3α-acetoxy-11α-hydroxy-7-keto-Δ⁸-cholenate, m.p. 168–169° (no depression in mixed m.p.), α^{24}_D +3 ± 1° Chf, λ^{EtOH} 252 mμ (8,580).

Hydrogen Peroxide–Ferrous Sulfate (W.-Y. H.).—A solution of 1 g. of methyl 3α-acetoxy-Δ$^{7,9(11)}$-choladienate in 200 cc. of acetic acid was stirred mechanically while 25 cc. of 30% hydrogen peroxide and 50 cc. of 5% ferrous sulfate heptahydrate were dropped in simultaneously in the course of 10 min. at 40°. Stirring was continued at 40° for 8 hr. and the brown solution was left overnight at 25°, treated with sodium bisulfite to destroy any oxidizing agent, and evaporated in vacuum to a small volume. This was extracted with ether in a continuous extractor and the residue from evaporation of the ether was treated with excess diazomethane. Chromatography on 25 g. of alumina gave solid material only in the benzene eluate, which afforded about 40 mg. of slightly yellowish material, m.p. 165–170°, which appeared to be a mixture of **methyl 3α-acetoxy-7-keto-Δ$^{9(11)}$- and Δ^{8}-cholenates.** Crystallized from methanol, it had the constants: m.p. 173–174°, λ^{EtOH} 254 mμ (3,450), λ^{Chf} 5.78, 5.83, 5.97, 6.25, 7.94 μ. A 20-mg. portion was refluxed for 2 hr. with potassium hydroxide in aqueous methanol and the material obtained on acidification was crystallized from acetone and gave **7-keto-Δ⁸-lithocholenic acid**, m.p. 210–213° (no depression on admixture), λ^{EtOH} 253.5 mμ (8,600).

Silver Benzoate–Iodine (W.-Y. H.).—In a preliminary experiment 430 mg. of methyl 3α-acetoxy-Δ$^{7,9(11)}$-choladienate treated with excess reagent afforded on chromatography (benzene eluate) 80 mg. of material m.p. 132–137°. Crystallized from methanol, it melted at 142–143°, α_D +31.4 ± 0.5° Chf, λ^{EtOH} 231.5 mμ (44,400), λ^{Chf} 2.75, 2.91, 5.85, 5.87, 6.25, 7.9 μ. The analysis is in fair agreement with that for a product of the addition of two benzoate groups containing a mole of methanol.

Anal. Calcd. for $C_{42}H_{64}O_9$ (702.85): C, 71.77; H, 7.74. Found: C, 72.00, 71.47; H, 7.36, 7.53.

The material was refluxed with methanolic sodium hydroxide for 2 hr. and then treated with dichromate in acetic acid at 25°; the resulting material still showed benzoate absorption at about 230 mμ and no absorption at 270 mμ.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, HARVARD UNIVERSITY]

Synthesis of 11-Ketosteroids. II. 11-Ketocholestanol

BY LOUIS F. FIESER AND JOSEF E. HERZ[1]

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Dichromate oxidation of Δ$^{7,9(11)}$-cholestadienyl benzoate (I) gave, in yields of a few per cent. only, the Δ⁸-7,11-diketone (II) and the Δ$^{9(11)}$-7-ketone III. Reduction of II with zinc and acetic acid followed by Wolff–Kishner reduction afforded 11-ketocholestanol (XI). 7-Keto-Δ⁸-cholestenyl benzoate (VII) was isolated from the mixture resulting from refluxing the total oxidation product with zinc and acetic acid. Oxidation of I with hydrogen peroxide and ferrous sulfate gave the 9α,11α-oxido-7-ketone V, a substance of a type first described by the Syntex group and convertible through IX into X by the methods they have reported.

