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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RECEIVED AUGUST 28, 1952

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.

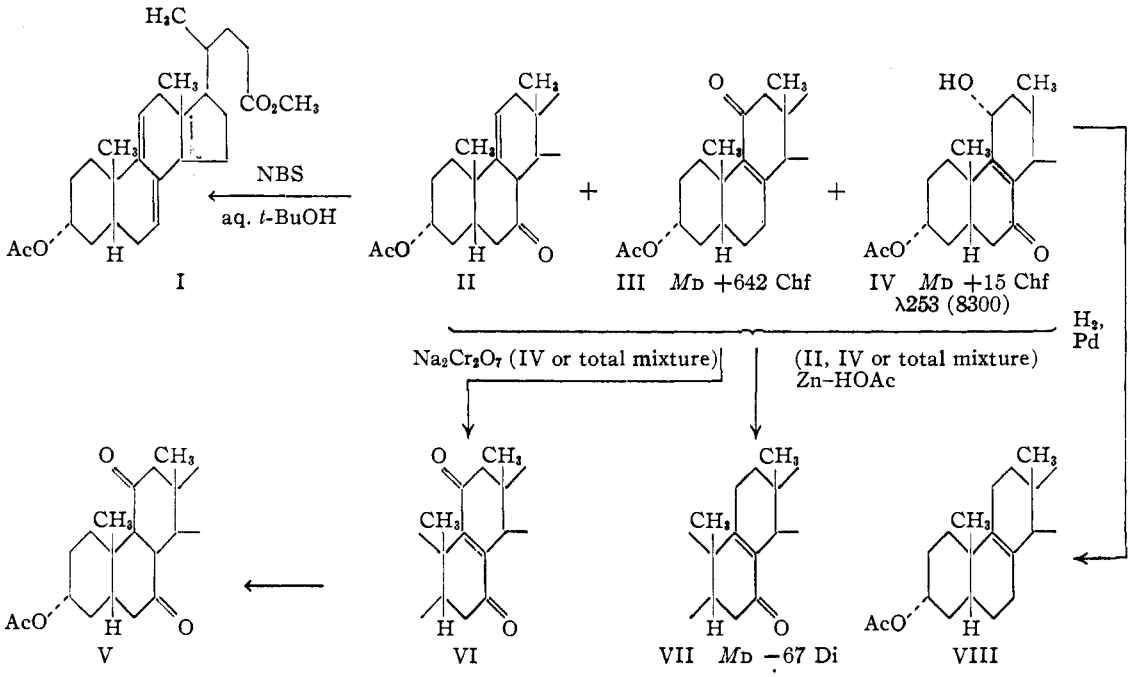
In addition to other oxidizing agents explored in our laboratory for the conversion of steroid Δ⁷·⁹⁽¹¹⁾-dienes into 11-oxygenated intermediates,[3,4] N-bromosuccinimide was investigated, first for the oxidation of methyl 3α-acetoxy-Δ⁷·⁹⁽¹¹⁾-choladienate (I). In a solution of *t*-butanol and dilute sulfuric 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

(1) Postdoctoral Research Fellow on an institutional grant from the American Cancer Society.

(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).



the same sequence of steps $\Delta^{7,9(11),22}$-ergostatrienyl acetate afforded 7,11-diketo-Δ^{22}-ergostenyl acetate[5] and $\Delta^{7,9(11)}$-cholestadienyl benzoate gave 7,11-diketocholestanyl benzoate.[4a] The last-named compound was also obtained by the same procedure directly from Δ^{7}-cholestenyl benzoate, which has been shown to be dehydrogenated to the $\Delta^{7,9(11)}$-diene by N-bromosuccinimide.[4b]

