and then distilled under a reduced pressure. Faint yellow esters (total amount, about 60 g.) were obtained. The esters were dissolved in carbon tetrachloride and the unsaturated fatty acids present in small quantities in it were removed by ozonization (inspection of the ozonides was not carried out).

Rectification—The fatty acid esters (about 57 g.) were fractionally distilled in 5° fractions, using the Klenk fractional distillation apparatus[4]. The result of the fractional distillation is shown in Fig. 1.

Confirmatory reactions—The five fractions, corresponding to the tops of the curve, were converted to the amides and 2-alkylbenzimidazoles according to the confirmatory reactions of the acids, and the results obtained are shown in Table I. The melting points of the derivatives were not depressed on admixture with the authentic specimens prepared from the pure acids, from which the presence of the normal fatty acid nitriles were confirmed.

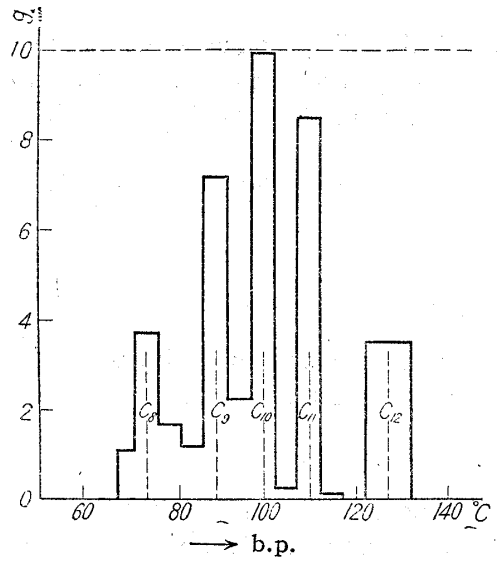

Fig. 1. Fractional Distillation Curve of Methyl Esters Separated from the Light Oil.

TABLE I

Normal fatty acids	Methyl Esters $b.p_{10}$ °C	Derivatives m.p. °C: Amides	Derivatives m.p. °C: 2-Alkylbenzimidazoles
C_8 Caprylic	72～ 77	104.5	143.5
C_9 Pelargonic	87～ 92	99.0	139.5
C_{10} Capric	97～ 92	98.0	127.0
C_{11} Undecanoic	107～112	96.5	114.5
C_{12} Lauric	126～131	98.5	—

Summary

The nitriles obtained from the crude light oil, b.p. 200～280°, of Fushun shale oil in Manchuria were studied, and caprylo-, pelargo-, capro-, hendecano-, and lauro-nitriles were identified.

(Received May 21, 1953)

4) Z. Physiol. Chem., 224, 250 (1936).

50. Ko Arima and Ryoichi Hayatsu: Studies on Cholestapolyenes. I. Syntheses of Bicholestatriene A and 7-Dehydrocholesterol.

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There are many methods of preparing provitamin D_3 by the dehydrohalogenation of 7-halocholesteryl ester. In the present series of experiments, 7β-bromocholesteryl benzoate (I) was treated with sodium iodide and two kinds of new hydrocholesteryl benzoate possessing one tertiary hydroxyl group were obtained. These compounds were dehydrated by heating in vacuo by which provitamin D_3 was prepared with a comparatively good yield. Dehydration in glacial acetic acid was attempted but this failed to give provitamin and in its stead, yellow hydrocarbon, $C_{54}H_{82}$, was obtained in a comparatively good yield. These are described in the present paper.

