$-26.6°$, $[\alpha]_{589} - 37.2°$, $[\alpha]_{290} - 250.4°$; $c = 1.00$; temp. 24–25°. Drude equation: $[M] = -48.2/(\lambda^2 - 0.0387) + 4.37/\lambda^2$; λ_0 197 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±0.9%, 620–310 mμ; ±1.6%, 650–300 mμ.

Δ^6-Cholesten-3β-ol-acetate (VI), m.p. 106–108°, furnished by Dr. O. Wintersteiner, E. R. Squibb & Sons. R. D. (Fig. 1): $[\alpha]_{700}$ −64.8°, $[\alpha]_{589}$ −88.4°, $[\alpha]_{300}$ −642.6°; $c = 1.00$; temp. 24–25°. Drude equation: $[M] = -170/(\lambda^2 - 0.0414) + 58.1/\lambda^2$; λ_0 203 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±0.8%, 620–310 mμ; ±1.5%, 620–300 mμ; ±2.5%, 650–300 mμ.

Δ^4-Cholesten-3-one (VII), m.p. 80–81°; $\lambda_{max.}$ 320–323, 327–332 mμ, log ε 2.00, 2.00, shoulder 349 mμ, log ε 1.81; inflections 357, 367 mμ, log ε 1.62, 1.49. R. D. (Fig. 2): $[\alpha]_{700}$ + 60°, $[\alpha]_{589}$ + 82°, $[\alpha]_{280}$ + 1900°, "max." $[\alpha]_{420}$ + 161, "min." $[\alpha]_{365}$ − 123°, "max." $[\alpha]_{360}$ − 80°, "min." $[\alpha]_{350}$ − 164°, "max." $[\alpha]_{285-290}$ +2006°; $c = 0.10$; temp. 24–25°. R. D.: $[\alpha]_{700}$ +56.9°, $[\alpha]_{589}$ +82.2°, $[\alpha]_{390}$ + 127.2°, "max." $[\alpha]_{415-420}$ +152.4°; $c = 1.00$; temp. 24–25°. Drude equation: $[M] = 101/(\lambda^2 - 0.0301)$, from $c = 1.00$ data; λ_0 173 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±1.1%, 700–525 mμ; ±1.9%, 700–500 mμ; ±2.8%, 700–475 mμ.

Δ^1-Cholesten-3-one (VIII), m.p. 93.5–95°; $\lambda_{max.}$ 316–326 mμ, log ε 1.93; inflections 343, 357, log ε 1.83, 1.67. R. D. (Fig. 2): $[\alpha]_{700}$ +44.2°, $[\alpha]_{589}$ +59.6°, $[\alpha]_{300}$ +1097°, "max." $[\alpha]_{470}$ +84°, "min." $[\alpha]_{382.5}$ −212°, "max." $[\alpha]_{370-372.5}$ −78°, "min." $[\alpha]_{365}$ −110°, "max." $[\alpha]_{315}$ + 1205°; $c = 0.10$; temp. 24°.

Cholestan-3-one (IX), m.p. 129–130°; $\lambda_{max.}$ 284–292 mμ, log ε 1.46. R. D. (Fig. 2): $[\alpha]_{700}$ +29.3°, $[\alpha]_{589}$ + 40.2°, $[\alpha]_{285}$ −466°, "max." $[\alpha]_{315}$ +692°; $c = 1.00$ from 700–310 mμ, $c = 0.10$ from 360–285 mμ; temp. 23–24°. Drude equation: $[M] = 17.4/(\lambda^2 - 0.0970) + 29.6/\lambda^2$; λ_0 311 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±1.4%, 650–350 mμ.

3,5-Cyclocholestan-6-one (X), m.p. 100–102°; $\lambda_{max.}$ 287–289 mμ, log ε 1.65. R. D. (Fig. 2): $[\alpha]_{700}$ + 35.4°, $[\alpha]_{589}$ + 48.0°, $[\alpha]_{295}$ + 515°, "max." $[\alpha]_{410}$ + 82.8°, "min." $[\alpha]_{317.5}$ − 664°; $c = 1.00$ from 700–340 mμ, $c = 0.10$ from 340–295 mμ; temp. 24–25°. Drude equation: $[M] = -19.7/(\lambda^2 - 0.149) + 67.4/\lambda^2$; λ_0 386 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±0.3%, 650–440 mμ.