In a first exploration of the course of the reaction, we treated methyl 3α-acetoxy-$\Delta^{7,9(11)}$-choladienate (I) with excess N-bromosuccinimide as before and reduced the total crude product with zinc and acetic acid. Chromatography afforded only one crystalline product which was identified as methyl 3α-acetoxy-7-keto-Δ^{8}-cholenate (VII). We reported this result in a communication[6] and suggested that the product VII might come from an 11-bromo-Δ^{8}-ene-7-one. However, no such compound was encountered in a later experiment in which the total crude oxidation mixture was chromatographed without prior treatment with either zinc dust or silver nitrate. Three halogen-free products were isolated and characterized as having the structures II, III and IV. The non-conjugated unsaturated ketone II was identical with that described in paper I,[3] and the conjugated isomer (III) was identical with methyl 3α-acetoxy-11-keto-Δ^{8}-cholenate, described by Heymann and Fieser.[7] The third product was characterized as an 11-hydroxy-Δ^{8}-ene-7-one (IV) by analysis, oxidation to the Δ^{8}-ene-7,11-dione VI, hydrogenation with palladium in acetic acid to methyl 3α-acetoxy-Δ^{8}-cholenate (VIII) and reduction with zinc and acetic acid to the Δ^{8}-ene-7-one[3] VII. Since the $\Delta^{9,11}$-ene-7-one (II) is isomerized by zinc–acetic acid to the conjugated ketone VII,[3] II and IV are both precursors of the product (VII) isolated on reduction of the total oxidation mixture. Comparison of the molecular rotations of the 11-hydroxy compound IV and the parent Δ^{8}-ene-7-one (VII) shows that introduction of the 11-hydroxyl group is attended with a positive shift, $\Delta^{11-OH} = +82$ (Di *vs.* Chf). The fact that 7-keto-Δ^{8}-cholestene-3β,11α-diol[4a] differs from the parent 7-keto-Δ^{8}-cholestene-3β-ol[4a] by an increment that is also strongly positive ($\Delta^{11\alpha-OH} = +146$ Di) suggests that the 11-hydroxyl group of the bile acid derivative is also α-oriented. Although the rotational evidence is weakened by the differences between the two series in the configurations at C_3 and C_5 and in the nature of the functions at C_3, the conclusion is supported by the fact that the same enolone (IV) was obtained by perphthalic acid oxidation of the enol acetate of methyl 3α-acetoxy-7-keto-Δ^{8}-cholenate (see XI, paper I[3]), a reaction demonstrated by the Syntex group[8] to give Δ^{8}-ene-11α-ol-7-ones, at least in the allo series. The compounds of the two series differ in their behavior on hydrogenation. Our compound IV suffers hydrogenolysis with elimination of both oxygen functions (Pd–HOAc), whereas Δ^{8}-ene-11α-ol-7-ones of the allo series are reduced to the saturated 11α-ol-7-ones (Pd–EtOH).[8] The difference seems attributable to the different orientation at C_5 and not to a solvent effect, since paper II[4] reports hydrogenation of 7-keto-Δ^{8}-cholestenyl benzoate to the saturated 7-ketone (Pd–HOAc).

With regard to the question of mechanisms, the oxidation of a $\Delta^{7,9(11)}$-diene to a Δ^{8}-ene-11α-ol-7-one appears analogous to the oxidation of cholesterol to cholestane-3β,5α-diol-6-one with aqueous N-bromosuccinimide.[9]

(5) E. M. Chamberlain, W. V. Ruyle, A. E. Erickson, J. M. Chemerda, L. M. Aliminosa, R. L. Erickson, G. E. Sita and M. Tishler, THIS JOURNAL, **73**, 2396 (1951).

(6) L. F. Fieser, J. C. Babcock, J. E. Herz, W.-Y. Huang and W. P. Schneider, *ibid.*, **73**, 4053 (1951).

(7) H. Heymann and L. F. Fieser, *ibid.*, **73**, 5252 (1951).

(8) G. Stork, J. Romo, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 3546 (1951).

(9) L. F. Fieser and S. Rajagopalan, *ibid.*, **71**, 3938 (1949).

