gressed. The cooled reaction mixture was poured over crushed ice and the precipitated diiodo-diacetal removed by filtration and recrystallized from 80 parts of absolute alcohol. The compound crystallized in quadrilateral plates which melted with decomposition at 162–163° (cor.). The yield was 0.5 g. (quantitative).

Anal. Calcd. for $C_{20}H_{20}O_4I_2$: C, 41.54; H, 3.49. Found: C, 41.42; H, 3.67.

Disubstituted Derivatives of 2,3,4,5-Dibenzylidene-dulcitol I.—These compounds were prepared in the same manner as the isomeric compounds of 2,3,4,5-dibenzylidene-dulcitol II. (a) The **1,6-dityril-2,3,4,5-dibenzylidene-dulcitol I** deposted from its solution in 5 parts of dioxane in the form of fine needles which melted at 184–186° (cor.).

Anal. Calcd. for $C_{58}H_{50}O_6$: C, 82.63; H, 5.98. Found: C, 82.76; H, 6.02.

(b) **1,6-Ditosyl-2,3,4,5-dibenzylidene-dulcitol I** was obtained in a yield of 91% in the form of fine needles. It was recrystallized from 5 parts of dioxane and melted when pure at 167–168° (cor.).

Anal. Calcd. for $C_{34}H_{34}O_{10}S_2$: C, 61.24; H, 5.14. Found: C, 61.40; H, 5.14.

(c) **1,6-Diiodo-2,3,4,5-dibenzylidene-dulcitol I** formed in elongated prisms upon cooling its solution in 70 parts of absolute alcohol. It melted at 127–128° (cor.). The yield was quantitative.

Anal. Calcd. for $C_{20}H_{20}O_4I_2$: C, 41.54; H, 3.49. Found: C, 41.56; H, 3.49.

Summary

The condensation of 1,6-dibenzoyl-dulcitol and benzaldehyde by fused zinc chloride at 60° yielded the 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol of melting point 119–120° (cor.) previously obtained when gaseous hydrochloric acid was employed as a condensing agent; it is now designated the stable isomer (I). When the condensation through zinc chloride was conducted at 20° an isomeric 1,6-dibenzoyl-2,3,4,5-dibenzylidene-dulcitol melting at 147–148° (cor.) was obtained. The latter isomer, because of its ease of conversion into the stable isomer (I) of melting point 119–120° (cor.), will be designated the unstable isomer (II). Both compounds yield 1,6-dibenzoyl-2,3,4,5-tetra-acetyl-dulcitol upon treatment with an acid acetylating mixture, hence their isomerism is due to position or stereo-isomerism of the benzylidene groups. The compounds upon debenzoylation yield two different 2,3,4,5-dibenzylidene-dulcitols, from which two corresponding series of disubstituted derivatives differing in melting point and other physical properties may be obtained.

BETHESDA, MARYLAND RECEIVED OCTOBER 31, 1941

[CONTRIBUTION FROM THE ANIMAL CHEMISTRY AND NUTRITION SUBSECTION OF IOWA STATE COLLEGE]

The Preparation of $\Delta^{6,8(14)}$-, $\Delta^{7,9(11)}$-, $\Delta^{7,14}$- and $\Delta^{8,14}$-Cholestadienes[1]

BY J. C. ECK AND E. W. HOLLINGSWORTH

The preparation of various cholestane derivatives possessing di-unsaturation in rings B and C or rings B and D was made possible by the recent preparation[2] of Δ^8- and $\Delta^{8(14)}$-cholestenes which possess mono-unsaturation in ring C. Thus, $\Delta^{6,8(14)}$-, $\Delta^{7,9(11)}$-, $\Delta^{7,14}$- and $\Delta^{8(14)}$-cholestadienes were prepared from Δ^8- and $\Delta^{8(14)}$-cholestenes by various methods. The methods of preparation and the specific rotations of these cholestadienes were compared with those of known analogous steroid derivatives possessing di-unsaturation in rings B and C or rings B and D. The double bonds are located in ring A or B or rings A and B in the hitherto known cholestadienes which are $\Delta^{2,4}$-cholestadiene ($\Delta^{2,4}$-coprostadiene), $\Delta^{3,5}$-cholestadiene, $\Delta^{4,6}$-cholestadiene (referred to as "7-dehydrocholestene isomer")[3] and $\Delta^{5,7}$-cholestadiene (referred to as 7-dehydrocholestene).[4]