3,5-Cyclo-Δ^6-cholestene (XI), m.p. 69–70°; slight $\lambda_{max.}$ 265–267 mμ, log ε 2.04, shoulders 289, 277 mμ, log ε 1.72, 1.86; inflection 285 mμ, log ε 1.79. R. D. (Fig. 2): $[\alpha]_{700}$ − 25.8°, $[\alpha]_{589}$ − 36.4°, $[\alpha]_{300}$ − 320°; $c = 1.00$ from 700–325 mμ, $c = 0.10$ from 330–300 mμ; temp. 23–25°. Drude equation: $[M] = 288/(\lambda^2 - 0.0199) - 261/\lambda^2$; λ_0 141 mμ; % deviation $[M]_{obsd} - [M]_{calcd}$: ±0.7%, 520–350 mμ; ±2.2%, 550–315 mμ.

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DETROIT, MICHIGAN

[CONTRIBUTION FROM THE SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH]

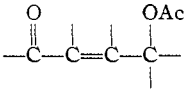
Deacetoxylation of Steroid Ring C Ketol Acetates[1]

BY R. S. ROSENFELD AND T. F. GALLAGHER

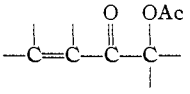
RECEIVED MARCH 14, 1955

When methyl 3α,11β-diacetoxy-12-ketocholanate or methyl 3α,12α-diacetoxy-11-ketocholanate, which have the ring C acetoxy group in the axial conformation, are refluxed with zinc in glacial acetic acid, methyl 3α-acetoxy-12-ketocholanate and methyl 3α-acetoxy-11-ketocholanate, respectively, are obtained in good yields. However, when methyl 3α,11α-diacetoxy-12-ketocholanate and methyl 3α,12β-diacetoxy-11-ketocholanate, ring C acetoxy groups equatorial, are subjected to the same reaction conditions, the yield of the corresponding monoacetoxy keto cholanic ester is markedly diminished. A similar deacetoxylation has been observed in the sapogenin series.

Several examples of the deacetoxylation of ketol acetates by means of zinc and acetic acid have been reported. Two types of ketol acetates have been shown to undergo deacetoxylation under these conditions: (1) 1,4-ketol acetates, where the functional groups are separated by unsaturation[2]



and (2) 1,2-ketol acetates, in which the ketone is part of an α,β-unsaturated system.[3]



This investigation deals with deacetoxylation of steroid ring C ketols with no unsaturation near the reactive centers. The yield in the removal of the acetoxy group depends on its conformation.

When methyl 3α,11β-diacetoxy-12-ketocholanate (I), with the C-11 substituent axial,[4] was refluxed in glacial acetic acid with powdered zinc for 7 hours, the only product isolated was methyl 3α-acetoxy-12-ketocholanate (II) which crystallized directly from the reaction mixture in 64% yield. The epimer of I, methyl 3α,11α-diacetoxy-12-ketocholanate (III), C-11 acetoxy equatorial, would not deacetoxylate under these conditions. However, when the reflux time was extended to 24 hours, partial deacetoxylation of III took place yielding 28% of II and the remainder was the starting ketol acetate III.