Experimental

Conversion of the Diene I to Methyl 3α-Acetoxy-7,11-diketocholanate (V, W.P.S.).—Methyl 3α-acetoxy-$\Delta^{7,9(11)}$-choladienate (430 mg., m.p. 148–149°) was dissolved in 50 cc. of *t*-butanol by warming and the solution was cooled, treated with 20 cc. of 0.05 *N* sulfuric acid (clear solution) and stirred in an ice-bath during addition of 470 mg. (2.6 equiv.) of N-bromosuccinimide in portions during 1/2 hr. After standing for 3/4 hr. a 1-cc. sample was withdrawn and found to show λ^{EtOH} 250 mμ (3,500). A trace of sodium dichromate was added as indicator and 5% silver nitrate was added until bromide precipitation was complete. Then 300 mg. more silver nitrate was added in a little water followed by 0.9 g. of chromic anhydride in 5 cc. of water and the mixture was stirred at 25° for 6 hr. The absorption gradually shifted toward the red as follows: 1 hr., λ^{EtOH} 250 mμ (5,100); 6 hr., 260 mμ (5,000). The mixture was filtered, diluted, extracted with ether and the yellow extract was washed neutral, dried and evaporated. Two 10-cc. portions of benzene were added and evaporated at reduced pressure and the oily residue was then dissolved in benzene and adsorbed onto 17 g. of alumina. Benzene eluted 23 mg. of material that gave a red fluorescence (ultraviolet light) on the column and probably contained dienones (λ^{EtOH} about 300 mμ). Then 1:9 ether–benzene eluted two yellow fractions, the first of which was evidently largely the Δ^8-7,11-diketone VI: 123 mg., m.p. 110–118°, λ^{EtOH} 272 mμ (6,500) and 29 mg. of semi-solid, λ^{EtOH} 272 mμ (5,200). Ether and methanol eluates were yellow oils giving a positive Beilstein test and absorbing around 250 mμ.

The two fractions exhibiting enedione absorption at 272 mμ were combined and refluxed with 1 g. of zinc in 9 cc. of acetic acid and 1 cc. of water with stirring for 0.5 hr. The colorless solution was filtered, the zinc washed with hot acetic acid and the combined solution diluted carefully with water to the point of crystallization. Long needles separated (119 mg.), m.p. 135–148°. Recrystallization from benzene–ligroin and finally from methanol, and reworking the mother liquors gave a total of 90 mg. (19% from I) of methyl 3α-acetoxy-7,11-diketocholanate, m.p. 160–162°. The analytical sample, recrystallized from methanol, formed flat blades or rods, m.p. 161–162°, $\alpha^{23}D$ +26.7 ± 0.5° Di.

Anal. Calcd. for $C_{27}H_{40}O_6$ (460.59): C, 70.40; H, 8.75. Found: C, 70.51; H, 8.96.

The m.p. of the material was undepressed on admixture with the sample described in paper I. The substance shows low intensity absorption around 280–290 mμ (500), probably due to the carbonyl groups. It crystallizes from benzene–ligroin in transparent, glassy prisms that crumble on drying in vacuum at 80°. Trials were also made of the reaction of 3α-acetoxy-$\Delta^{7,9(11)}$-choladienate with N-bromosuccinimide in aqueous acetone containing acetic acid, a trace of hydrobromic acid or acetic acid–sodium acetate.[10] In each case fractions showing absorption at 272 mμ were obtained, but in lower yield than in the procedure above; larger amounts of the dienone fraction (λ^{EtOH} 300 mμ, red fluorescence on the column) were found. The procedure of the N-bromosuccinimide reaction is similar to that employed by Sarett[11] for formation of bromohydrins from 11,12-enes.