$\Delta^{6,8(14)}$-Cholestadiene (I) was prepared by the alcoholic hydrochloric acid dehydration of Δ^8-cholesten-7-ol (II) which was obtained by the aluminum isopropoxide reduction of Δ^8-cholesten-7-one (III).[2] The double bond probably rearranges from the 8- to the 8(14)-position during the treatment with alcoholic hydrochloric acid. The structure of $\Delta^{6,8(14)}$-cholestadiene (I) is supported by its method of preparation, its non-formation of a maleic anhydride addition product and its absorption spectrum maximum at about 245 mμ. Only one steroid derivative is known to contain a $\Delta^{6,8(14)}$-unsaturated structure and this compound, $\Delta^{6,8(14)}$-cholestadiene-3,9-diol ($[\alpha]D$ −19.7°), was prepared by the action of perbenzoic acid on $\Delta^{6,8}$-cholestadiene-3-ol.[5] The structure of cholestadieneol-3C is not known,[5] al-

(1) Journal Paper No. J915 of the Iowa Agricultural Experiment Station, Project No. 506.

(2) Eck and Hollingsworth, THIS JOURNAL, **63**, 2986 (1941).

(3) Eck and Hollingsworth, *ibid.*, **63**, 107 (1941).

(4) Dimroth and Trautmann, *Ber.*, **69B**, 669 (1936).

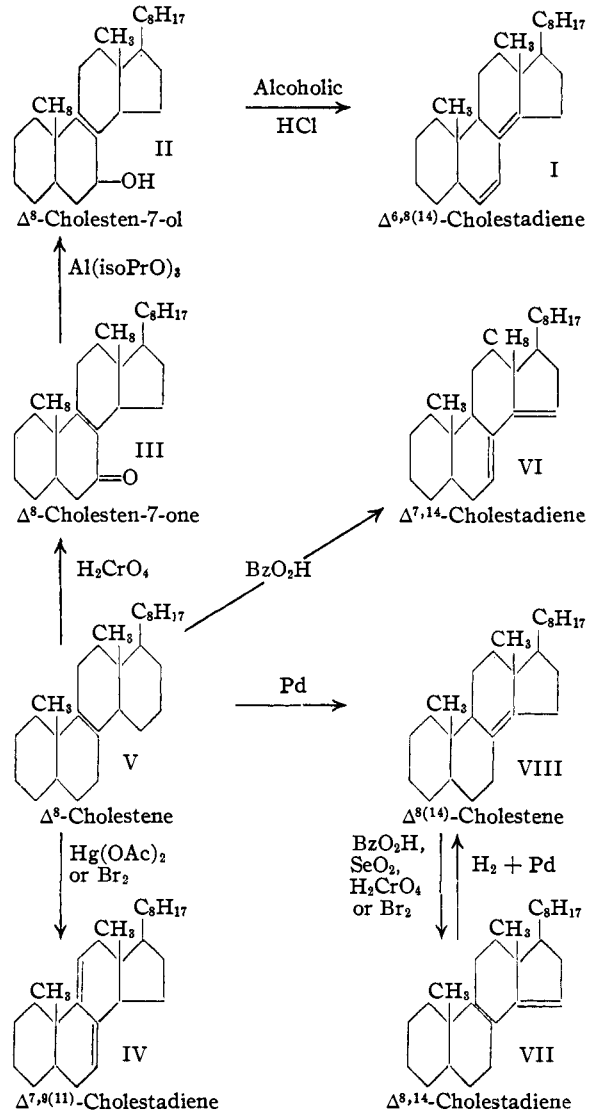
(5) Windaus, Linsert and Eckhardt, *Ann.*, **534**, 22 (1938).