Schenck, Buchholz and Wiese[2] prepared Δ⁷-cholestenol by reduction of 7-dehydrocholesterol with sodium and ethanol and obtained material, m.p. 122–123°, α_D 0° Chf; acetate, m.p. 118–119°, α_D 0° Chf. By dehydration of 7α-hydroxycholestanyl acetate and purification of the resulting stenyl acetate mixture by chromatography and crystallization, Wintersteiner and Moore[3] obtained stenol of m.p. 122–123°, α_D +6.5° Chf; acetate, m.p. 118–119°, α_D +4.2° Chf.[4] We first tried hydrogenation of 7-dehydrocholesterol, kindly supplied by the du Pont Company, with platinum catalyst in ethyl acetate, but obtained partially isomerized material, possibly due to a trace of acetic acid in the solvent. Following a suggestion of Dr. Max Tishler, we then tried hydrogenation in dioxane in the presence of Raney nickel and regularly obtained very satisfactory material in 80% yield. Our most highly purified sample of Δ⁷-cholestenol[5] had the constants: m.p. 125–126°, α_D +3.9° Chf, +10.0° Di; acetate m.p. 118–119°, α_D +2.4°, Chf, +9.4° Di.

Dehydrogenation of Δ⁷-cholestenol with mercuric acetate[6] in chloroform–acetic acid under nitrogen at 25° and benzoylation gave the starting material, Δ$^{7,9(11)}$-cholestadienyl benzoate (I) in 43.5% overall yield. Oxidation with sodium dichromate in benzene–acetic acid at 25° gave a mixture from which two components were isolated by chromatography. One is characterized as the Δ⁸-7,11-diketone II by its yellow color, low-intensity absorption at 268 mμ and reduction with zinc dust to the saturated 7,11-diketone VI. The other is a monooxygen derivative showing no ultraviolet absorption and isomeric with the conjugated Δ⁸-7-ketone VII, which was isolated along with the saturated 7,11-diketone VI by chromatographing the mixture resulting from zinc–acetic acid reduction of the total oxidation mixture. The conjugated ketone VII could be selectively hydrogenated to a saturated ketone identified, after hydrolysis, as 7-ketocholestanol (VIII), which fixes the position of the carbonyl group. An attempt to prove the position of the double bond in VII by Wolff–Kishner reduction gave a stenyl mixture of α_D +20° Di that was found on selenium dioxide analysis[7] to contain 31.5% Δ⁷-cholestenol. Since the latter substance is almost optically inactive, the main component must be rather strongly dextrorotatory and hence is probably Δ⁸-cholestenol (α_D +50° Chf) rather than Δ$^{8(14)}$-cholestenol (α_D +20° Chf). Our 7-keto-Δ⁸-cholestenyl benzoate differs in M_D from the value + 141° Di calculated[8] for cholestanyl benzoate by the increment − 207 Di; the increment found for the corresponding acetates is −203 Chf.[9]

(1) Abbott Laboratories predoctoral fellow, 1950–1951.

(2) Fr. Schenck, K. Buchholz and O. Wiese, *Ber.*, **69**, 2696 (1936).

(3) O. Wintersteiner and M. Moore, THIS JOURNAL, **65**, 1507 (1943).

(4) W. Buser, *Helv. Chim. Acta*, **30**, 1379 (1947), obtained impure material (α_D −20°) by the method of Schenck, Buchholz and Wiese; by the method of Wintersteiner and Moore he obtained stenyl acetate, m.p. 116–119°, α_D +0.6° chf.

