in dilute dioxane containing one drop of acetic acid, the material which precipitated gradually over several days was a sharp melting mixture (m.p. 150–150.5°) identified by infrared and ultraviolet absorptions as stigmastadienone and the starting enamine.

When the conjugate acids of enamines were treated with dilute alkali, the absorption near 278 mμ was rapidly replaced by the absorption of the Δ^4-3-ketone near 240 mμ. The same change occurred at a somewhat slower rate when enamines were treated directly with alkali.

Recovery of Enamines from Their Conjugated Acids.—An ether suspension of testosterone pyrrolidinyl enamine hydrochloride was treated with excess piperidine and stirred for 10 minutes. The mixture was filtered and the filtrate taken to dryness *in vacuo*. Trituration of the residue with methanol gave testosterone pyrrolidinyl enamine.

Ultraviolet spectra and rotations of the hydrochloride salts of enamines of Δ^4-3-ketones were not altered by addition of triethylamine, but addition of diethylamine or piperidine converted the conjugate acids to the free bases.

Separation of Progesterone from Pregnenolone Using Enamine Salts.—A mixture of 3.14 g. of progesterone and 3.16 g. of pregnenolone was dissolved in 50 ml. of benzene. The solution was treated with 1.67 ml. of pyrrolidine and 20 mg. of *p*-toluenesulfonic acid and stirred at reflux under a water trap for 2.25 hours, during which time 0.18 ml. of water was collected. The reaction mixture was evaporated to dryness *in vacuo* and the residue redissolved in 50 ml. of a mixture of benzene–ether (1:1). An ether solution of anhydrous hydrogen chloride was added slowly with stirring until no further precipitation occurred. The insoluble enamine hydrochloride of progesterone, A, was recovered by filtration, washed with ether and dried, and the filtrate saved.

The hydrochloride A was dissolved in 100 ml. of methanol and 25 ml. of 5% aqueous sodium hydroxide was added. The solution was warmed at 50° for 20 minutes, acidified with glacial acetic acid, and concentrated to dryness *in vacuo*. The residue was recrystallized from dilute methanol to give 2.79 g. of progesterone, m.p. 120–129°, identical with authentic progesterone by melting point and infrared spectrum.

The filtrate B was washed free of acid. Evaporation of the solvent gave 2.98 g. of good quality pregnenolone, m.p. 187–190°, identified by comparison of melting point and infrared spectrum.

KALAMAZOO, MICHIGAN

[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF ARTHRITIS AND METABOLIC DISEASES, NATIONAL INSTITUTES OF HEALTH]

The Anthrasteroid Rearrangement. IV. The Preparation of Several New Anthrasteroids and Some Observations on the Dehydrobromination of 7-Bromo-Δ^5-steroids[1]

BY WILLIAM R. NES, ROBERT B. KOSTIC AND ERICH MOSETTIG

RECEIVED AUGUST 19, 1955

Anthracholestatetraene, anthracholestatriene, methyl anthrabisnorcholatetraenate and methyl anthrabisnorcholatrienate have been prepared from the corresponding steroidal 5,7,9(11)-trienes. The molecular rotations of these anthrasteroids and those of the corresponding derivatives in the ergosterol series exhibit consistent ΔM_D values for hydrogenation of the conjugated double bond. This is interpreted as evidence for a common position of the conjugated double bond in the various anthrasteroids and, consequently, for a dominant pathway for the over-all conversion. Rearrangement in the 17-ketosteroid series gave in poor yield the corresponding chloroanthrastatrienone. This compound exhibited the normal ultraviolet spectrum of anthrastatrienes and possessed an infrared spectrum which showed the presence of an unconjugated carbonyl group. This is considered as corroborating earlier evidence that anthrasteroids possess an aromatic B-ring and not an aromatic C-ring. A study of the influence of temperature on the dehydrobromination of 7-bromocholesteryl acetate revealed that the yield of $\Delta^{5,7}$-steroid decreases with decreasing temperature while the formation of the 4,6-isomer was not appreciably affected. The isocaproates of cholesterol and dehydroepiandrosterone gave better yields of the corresponding $\Delta^{5,7}$-steroid than did the acetates.

The application of the anthrasteroid rearrangement in the ergosterol and lumisterol[3] series has been described previously.[1a] The present paper deals with the extension of this reaction to the 5,7,9(11)-trienes derived from cholesterol, methyl 3β-hydroxybisnor-5-cholenate and dehydroepiandrosterone.

Applied to compounds I and II, the rearrangement proceeded smoothly and the corresponding anthrasteroids III and IV were obtained. These were reduced to the trienes V and VI, respectively, with platinum oxide in ethyl acetate–acetic acid. Sufficient material was available only in the cholesterol series to carry out dehydrogenation experiments, and anthracholestatetraene (III) was converted readily to an oily anthracene derivative by heating with palladium-on-charcoal.