though it is possible that it could possess the structure of $\Delta^{6,8(14)}$-cholestadiene-3-ol. Cholestadieneol-3C was obtained[5] as a by-product in the treatment of $\Delta^{6,8}$-cholestadiene-3-ol with maleic anhydride. A $\Delta^{6,8(14)}$-unsaturated structure for cholestadieneol-3C is in agreement with its absorption spectrum maximum at 248 mμ, its non-formation of a maleic anhydride addition product and its specific rotation. The specific rotation of cholestadieneol-3C ($[\alpha]_D$ $-2.7°$) is comparable with that of $\Delta^{6,8(14)}$-cholestadiene ($[\alpha]_D$ $+1.1°$) in numerical value and with respect to the differences (32.4° and 23.7°, respectively) in specific rotation from the corresponding saturated derivatives, cholestan-3(β)-ol ($[\alpha]_D$ $+29.7°$) and cholestane ($[\alpha]_D$ $+24.8°$).

$\Delta^{7,9(11)}$-Cholestadiene (IV) was prepared from Δ^{8}-cholestene (V) by the action of mercuric acetate, and also by the addition of a molar equivalent of bromine followed by the spontaneous cleavage of two molar equivalents of hydrogen bromide. The structure of $\Delta^{7,9(11)}$-cholestadiene (IV) is supported by its method of preparation, its non-formation of a maleic anhydride addition product and its absorption spectrum maximum at 243 mμ. A $\Delta^{7,9(11)}$-unsaturated structure has been suggested[5] for cholestadieneol-D ($\Delta^{7,9(11)}$-cholestadiene-3-ol) which was prepared by the treatment of Δ^{8}-cholesten-3-ol (δ-cholestenol) with perbenzoic acid. The specific rotation of cholestadieneol-D was, however, unfortunately not reported, so a comparison of specific rotations is not possible as a verification of structure.

$\Delta^{7,14}$-Cholestadiene (VI) was prepared by the treatment of Δ^{8}-cholestene (V) with perbenzoic acid. The structure of $\Delta^{7,14}$-cholestadiene (VI) is supported by its strong levorotation, its formation of a maleic anhydride addition product and its absorption spectrum data. Its method of preparation and its formation of a maleic anhydride addition product could possibly suggest a $\Delta^{8(14),9(11)}$-unsaturated structure. However, a structure with two double bonds in conjugation in the same ring was not indicated since an absorption spectrum maximum for such a structure (about 270 to 280 mμ) was not found. Two maxima were found (242 and 250 mμ) which indicated a structure with two double bonds in conjugation in two different rings. One of these maxima may be due to an inseparable impurity or to a rearrangement product formed during the irradiation in obtaining the absorption spectrum data. The instability of $\Delta^{7,14}$-cholestadiene was indicated by a repeated recrystallization of a sample of $\Delta^{7,14}$-cholestadiene which resulted in a lower levorotation ($[\alpha]_D$ $-69°$).

In addition to the formation of a maleic anhydride addition product, a cholestadiene with a specific rotation of $+27°$ was produced as a by-product in the treatment of $\Delta^{7,14}$-cholestadiene with maleic anhydride. This cholestadiene could be $\Delta^{7,9(11)}$-cholestadiene since its properties were found to be in agreement with those of $\Delta^{7,9(11)}$-cholestadiene. A similar rearrangement of a diunsaturated steroid derivative by the action of maleic anhydride has been reported.[6] $\Delta^{6,8}$-Coprostadiene-3-ol ($[\alpha]_D$ $+127°$) was rearranged to an isomeric compound ($[\alpha]_D$ $-48°$) by treatment



(6) Windaus and Zühlsdorff, *Ann.*, **536**, 204 (1938).