Comparable results were obtained with 11-keto-12-acetoxy compounds. Thus, when methyl 3α,-12α-diacetoxy-11-ketocholanate (IV), C-12-acetoxyl group axial, was refluxed with zinc in glacial acetic acid for 24 hours, methyl 3α-acetoxy-11-ketocholanate (V) was directly crystallized from the reaction product in 44% yield. Examination of

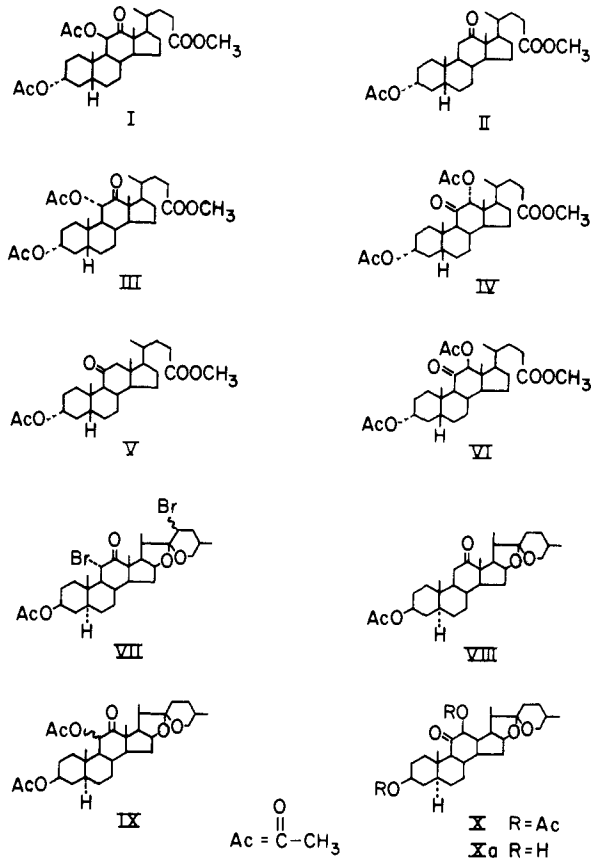
(1) This investigation was supported by grants from the Anna Fuller Fund, the Lillia Babbitt Hyde Foundation, and the National Cancer Institute of the National Institutes of Health, United States Public Health Service (C-440).

(2) C. Amendolla, G. Rosenkranz and F. Sondheimer, *J. Chem. Soc.*, 1226 (1954); L. F. Fieser, THIS JOURNAL, **75**, 4377 (1953); S. A. Knight, J. F. McGhie and M. J. Birchenough, *Chemistry and Industry*, 822 (1953).

(3) W. R. Nes and H. L. Mason, THIS JOURNAL, **73**, 4765 (1951); F. Sondheimer, St. Kaufman, J. Romo, H. Martinez and G. Rosenkranz, *ibid.*, **75**, 4712 (1953); M. Roth, G. Saucy, R. Anliker, O. Jeger and H. Heusser, *Helv. Chim. Acta*, **36**, 1908 (1953).

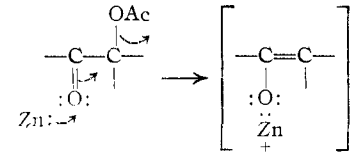
(4) E. J. Corey, THIS JOURNAL, **76**, 175 (1954).

the mother liquors by infrared spectrometry showed V to be the main product and no starting material was detected. The epimer with the substituent at C-12 equatorial, methyl 3α,12β-diacetoxy-11-ketocholanate (VI) was treated in an identical fashion and the deacetoxylation product V was obtained in 7% yield; starting substance comprised the balance of the recovered material.