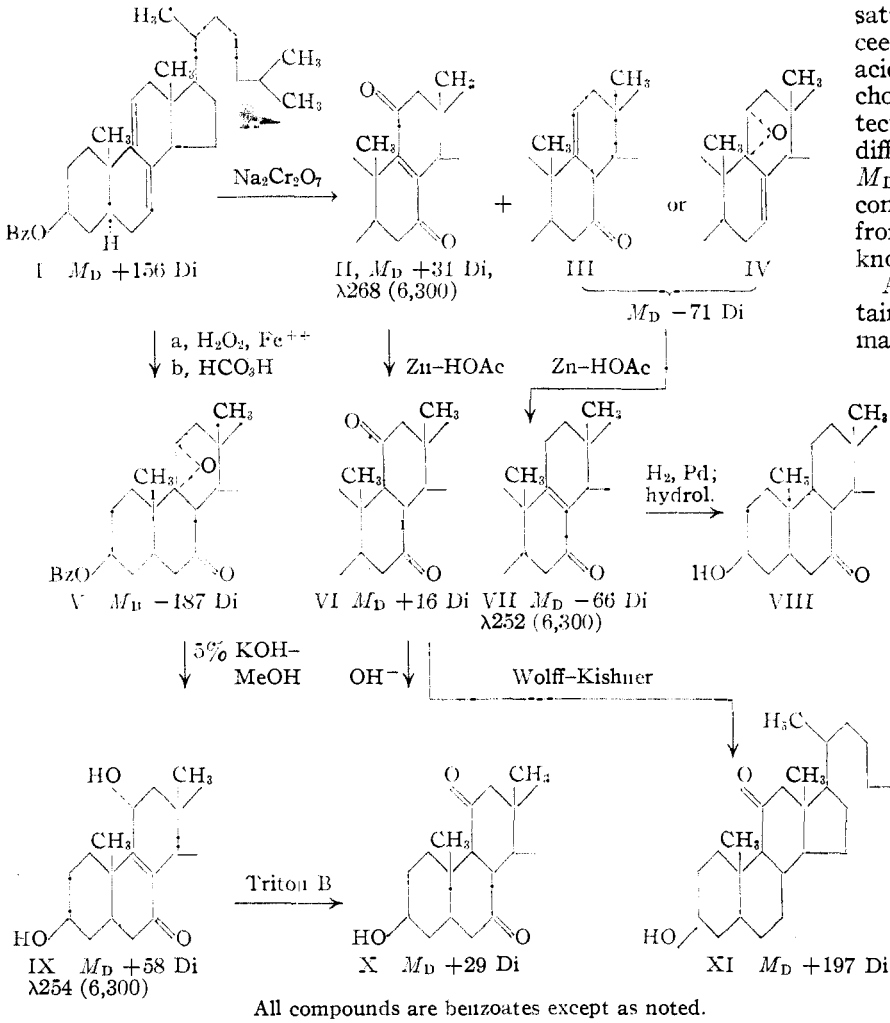
(5) L. F. Fieser, THIS JOURNAL, **73**, 5007 (1951).

(6) A. Windaus and E. Auhagen, *Ann.*, **472**, 185 (1929).

(7) Method of Koji Nakanishi, see ref. 5.

(8) L. F. Fieser, J. E. Herz, M. W. Klohs, M. A. Romero and T. Utne, THIS JOURNAL, **74**, 3309 (1952).

(9) L. F. Fieser, unpublished.



All compounds are benzoates except as noted.

The non-absorbing product of oxidation is evidently at least one of the precursors of the isomeric conjugated 7-ketone VII and it probably is either the non-conjugated ketone III, corresponding to one of the oxidation products in the bile acid series,[10] or a monoöxide such as IV. The presence of the benzoate group prevented infrared characterization of a possible carbonyl group and the appearance of a carbonyl band on saponification is not decisive because of possible rearrangement in the process. From the reaction of the diene I with perphthalic acid, Heusser, *et al.*,[11] isolated a substance different from our product which they formulated as the Δ^7-9,11-oxide IV; the M_D difference between this substance and the starting diene I of −239 Chf is in fair agreement with that of −276 Chf for the more fully characterized Δ^7-9,11-oxide from ergosterol-D acetate.[12,13] Hence our product very probably is the $\Delta^{9(11)}$-7-ketone III.

Wolff–Kishner reduction (Huang-Minlon) of the saturated 7,11-diketone proceeded better than in the bile acid series[10] and gave 11-ketocholestanol (XI) as the only detected product. The 11-ketone differs from cholestanol[14] by the M_D increment +101 Di, as compared with values ranging from +60 to +96 Chf for five known examples.[15]

Although the goal was attained, the process of dichromate oxidation proceeds so poorly that the yields of usable products (II, VI and VII) are all well under 10% and the mixtures are separable only with difficulty. As an alternative, we explored oxidation of the $\Delta^{7,9(11)}$-diene I with hydrogen peroxide and ferrous sulfate,[16] which furnishes hydroxyl radicals, and isolated easily a product of the composition of a dioxide or ketoxide that afforded on treatment with base a free alcohol characterized by spectroscopy as an α,β-unsaturated ketone. At this point we learned from Dr. Gilbert Stork of the work of the Syntex group,[17] who by oxidation of $\Delta^{7,9(11)}$-dienes with performic acid had obtained compounds similar to ours which they characterized as 9α,11α-oxido-7-ketones (V) convertible through 11α-hydroxy-Δ^8-7-ketones (IX) into the saturated 7,11-diketones (X). We then found that performic acid oxidation of I gave a product identical with that of the hydroxyl radical reaction (V) and completed the conversion through IX to X by the methods reported from Mexico. We also explored briefly the action of osmium tetroxide on I and isolated in low yield a substance having the composition of a cholestenetriol benzoate.