with hydrogen chloride in chloroform. The structure of this isomeric compound is not known, although it is possible that this compound could possess the structure of $\Delta^{7,14}$-coprostadiene-3-ol since the increase in levorotation (175°) resulting from this rearrangement is large and is similar to the increase in levorotation (127.6°) in the hydrogen chloride rearrangement of $\Delta^{6,8}$-cholestadiene-3-ol ($[\alpha]D$ −17.9°) to $\Delta^{7,14}$-cholestadiene-3-ol (dehydrocholesterol B_3) ($[\alpha]D$ −145.5°).[5] The isomeric compound was found to be converted back to $\Delta^{6,8}$-coprostadiene-3-ol when heated with maleic anhydride. These reactions may be similar although it was found that $\Delta^{7,9(11)}$-cholestadiene was not appreciably affected when treated with hydrogen chloride in chloroform. In addition to the above mentioned $\Delta^{7,14}$-unsaturated steroid derivatives, hydrogen chloride in chloroform was used also in preparing $\Delta^{7,14}$-cholestadiene-3-ol from $\Delta^{5,7}$-cholestadiene-3-ol (7-dehydrocholesterol)[7] and $\Delta^{7,14,22}$-ergostatriene-3-ol (ergosterol B_3) together with ergosterol B_1 and ergosterol B_2 from $\Delta^{5,7,22}$-ergostatriene-3-ol (ergosterol).[8]

$\Delta^{8,14}$-Cholestadiene (VII) was prepared from $\Delta^{8(14)}$-cholestene (VIII) by the action of bromine, perbenzoic acid, selenium dioxide or chromic acid. The dehydrogenating action of bromine has been used in the conversion of Δ^{14}-ergosten-3-ol (β-ergostenol) to $\Delta^{8,14}$-ergostadiene-3-ol (dehydro-α-ergostenol).[9] Selenium dioxide has been used in the conversion of $\Delta^{8(14)}$-ergosten-3-ol (α-ergostenol) to $\Delta^{8(14)}$-ergostadiene-3-ol[9] and of $\Delta^{8(14),22}$-ergostadiene-3-ol (dihydroergosterol) to a mixture of $\Delta^{8,14,22}$-ergostatriene-3-ol (ergosterol D) and $\Delta^{7,14,22}$-ergostatriene-3-ol.[9] The action of perbenzoic acid is known to convert Δ^{14}-α_1-sitostan-3-ol acetate to $\Delta^{8,14}$-α_1-sitostadiene-3-ol,[10] $\Delta^{8(14)}$- or Δ^{14}-ergostene (α- or β-ergostene) to $\Delta^{8,14}$-ergostadiene (dehydroergostene)[9] and $\Delta^{8(14)}$- or Δ^{14}-ergosten-3-ol to $\Delta^{8,14}$-ergostadiene-3-ol.[9] The proposed structure of $\Delta^{8,14}$-ergostadiene for dehydroergostene is based on its methods of preparation and its specific rotation of −15°. The formation of additional unsaturation by the action of chromic acid was suggested[2] by the presence of a cholestadiene in the hydrocarbon fraction recovered from the chromic acid oxidation product of Δ^{8}-cholestene.

(7) Schenck, Buchholz and Wiese, *Ber.*, **69B**, 2696 (1936).
(8) Windaus, Dithmar, Murke and Suckfüll, *Ann.*, **488**, 91 (1933).
(9) Morrison and Simpson, *J. Chem. Soc.*, 1710 (1932).
(10) Bernstein and Wallis, THIS JOURNAL, **61**, 2308 (1939).

The structure of $\Delta^{8,14}$-cholestadiene (VII) is supported by its methods of preparation, its nonformation of a maleic anhydride addition product and its absorption spectrum maximum at 245 mμ. The levorotation of $\Delta^{8,14}$-cholestadiene ($[\alpha]D$ −23.0°) is comparable with that of $\Delta^{8,14}$-ergostadiene ($[\alpha]D$ −15.0°) and $\Delta^{8,14}$-ergostadiene-3-ol ($[\alpha]D$ −17.5°); the specific rotations of ergostane and ergostan-3-ol are +19.9° and +15.5°, respectively. Normal catalytic hydrogenation of $\Delta^{8,14}$-cholestadiene was found to result in its conversion back to $\Delta^{8(14)}$-cholestene. Similar to Δ^{8}-, $\Delta^{8(14)}$- and Δ^{14}-cholestenes,[2] the $\Delta^{6,8(14)}$-, $\Delta^{7,9(11)}$-, $\Delta^{7,14}$- and $\Delta^{8,14}$-cholestadienes were found by titration to consume more bromine than $\Delta^{3,5}$-cholestadiene.