Treatment of 7β-bromocholesteryl benzoate[1] (I) in a solution of anhydrous sodium iodide in dehydrated acetone at a low temperature gives 7β-iodocholesteryl benzoate[2] (II) which

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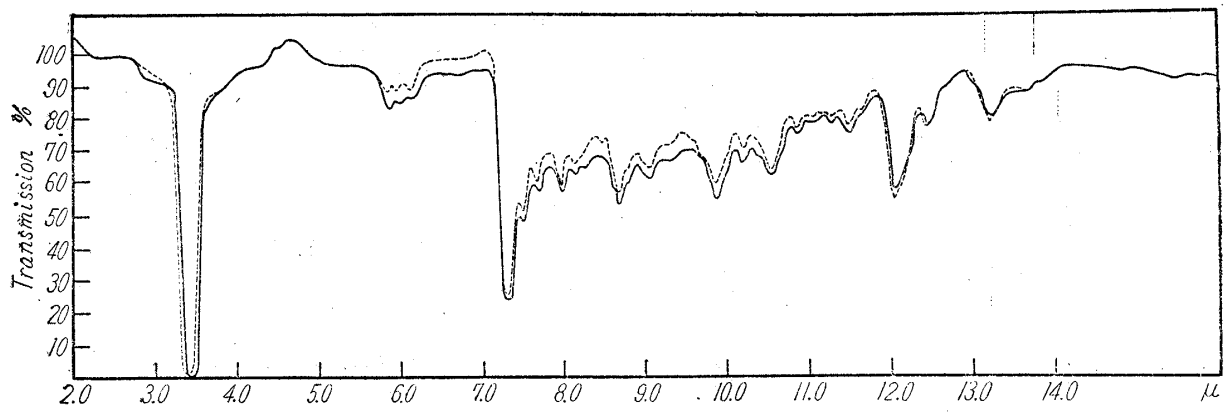
1) H. Schaltegger: Helv. Chim. Acta, 29, 285(1946).

2) H.B. Heubest: J. Chem. Soc., 1948, 1788.

undergoes resination in cold, polar solvent but does not resinify in the presence of alcohols. Under some conditions, two kinds of new hydroxycholesteryl benzoates are formed. When



—— Hydroxycholesteryl benzoate A ····· Hydroxycholesteryl benzoate B

Fig. 1. Infrared Absorption Spectrum of Bicholestatriene A

the mixture of chloroform and methanol is completely dehydrated, hydroxycholesteryl benzoate A(IV), m.p. 155~156°, is formed. The formation of hydroxycholesteryl benzoate B(V), m.p. 135~136°, is varied according to the manner of hydration at the time of the preparation and is more difficult to obtain than the former. A(IV) can be obtained in an average of 40% yield. A(IV) can also be obtained by the application of sodium iodide on (I) in warm methanol or by warming 7α-bromocholesteryl benzoate (III) in dehydrated methanol. Both A and B, when dehydrated by heating in vacuo at around their respective melting point, yield crystals (VI) of m.p. 138~140° which failed to show any depression of the melting point when admixed with 7-dehydrocholesteryl benzoate[1] prepared by the dehydrobromination of 7β-bromocholesteryl benzoate with dimethylaniline. Saponification of (VI) with methanolic potassium hydroxide in nitrogen stream yields crystals of m.p. 140~142° which was determined as provitamin D_3 of 80% purity from the determination of its ultraviolet absorption spectrum.

Dehydration of hydroxycholesteryl benzoate A and B by boiling in glacial acetic acid failed to form provitamin D_3 and in its stead, yellow needles (VII), m.p. 242~244° (decomp.), were obtained. Its analytical values coincide with $C_{54}H_{82}$. The fact that the crystals formed from A and B were identical was proved by mixed fusion and by the identity of analytical values, ultraviolet and infrared absorption spectra (Fig. 1). (VII), obtained by two recrystallizations from benzene, gave an m.p. of 260~262° and not the decomposition point when the bath for determining the melting point was preheated to 250°, and the melting point determined within 1 minute. The yellow hydrocarbon obtained by Tsuda and others[3] is identical with (VII) in the decomposition point, analytical values, and ultraviolet absorption. The maximum of absorption of (VII) determined in the present experiments was $\lambda_{max}^{Et_2O}$ 352 mμ and 369.5 mμ, while that of Tsuda was 348 mμ and 365 mμ, showing a slight difference in the values but the two substances may be assumed to be identical. It is assumed that hydroxycholesteryl benzoate A and B are one of Δ^7-5α-(VIII), Δ^7-5β-(IX), or Δ^5-8-hydroxycholesteryl benzoate (X), but no definite confirmation has yet been obtained.