The molecular rotations of the new anthrasteroids are compared with those of anthraergostatetraene and anthraergostatriene in Table I, and the increments for hydrogenation of the conjugated double bond have been calculated. The consistency of the individual values (+244° ± 6°) suggests strongly that the various samples of the anthrasteroids were homogeneous and, moreover, that all three types have a common position for the conjugated double bond. This is significant for answering the question of the pathway for the over-all conversion, since there is the possibility that more than one unsaturated steroidal intermediate could undergo rearrangement to give isomeric anthrasteroids. The fact, however, that the 5,7,9(11)-trienes appear to be converted principally or solely to but one isomer indicates the predominance of a single pathway.

TABLE I

ΔM_D FOR HYDROGENATION

Side chain related to	M_D of anthrasteroid containing (A) a conjugated double bond	(B) no conjugated double bond	M_D(B) − M_D(A)
Ergosterol	−163°[a]	+80°[b]	+243°
Cholesterol	−128	+110	+238
Methyl bisnorcholenate	−152	+98	+250

[a] Calcd. for M_D of anthraergostapentaene[1a] using an increment of +103° for saturation of the Δ^{22}-bond (D. H. R. Barton, J. D. Cox and N. J. Holness, *J. Chem. Soc.*, 1771 (1949)). [b] See ref. 1a.

(1) (a) Part I, W. R. Nes and E. Mosettig, THIS JOURNAL, **76**, 3182 (1954); (b) part II, *ibid.*, **76**, 3186 (1954); (c) part III, W. R. Nes, *ibid.*, **78**, 193 (1956).

The rearrangement of 5,7,9(11)-androstatrien-3β-ol-17-one isocaproate (VII) gave two products each in a poor yield. The ultraviolet spectrum of the crude reaction mixture indicated that the expected keto-tetraene had not been formed in the usual *ca.* 50% yield. Elemental analysis of the two compounds isolated showed that the oxygen function at C-3 had been eliminated, and the infrared spectra of both compounds showed a band at 5.74 μ for the unconjugated carbonyl group in the five-membered ring. However, neither compound had the infrared or ultraviolet spectrum characteristic of the expected keto-tetraene.[2] The two products were isolated by chromatography. The first one (VIII) to be eluted may be an aromatic compound, for it showed a number of bands in the 11–15 μ region one of which was particularly strong at 12.76 μ. (Anthraergostapentaene[1a] and compounds I and II exhibit a strong band near 12.3 μ.[2]) The ultraviolet spectrum (Fig. 1) is suggestive of the absorption of the expected aromatic tetraene but is shifted 10–15 mμ toward the red. Lack of material prevented further study on the structure of this compound. The second product (IX) to be eluted was a chloro derivative. The empirical formula ($C_{19}H_{23}OCl$) and the infrared and ultraviolet spectra (λ_{max} 11.60 μ; λ_{max} 281.5, 276.5 and 272.0 mμ, ϵ 774, 634 and 720) were in agreement with the structure of a chloroanthrastatrienone (IX).[2] It is of interest that both the ultraviolet and infrared spectra of this compound show that the carbonyl group is unconjugated which is an additional proof[1a] that anthrasteroids possess an aromatic B-ring and not an aromatic C-ring. If ring C were aromatic, conjugation of the carbonyl group with the benzenoid nucleus in IX should be expected.

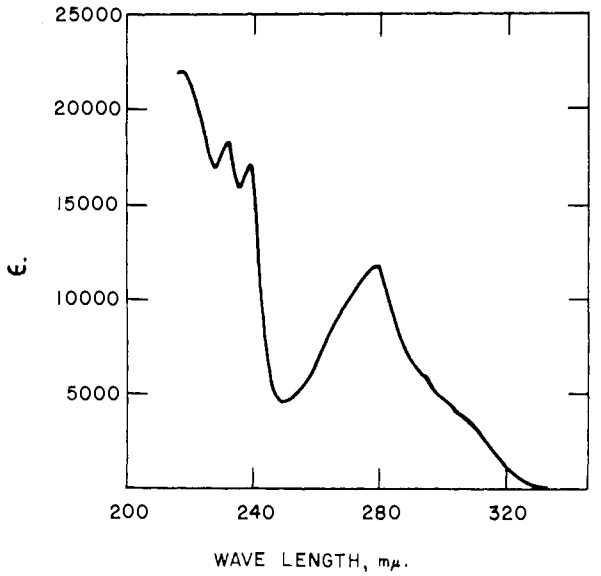


Fig. 1.