Experimental

Preparation of $\Delta^{6,8(14)}$-Cholestadiene.—In a 200-cc. round-bottom flask provided with a fractionating column supplied with a distillation condenser, a mixture of 500 mg. of Δ^{8}-cholesten-7-one,[2] 2 g. of aluminum isopropoxide and 100 cc. of dry isopropyl alcohol was heated at such a rate that a slow distillation occurred over a period of ten hours. The reaction product was poured into 150 cc. of 4% potassium hydroxide and the resulting mixture was extracted with ether after standing several hours. The ether extract was washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was crystallized from methanol to yield 220 mg. of Δ^{8}-cholesten-7-ol in the form of plates, m. p. 79–80°, $[\alpha]^{24}D$ +4.2° (*c*, 1.72 in carbon tetrachloride).

Anal. Calcd. for $C_{27}H_{46}O$: C, 83.86; H, 12.00. Found: C, 83.48; H, 12.42.

In a 50-cc. Erlenmeyer flask provided with a reflux condenser, a mixture of 100 mg. of Δ^{8}-cholesten-7-ol and 20 cc. of alcohol containing 0.2 cc. of concentrated hydrochloric acid was refluxed for forty minutes. The reaction product was concentrated *in vacuo*, and the residue dissolved in 20 cc. of petroleum ether (b. p. 30–40°) was passed through an 8 × 55 mm. column of activated alumina. The filtrate was concentrated *in vacuo* and the residue on crystallization from acetone-methanol yielded 65 mg. of $\Delta^{6,8(14)}$-cholestadiene in the form of plates, m. p. 84–85°, $[\alpha]^{24}D$ +1.1° (*c*, 1.90 in carbon tetrachloride). The $\Delta^{6,8(14)}$-cholestadiene possessed an absorption spectrum maximum at about 245 mμ, remained unchanged when refluxed with maleic anhydride in benzene for four hours and gave a negative[11] Liebermann-Burchard color reaction (purple).

Anal. Calcd. for $C_{27}H_{44}$: C, 87.96; H, 12.04. Found: C, 87.60; H, 12.12.

Preparation of $\Delta^{7,9(11)}$-Cholestadiene.—$\Delta^{7,9(11)}$-Cholestadiene was prepared from Δ^{8}-cholestene by the action of mercuric acetate in a manner similar to that used in the dehydrogenation of ergosterol.[12] In a 200-cc. round-bottom flask provided with a reflux condenser, a mixture of 1

(11) Eck and Thomas, *J. Biol. Chem.*, **128**, 267 (1939).
(12) Windaus and Linsert, *Ann.*, **465**, 148 (1928).

g. of Δ^8-cholestene and 100 cc. of alcohol was heated to boiling. A solution of 2.28 g. of mercuric acetate in a mixture of 20 cc. of acetic acid and 20 cc. of alcohol was added and the resulting reaction mixture was gently refluxed for one hour, during which time mercurous acetate separated and caused bumping. The slightly yellow decanted solution was concentrated *in vacuo*, and the residue was extracted with 50 cc. of petroleum ether. The petroleum ether extract was passed through a 10 × 50 mm. column of activated alumina and the combined petroleum ether filtrate and washings were concentrated *in vacuo*. The residue was crystallized from acetone–methanol to yield 0.5 g. of $\Delta^{7,9(11)}$-cholestadiene, m. p. 83–84°, $[\alpha]^{30}D$ +31.3° (*c*, 0.84 in chloroform). $\Delta^{7,9(11)}$-Cholestadiene displayed an absorption spectrum maximum at 243 mμ and was recovered unchanged after being refluxed with maleic anhydride in toluene for nine hours, and also after treatment with hydrogen chloride in chloroform solution.