In order to examine the reaction in another series 11α,23-dibromo-3β-acetoxy-5α,22a-spirostane-12-one (dibromohecogenin acetate) (VII) was hydrolyzed with dilute alcoholic potassium hydroxide. Under the conditions of the experiment, replacement of the labile bromine (at C-11) by hydroxyl was complete after 1 hour. The reaction product, without characterization, was acetylated and the crude material was refluxed with zinc in acetic acid. Chromatography on alumina yielded two principal products: 3β-acetoxy-5α,22a-spirostane-12-one (hecogenin acetate) (VIII) in yields varying from 38 to 88% and a substance, m.p. 138–139°, which crystallized with one molecule of methanol. This substance when dried under vacuum at the melting point gave a semi-crystalline material whose elementary analysis corresponded to 3β,11-diacetoxy-5α,22a-spirostane-12-one (IX). The formation of an oxime was in accord with the presence of a 12-ketone group. With the sapogenin derivative it is assumed that replacement of the 11α-bromine atom in VII by hydroxyl occurs with inversion of configuration. However, the presence of IX in the reaction product remains to be explained, since; (1) methyl 3α,11β-diacetoxy-12-ketocholanate (I) is converted to the C-11 deacetoxylated product II with no starting material recovered and (2) the rigidity of the sapogenin rings E and F leaves ring C comparatively unhindered for the deacetoxylation reaction.[5] That inversion to the β-configuration at C-11 occurred is borne out by the deacetoxylation and debromination of the intermediate 23-bromo-3β,11-diacetoxy-5α,22a-spirostane-12-one to hecogenin acetate (VIII). In addition, some 11α-hydroxy-12-keto compound might arise through an intermediate Δ^{11}-11,12-diol by enolization during deacetoxylation. Thus 3β,11-diacetoxy-5α,22a-spirostane-12-one (IX) might possess the 11α-configuration which would account for its presence and resistance to further reaction. It should be noted that the configuration at C-11 of ring C ketols in the sapogenin series has not been firmly established.[5,6] That one of the bromine atoms occupied the 11-position of 11α,23-dibromo-3β-acetoxy-5α,-22a-spirostane-12-one (VII) was shown by vigorous hydrolysis in alkali which, after acetylation and debromination, gave 3β,12β-diacetoxy-5α,22a-spirostane-11-one (11-ketorockogenin diacetate) (X) in 92% yield. Additional evidence for the structure of 3β,11-diacetoxy-5α,22a-spirostane-12-one (IX) was secured by a conversion of IX to 11-ketorockogenin (Xa) in 90% yield by treatment with strong alkali.[7]

A mechanism for such deacetoxylations has been proposed by Woodward and his collaborators who deacetoxylated *trans*-1-acetoxy-2-keto-10-methyl-$\Delta^{3,6}$-hexahydronaphthalene with zinc in refluxing acetic anhydride or xylene.[8] They propose an attack by the zinc metal on the ketone with concomitant formation of the double bond and removal of the acetoxy anion; thus



Although a similar mechanism must be operative in the removal of the acetoxy group in ring C ketol acetates, it appears that reducing conditions are advantageous. Methyl 3α,11β-diacetoxy-12-ketocholanate (I) in zinc–acetic anhydride yielded about 30% of the deacetoxylated product II, while 42% of the starting material was recoverable. With zinc dust in refluxing toluene I failed to react and only the starting material was recovered.

The results of these experiments are entirely in accord with observations of Barton and others[9] who have shown that (1) the four centers involved in 1,2-eliminations should lie in one plane for facile reaction and (2) the participants should be *trans* and axial. Methyl 3α,11β-diacetoxy-12-ketochol-

(5) G. P. Mueller, L. L. Norton, R. E. Stobaugh, L. Tsai and R. S. Winniford, THIS JOURNAL, **75**, 4892 (1953).

(6) G. P. Mueller, R. E. Stobaugh and R. S. Winniford, *ibid.*, **73**, 2400 (1951).

(7) T. F Gallagher, *J. Biol. Chem.*, **162**, 539 (1946).

(8) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

(9) D. H. R. Barton, *Experientia*, **6**, 316 (1950); D. H. R. Barton and W. J. Rosenfelder, *J. Chem. Soc.*, 1048 (1951); D. H. R. Barton and E. Miller, THIS JOURNAL, **72**, 1066 (1950).

anate (I) could be activated by hydride ion (or zinc) attack at the keto group to form an intermediate ion which fits the criteria mentioned. The electron pair at C-12 participates as reacting center. As has been shown, I deacetoxylates in good yield. On the other hand, the epimeric methyl 3α,11α-diacetoxy-12-ketocholanate reacts less readily with zinc and acetic acid since the 11α-acetoxy group in the equatorial conformation cannot form an intermediate with the required coplanarity. The same considerations are valid in the isomeric 11-keto-12-acetoxy series. Methyl 3α,12α-diacetoxy-11-ketocholanate (IV) with the ring C acetoxyl group axial deacetoxylates to form V more readily than its 12β-acetoxy epimer VI.

