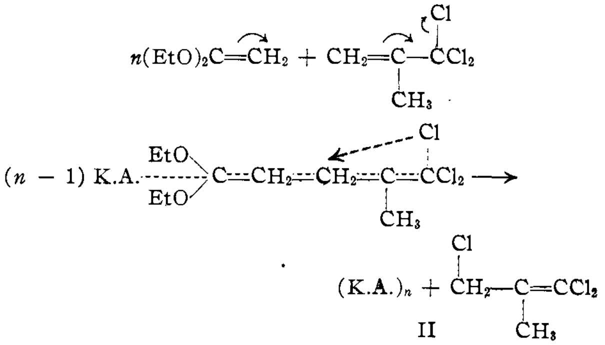
It seems that the most significant finding here is the facile conversion of TMP *via* an allylic rearrangement over to the allyl TMP by means of a strong electron donor agent such as ketene acetal. Previously, conversion of TMP to this allylic isomer was brought about by heating 10 g. of TMP with 0.1 g. of hydrogen chloride at 200° overnight.[6]

The mechanism for ketene acetal causing facile conversion of TMP to the allylic isomer appears interesting. The following seems reasonable, and is postulated (K. A. stands for ketene acetal).



II

Experimental

Starting Materials.—1,1,1-Trichloro-2-methylpropene-2 (TMP) was prepared along the lines of the method of McElvain and Stevens[6] except that a longer reaction period of 20–30 hr. was used. TMP having b.p. 132–135° was used. *Ketene acetal* was prepared by the method of McElvain and Kundiger.[7] *Ethyl orthoacetate* was prepared for a control experiment by treating 5.8 g. (0.05 mole) of ketene acetal with 100% absolute alcohol (2.8 g., slightly more than 0.05 mole). These materials were heated under anhydrous conditions at 95–100° for 15 minutes; then distillation gave 6.5 g. of ethyl orthoacetate, observed b.p. 146–150°.

Reaction of 1,1,1-Trichloro-2-methylpropene-2 (TMP) with Ketene Diethylacetal. Formation of 1,1,3-Trichloro-2-methylpropene-1 (allyl TMP).—To a 100-ml. round-bottom flask fitted with a reflux condenser connected to a Dry Ice cooled trap, a mercury sealed mechanical stirrer and a dropping funnel, there was added TMP (35.5 g., 0.221 mole). Ketene acetal (25.8 g. (0.221 mole)) was added dropwise to the TMP (constant stirring), beginning at room temperature. There was spontaneous rise of temperature in the reaction mixture to only 40°. Then, the reaction mixture was stirred and held at 100° by a bath for 48 hours. Indication of deep red dealcoholated polymers of ketene acetal was obtained because the mixture became a clear deep red solution. Ethyl chloride, b.p. 12° (3.5 g.) collected in the Dry Ice trap. Distillation of the reaction mixture through a column fractionating setup gave the following significant fractions: (a) 3.1 g., b.p. 47–49° at a pressure of 145 mm. (This material redistilled at 71–78°, had a strong odor of ethyl acetate and contained admixed ethanol since it gave the proper ceric nitrate test and also gave the 3,5-dinitrobenzoate derivative of ethanol, m.p. 95–96°, no depression of m.p. on admixture with an authentic sample); (b) 3.2 g., b.p. 100–102° (145 mm.); (c) 26.8 g., b.p. 96–100° (125 mm.); (d) 5.6 g., b.p. 50–53° (2 mm.); (e) 3.5 g., b.p. 70–129° (2 mm.) and (f) 7.5 g., b.p. rising constantly above 129° (2 mm.).

The above fractions (b), (c) and (d) were found to be a mixture of allyl-TMP, b.p. 154° (Cl content 66.4%) and ethyl orthoacetate, b.p. 146°. These combined fractions (b), (c) and (d)—termed "product A"—redistilled at atmospheric pressure at b.p. 142–154° and 88% of it at b.p. 149–154°. Carius analyses of "product A" gave total Cl content: 52.5, 52.2, 52.7%. Based on these Carius analyses and the wt. of "product A" (35.4 g.), this mixture was 86.8% allyl TMP and 13.2% ethyl orthoacetate. Standard Zeisel semi-micro ethoxyl determinations were also carried out on "product A." Various samples of this product had 12.2 to 13.5% ethoxyl, also indicating the ethyl orthoacetate content.

Acid hydrolysis of "product A" to remove the ethyl orthoacetate and prove its presence was carried out thus: To a 100-ml. round-bottom 3-necked flask fitted with a reflux condenser, a mercury sealed stirrer, and a dropping funnel, there were added 20.5 g. of "product A"; and then with very rapid stirring throughout, 60 ml. of 5% hydrochloric acid was added from the dropping funnel, and the resulting mixture boiled vigorously for ten minutes. The mixture was cooled to 25°, the water-insoluble layer separated and, on distilling it, the lower fractions had no definite b.p. but had a strong odor of ethyl acetate; the major fraction came over at b.p. 153–155°, corresponding with the b.p. of the allyl TMP, *i.e.*, II. Carius analyses on this fraction gave 65.8% Cl as compared to 66.1% Cl obtained on known allyl TMP (calcd. Cl, 66.4).