The 5,7,9(11)-trienes used in this investigation were prepared from the corresponding 5,7-dienes by dehydrogenation with mercuric acetate. The 5,7-dienes[3] were prepared by bromination of the Δ^5-compound with N-bromosuccinimide and subsequent dehydrobromination. Several groups of investigators have shown that the 5,7-diene is accompanied by the 4,6-isomer.[4] We decided to study the influence of temperature on the ratio of these isomers formed in the dehydrobromination reaction and found that in the range of 110–140°, when the reaction was carried out in a dilute *s*-collidine solution, the 5,7-isomer was formed in a somewhat greater amount than was the 4,6-isomer. At lower temperatures (down to 37°) the content of the 5,7-isomer decreased by a factor of ten, but the content of the 4,6-isomer remained essentially constant. The total percentage of conjugated dienes in the reaction mixture was always less than the percentage of recovered *s*-collidine hydrobromide in the temperature range of 37–80°.[5] Our experiments indicated that a minimum temperature of near 100° is required to give fair yields of the conjugated 5,7-isomer. At temperatures above 160° the 5,7-diene content remained at 50–65%, but the 4,6-isomer which formed was pyrolyzed to a hydrocarbon ($C_{27}H_{42}$) (m.p. 72–74°, $[\alpha]_D$ +3°, λ_{max} 296, 304 and $\lambda_{infl.}$ 320 mμ, ϵ 14,380, 13,640 and 8,720; Fig. 2); this is apparently 2,4,6-cholestatriene.[6] Unfortunately, we were not able to chromatograph the mixture on alumina and recover the 5,7-sterol in the anticipated yield (based on the ultraviolet spectrum of the reaction mix-

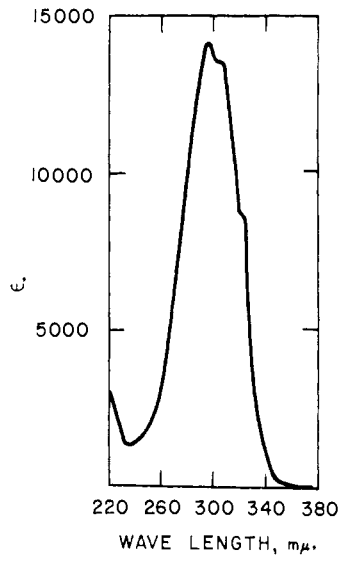


Fig. 2.

(2) For a detailed discussion of the infrared and ultraviolet spectra of anthrasteroids and other aromatic compounds see I. Scheer, W. R. Nes and P. Smeltzer, *ibid.*, **77**, 3300 (1955).

(3) Methyl 3β-acetoxy-5,7-choladienate was purchased from the Glidden Co.

(4) (a) A. E. Bide, H. B. Henbest, E. R. H. Jones, R. W. Peevers and P. A. Wilkinson, *J. Chem. Soc.*, 1783 (1948); (b) S. Bernstein, L. J. Binovi, L. Dorfman, K. J. Sax and Y. SubbaRow, *J. Org. Chem.*, **14**, 433 (1949).

(5) K. Tsuda, K. Arima and R. Hayatsu [THIS JOURNAL, **76**, 2933 (1954)] have found that 7-bromocholesterol can give rise to an unconjugated diene. The presence of such diene may account for our results.

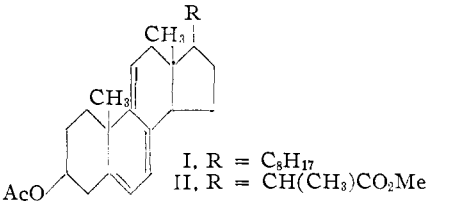
(6) J. Schmutz, H. Schaltegger and M. Sanz, *Helv. Chim. Acta*, **34**, 1111 (1951), have prepared 2,4,6-cholestatriene and proved its structure. The compound (m.p. 71–72°, $[\alpha]_D$ −14°) exhibits a maximum at 306 mμ, ϵ 15,700, and two inflections at 295–300 mμ and *ca.* 320 mμ, respectively. It is therefore most likely that our sample contains an impurity absorbing near 296 mμ.

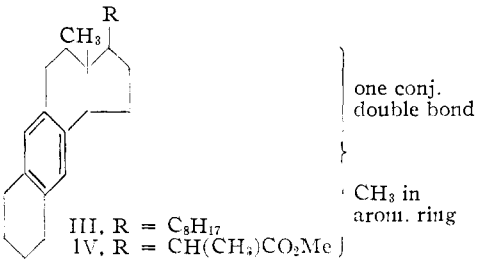
ture). The hydrocarbon separated without difficulty, but the eluted sterol was impure. Thus, the pyrolysis technique could not be used as a method for separating the original mixture of isomeric sterols. We have also tried other amines in the dehydrobromination reaction but have been unable to obtain significant correlations beyond the fact that dimethylaniline appeared to promote the formation of the hydrocarbon. A study of various esters of cholesterol revealed that some improvement in the yield of the 7-dehydro compound could be obtained by using the isocaproate. We have been able to obtain pure 7-dehydrocholesteryl isocaproate in an over-all yield of 35% from the Δ^5-steroid. The use of the corresponding acetate gave significantly lower yields of isolable, pure 7-dehydrosteroid. When the isocaproate of dehydroepiandrosterone was brominated and dehydrobrominated, pure 5,7-androstadien-3β-ol-17-one isocaproate was also obtained in a 30–40% yield.