Experimental[10]

Reaction of Methyl 3α,11β-Diacetoxy-12-ketocholanate (I) with Zinc–Acetic Acid.—A solution of 59 mg. of I in 15 ml. of glacial acetic acid was refluxed with 600 mg. of zinc dust for 7 hours, cooled and the solution was filtered from the zinc. Ether was added to the filtrate which was washed with 5% sodium hydroxide, then water. The alkaline and aqueous washes were re-extracted with 400 ml. of ether. The combined ether solution was concentrated and yielded 59 mg. of crystalline product. Recrystallization from methanol afforded 33 mg. (64%) of methyl 3α-acetoxy-12-ketocholanate (II), m.p. 149–151°, $[\alpha]_D$ +107° ($CHCl_3$); no depression in melting point when admixed with authentic II. The infrared spectrum of the isolated material was identical with that of authentic II.

Reaction of Methyl 3α,11α-Diacetoxy-12-ketocholanate (III) with Zinc–Acetic Acid.—Sixty-five milligrams of methyl 3α,11α-diacetoxy-12-ketocholanate (III) was refluxed in 45 ml. of glacial acetic acid containing 6.5 g. of zinc dust for 24 hours. Isolation of the reaction product as described above afforded 49 mg. of oil which was chromatographed on 5 g. of Merck acid-washed alumina. The benzene eluates, which by infrared spectrometry contained predominantly starting material, after repeated crystallization from methanol gave a small amount of substance, m.p. 141–149°, $[\alpha]_D$ + 106° ($CHCl_3$). This was identified from the infrared spectrum as methyl 3α-acetoxy-12-ketocholanate (II). The total product was recombined and chromatographed on 7 g. of silica gel. Two crystalline substances were eluted with petroleum ether–ether (4:1). The first compound eluted, 16 mg. (28%), was methyl 3α-acetoxy-12-ketocholanate (II); after two recrystallizations from methanol the m.p. was 150–152°, $[\alpha]_D$ +106° ($CHCl_3$), infrared spectrum identical with authentic II. The fractions containing the second substance were combined and yielded 23 mg. (35%) of III, which after one recrystallization from methanol melted at 151–152°, infrared spectrum identical with authentic methyl 3α,11α-diacetoxy-12-ketocholanate. A mixture of the two substances isolated melted at 136–138°.

Reaction of Methyl 3α,12α-Diacetoxy-11-ketocholanate (IV) with Zinc–Acetic Acid.—When 30 mg. of IV in 20 ml. of glacial acetic acid and 3.0 g. of zinc dust was refluxed for 24 hours a crystalline product was isolated in the usual fashion. Recrystallization from methanol afforded 11 mg. (42%), m.p. 131–132°, $[\alpha]_D$ +66° ($CHCl_3$), which did not depress the melting point on admixture with methyl 3α-acetoxy-11-ketocholanate (V). The infrared spectrum was identical with authentic V, and no substance other than V was detected in the mother liquors by infrared spectrometry.

Reaction of Methyl 3α,12β-Diacetoxy-11-ketocholanate (VI) with Zinc–Acetic Acid.—When 109 mg. of VI was refluxed for 24 hours in 75 ml. of glacial acetic acid and 11.2 g. of zinc dust, 92 mg. of oil was obtained after the usual isolation procedure. On infrared examination the substance appeared to be predominantly VI. Chromatography on 8 g. of alumina followed by repeated crystallization from methanol gave 7 mg. (7%) of crude methyl 3α-acetoxy-11-ketocholanate (V), m.p. 123–132°, infrared spectrum identical with that of authentic material. The mother liquors were methyl 3α,12β-diacetoxy-11-ketocholanate (VI) from the infrared spectrum and after two recrystallizations from methanol the product melted at 80–86°.