Experimental

Δ^7-Cholestenol.—7-Dehydrocholesterol was kindly supplied to us by the du Pont Co. as a paste in methanol (stabilizer) containing 83% solids of which 89% consisted in the $\Delta^{5,7}$-diene. Material suitable for hydrogenation was prepared as follows and used at once, since the dry solid undergoes rapid autoxidation. A 50-g. portion of paste was dissolved in 500 cc. of hot acetone and the solution was filtered by suction through Supercel and cooled. The product consisted of fine needles, m.p. 151–153° (vac.), yield 33 g. (89%).

(10) L. F. Fieser, W.-Y. Huang and J. C. Babcock, THIS JOURNAL, **75**, 116 (1953).

(11) H. Heusser, K. Heusler, K. Eichenberger, C. G. Honegger and O. Jeger, *Helv. Chim. Acta*, **35**, 295 (1952).

(12) E. M. Chamberlin, M. Tishler, *et al.*, THIS JOURNAL, **73**, 2396 (1951).

(13) H. Heusser, K. Eichenberger, P. Kurath, H. R. Dällenbach and O. Jeger, *Helv. Chim. Acta*, **34**, 2106 (1951).

(14) For cholestanol crystallized from ligroin we find the constants m.p. 143–144°, α_D +23.8° Chf, +24.8° Di.

(15) D. H. R. Barton and W. Klyne, *Chemistry and Industry*, **26**, 755 (1948).

(16) G. R. Clemo, M. Keller and J. Weiss, *J. Chem. Soc.*, 3470 (1950).

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

Hydrogenation was accomplished with 25 g. of 7-dehydrocholesterol in 250 cc. of dioxane at atmospheric temperature in the presence of Raney nickel. After 24 hr. 1660 cc. of hydrogen had been taken up (theory 1650 cc.). The solution was filtered and diluted with water containing sodium chloride. Crystallization from aqueous acetone gave fine needles of Δ^7-cholestenol, m.p. 123–125°,[18] yield 20.5 g. (82%).

$\Delta^{7,9(11)}$-Cholestadienol.—Solutions of 1 g. of Δ^7-cholestenol in 45 cc. of chloroform and of 2.3 g. of mercuric acetate in 40 cc. of acetic acid were mixed under nitrogen and let stand for 24 hr. at 25°. The precipitated mercurous acetate was removed by filtration and the solution washed free of acid with water, dried and evaporated in vacuum. Crystallization of the residue from aqueous acetone gave 0.6 g. (59%) of colorless needles, m.p. 107–110° (vac.), α_D +39 ± 2° Di, λ^{EtOH} 242 mμ (10,000).

Anal. Calcd. for $C_{27}H_{44}O$ (384.35): C, 84.30; H, 11.54. Found: C, 84.31; H, 11.65.

The acetate was obtained only in low yield by dehydrogenation of Δ^7-cholestenyl acetate (1.8 g.) as above (4.3 g. mercuric acetate); crystallization from aqueous methanol gave colorless needles (0.1 g.), m.p. 117–119° (vac.), α_D +63 ± 2° Di, λ^{EtOH} 236, 243, 250 mμ (12,600, 14,200, 9,130).

Anal. Calcd. for $C_{29}H_{46}O_2$ (426.65): C, 81.63; H, 10.87. Found: C, 81.84; H, 11.13.