Anal. Calcd. for $C_{27}H_{44}$: C, 87.96; H, 12.04. Found: C, 87.65, 87.78; H, 12.14, 12.21.

$\Delta^{7,9(11)}$-Cholestadiene was prepared also by the treatment of Δ^8-cholestene with bromine. A solution of 0.212 cc. of bromine (1.05 moles per mole of Δ^8-cholestene) in 15 cc. of dry chloroform at −75° was added all at once to a solution of 1.5 g. of Δ^8-cholestene in 100 cc. of dry chloroform at −75°. The resulting mixture was allowed to stand for one hour although it was not found necessary to maintain the temperature of the mixture at −75° during this hour. The solvent was removed *in vacuo*, and the residue dissolved in 50 cc. of petroleum ether was passed through an 18 × 70 mm. column of activated alumina. The column was washed with 50 cc. of petroleum ether and the combined filtrate and washings were concentrated *in vacuo*. The residue was crystallized from acetone–methanol and the 1.05 g. of plates on repeated recrystallization yielded $\Delta^{7,9(11)}$-cholestadiene, m. p. 83–84°, $[\alpha]^{23}D$ +32.2° (*c*, 1.96 in carbon tetrachloride).

Preparation of $\Delta^{7,14}$-Cholestadiene.—A solution of 2 g. of Δ^8-cholestene and 1.5 g. of perbenzoic acid (2 moles per mole of Δ^8-cholestene) in 20 cc. of chloroform was allowed to stand stoppered at 0° for eight days. The solvent was removed *in vacuo*, and the residue was dissolved in 100 cc. of ether. The ether solution was washed with 5% sodium hydroxide and with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue, dissolved in 75 cc. of petroleum ether, was passed through an 18 × 190 mm. column of activated alumina. The column was washed with 75 cc. of petroleum ether and the combined filtrates were concentrated *in vacuo*. The residue was crystallized from acetone–methanol to yield 0.6 g. of $\Delta^{7,14}$-cholestadiene in the form of thick plates, m. p. 82–83°, $[\alpha]^{21}D$ −93.2° (*c*, 1.27 in carbon tetrachloride). $\Delta^{7,14}$-Cholestadiene displayed absorption spectrum maxima at 242 and 250 mμ.

Anal. Calcd. for $C_{27}H_{44}$: C, 87.96; H, 12.04. Found: C, 87.89, 87.71; H, 12.13, 12.02.

A solution of 250 mg. of $\Delta^{7,14}$-cholestadiene, 150 mg. of maleic anhydride and 30 cc. of toluene was refluxed for ten hours. The solvent was removed *in vacuo*, and the residue dissolved in 60 cc. of ether was washed with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue was dissolved in 25 cc. of petroleum ether and the petroleum ether solution was passed through an 8 × 60 mm. column of activated alumina. The column filtrate was concentrated *in vacuo*, and the residue was crystallized from alcohol to yield 120 mg. of a compound in the form of plates, m. p. 82–83°, $[\alpha]^{24}D$ +27.3° (*c*, 2.18 in carbon tetrachloride), which gave no depression in mixed melting point with $\Delta^{7,9(11)}$-cholestadiene. The column was eluted with 100 cc. of ether and the ether eluate was concentrated *in vacuo*. The residue was crystallized from petroleum ether to yield a maleic anhydride addition product, m. p. 170–174°.

Anal. Calcd. for $C_{31}H_{46}O_3$: C, 79.66; H, 10.04. Found: C, 79.92; H, 10.32.