Treatment of 11α,23-Dibromo-3β-acetoxy-5α,22a-spirostane-12-one (Dibromohecogenin Acetate) (VII) with Dilute Alkali and Reaction of the Acetylated Hydrolysis Product with Zinc–Acetic Acid. A.—Crude 11α,23-dibromohecogenin acetate (VII) was crystallized from ethyl acetate giving rectangular plates, m.p. 179–180° dec., $[\alpha]_D$ −37° ($CHCl_3$).

Anal. Calcd. for $C_{29}H_{42}O_5Br_2$: C, 55.25; H, 6.72; Br, 25.35. Found: C, 55.18; H, 6.73; Br, 25.42.

In a 200-ml. volumetric flask 1.0225 g. of VII was dissolved in 150 ml. of ethanol and 25 ml. of acetone. Eighteen ml. of 1.74 *N* potassium hydroxide was added and the volume was brought to 200 ml. with ethanol. The temperature was maintained at 28° and 10-ml. portions were removed at intervals and mixed with 20 ml. of water and 0.5 ml. of 8 *N* nitric acid. The acidified aliquots were analyzed for ionic bromine by the silver nitrate–potassium thiocyanate titration. Assuming one bromine atom (at C-11) is labile under conditions of the hydrolysis 93% of the replaceable bromine was released in 25 minutes and 97% had been released after 32 minutes. In a duplicate experiment, 98% of the labile bromine had been replaced in 46 minutes. After about 1 hour the solution was acidified with 200 ml. of 0.2 *N* nitric acid and extracted twice with 400-ml. portions of ether. The ether solution was washed with water and dried over sodium sulfate. The ether was removed and the 808 mg. of product was acetylated with acetic anhydride and a trace of perchloric acid. The acetate was refluxed for 9 hours in 100 ml. of glacial acetic acid containing 1 g. of zinc dust. After the usual procedures of filtration, dilution with water and ether extraction, the crystalline residue (m.p. 200–227°) was chromatographed on 60 g. of alumina. Two crystalline materials were obtained, 288 mg. eluted with benzene and 255 mg. recovered from the benzene–ether eluates (9:1 to 1:1). The combined material from the benzene eluates was crystallized from ethyl acetate as needles; m.p. 245–247°, $[\alpha]_D$ +1.1° ($CHCl_3$), infrared spectrum identical with hecogenin acetate (VIII).

Anal. Calcd. for $C_{29}H_{44}O_5$: C, 73.67; H, 9.38. Found: C, 73.37; H, 9.05.

The second fraction afforded feathery needles from methanol, m.p. 138–139°, $[\alpha]_D$ +39° ($CHCl_3$). This was assumed to be 3β,11-diacetoxy-5α,22a-spirostane-12-one (IX) with methanol of crystallization.

Anal. Calcd. for $C_{31}H_{46}O_7 \cdot CH_3OH$: C, 68.3; H, 8.95. Found: C, 68.35, 68.53; H, 9.25, 9.39. Infrared spectrum (CS_2): ketol acetate (1752, 1719 cm.$^{-1}$); 3-acetoxy (1736, 1238 cm.$^{-1}$); 11-acetoxy (1222 cm.$^{-1}$).

When this substance was heated for 4 hours at 132° *in vacuo*, a semi-crystalline material was recovered; the infrared spectrum was identical with that of the solvate.

Anal. Calcd. for $C_{31}H_{46}O_7$: C, 70.16; H, 8.74. Found: C, 70.37, 70.21; H, 8.91, 8.68.

This substance reacted with hydroxylamine hydrochloride in 80% alcohol containing sodium acetate to form a crystalline oxime, m.p. 199–201°, with loss of an acetoxy group.

Anal. Calcd. for $C_{29}H_{45}O_6N$: C, 69.15; H, 9.01; N, 2.78. Found: C, 69.06; H, 8.96; N, 2.83.

In other experiments similar to the one described above hecogenin acetate (VIII) was obtained in 69 and 88% yield. The increased yield may be due to the larger quantity of zinc (10-fold instead of 1:1) used in the deacetoxylation–debromination.