The authors take this opportunity to express their deep gratitude to Prof. K. Tsuda of the University of Kyushu, Mr. Sudo, Director of the Shinagawa Plant of this firm, and Mr. Matsui, the Vice-Director of the same, for their unfailing guidance and kind advices. The authors are also greatful to Messrs. Hirai, Kawamoto, Furukawa, and Maruyama for analyses and determination of spectra.

3) Tsuda, *et al.*: J. Pharm. Soc. Japan, 71, 273(1951) (C.A., 45, 8150(1951)); *Ibid.*, 72, 182(1952) (C.A., 47, 2190(1953)).

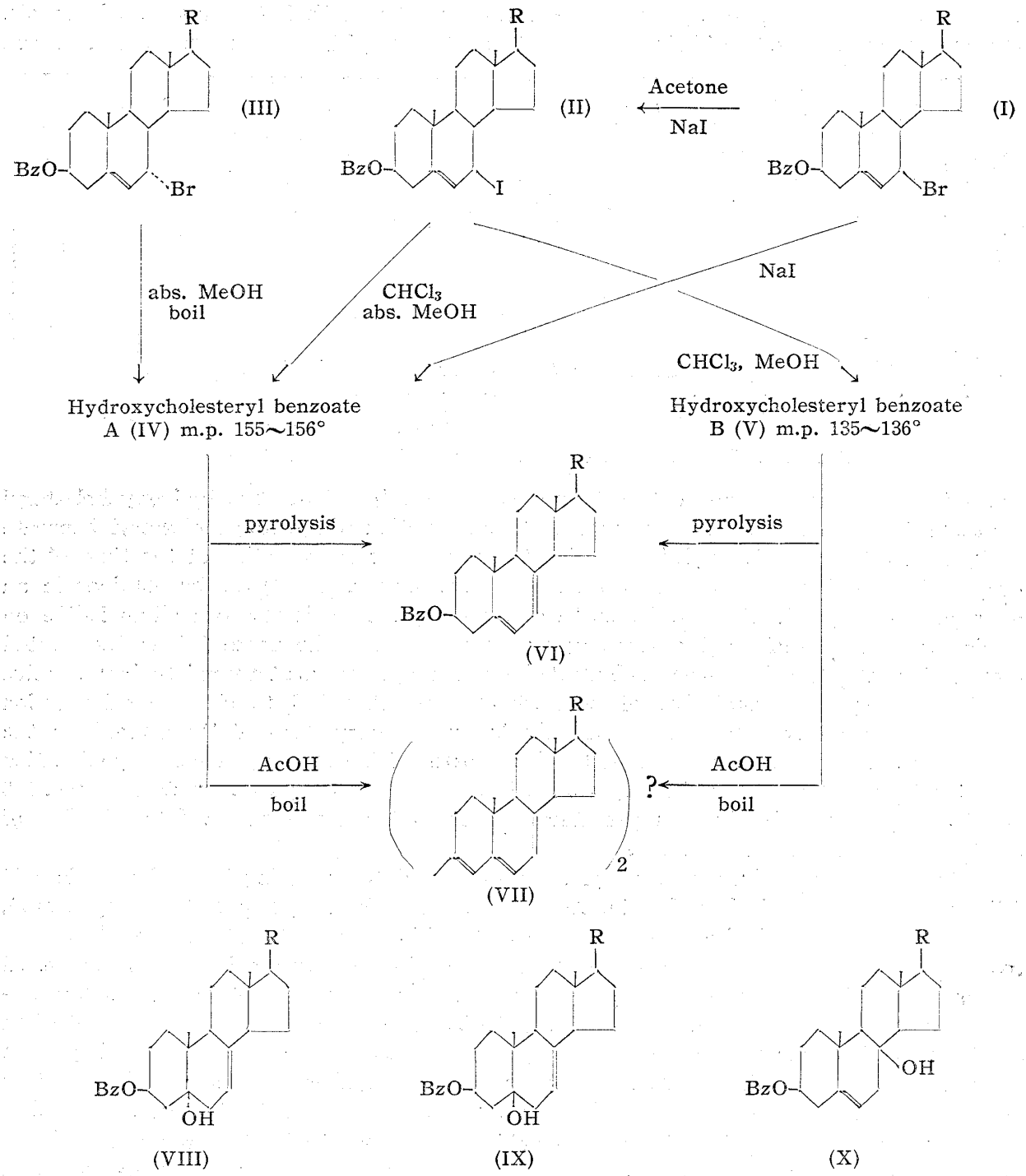


Fig. 2. Preparation Routes for Bicholestatriene A and 7-Dehydrocholesterol

Experimental

1) Preparation of crude 7β-iodocholesteryl benzoate (II)—To 8 g. of anhydrous sodium iodide dissolved in dehydrated acetone, while being stirred at 0°, 10 g. of powdered 7β-bromocholesteryl benzoate (I), m.p. 139~140°, was added in small portions. After 30 minutes, the reaction mixture was filtered, and the solid on the filter was washed with acetone until colorless. After washing with water, it was dried in a vacuum desiccator. m.p. 95~96°. Can be recrystallized from petroleum benzine but liable to decompose during recrystallization. This crude product can be used for the next reaction.

2) Preparation of hydroxycholesteryl benzoate B(V) — Ten g. of (II) was dissolved in 100 cc. of a cold mixture of chloroform and methanol. When the solution was allowed to stand at