Preparation of $\Delta^{8,14}$-Cholestadiene.—A mixture of 1 g. of $\Delta^{8(14)}$-cholestene and 0.75 g. of perbenzoic acid (two moles per mole of $\Delta^{8(14)}$-cholestene) dissolved in 30 cc. of chloroform was allowed to stand stoppered at 0° for eight days. The reaction product was washed with 5% sodium hydroxide and with water, dried over anhydrous sodium sulfate and concentrated *in vacuo*. The residue, dissolved in 100 cc. of methanol containing 1 cc. of dilute sulfuric acid (1:1), was refluxed for fifteen minutes. The solution was neutralized with 35% sodium hydroxide and concentrated *in vacuo*. The residue was extracted with 75 cc. of petroleum ether, and the extract was passed through an 18 × 170 mm. column of activated alumina. The column was washed with 125 cc. of petroleum ether, and the combined filtrates were concentrated *in vacuo*. The residue was crystallized from acetone-methanol and the 190 mg. of product in the form of plates on repeated recrystallization yielded $\Delta^{8,14}$-cholestadiene, m. p. 83–84°, $[\alpha]^{20}D$ −23.0° (*c*, 1.08 in carbon tetrachloride). $\Delta^{8,14}$-Cholestadiene displayed an absorption spectrum maximum at 245 mμ.

Anal. Calcd. for $C_{27}H_{44}$: C, 87.96; H, 12.04. Found: C, 87.89, 87.74; H, 12.22, 12.32.

A mixture of 200 mg. of $\Delta^{8(14)}$-cholestene, 200 mg. of selenium dioxide and 40 cc. of alcohol was refluxed for six hours. The solvent was removed *in vacuo*, and the residue, dissolved in 25 cc. of petroleum ether, was passed through an 18 × 120 mm. column of activated alumina. The column was washed with 40 cc. of petroleum ether, and the combined filtrates were concentrated *in vacuo*. Repeated recrystallization of the 30 mg. of plates obtained by crystallization of the residue from alcohol yielded $\Delta^{8,14}$-cholestadiene, m. p. 83–84°, $[\alpha]^{23}D$ −19.7° (*c*, 1.05 in carbon tetrachloride), which gave no depression in mixed melting point with the sample of $\Delta^{8,14}$-cholestadiene obtained by treatment of $\Delta^{8(14)}$-cholestene with perbenzoic acid.

A methanol solution of 260 mg. of bromine (3 moles per mole of $\Delta^{8(14)}$-cholestene) was added to 200 mg. of $\Delta^{8(14)}$-cholestene dissolved in 75 cc. of methanol–ether (1:1). The mixture was allowed to stand in a refrigerator for one day and then concentrated *in vacuo*. The residue was extracted with petroleum ether, and the extract was passed through an 8 × 50 mm. column of activated alumina. The filtrate of the column was concentrated *in vacuo*, and the residue was crystallized from acetone–methanol to yield 18 mg. of $\Delta^{8,14}$-cholestadiene in the form of plates which, after recrystallization, melted at 82–83° and gave no depression in mixed melting point with $\Delta^{8,14}$-cholestadiene obtained by the action of perbenzoic acid on $\Delta^{8(14)}$-cholestene.

$\Delta^{8(14)}$-Cholestene (300 mg.) was oxidized with chromic acid by the same procedure as used in the oxidation of Δ^{8}-cholestene,[2] and the reaction product was divided into a ketone and a hydrocarbon fraction. The ketone fraction was indicated to contain a mixture of ketones since a crystalline product was not obtained either directly or as a semicarbazone or an oxime. The hydrocarbon fraction on repeated recrystallization from acetone–methanol yielded 12 mg. of $\Delta^{8,14}$-cholestadiene, m. p. 83–84°, which gave no depression in mixed melting point with a sample of $\Delta^{8,14}$-cholestadiene obtained by the action of perbenzoic acid on $\Delta^{8(14)}$-cholestene.

$\Delta^{8,14}$-Cholestadiene was recovered unchanged after being refluxed with maleic anhydride in benzene for nine hours. Catalytic hydrogenation of $\Delta^{8,14}$-cholestadiene in ethyl acetate with palladium catalyst yielded a compound in the form of needles, m. p. 52–54°, which gave no depression in mixed melting point with $\Delta^{8(14)}$-cholestene.