B. Hydrolysis of 11α,23-Dibromo-3β-acetoxy-5α,22a-spirostane-12-one (VII) with Alkali for 20 Hours.—Eighty-eight mg. of VII was dissolved in 80 ml. of 0.3 *N* 80% ethanolic potassium hydroxide and the solution was kept at room temperature for 20 hours. After this, the procedures of extraction, acetylation and zinc–acetic acid reduction were identical with those in part (A). From the zinc–acetic acid reaction 68 mg., m.p. 215–224°, was recovered (92% yield). Recrystallization from ethanol afforded short needles, m.p. 221–224°. The infrared spectrum of the material was identical with that of 3β,12β-diacetoxy-5α,22a-spirostane-11-one (11-ketorockogenin diacetate) (X).

Vigorous Hydrolysis of 3β,11-Diacetoxy-12-keto-5α,22a-spirostane (IX).—Twenty-two mg. of IX was dissolved in

(10) All melting points are corrected.

50 ml. of 0.4 *N* potassium hydroxide (80% ethanol) and the solution was refluxed for 4 hours. The cooled solution was extracted twice with 200-ml. portions of ether and the ether extracts washed with water, combined and dried over sodium sulfate. Concentration of the ether solution yielded 16 mg. (92%) of crystalline material which melted at 209–210°, after recrystallization from ethanol. A mixture of this product and authentic 11-ketorockogenin (Xa), melted at 209–210°. The infrared spectrum of the isolated Xa was identical with that of a standard sample.

Reaction of Methyl 3α,11β-Diacetoxy-12-ketocholanate (I) with Zinc–Acetic Anhydride.—One hundred twenty-two mg. of I was refluxed for 20 hours in 75 ml. of acetic anhydride containing 12 g. zinc dust. On cooling, the mixture was added to cold aqueous methanolic sodium hydroxide solution and filtered after 1 hour. The filtrate was extracted three times with 200-ml. portions of ether and the ether solution was washed with dilute alkali, water and dried over sodium sulfate. Concentration of the solution afforded an oil which was chromatographed on 20 g. of silica gel. Two substances were eluted in petroleum ether–ether (4:1). The first material, 35 mg. (32%), was shown by comparison of its infrared spectrum with authentic II to be methyl 3α-acetoxy-12-ketocholanate (II). One recrystallization from methanol gave material, m.p. 150–152°, which did not depress the melting point of a known sample of II. The second crystalline substance, 51 mg., had an infrared spectrum identical with I.

Reaction of Methyl 3α,11β-Diacetoxy-12-ketocholanate (I) with Zinc–Toluene.—Seventy-five ml. of toluene and 132 mg. of I were refluxed for 20 hours with 12 g. of zinc dust. After cooling, the reaction mixture was shaken with 100 ml. of 50% glacial acetic acid and then filtered from the zinc. The filtrate was processed as in the previous experiment and afforded 130 mg. of an oil, 100 mg. of which was chromatographed on 15 g. of silica gel. From the fractions washed from the column with petroleum ether–ether (17:3), 89 mg. (89%) of the starting material I was recoverable. After one recrystallization from methanol the substance melted at 109–111°; admixture of the product with authentic methyl 3α,11β-diacetoxy-12-ketocholanate (I) showed no change in melting point. The infrared spectrum of the reaction product was indistinguishable from that of starting material. No other material was identified in the chromatogram.

Acknowledgment.—The authors are indebted to Dr. Carl Djerassi of Wayne University, and Dr. George Rosenkranz of Syntex, S. A., Mexico City, for their generous gift of dibromohecogenin acetate.

NEW YORK, N. Y.