Heating of 50 g. of TMP at 100° for 48 hr. resulted in practically no rearrangement to allyl TMP. The original TMP was recovered practically quantitatively.

Two other runs of TMP mixed with ketene acetal were made for 72 hr. and the methods and results checked those described above.

Acknowledgment.—We wish to thank Mr. H. Pledger, Jr., who aided materially in developing successful syntheses of TMP.

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[6] S. M. McElvain and C. L. Stevens, THIS JOURNAL, **69**, 2669 (1947).

[7] S. M. McElvain and D. G. Kundiger, *Org. Syn.*, **23**, 45 (1943).

The Dehydration of a Steroidal Δ^8-11α-Hydroxy-7-ketone

BY A. J. LEMIN,[1] G. ROSENKRANZ[2] AND CARL DJERASSI

RECEIVED NOVEMBER 13, 1952

In a recent synthesis of cortisone,[3] there was investigated the isomerization of the unsaturated ketol I to the corresponding saturated 7,11-dione and it was found that this could be accomplished in nearly quantitative yield by treatment with a strong base such as potassium *t*-butoxide. However, all attempts to employ acidic reagents resulted in dehydration to a dienone with ultraviolet absorption maxima at 226 and 298 mμ to which was assigned the structure of a $\Delta^{8,11}$-dien-7-one II. Since this dehydration product proved to be useless as far as the synthesis of 11-keto steroids was concerned, no further work was done with this substance.

Recently, Halsall, Jones and Lemin[4] in their degradation of the triterpene polyporenic acid A were able to demonstrate that the vinylogous β-acetoxy ketone V smoothly underwent deacetoxylation on boiling with acetic acid to afford a dienone VI with an ultraviolet absorption maximum at 318 mμ (log ϵ 3.88) in excellent agreement with the maximum (314 mμ, log ϵ 3.88) found for $\Delta^{2,4}$-cholestadien-6-one.[5] Since the chromophore in the last two mentioned substances is identical with that present in the proposed[3] structure of the dehydration product II, which, however, exhibited a maximum at 298 mμ, it was considered worthwhile to reinvestigate the structure of that substance.

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[1] Syntex Postdoctorate Fellow at Wayne University, 1952–1953.

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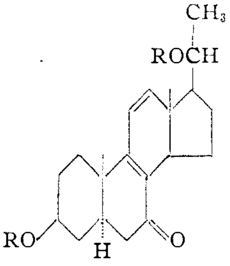
[3] J. Romo, G. Stork, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **74**, 2918 (1952).

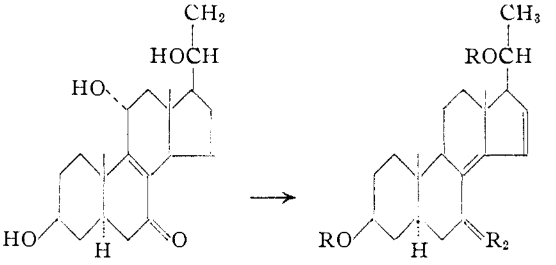
[4] T. G. Halsall, E. R. H. Jones and A. J. Lemin, *J. Chem. Soc.*, in press (1953).

[5] H. Reich, F. E. Walker and R. W. Collins, *J. Org. Chem.*, **16**, 1753 (1951).

If structure II were correct, then reduction of the 7-keto function[6] should afford a homoannular diene with a characteristic ultraviolet absorption maximum above 260 mμ. When the diacetate of the dehydration product of I was reduced with sodium borohydride, there was obtained an oil with an ultraviolet absorption maximum at 246 mμ. The acetylation product IIIc similarly failed to crystallize but the free triol IIId was obtained as a crystalline solid with an ultraviolet absorption maximum at 247 mμ, log ε 3.90. The position of this maximum completely eliminates a homoannular diene structure II from consideration and makes it appear most likely that the acidic dehydration of the Δ^8-11α-ol-7-one leads to a $\Delta^{8(14)15}$-dien-7-one IIIa. The positions of the ultraviolet absorption maxima (298 mμ for IIIa and 247 mμ for IIIb-d) are in excellent agreement with the proposed structures; the relatively low extinction (log ε *ca.* 3.9) is noteworthy. It is generally accepted now[7] that ionic 1,2-elimination in alicyclic systems proceeds most readily when both substituents are polar. Since the 11α-hydroxy group is equatorial and should thus be eliminated toward C-12 only with difficulty, the dehydration probably proceeds as indicated in IV, the initially formed $\Delta^{8(14),9(11)}$-diene rearranging in the acid medium to the thermodynamically more stable linear dienone structure IIIa.