The benzoate (I) was prepared by dehydrogenating 20.5 g. of Δ^7-cholestenol in 400 cc. of chloroform with 46 g. of mercuric acetate in 400 cc. of acetic acid (16 hr. at 25° under nitrogen; 37 g. of precipitated mercurous acetate = 98% of theory). The glassy residue left on evaporation of the washed and dried chloroform solution was dissolved in 175 cc. of pyridine and 50 cc. of dioxane and the solution was cooled in ice during addition of 20 cc. of benzoyl chloride. After standing for 24 hr. under nitrogen, the solution was poured onto ice, acidified with hydrochloric acid and the gummy precipitate filtered. Two crystallizations from acetone–dioxane–water gave slightly yellow needles, m.p. 132–134° (vac.), yield 11.3 g. (43.5%). Analytical sample: colorless needles, m.p. 135–137° (vac.), α_D +32 ± 2° Di.

Anal. Calcd. for $C_{34}H_{48}O_2$ (488.72): C, 83.55; H, 9.90. Found: C, 83.81; H, 10.05.

The Swiss workers[11] report m.p. 132.5–133.5°, α_D +52° Chf.

Oxidation of $\Delta^{7,9(11)}$-Cholestadienyl Benzoate.—A solution of 3.6 g. of sodium dichromate dihydrate in 35 cc. of acetic acid was added to a solution of 2 g. of the diene benzoate in 25 cc. of benzene and 30 cc. of acetic acid and the solution was let stand at 25° for 24 hr. and then diluted with water and extracted with ether. The crude reaction product, a greenish oil, was adsorbed onto 40 g. of acid-washed alumina and separated into the following fractions: A, eluted by 4:1 petroleum ether–benzene (white, 100 mg.); B, eluted by a 2:1 mixture of the same solvents (yellow, 300 mg., m.p. 156–158°); C, eluted later by the 2:1 mixture (yellow, 180 mg.).

Fraction A. 7-Keto-$\Delta^{9(11)}$-cholestene-3β-ol Benzoate (III).—Crystallization of the early eluate from methanol gave 100 mg. of colorless needles, m.p. 126–128°, α_D −14 ±2° Di. The infrared spectrum (CS_2) indicated the absence of a hydroxyl group or an α,β-unsaturated ketonic group.

Anal. Calcd. for $C_{34}H_{46}O_3$ (504.72): C, 80.90; H, 9.58. Found: C, 80.67; H, 9.65.

Saponification of a small sample gave non-crystalline material with infrared spectrum indicative of the presence of a hydroxyl group and an α,β-unsaturated 7-keto group (absorption at 1720 cm.$^{-1}$; determination made at the Syntex laboratory through the courtesy of Dr. Carl Djerassi).

7,11-Diketo-Δ^8-cholestene-3β-ol 3-Benzoate (II).—Repeated crystallization of the combined eluates of fraction C from methanol gave 150 mg. of yellow needles, m.p. 148–150°, α_D +6 ± 2° Di, λ^{EtOH} 268 mμ (6,300) λ^{CS_2} 5.95 μ.

Anal. Calcd. for $C_{34}H_{46}O_4$ (518.71): C, 78.72; H, 8.94. Found: C, 78.77; H, 9.19.

Oxidation of $\Delta^{7,9(11)}$-Cholestadienyl Benzoate Followed by Reduction.—The successive eluates of the above fraction B on crystallization from methanol melted in the range 140–146°, but analyses indicated variable composition. Five recrystallizations gave yellow needles, m.p. 156–158°, α_D −30 ± 2° Di, of analysis approximating $C_{34}H_{48}O_4$ (found: C, 78.74; H, 9.14). The total material (300 mg.) was then refluxed with 0.5 g. of zinc dust, 20 cc. of acetic acid, and 1 cc. of water for 12 hr. and the "reduced fraction B" processed as described below.

A second oxidation was conducted with 8 g. of diene benzoate in 100 cc. of benzene and 120 cc. of acetic acid with 14.4 g. of dichromate in 145 cc. of acetic acid. After 24 hr. at 25°, 20 cc. of absolute ethanol was added, the benzene was boiled off, 3 g. of zinc dust (activated with 10% hydrochloric acid and a little copper sulfate) and 10 cc. of water were added, and the mixture was refluxed for 15 hr. The neutral fraction extracted with ether when triturated with methanol afforded 3.5 g. of greenish crystalline product that was separated by chromatography on 150 g. of alumina into fractions as follows. **Fraction D**, eluted by 1:1 petroleum ether–benzene, on crystallization from acetone–water afforded 150 mg. of white needles, m.p. 140–142°, α_D −10 ± 2° Di. The analysis and constants suggest that the substance is cholesteryl benzoate (m.p. 145.5°, α_D −14° Chf).