[CONTRIBUTION FROM THE IPATIEFF HIGH PRESSURE AND CATALYTIC LABORATORY, DEPARTMENT OF CHEMISTRY, NORTHWESTERN UNIVERSITY]

Studies in the Terpene Series. XXIII.[1,2] Pyrolysis of *d*-Limonene and of Related Hydrocarbons. Mechanisms of Pyrolysis

BY HERMAN PINES AND JACK RYER[3]

RECEIVED FEBRUARY 9, 1955

The pyrolysis of *d*-limonene and of a mixture consisting of α- and β-pyronene and of 1,5-dimethyl-5-ethyl-1,3-cyclohexadiene (V) over copper pellets at 450° and at atmospheric pressure was studied. It was found that *d*-limonene formed 9% aromatic hydrocarbons containing as the major constituents *p*-cymene, 1,2,3,5-tetramethylbenzene, *m*-xylene and trimethylbenzenes. The non-aromatic hydrocarbons contained geminal and non-geminal alkylcyclohexanes, which on dehydrogenation formed polymethylated alkylbenzenes. The mixture of pyronenes (VII and IX) and of compound V on pyrolysis formed products having composition similar to that obtained from *d*-limonene. A biradical mechanism is proposed to explain the formation of the various compounds.

Introduction

The catalytic rearrangement of terpenes and related compounds at elevated temperatures has been a subject of extensive studies in this Laboratory. Inasmuch as terpenes and certain bicyclic dihydroterpenes may undergo changes when exposed to high temperatures in the absence of catalysts it was deemed necessary to investigate the extent to which these pyrolytic reactions were responsible for the rearrangement of the terpenes studied. For that reason the pyrolysis of pinane[4a,b] and 6,6-dimethylnorpinane[5] were investigated. It was found that pinane rearranges at 400–500° to 3,7-dimethyl-1,6-octadiene and to *cis, cis, cis* and *cis, trans, cis*-1,2-dimethyl-3-isopropenylcyclopentane. Dimethylnorpinane forms similar compounds, namely, 7-methyl-1,6-octadiene and *trans*-1-methyl-2-isopropenylcyclopentane.

Of the terpenes only the pyrolysis of α- and β-pinene and of alloöcimene have been studied extensively. Fuguitt and Hawkins[6] on the basis of a kinetic study, concluded that several processes occurred simultaneously when α-pinene was heated at 200–500°. These processes included the racemization of α-pinene, isomerization to almost optically inactive limonene (dipentene) and isomerization to alloöcimene through an intermediate ocimene.[7] At higher temperatures pyronenes[8] and other cyclic hydrocarbons were produced.

The products of the pyrolytic isomerization of β-pinene were not identical with those of α-pinene. They consisted of optically active limonene and myrcene.[9]

Burwell[10] has proposed a mechanism for the pyrolysis of pinenes, involving biradical intermediates, which is in accord with all of the above indicated facts.

The pyrolysis of alloöcimene was studied by Parker and Goldblatt.[11] They found that the product contained besides α- and β-pyronene a substantial

(1) For previous paper of this series see H. Pines and J. Maréchal, THIS JOURNAL, **77**, 2819 (1955).

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(3) Taken in part from the Doctoral Dissertation submitted to the Department of Chemistry, Northwestern University, Evanston, Illinois, January, 1954.

(4) (a) V. N. Ipatieff, W. D. Huntsman and H. Pines, THIS JOURNAL, **75**, 6222 (1953); (b) H. Pines, N. E. Hoffman and V. N. Ipatieff, *ibid.*, **76**, 4412 (1954).

(5) H. Pines and N. E. Hoffman, *ibid.*, **76**, 4417 (1954).

(6) R. E. Fuguitt and E. J. Hawkins, *ibid.*, **67**, 242 (1945).

(7) E. J. Hawkins and H. G. Hunt, *ibid.*, **73**, 5379 (1951).

(8) G. Dupont and R. Dulou, *Compt. rend.*, **201**, 219 (1935).

(9) L. A. Goldblatt and S. Palkin, *ibid.*, **63**, 3517 (1941).

(10) R. L. Burwell, Jr., *ibid.*, **73**, 4461 (1951).

(11) E. E. Parker and L. A. Goldblatt, *ibid.*, **72**, 2151 (1950).