Methyl 3α-Acetoxy-7-keto-Δ^8-cholenate (VII, W.-Y. H.).—An 860-mg. batch of the diene I was oxidized with N-bromosuccinimide (940 mg.) in aqueous *t*-butanol–sulfuric acid at 0° exactly as in the preceding experiment. The reaction mixture was let stand at 0° for 15 min. and sodium bisulfite was added to destroy excess reagent. Dilution with water and extraction with benzene afforded a bright yellow oil that was taken up in 20 cc. of acetic acid. After addition of 2 g. of zinc dust and 2 cc. of water, the mixture was heated at 50–70° with occasional swirling for 1 hr., diluted with water and extracted with ether. The washed (water, bicarbonate, brine) and dried extract on evaporation left an oil that was dissolved in 3 cc. of benzene and chromatographed on 30 g. of alumina. The eluates were collected in 30-cc. portions starting with 1:1 petroleum ether–benzene and the residues obtained on evaporation of the solvent were crystallized from methanol. Fractions 8–10, eluted by 94:6 to 90:10 benzene–ether and totalling 49 mg., melted in the range 159–177° and showed absorption at 254 mμ (3,260 to 7,350); later fractions were yellow oils giving a positive Beilstein test and absorbing at about 255 mμ. Fraction 8 (12 mg.) on recrystallization from methanol afforded pure VII, m.p. 179–180°, λ^{EtOH} 254, 310 mμ (7,600, 700); no depression in mixed m.p. with an authentic sample.

Anal. Calcd. for $C_{27}H_{40}O_5$ (444.59): C, 72.94; H, 9.07. Found: C, 72.68; H, 9.52.

Isolation of the Primary Oxidation Products II, III and IV (W.-Y. H.).—N-Bromosuccinimide (3.0 g.) was added in small portions to an ice-cooled solution of 3.4 g. of methyl 3α-acetoxy-$\Delta^{7,9(11)}$-choladienate (I) in 250 cc. of *t*-butanol and 150 cc. of 0.05 *N* sulfuric acid in 20 min. with occasional swirling. The resulting solution had a slightly yellow color that disappeared in about half an hour. An additional 244-mg. portion of NBS was added and the mixture let stand at 25° for 20 hr. Excess reagent was destroyed with sodium bisulfite and the mixture was diluted well with water and extracted with ether. The extract contained a considerable amount of *t*-butanol; it was washed several times with water, then with brine, dried, evaporated at reduced pressure below 40° and further evaporated after addition of benzene. The residue was dissolved in a small amount of benzene, adsorbed onto 80 g. of alumina and the column eluted with 100-cc. portions of solvents with the results

Fraction	Solvent[a]	Wt., mg.	M.p., °C.
1	1:1 PE–B	225	139–158
2	1:1 PE–B	240	120–124
3	3:1 PE–B	100	162–170
4	B	57	165–170
5	19:1 B–E	34	163–170
6	9:1 B–E	15	185–195
7	4:1 B–E	18	215–218
8	1:1 B–E	128	165–169
9–11	E	Oils	

[a] PE = Petroleum ether, B = benzene, E = ether.

Fraction 2 on three recrystallizations from methanol gave pure **methyl 3α-acetoxy-7-keto-$\Delta^{9(11)}$-cholenate** (II), m.p. 181–181.5°, α_D +20.4° Di, which showed no depression in mixed m.p. with the sample of paper I. The mother liquor of the first crystallization on further concentration deposited a crystalline product, m.p. 126–128°, α_D +112 ± 1° Chf, λ^{EtOH} 254 mμ (6,900), that appears to be slightly impure **methyl 3α-acetoxy-11-keto-Δ^8-cholenate** (III); a mixed m.p. with an authentic sample[7] (m.p. 129–130°) showed no depression.

Anal. Calcd. for $C_{27}H_{40}O_5$ (444.59): C, 72.94; H, 9.07. Found: C, 72.28; H, 8.78.

Fractions 3–7 showed absorption at 250–255 mμ not altered by treatment with sodium dichromate in acetic acid at 25° for 3 hr.

Fraction 8 on recrystallization from methanol gave methyl **3α-acetoxy-11α-hydroxy-7-keto-Δ^8-cholenate** (IV), m.p. 169–170°, α_D +3.2 ± 0.4° Chf, λ^{EtOH} 253 mμ (8,300), λ^{Chf} 2.78, 2.98, 5.87, 6.04, 8.0 μ.

Anal. Calcd. for $C_{27}H_{40}O_6$ (460.59): C, 70.40; H, 8.75. Found: C, 70.34; H, 8.55.