Anal. Calcd. for $C_{34}H_{50}O_2$ (490.74): C, 83.21; H, 10.27. Found: C, 82.68; H, 10.25.

Fraction E (800 mg., VII) was eluted by 1:3 petroleum ether–benzene, and **fraction F** (300 mg., VI) was eluted later by the same solvent mixture. Still later fractions were yellow oils that did not crystallize.

7-Keto-Δ^8-cholestene-3β-ol Benzoate (VII).—The various eluates comprising **fraction B** of the oxidation mixture were of varying melting point and analysis, and the composition and results of reduction suggest the presence of the non-conjugated ketone III and possibly a monoöxide and the 7,11-diketo-8,9-oxide. The total material (300 mg.) was reduced with zinc and acetic acid and the product chromatographed. Eluates 6–12 (1:1 benzene–petroleum ether) gave solids melting in the range 157–170° and several crystallizations from aqueous acetone afforded 150 mg. (8%) of the Δ^8-7-ketone as colorless prismatic needles, m.p. 148–150°, α_D −13 ± 2° Di, λ^{EtOH} 252 mμ (6,300), λ^{Chf} 5.95 μ.

Anal. Calcd. for $C_{34}H_{48}O_3$ (504.72): C, 80.90; H, 9.58. Found: C, 81.02; H, 9.87.

Fraction E (800 mg., m.p. 135–146°) resulting from reduction of the total oxidation mixture, on three crystallizations from methanol–water, yielded 600 mg. of pure Δ^8-7-ketone (VII).

7,11-Diketocholestane-3β-ol Benzoate (VI).—Eluates 13–21 (1:1 petroleum ether–benzene) from **fraction B**, of m.p. in the range 184–192°, afforded after several crystallizations from aqueous acetone 100 mg. (4%) of the saturated diketone as shiny plates, m.p. 199–201°, α_D +3 ± 2° Di.

Anal. Calcd. for $C_{34}H_{48}O_4$ (520.72); C, 78.42; H, 9.29. Found: C, 78.37; H, 9.71.

Zinc and acetic acid reduction of 7,11-diketo-Δ^8-cholestene-3β-ol benzoate gave saturated diketone, m.p. 199–201°, in 65% yield. The oxidation–reduction experiment afforded the same compound in **fraction F** (300 mg., m.p. 155–177°); crystallization gave 100 mg. of product, m.p. 189–192°.

7,11-Diketocholestane-3β-ol.—Saponification of the benzoate and crystallization of the product from aqueous methanol yielded colorless plates, m.p. 187–189°, α_D +7 ± 2° Di.

Anal. Calcd. for $C_{27}H_{44}O_3$ (416.62): C, 77.83; H, 10.65. Found: C, 77.51; H, 10.89.

11-Ketocholestane-3β-ol (XI).—A mixture of 120 mg. of 7,11-diketocholestane-3β-ol benzoate, 300 mg. of potassium hydroxide pellets, 0.3 cc. of 85% hydrazine hydrate and 10 cc. of triethylene glycol was refluxed for 0.5 hr., the temperature was raised to 195° in 1 hr. and kept there for 2 hr. longer. The dark brown mixture was poured into dilute acid and the product isolated by extraction with ether and chromatography. The column was first washed well with 25:1 benzene–ether and then elution with ether eluted the 11-ketone, which formed fine colorless needles from aqueous methanol; yield 40 mg. (44%), m.p. 149–151°, α_D +49 ±2° Di, λ^{CCl_4} 5.89 μ.

Anal. Calcd. for $C_{27}H_{46}O_2$ (402.64): C, 80.54; H, 11.52. Found: C, 80.66; H, 11.49.