Bromine Titrations.—The cholestadienes were titrated with bromine in the same manner as that described for the titration of Δ^{8}-, $\Delta^{8(14)}$- and Δ^{14}-cholestenes.[2] It was found that $\Delta^{3,5}$-cholestadiene, $\Delta^{6,8(14)}$-cholestadiene, $\Delta^{7,9(11)}$-cholestadiene, $\Delta^{7,14}$-cholestadiene and $\Delta^{8,14}$-cholestadiene in chloroform solution consumed 1.01, 2.24, 3.04, 2.66 and 3.22 molar equivalents of bromine, respectively, dissolved in chloroform. Using a methanol solution of the compound and a methanol solution of bromine, the same compounds consumed 1.02, —, 1.65, 1.76 and 1.83 molar equivalents of bromine, respectively.

The authors wish to express their appreciation to Mr. E. M. Gladrow of the physical chemistry department for helpful assistance in obtaining the absorption spectrum data.

Summary

$\Delta^{6,8(14)}$-, $\Delta^{7,9(11)}$-, $\Delta^{7,14}$- and $\Delta^{8,14}$-cholestadienes were prepared. The methods of preparation and the specific rotations of these cholestadienes were compared with those of the known analogous unsaturated steroid derivatives.

AMES, IOWA RECEIVED AUGUST 2, 1941

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY AND LOUISIANA STATE UNIVERSITY]

American Musk. I. The Chemical Constitution of the Musk of the Louisiana Muskrat[1]

BY PHILIP G. STEVENS[2] AND J. L. E. ERICKSON[3]

It is now 36 years since Walbaum[4] discovered that the essential principle of musk was muscone, 30 years since Sack[5] isolated civetone from civet, and 16 years since the classic work of Ruzicka[6] who elucidated the structure of these curious compounds. Yet in spite of the interest shown in this field, the most abundant natural source[7] of the large ring compounds—the scent glands of the common muskrat—apparently has been overlooked by organic chemists, a remarkable fact, since from the name *musk*rat, one would have expected an investigation to have been made long ago.

The presence of substances with a musk odor in muskrat scent glands has, however, been long suspected, but very little attention has been given them, although they have been reported[8] as being about equal to civet and musk-xylene, a very shrewd estimation as this work will reveal. The only prior chemical work in the literature is an analysis of the fatty acids of these glands.[9]

The scent glands investigated in this work were those of the Louisiana muskrat, *Ondatra zibethicus rivalicius*, a typical North American muskrat. Both sexes have these glands,[10] just as does the beaver, and the civet cat of Abyssinia, in contrast to the musk deer of Asia, the male of which alone produces musk.

Isolation of the Crude Musk.—The scent glands, varying in size from 0.6 g. to 1.8 g. (average, 1.25 g.),[11] were obtained directly from the trapper (December–February) who merely cut them from the carcass and stored them in jars of alcohol. The glands, which had a characteristic, not unpleasant, musky odor, were drained from the

(1) Preliminary work was started at the Massachusetts Institute of Technology and Louisiana State University, and continued at McGill University. The final and successful work, however, was carried out at Harvard University and Louisiana State University.

(2) Present address: Department of Chemistry, Yale University.

(3) Present address: Department of Chemistry, Louisiana State University.

(4) Walbaum, *J. prakt. Chem.*, [2] **73**, 488 (1906).

(5) Sack, German Patent 279,313 (1912); *Chem.-Ztg.*, **39**, 538 (1915).

(6) Ruzicka, *Helv. Chim. Acta*, **9**, 230, 715 (1926).

(7) Approximately 6 million muskrats are trapped annually in Louisiana alone.

(8) Redgrove, *Chemist and Druggist*, **112**, 288 (1930).

(9) Simmons and Hills, *Analyst*, **58**, 154 (1933).

(10) The purposes of these preputial glands is not fully established, but it is said that their secretions assist the muskrat to become aware of other members of the specie, even at great distances. Any sexual significance is problematical, but this seems likely, since in both sexes the musk glands reach their maximum development in the rutting season (Grinnell, Dixon and Linsdale, "Fur Bearing Animals of California," Vol. II, University of California Press, Berkeley, California, 1937, p. 744.

(11) Dry weight about one-half this.