II



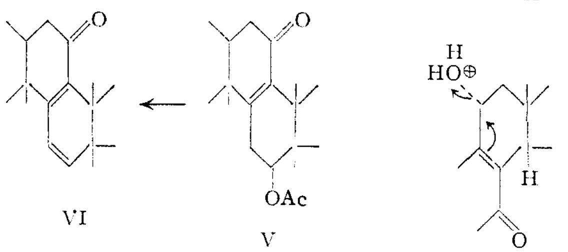
I

IIIa R = Ac; $R_2' = O$

b R = Ac; $R_2' = <^{OH}_{H}$

c R = Ac; $R_2' = <^{OAc}_{H}$

d R = H; $R_2' = <^{HO}_{H}$



VI V IV

Experimental[8]

A mixture of 0.55 g. of Δ^8-allopregnene-3β,11α,20β-triol (I)[9] (m.p. 249–251°) was refluxed for one hour with 40 cc. of methanol and 1 cc. of concd. hydrochloric acid and then diluted with water. Filtration afforded 0.48 g. of colorless crystals with m.p. 220–225°, $\lambda_{\max}^{\mathrm{EtOH}}$ 225 and 298 mμ, log ε 4.20 and 3.77, $\lambda_{\max}^{\mathrm{Nujol}}$ 1665 cm.$^{-1}$ and free hydroxyl band. The physical constants are in good agreement with those reported earlier,[3] but the yield has been markedly improved. Acetylation produced **$\Delta^{8(14)15}$-allopregnadiene-3β,20β-diol-7-one diacetate** (IIIa) with m.p. 158–160°. $\lambda_{\max}^{\mathrm{EtOH}}$ 225 and 298 mμ, log ε 4.27 and 3.80, $\lambda_{\max}^{\mathrm{CHCl_3}}$ 1730 and 1665 cm.$^{-1}$.

The above diacetate IIIa (0.175 g.) in 5 cc. of methanol and 1 cc. of dioxane was allowed to stand at room temperature for one hour with 0.01 g. of sodium borohydride. Dilution with water, extraction with ether, washing, drying and evaporation afforded 0.175 g. of an oil, IIIb, $\lambda_{\max}^{\mathrm{EtOH}}$ 246 mμ, log ε 3.85. Acetylation similarly produced an oil $\lambda_{\max}^{\mathrm{EtOH}}$ 246 mμ, log ε 3.90, but saponification of the triacetate (IIIc) with methanolic potassium hydroxide (2 hours refluxing) followed by recrystallization from acetone led to colorless crystals of **$\Delta^{8(14)15}$-allopregnadiene-3β,7,20β-triol** (**IIId**) with m.p. 198–200°, $\lambda_{\max}^{\mathrm{EtOH}}$ 247 mμ, log ε 3.90.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.90; H, 10.17.

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(6) Such a procedure was employed by L. F. Fieser in the structure proof of a similar dienone in the cholesterol series (Abstracts of Ciba Foundation Conference, London, July 7-10, 1952).

(7) *Cf.* D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951).

(8) Melting points are uncorrected and were taken on the Fisher block. Ultraviolet absorption spectra were determined in absolute ethanol solution; infrared spectra were measured with a Baird double beam infrared spectrometer.

(9) G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, THIS JOURNAL, **73**, 3546 (1951).

Fractionation of an Enzyme by Foaming[1]

BY MORRIS LONDON, MARTIN COHEN AND PERRY B. HUDSON[2]

RECEIVED NOVEMBER 8, 1952

In this Laboratory a 15-fold purification of prostatic acid phosphatase[3] was obtained from an enzyme fraction already 300-fold purified on a wet tissue weight basis, by foaming off inactive protein. Several recent papers[4,5,6] have dealt with the foaming power and foam stability of protein solutions. Some authors have attempted to use these properties for the analysis of protein mixtures,[7] and two other investigators[8,9] used the method of foaming for preparing more or less pure proteins from a mixture of proteins.

This is a report on a series of experiments carried out on jackbean urease (Arlco brand) with the view of ascertaining the effect of various conditions on

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(1) This research was supported by grants from the American Cancer Society, and the Damon Runyon Memorial Fund.

(2) Damon Runyon Memorial Fellow.

(3) The purification of this enzyme is the subject of another paper in preparation.

(4) H. Kimizuka and T. Sasaki, *Bull. Chem. Soc. Japan*, **24**, 230 (1951).

(5) F. Schütz, *Trans. Faraday Soc.*, **42**, 437 (1946).

(6) Wo. Ostwald and A. Siehr, *Kolloid-Z.*, **76**, 33 (1936).

(7) D. Peters, *ibid.*, **125**, 157 (1952).

(8) A. Dognon, "Surface Chemistry," Butterworth, London, 1949, page 253.

(9) F. Schütz, R. Bader and M. Stacey, *Nature*, **154**, 183 (1944).