7-Keto-Δ^8-cholestene-3β-ol, obtained by saponification of the benzoate, crystallized from aqueous methanol in shiny plates, m.p. 114–116°, α_D −22 ± 2° Di.

(18) See Theoretical Part for constants of fully purified material.

Anal. Calcd. for $C_{27}H_{44}O_2$ (400.62): C, 80.94; H, 11.07. Found: C, 81.11; H, 11.27.

7-Ketocholestane-3β-ol from the Δ⁸-7-Ketone.—A solution of 135 mg. of 7-keto-Δ⁸-cholestene-3β-ol benzoate in 25 cc. of acetic acid was hydrogenated in the presence of 100 mg. of 10% palladium–charcoal. When the theoretical amount of hydrogen (7 cc.) had been taken up the solution was filtered, the solvent blown off with air and the residue hydrolyzed with methanolic potassium hydroxide. Several crystallizations from aqueous methanol yielded colorless plates, m.p. 159–161°, undepressed on admixture with authentic 7-ketocholestane-3β-ol (m.p. 162°).

Wolff–Kishner Reduction of 7-Keto-Δ⁸-cholestene-3β-ol Benzoate (VII).—Chromatography of the reaction mixture and crystallization from aqueous methanol afforded needles, m.p. 121–123° (sintering at 110°), α_D +20 ± 2° Di. A mixture with Δ⁸⁽¹⁴⁾-cholestenol (m.p. 118–120°) melted at 112°. An analysis[7] by Koji Nakanishi indicated the presence of 31.5% of Δ⁷-cholestenol.

7-Keto-Δ⁸-cholestene-3β-ol-7-ethylenethioketal Benzoate.—A solution of 200 mg. of the Δ⁸-7-keto benzoate in 5 cc. of ethylene dithiol was treated at −15° with hydrogen chloride for 0.5 hr. and left at 0° for 3 hr. Excess anhydrous sodium carbonate was added and the mixture was extracted with ether. After washing with 10% alkali and with water and drying, evaporation left an oily residue that crystallized when triturated to give 200 mg. (87%) of large colorless needles, m.p. 186–189°. Crystallization from methanol–ether raised the m.p. to 188–191°.

Anal. Calcd. for $C_{36}H_{52}O_2S_2$ (580.90): C, 74.43; H, 9.02; S, 11,04. Found: C, 74.88; H, 9.22; S, 11.62.

Refluxing with Raney nickel in ethanol for 12 hr. and crystallization of the product from methanol gave needles of an unidentified benzoate mixture, m.p. 143–146°, α_D +23 ± 2° Di.

Reaction of Δ⁷,⁹⁽¹¹⁾-Cholestadienyl Benzoate with Osmium Tetroxide.—A solution of 900 mg. of diene benzoate, 550 mg. (1 equiv.) of osmium tetroxide and 2 cc. of pyridine in 40 cc. of ether was let stand at 25° for 72 hr. The solvent was evaporated and a solution of the residue in ethanol treated with 5.4 g. of sodium sulfite in 40 cc. of water and the mixture refluxed for 12 hr. The dark precipitate was removed and washed with ethanol and the product recovered from the filtrate by ether extraction (300 mg.) and chromatographed. Benzene–ether (25:1) eluted 150 mg. of a **cholestene-3β,?,?-triol benzoate**, which crystallized from aqueous methanol in needles, m.p. 173–175°, α_D +31 ± 2° Di.

Anal. Calcd. for $C_{34}H_{50}O_4$ (522.74): C, 78.11; H, 9.64. Found: C, 78.11; H, 9.62.

7-Keto-9α,11α-oxidocholestane-3β-ol Benzoate (V). (a).—A solution of 1 g. of Δ⁷,⁹⁽¹¹⁾-cholestadienyl benzoate in 100 cc. of dioxane and 200 cc. of acetic acid was stirred at 35–40° during simultaneous addition of 25 cc. of 30% hydrogen peroxide and 50 cc. of 5% ferrous sulfate. Stirring at 35–40° was continued for 12 hr. and the solution was evaporated to half its volume, diluted with water, extracted with ether, and the solution washed, dried and evaporated. Two crystallizations of the residue from acetone–water yielded 250 mg. (24%) of needles, m.p. 201–202°, α_D −36 ± 2° Di. A mixture with 7,11-diketocholestane-3β-ol benzoate melted at 154–162°.

