5 spoonfuls of ethanolic suspension) and refluxed overnight. Filtration and evaporation of the solvent gave a crystalline residue which after recrystallization from ether–hexane gave 0.55 g. of **20**, m.p. 155–156°, $[\alpha]_D$ −0.6°, λ^{KBr} 5.75 μ. In the n.m.r. spectrum signals were observed at 38 (C-19 methyl), 47 (C-18 methyl), 52 (C-2 methyl), 122 (C-17 acetoxy), and 128 c.p.s. (C-2 acetyl).

Anal. Calcd. for $C_{24}H_{38}O_3$: C, 76.96; H, 10.28. Found: C, 76.82; H, 10.19.

Pyrolysis of the Dimeric Ketone 21.—The diketone **21** (0.05 g.) was heated in an evacuated tube (25 mm.) at 250° for 5 min. Then the tube was evacuated further under high vacuum (0.1 mm.) and the products were sublimed at the same temperature. The sublimed material had m.p. 130–150°, λ_{max}^{EtOH} 241 mμ (ϵ 5100), and in the n.m.r. peaks were observed attributed to both products **16** and **17**. The signals of 2-methyl ketone **16** were found at 48.5 (C-18 methyl), 61 (doublet, J = 8 c.p.s., C-2 methyl), 65 (C-19 methyl), and 124 c.p.s. (C-17 acetate). Those assigned to the Δ^1-3-ketone **17** are at 50 (C-18 methyl), 60 (C-19 methyl), 107 [C-2 methyl, doublet (J = 1.5 c.p.s.)], and 124 c.p.s. (C-17 acetate). The integration of the main peaks gave the ratio of the two isomers as 1:1.

5α-Androst-2-ene-3,17β-diol d_6-Diacetate (22).—5α-Androstan-3-on-17β-ol (3 g.) was treated with d_6-acetic anhydride (4 cc.) and a few crystals of p-toluenesulfonic acid. The mixture was heated for 3 hr. at 110° and then for 2 hr. at 140°. The resulting solution was cooled and the produced crystals filtered and washed with pentane and recrystallized twice from ether–pentane. The d_6-diacetate **22** obtained (2 g.) had m.p. 175–176°. Its n.m.r. was similar to that of diacetate **11** in which the two peaks at 123 and 132 c.p.s. (attributed to the acetoxy and acetyl hydrogens at C-17 and C-3) were absent.

Photolysis of Enol Acetates Mixtures.—(a) A solution of 1.5 g. of cholest-2-en-3-ol acetate (**11**) and 0.5 g. of 5α-androst-2-ene-3,17β-diol d_6-diacetate (**22**) in 170 cc. of cyclohexane was irradiated until its ultraviolet absorption at 283 mμ reached a constant value (ϵ 1300 in 20 hr.). The solvent was evaporated and the residue chromatographed on silica gel (60 g.),

The first fraction eluted with pentane gave, after two recrystallizations from ether–methanol, cholest-2-en-3-ol acetate (**11**, 0.15 g., m.p. 93–94°). In its n.m.r. spectrum the signal at 123 c.p.s. attributed to the acetoxy group had the same integration area as the starting material **11**, indicating that no observable deuteration occurred.

The next fraction eluted with the same solvent (0.75 g.) consisted of a mixture of the diacetate **11** and 2-acetylcholestan-3-one (**12**, ultraviolet and infrared spectrum).

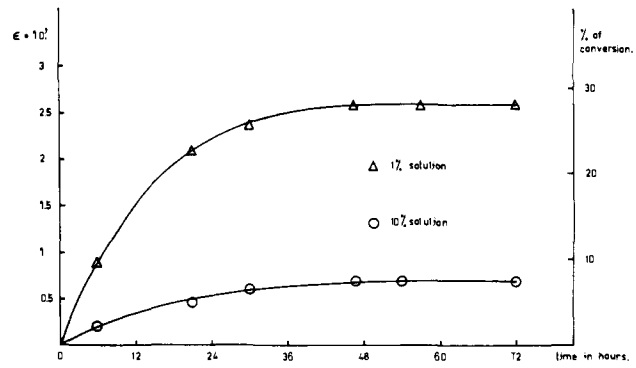


Fig. 4. —The rate of formation of acetylacetone (**2**) from isopropenyl acetate (**1**).