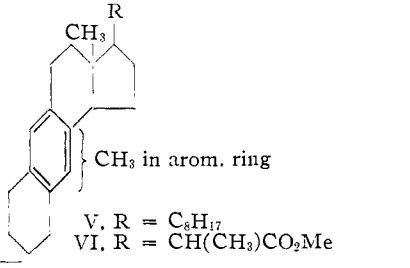
Experimental[7]

Cholesteryl Isocaproate.—The ester, prepared in the usual manner from cholesterol, pyridine and isocaproyl chloride, formed fine needles, m.p. 98–99°.

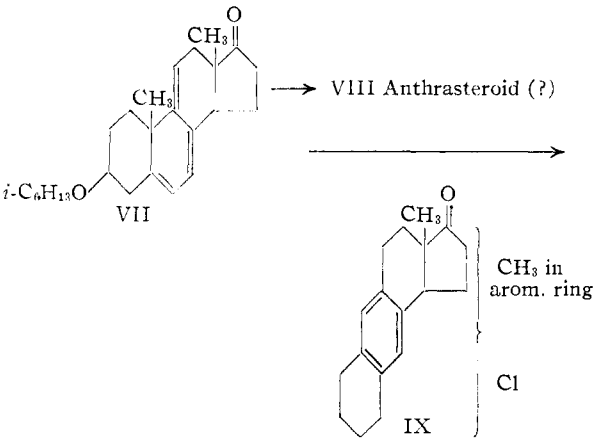
Anal. Calcd. for $C_{33}H_{56}O_2$: C, 81.75; H, 11.65. Found: C, 81.66; H, 11.43.







(7) All melting points were determined on a Kofler block and are recorded as read. Rotations were determined in chloroform at 20° in *ca.* 1% solution. Ultraviolet spectra were determined in absolute ethanol (unless otherwise noted) on a Cary recording spectrophotometer with the assistance of Mrs. Anne Wright. Infrared spectra were determined in carbon disulfide solution on a Perkin–Elmer double beam spectrophotometer by Mr. H. K. Miller. Microanalyses were performed in the Analytical Service Laboratory of this Institute under the direction of Dr. William C. Alford. The petroleum ether used in this investigation was purified by shaking extensively with concentrated sulfuric acid; after being washed and dried, it was distilled and the fraction boiling at 30–60° was used (unless otherwise noted). The alumina for chromatography was purchased from the Aluminum Company of America and was Grade F-20.



7-Dehydrocholesteryl Isocaproate.—A solution of 9.85 g. of cholesteryl isocaproate in 116 ml. of petroleum ether (b.p. 60–71°) was refluxed 15 minutes with 4.6 g. of N-bromosuccinimide, the heat being supplied by two General Electric RSP-2 photospot lamps. The mixture was cooled, filtered and the filtrate evaporated to dryness in a vacuum. The residual oil was taken up in 30 ml. of xylene and added dropwise during 20 minutes to a solution of 60 ml. of xylene and 12 ml. of *s*-collidine which was refluxing at 138°. The reaction mixture was refluxed an additional 10 minutes, cooled and the collidine hydrobromide filtered off. The filtrate was evaporated in a vacuum to dryness, and the residual oil was crystallized from acetone–methanol and yielded crystals mixed with oil. Three recrystallizations from acetone gave 3.45 g. (35%) of plates melting at 99–101° resolidifying at 108° and remelting at 112–116°, $\lambda_{max}^{isooctane}$ 271, 282 and 294 mμ (ϵ 10,850, 11,370 and 6,480). The analytical sample melted at 101–103°, resolidified at 108° and remelted at 114–118°, $\lambda_{max}^{isooctane}$ 271, 282 and 294 mμ (ϵ 11,400, 11,900 and 6,800).

Anal. Calcd. for $C_{33}H_{54}O_2$: C, 82.09; H, 11.28. Found: C, 82.15; H, 11.41.

Bernstein, *et al.*,[4b] have reported a yield of 24% for pure 7-dehydrocholesteryl acetate. However, in repeated experiments in this Laboratory by essentially the same procedure as used by these authors we were unable to obtain a yield as high as this. The over-all yield of 7-dehydrocholesteryl acetate obtained by the 3,5-dinitrobenzoate technique of Bide, *et al.*,[4a] also failed to give yields comparable with those obtained with the isocaproate.