In a separate run, 860 mg. of diene I afforded 77 mg. of pure IV.

Oxidation of IV to **methyl 3α-acetoxy-7,11-diketo-Δ^8-cholenate** (VI) was accomplished by mixing solutions of 30 mg. of IV and 65 mg. of sodium dichromate dihydrate in 1-cc. portions of acetic acid at 25°. Dilution with water after 2 hr. gave a yellow crystalline product that on recrystallization from methanol afforded 25 mg. of pure V, m.p. 115–116°; λ^{EtOH} 271 mμ (7,900), undepressed on admixture with authentic material (paper I).

For reduction of IV to **methyl 3α-acetoxy-7-keto-Δ^8-cholenate** (VII) a mixture of 70 mg. of IV, 0.2 g. of zinc dust, 5 cc. of acetic acid and 0.5 cc. of water was heated on the steam-bath for 2 hr. Filtration and dilution with water gave a solid that on recrystallization from methanol yielded 33 mg. of VII, m.p. 181°, λ^{EtOH} 254 mμ (8,300); mixed m.p. with earlier sample (paper I) undepressed.

Hydrogenation of Methyl 3α-Acetoxy-11α-hydroxy-7-keto-Δ^8-cholenate (IV).—Hydrogenation of 90 mg. of IV in 10 cc. of acetic acid in the presence of 50 mg. of 10% palla-

(10) See J. v. Euw and T. Reichstein, *Helv. Chim. Acta*, **29**, 1913 (1946).

(11) L. H. Sarett, *J. Biol. Chem.*, **162**, 601 (1946).

dium–charcoal was conducted for 24 hr. Dilution of the filtered solution gave a solid product that after one recrystallization from methanol melted at 137–139° and gave a positive test with tetranitromethane. A second recrystallization gave a small amount of material, m.p. 142–143°, that gave no depression in m.p. when mixed with a sample of methyl 3α-acetoxy-Δ^8-cholenate (VIII, paper I).

7,11-Diketo-Δ^{22}-ergostenyl Acetate (W.P.S.).—The starting material was prepared from ergosterol *via* **5-dihydroergosteryl acetate**,[12,13] m.p. 180–182°, λ 282 mμ (370), which on dehydrogenation with mercuric acetate[14] afforded in 49% yield **$\Delta^{7,9(11),22}$-ergostatrienyl acetate**, m.p. 174–175.5°, α^{23}_D +28.7 ± 0.4° Di, λ^{EtOH} 236, 243, 251 mμ (15,900, 17,400, 11,500).

A solution of 500 mg. of this triene in 60 cc. of warm *t*-butanol was cooled and treated with 20 cc. of 0.05 *N* sulfuric acid, when a cloudy precipitate separated. The suspension was stirred in an ice-bath during addition over one-half hour of 500 mg. of N-bromosuccinimide; the precipitate dissolved after 420 mg. had been added. The pale yellow solution was stirred at 0° for 1 hr., 5% silver nitrate was added until precipitation of bromide was complete and 0.9 g. of chromic anhydride in a little water was added. After stirring for 4 hr. the mixture was processed as described in the bile acid series and the crude product, a yellow oil, was chromatographed on 18 g. of alumina. Petroleum ether–benzene eluted a small fraction showing red fluorescence on the column and then benzene eluted 170 mg. of yellow solid, m.p. 128–139°, λ^{EtOH} 270 mμ. Ether–benzene mixtures and ether eluted Beilstein-positive yellow glasses, λ^{EtOH} 245–255 mμ, and methanol–acetic acid eluted 140 mg. of brown oil.

The crude enedione fraction (170 mg.) was refluxed for 20 min. with 1 g. of zinc dust in 9 cc. of acetic acid and 1 cc. of water. Dilution of the filtered solution gave a gelatinous precipitate that when dried melted at 160–175°. Crystallization from methanol–acetone and finally from benzene–ligroin gave 75 mg. of the $\Delta^{8,22}$-7,11-diketone as colorless needles, m.p. 197–199°, α^{24}_D −29.5 ± 1° Chf, in agreement with the constants reported by the Merck group.[5]

Anal. Calcd. for $C_{30}H_{46}O_4$ (470.67): C, 76.55; H, 9.85. Found: C, 76.47; H, 9.77.