Anal. Calcd. for $C_{34}H_{48}O_4$ (520.72): C, 78.42; H, 9.29. Found: C, 78.42; H, 9.18.

The substance was recovered unchanged after brief treatment with chromic acid in hot acetic acid–water.

(b).—A solution of 500 mg. of the diene benzoate in 15 cc. of dioxane was warmed on the steam-bath, 20 cc. of 88% formic acid was added and the solution quickly cooled to 25° to produce a fine suspension. This was stirred at 40°, 0.8 cc. of 30% hydrogen peroxide was added and stirring was continued for 1 hr., when the solid had all dissolved. Dilution with water precipitated an oil that afforded crystals from aqueous acetone. Several crystallizations gave 70 mg. (13%) of satisfactory ketoöxide, m.p. 198–200°, not depressed on admixture with (a).

7-Keto-Δ⁸-cholestene-3β,11α-diol (IX).—The benzoate (75 mg.) was refluxed for 0.5 hr. with 10 c. of 5% methanolic potassium hydroxide and the solution was acidified and diluted with water. The solid precipitate on crystallization from aqueous acetone gave 30 mg. (50%) of long needles, m.p. 171–173°, α_D +14 ± 2° Di, λ^{EtOH} 254 mμ (6,300), λ^{Chf} 5.95 μ.

Anal. Calcd. for $C_{27}H_{44}O_3$ (416.63): C, 77.83; H, 10.65. Found: C, 77.57; H, 10.94.

Isomerization of this substance was effected by refluxing 20 mg. in 5 cc. of methanol and 1 cc. of 40% Triton B solution overnight. Extraction with ether and chromatography afforded **7,11-diketocholestane-3β-ol**, m.p. 187–189°, undepressed by admixture with material described above.

CAMBRIDGE, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, HARVARD UNIVERSITY]

Synthesis of 11-Ketosteroids. III. Oxidation of Δ⁷,⁹⁽¹¹⁾-Dienes with N-Bromosuccinimide

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Δ⁷,⁹⁽¹¹⁾-Dienes of the bile acid, cholesterol and ergosterol series have been converted into the saturated 7,11-diketones by reaction with N-bromosuccinimide in *t*-butanol–dilute sulfuric acid, followed by further oxidation with silver chromate and reduction with zinc and acetic acid. In the bile acid series initial products of reaction with the bromoimide have been characterized as the Δ⁹⁽¹¹⁾-ene-7-one II, the Δ⁸-ene-11-one III and the Δ⁸-ene-11α-ol-7-one IV.

In addition to other oxidizing agents explored in our laboratory for the conversion of steroid Δ⁷,⁹⁽¹¹⁾-dienes into 11-oxygenated intermediates,[3,4] N-bromosuccinimide was investigated, first for the oxidation of methyl 3α-acetoxy-Δ⁷,⁹⁽¹¹⁾-choladienate (I). In a solution of *t*-butanol and dilute sulfuric acid at 0°, the bromoimide attacks the diene rapidly and after about an hour the intense diene absorption band at 244 mμ disappears and the solution shows distinct absorption at 250 mμ. Silver nitrate solution was added until no further silver bromide precipitated and then oxidation was continued with silver chromate, when the absorption slowly shifted to the region of longer wave length. Chromatography afforded a yellow fraction showing absorption at 272 mμ indicative of the presence of the Δ⁸-ene-7,11-dione (VI) and this on reduction with zinc dust and acetic acid gave a colorless product identical with the previously described[3] methyl 7,11-diketocholanate (V). The over-all yield was 19%, which at least is an improvement over that in the dichromate process.[3,4] By

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(2) National Institutes of Health predoctoral fellows, 1950-1952.

(3) L. F. Fieser, W.-Y. Huang and J. C. Babock, THIS JOURNAL, **75**, 116 (1953).

(4) (a) L. F. Fieser and J. E. Herz, *ibid.*, **75**, 121 (1953); (b) L. F. Fieser, *ibid.*, **73**, 5007 (1951).