5,7,9(11)-Cholestatrien-3β-ol Acetate (I).—To a refluxing solution of 2.0 g. of 7-dehydrocholesteryl acetate in 10 ml. of carbon tetrachloride and 33 ml. of absolute ethanol was added a hot solution of 4.7 g. of mercuric acetate, 4.7 ml. of glacial acetic acid and 13 ml. of absolute ethanol. The mixture was refluxed for 3 hours, slowly cooled for an additional 1.25 hours, and filtered. The filtrate was diluted to 180 ml. with water and extracted with carbon tetrachloride. The organic layer was washed with water, dried over sodium sulfate and evaporated to dryness. The residual oil gave gummy crystals from acetone–methanol. Two recrystallizations from methanol gave 0.3 g. (15%) of plates, m.p. 88–89°, lit.[8] m.p. 88.5–90.5°.

Anthracholestatetraene (III).—5,7,9(11)-Cholestatrien-3β-ol acetate (I) (7.7 g.) was dissolved in 170 ml. of a 0.06 *M* solution of hydrogen chloride in chloroform at room temperature. After one hour the reaction solution was washed with Na_2CO_3 and water, dried over Na_2SO_4 and evaporated to dryness *in vacuo*. The residual oil was adsorbed on a column of 130 g. of alumina. The fractions eluted with 600 ml. of a 2% solution of benzene in petroleum ether were collected and evaporated to dryness. The oil residue was crystallized from acetone–methanol to give 2.0 g. of needles, m.p. 109–112°. Two recrystallizations from acetone–methanol gave 1.28 g. of needles, m.p. 116–117°, $[\alpha]_D$ −34°, $\lambda_{max}^{isooctane}$ 222, 227, 266, 296 and 308 mμ (ϵ 23,630, 25,200, 16,700, 2,490 and 2,060).

(8) R. Antonucci, S. Bernstein, D. Giancola and K. J. Sax, *J. Org. Chem.*, **16**, 1159 (1951).

Anal. Calcd. for $C_{27}H_{40}$: C, 88.94; H, 11.06. Found: C, 88.92; H, 10.91.

Anthracholestatriene (V).—One gram of the tetraene III in a solution of 35 ml. of ethyl acetate and 16 ml. of glacial acetic acid in the presence of 200 mg. of platinum oxide was hydrogenated at room temperature and atmospheric pressure. One molecular equivalent of hydrogen was absorbed in 20 minutes. The catalyst was filtered and the filtrate evaporated to dryness in a vacuum. The resulting material was purified by chromatography on alumina and yielded 0.57 g. of colorless prisms, m.p. 71–73°, $[\alpha]_D$ +30°, $\lambda_{max}^{isooctane}$ 272.5, 277.5 and 282.5 mμ (ε 690, 541 and 647).

Anal. Calcd. for $C_{27}H_{42}$: C, 88.45; H, 11.55. Found: C, 88.58; H, 11.69.

Dehydrogenation of Anthracholestatetraene.—A mixture of 1.4 g. of III with 0.7 g. of 5% palladium–charcoal catalyst was heated at 300° for 3.5 hours. The reaction mixture was cooled and extracted with ether. The ethereal extract was filtered through Celite, and the filtrate was evaporated to dryness. The residual oil, 1.6 g., was adsorbed on a column of alumina in a solution of petroleum ether. The fractions eluted with 3 l. of 5% benzene–petroleum ether were combined, evaporated to dryness and rechromatographed on a column of alumina. The fractions eluted with 2.1 l. of 5% benzene–petroleum ether were combined and evaporated to dryness. The residual oil, 0.31 g., did not crystallize; $\lambda_{max}^{isooctane}$ 227, 234, 262, 338, 354, 372 and 391 mμ (ε 16,550, 17,550, 165,000, 2,750, 5,000, 7,420 and 7,520).

Anal. Calcd. for $C_{26}H_{32}$: C, 90.64; H, 9.36. Found: C, 90.19; H, 9.37.

Methyl 3β-Acetoxybisnor-5,7,9(11)-cholatrienate (II).—To a refluxing solution of 7.0 g. of methyl 3β-acetoxybisnor-5,7-choladienate[8] in 120 ml. of absolute ethanol and 35 ml. of carbon tetrachloride was added a hot solution of 22 g. of mercuric acetate, 22 ml. of glacial acetic acid and 60 ml. of absolute ethanol. The mixture was refluxed for 2 hours and then cooled slowly for 1.5 hours; the precipitate of mercurous acetate was filtered off. The filtrate was diluted with 4 volumes of water and the organic layer separated, washed twice with water, dried over sodium sulfate and evaporated to dryness in a vacuum. The oily residue was crystallized from methanol–water to give 1.7 g. of fine needles, m.p. 110–120°. Three recrystallizations from methanol–water gave 0.86 g. (12%) of thin needles, m.p. 124–125°, $\lambda_{max.}$ 311, 324 and 339 mμ (ε 10,500, 11,850 and 7,300), $[\alpha]_D$ +230°.