7,11-Diketocholestanyl Benzoate.[15]—$\Delta^{7,9(11)}$-Cholestadienyl benzoate (2 g.) was oxidized with N-bromosuccinimide and processed further exactly as described in the preceding example. Chromatography of the enedione fraction afforded, in the 3:1 petroleum ether–benzene eluate, 275 mg. (13%) of Beilstein-positive material that appeared to be impure 7,11-diketo-Δ^8-cholestene-3β-ol benzoate (paper II), m.p. 156–158°, α_D +46 ± 2° Di, λ^{EtOH} 269 mμ (6,300). Reduction with zinc dust and acetic acid gave pure 7,11-diketocholestane-3β-ol benzoate (paper II) as colorless needles, m.p. 197–199° (no depression in mixed m.p.).

In a second experiment 400 mg. of Δ^7-cholestenyl benzoate in 15 cc. of dioxane, 50 cc. of *t*-butanol and 15 cc. of 0.05 *N* sulfuric acid was treated at 0° with 750 mg. of N-bromosuccinimide. After further processing as before, chromatography gave 38 mg. of yellow needles, m.p. 136–140°. Zinc and acetic acid reduction gave 25 mg. of 7,11-diketocholestanyl benzoate, m.p. and mixed m.p. 199–201°.

Acknowledgments.—We are greatly indebted to the du Pont Company for supplies of 7-dehydrocholesterol and to Dr. Max Tishler of Merck and Co., Inc., for suggestions and coöperation.

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(13) S. v. Reichel, *Z. physiol. Chem.*, **226**, 146 (1934).
(14) A. Windaus and E. Auhagen, *Ann.*, **472**, 185 (1929).
(15) Experiments by Josef E. Herz.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

Studies of Configuration. II. The Configurations of the 3-Methylcyclohexylamines

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One pure isomer of 3-methylcyclohexanecarboxylic acid has been converted by a series of reactions which retain configuration to *cis*-1,3-dimethylcyclohexane and to *cis*-3-methylcyclohexylamine. The amine thus obtained is that which has previously been assigned the "*trans*" configuration. Thus another example of the inversion of configuration in the case of 1,3-disubstituted cyclohexane derivatives is established.

In the first paper of this series[1] it has been shown that the previous assignments of configuration of 3-methylcyclohexanol are inverted and must therefore be revised. It seemed likely that a similar situation prevailed with respect to the isomeric 3-methylcyclohexylamines, and it is the purpose of the present report to present evidence bearing on this problem.

Wallach[2] first prepared 3-methylcyclohexylamine (optically active) both by the reaction of ammonium formate with pulegone and by the reduction of 3-methylcyclohexanone oxime with sodium and alcohol. Knoevenagel and Klages[3] prepared a *dl*-3-methylcyclohexylamine. However, the first serious consideration of the preparation and characterization of the *cis* and *trans* isomer was given by Skita[4] who studied reduction of the toluidines and acetotoluides under a variety of conditions. The isomer which he called "*cis*," obtained by reduction in acid media, gave a benzamide, m.p. 95–96°, and that which he called "*trans*," by reduction in neutral or alkaline media, gave a benzamide, m.p. 126–127°. Skita comments on the physical properties of the two isomers by saying that the isomeric 3-methylcyclohexylamines are not in agreement with von Auwers[5] rule of relative density and index of refraction. Von Auwers[6] also discusses the isomer problem here.

More recently Mousseron[7] has reported numerous derivatives for optically active *cis*- and *trans*-3-methylcyclohexylamines.

The correlation of the amines with other compounds of known stereochemistry has not been accomplished. However, the reaction of these amines with nitrous acid[4,8] is suggestive. In light of the recent revision of the configuration of

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