The third fraction eluted with the same solvent gave, after recrystallization from methanol, 2-acetylcholestan-3-one (**12**), 0.075 g., m.p. 98–100°.

The fourth fraction eluted with pentane–ether (98:2), recrystallized from ether–pentane, yielded 0.36 g. of crystals, m.p. 175–176°, of 5α-androst-2-ene-3,17β-diol d_6-diacetate (**22**). Its n.m.r. spectrum was identical with that of the starting material **22** (no signals at 123 and 132 c.p.s. attributed to the nondeuterated acetoxy groups could be observed; Fig. 2 and 3).

The fifth fraction eluted with the same solvent mixture gave, after crystallization from ether–pentane, 0.2 g. of crystals which were rechromatographed on 10 g. of silica gel The fraction eluted with pentane–ether (98:2) was recrystallized twice from ether–pentane to give 0.075 g. of 2-d_3-acetyl-5α-androstan-3-on-17β-ol d_3-acetate (**23**), m.p. 177–178°, which did not give a melting point depression when admixed with the diketone **10**.

(b) A solution of 0.35 g. of cholest-2-en-3-ol acetate (**11**) and 1.04 g. of 5α-androst-2-ene-3,17β-diol d_6-diacetate (**22**) in 170 cc. of cyclohexane was irradiated for 18 hr. (the irradiation was stopped when the maximum absorption of the solution in the ultraviolet reached a constant value). Chromatography on silica gel resulted in the same four compounds isolated in the experiment a. The second compound (40 mg.) eluted from the column with pentane (positive ferric chloride test) was rechromatographed on 30 g. of silica. Elution with pentane and two recrystallizations from ether–methanol gave 0.025 g. of 2-acetylcholestan-3-one (**12**), m.p. 98–100°. Its n.m.r. spectrum was identical in all the details with that of the authentic diketone **12**.

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Photochemistry of Enolic Systems. II. Irradiation of Dienol Acetates[1]

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Irradiation of dienol acetates derived from testosterone and 4-methyltestosterone with a low pressure mercury lamp is described. The irradiation involves acetyl rearrangement from oxygen at C-3 to the carbon at C-4 and C-6. Thus androsta-3,5-diene-3,17β-diol diacetate (**1**) resulted in **2** and **8**; 4α-methylandrosta-3,5-diene-3,17β-diol diacetate (**13**) yielded the corresponding 4-methyl homologs **14** and **15**. The chemistry and stereochemistry of the isolated products support the previously postulated cage mechanism and stereoelectronic control for this photochemical reaction.[1b] The stability relations of the 6-acetyltestosterone epimers are discussed and compared with those of the corresponding epimeric saturated derivatives. The unusual stability of the 6β-acetyltestosterone is explained by electronic factors.

In the previous publication we described the irradiation of some enol acetates.[1b] We would now like to discuss the action of ultraviolet light on conjugated enol acetates. The systems chosen were the dienol acetates derived from Δ^4-3-keto steroids. These enol acetates have an extended conjugation and therefore show a strong ultraviolet absorption in the 200–260 mμ region. The light source used was again the low

(1) (a) Presented in part: 1, at 2nd International Symposium on the Chemistry of Natural Products, Prague, 1962; Abstracts of Communications, p. 115; 2, at 19th International Congress of Pure and Applied Chemistry, London, 1962; Abstracts A, p. 341; (b) Part I, A. Yogev, M. Gorodetsky, and Y. Mazur, *J. Am. Chem. Soc.*, **86**, 5208 (1964).