Anal. Calcd. for $C_{25}H_{34}O_4$: C, 75.34; H, 8.60. Found: C, 75.45; H, 8.87.

Methyl Anthrabisnorcholatetraenate (IV).—To a solution of 0.7 g. of II in 14 ml. of chloroform was added 6 ml. of a 0.4 *M* solution of HCl in chloroform. After standing at room temperature for 1 hour, the reaction mixture was washed with saturated sodium carbonate and water, dried over sodium sulfate and evaporated in a vacuum to dryness. The residual oil was chromatographed on a column of alumina. The fractions eluted with 135 ml. of petroleum ether–benzene (3/2) were combined, evaporated to dryness and the residual oil crystallized from methanol–water to give 0.18 g. of needles, m.p. 145–148°. Two recrystallizations from methanol gave 0.14 g. of needles, m.p. 154–155°, $[\alpha]_D$ −45°, 221, 227, 266, 296 and 308 mμ (ε 24,750, 26,300, 17,000, 2,400 and 1,980).

Anal. Calcd. for $C_{23}H_{30}O_2$: C, 81.61; H, 8.93. Found: C, 81.41; H, 9.04.

Methyl Anthrabisnorcholatrienate (VI).—A solution of 100 mg. of the tetraene IV in 5 ml. of ethyl acetate and 1.6 ml. of glacial acetic acid containing 20 mg. of platinum oxide catalyst was hydrogenated at 25° and atmospheric pressure. After one molecular equivalent of hydrogen had been absorbed, the catalyst was filtered off and the filtrate evaporated to dryness. The residue was chromatographed on alumina. The fractions eluted with 210 ml. of petroleum ether–benzene (3/2) were combined and evaporated to dryness. One crystallization from acetone–water and two recrystallizations from methanol gave 30 mg. of needles, m.p. 110–111°, $[\alpha]_D$ +29°, $\lambda_{max}^{isooctane}$ 272.5, 277 and 282 mμ (ε 705, 584 and 744).

Anal. Calcd. for $C_{23}H_{32}O_2$: C, 81.13; H, 9.47. Found: C, 80.82; H, 9.56.

Dehydroepiandrosterone Isocaproate.—Dehydroepiandrosterone was heated with pyridine and isocaproyl chloride for one hour at 100°. The product was isolated in the usual manner which yielded the ester as needles, m.p. 108–109°.

Anal. Calcd. for $C_{25}H_{38}O_3$: C, 77.67; H, 9.91. Found: C, 77.42; H, 10.01.

5,7-Androstadien-3β-ol-17-one Isocaproate.—A solution of 25 g. of dehydroepiandrosterone isocaproate in 450 ml. of petroleum ether and 50 ml. of carbon tetrachloride was refluxed for 15 minutes in the presence of 14.4 g. of N-bromosuccinimide.[9] The mixture was cooled, filtered and the filtrate evaporated to dryness at 25° in a vacuum. The semi-crystalline residue was dissolved in 120 ml. of xylene and added dropwise during 30 min. to a refluxing solution of 175 ml. of xylene and 20 ml. of *s*-collidine. The mixture was refluxed an additional 30 minutes, cooled, and filtered. The *s*-collidine hydrobromide was washed with petroleum ether and dried; wt. 11.1 g. (85%). The filtrate was evaporated to dryness in a vacuum, and the oily residue was crystallized from 30 ml. of methanol and 5 ml. of water to yield crystals mixed with oil. Three recrystallizations from methanol gave 10.4 g. (41%) of clusters of flat needles, m.p. 76–79°, $\lambda_{max.}$ 272, 282 and 293 mμ (ε 10,300, 10,760 and 6,280). A small portion was recrystallized twice more from methanol to give flat needles, m.p. 75–77°, $\lambda_{max.}$ 270, 281 and 293 mμ (ε 10,330, 10,800 and 6,270).

Anal. Calcd. for $C_{25}H_{36}O_3$: C, 78.08; H, 9.44. Found: C, 77.73; H, 9.54.

5,7,9(11)-Androstatrien-3β-ol-17-one Isocaproate (VII).—To a solution of 7.0 g. of 5,7-androstadien-3β-ol-17-one isocaproate in 100 ml. of absolute ethanol was added a hot solution of 20.3 g. of mercuric acetate, 100 ml. of absolute ethanol and 4.5 ml. of glacial acetic acid. The mixture was refluxed for 1.3 hr., cooled slowly for 1.5 hours and filtered. The filtrate was diluted with water and extracted twice with carbon tetrachloride. The organic layer was washed twice with water, dried over sodium sulfate and evaporated to dryness. The oily residue was crystallized from methanol–water and gave crystals mixed with oil. Four crystallizations from methanol gave 1.22 g. of needles, m.p. 134–135°, $\lambda_{max.}$ 321, λ_{infl} 311 and 336 mμ (ε 9,950, 11,250 and 6,950).

Anal. Calcd. for $C_{25}H_{34}O_3$: C, 78.49; H, 8.96. Found: C, 78.41; H, 9.08.

5,7,9(11)-Androstatriene-3β,17β-diol.—When 1.0 g. of VII was stirred for 50 minutes in 75 ml. of ether containing 2.0 ml. of 2.4 *M* ethereal lithium aluminum hydride, a voluminous precipitate formed. Ethyl acetate (3.0 ml.) and then water (2.0 ml.) was added and the precipitate was filtered off. The filtrate was concentrated on the steam-bath and finally refrigerated at −20°. The resulting colorless crystals, 0.57 g., after recrystallization from acetone–ether, melted at 176–180°. Recrystallization twice from acetone–methanol raised the melting point to 187–190° (opaque at 125–130°), lit.[8] m.p. 188–191°. The compound is reported[8] only as a solvate. It was obtained anhydrous by drying at 140° in a vacuum for 1.5 hours. The compound so obtained exhibited maxima at 312, 324 and 338 mμ (ε 9,500, 10,800 and 6,700).

Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.99; H, 9.39.

Rearrangement of 5,7,9(11)-Androstatrien-3β-ol-17-one Isocaproate (VII).—One hundred ml. of a 0.144 *M* solution of hydrogen chloride in chloroform was cooled to 20° and 1.92 g. of the ester was added. After 1.5 hours the mixture was evaporated to dryness at reduced pressure and the oily residue was adsorbed on a column of alumina. Elution with 600 ml. of benzene–petroleum ether (3/2) yielded an oil which crystallized from methanol–water as plates, wt. 50 mg., m.p. 97–101°. Four recrystallizations from methanol–water gave 20 mg. of VIII as plates, m.p. 106–107°, $\lambda_{max.}$ 231, 239 and 279 mμ (ε 18,300, 17,000 and 11,700) (Fig. 1), $\lambda_{max.}$ 5.74 (strong), 12.45 (moderate), 12.76 (strong), 13.71 (moderate) and 14.15 μ (moderate).

Anal. Calcd. for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 85.78; H, 8.30.

The second fraction was obtained by elution with 1 l. of benzene–petroleum ether (1/1). Evaporation of the sol-

(9) The N-bromosuccinimide was purified by recrystallization from hot glacial acetic acid.

vent in a vacuum gave an oil which did not crystallize. The oil was rechromatographed on a column of alumina, and the fractions eluted with 65 ml. of a petroleum ether–benzene mixture (7/3) yielded an oil which gave by treating with acetone–methanol crystals mixed with oil. Repeated recrystallizations from acetone–methanol gave 6 mg. of IX as fine needles, m.p. 129–130°, $\lambda_{max.}$ 272, 276.5 and 281.5 mμ (ϵ 720, 634 and 774), $\lambda_{max.}$ 5.74 (strong), 11.44 (moderate) and 11.60 μ (moderate).

Anal. Calcd. for $C_{19}H_{23}OCl$: C, 75.35; H, 7.65; Cl, 11.71. Found: C, 75.21; H, 7.47; Cl, 11.17.

The Influence of Temperature on the Dehydrobromination of 7-Bromocholesterol.—Cholesteryl acetate was brominated in a solution of refluxing petroleum ether using 120% of the calculated amount of freshly crystallized and dried N-bromosuccinimide.[9] General Electric RSP-2 Photospot lamps were used for illumination. After the mixture had refluxed for 15 min., it was cooled, filtered and evaporated to dryness at reduced pressure. The resulting crude 7-bromocholesterol was dissolved in the appropriate solvent (solvent/steroid = 4/1) and added dropwise to a hot, well-mixed solution of the same amount of solvent and a 300% excess of *s*-collidine (distilled from sodium). The approximate times required to obtain the percentage recoveries of collidine hydrobromide indicated below were determined empirically by carrying out the reactions for various intervals of time and weighing the recovered *s*-collidine hydrobromide. In the experiments listed below the percentage of conjugated diene or triene was measured spectrophotometrically using the maxima at 239, 282 and 305 mμ for the $\Delta^{4,6}$-, $\Delta^{6,7}$- and the $\Delta^{2,4,6}$-compounds, respectively.

When the dehydrobromination was carried out at 140° in the presence of dimethylaniline instead of *s*-collidine, none of the 4,6-isomer could be detected spectrophotometrically in the reaction mixture. However, strong absorption occurred in the 296–320 mμ region which was not present when *s*-collidine was used at the same temperature. This latter absorption is presumably attributable to 2,4,6-cholestatriene. The 5,7-diene was observable spectrophotometrically and apparently was not affected by the dimethylaniline.

Temp., °C.	Solvent	Time, hr.	No. of runs	C_8H_{12}-BrN recovd., %	% 4,6-diene	% 5,7-diene	% 2,4,6-triene	Total unsatd. mater., %
37	Toluene	99	1	100	60	6.3	..	66
55	Toluene	42	1	84	48	10	..	58
55	Toluene	19	1	79	53	8.3	..	61
68	Hexane	24	1	81	60	9.2	..	69
80	Benzene	5	2	89	65	17	..	72
91	Toluene	3	2	87	62	19	..	81
109	Toluene	2	4	86	38	51	..	89
140	Xylene	1	3	90	41	55	..	96
167	Decalin	0.5	2	96	46	44	13	103
174	Decalin	0.5	4	94	14	45	28	87

2,4,6-Cholestatriene.—Seventy-five grams of cholesteryl acetate was brominated with N-bromosuccinimide and dehydrobrominated with *s*-collidine in the manner described under the preparation of 7-dehydrocholesteryl acetate. After the *s*-collidine hydrobromide had been filtered off, the filtrate was evaporated in a vacuum on the steam-bath. A qualitative ultraviolet analysis on the residual oil showed characteristic peaks at 272, 282 and 295 mμ for 7-dehydrocholesteryl acetate and new peaks at 310 and 320 mμ; there was little or no absorption present at 239 mμ for the 4,6-isomer. The oil was crystallized from acetone giving 12.0 g. of crystals. The mother liquor was evaporated to dryness yielding 63 g. of material which was adsorbed on a column of 375 g. of Florisil in a mixture of benzene–petroleum ether (1/4). Elution with 2.5 l. of the same solvent mixture yielded an oil which was crystallized twice from acetone–methanol to give 3.7 g. of needles, m.p. 71–73.5°. One recrystallization from acetone–methanol gave thin needles, m.p. 72–74°, $[\alpha]D$ +3.4°, $\lambda_{max}^{isooctane}$ 296, 305 mμ and λ_{infl} 320 mμ (ϵ 14,380, 13,640 and 8,720)[5] (Fig. 2).

Anal. Calcd. for $C_{27}H_{42}$: C, 88.45; H, 11.55. Found: C, 88.74; H, 11.44.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Optical Rotatory Dispersion Studies. IV.[1] Steroidal Sapogenins[2]

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RECEIVED AUGUST 29, 1955

The rotatory dispersion curves of a variety of steroidal sapogenins are given and the changes produced by the introduction of carbonyl groups, halogen atoms and double bonds are discussed. The application to certain analytical problems also is mentioned.

In the preceding three papers[1,3,4] of this series, there was given the theoretical and experimental background to this study, which is concerned with an attempted correlation of the rotatory dispersion curves and certain structural features of steroids. The present investigation covers a series of closely related steroidal sapogenins, without, however, carrying out the earlier mathematical treatment[1] since it did not offer any advantages insofar as the correlation of chemical structure and rotatory dispersion is concerned.

The experimental procedure and definition of terms already has been outlined in detail[3] and has been followed in this paper as well. In contrast to the steroidal hydrocarbon, androstane, which showed[3] practically zero rotation over the spectral range (700–300 mμ) studied, the basic sapogenin skeleton, represented by 22a,25a,5α-spirostan (desoxytigogenin) (I)[5] shows an increasingly negative rotation (Fig. 1) down to the limit of measurement ($[\alpha]_{290}$ −358°). This curve should be considered the background against which the structural changes in the sapogenin molecule are to be discussed. The strong negative drift in the rotation is apparently a reflection of the spiroketal system attached to ring D and, as seen below, overshadows the possible recognition of more subtle effects which might be exerted by the introduction of

(1) Paper III, A. E. Lippman, E. W. Foltz and C. Djerassi, THIS JOURNAL, **77**, 4364 (1955).

(2) Supported by a research grant from the Damon Runyon Memorial Fund for Cancer Research. We are indebted to the National Science Foundation for funds covering the purchase of the spectropolarimeter.

(3) Paper I, C. Djerassi, E. W. Foltz and A. E. Lippman, THIS JOURNAL, **77**, 4354 (1955).

(4) Paper II, E. W. Foltz, A. E. Lippman and C. Djerassi, *ibid.*, **77**, 4359 (1955).

(5) For nomenclature, *cf.* C. Djerassi and J. Fishman, *ibid.*, **77**, 4291 (1955).