0° for 24 hours, needle crystals began to separate out. Further 50 cc. of methanol was added to allow separation of crystals, which were collected by filtration, washed until colorless with methanol, and recrystallized from ether to needles, m.p. 135~136°. Yield, 40% of theory. This reaction is accelerated by sunlight. *Anal.* Calcd. for $C_{34}H_{50}O_3$: C, 80.50; H, 9.88. Found: C, 80.80; H, 9.88. $[\alpha]_D^{29.5}$: +120° ($CHCl_3$).

By boiling 1 g. of hydroxycholesteryl benzoate B(V) with 0.5 g. of potassium carbonate, 2 cc. of water, and 100 cc. of methanol, saponification was effected when the crystals dissolved completely. The reaction mixture was poured into water, the crystals that separated out were collected by filtration, washed with water, and recrystallized from acetonitrile to colorless long needles, m.p. 149~150°. *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.60; H, 11.47. Found: C, 80.99; H, 10.99. $[\alpha]_D^{29.5}$: +130° ($CHCl_3$).

3) Hydroxycholesteryl benzoate A(IV)—(II) was treated exactly the same as in (2), using 1:1 mixture of chloroform, dehydrated with phosphorus pentoxide for 5 minutes, and methanol, dehydrated with metallic sodium. Needles, m.p. 155~156°, were obtained in an average yield of approximately 40% of the theoretical amount. *Anal.* Calcd. for $C_{34}H_{50}O_3$: C, 80.50; H, 9.88. Found: C, 80.64; H, 9.25. $[\alpha]_D^{28}$: +3° ($CHCl_3$).

Saponification as in the case of (2) and recrystallization from acetonitrile provided long needles, m.p. 142~144°. *Anal.* Calcd. for $C_{27}H_{46}O_2$: C, 80.60; H, 11.47. Found: C, 80.76; H, 10.66. $[\alpha]_D^{28}$: −26.3° ($CHCl_3$).

4) Preparation of hydroxycholesteryl benzoate A(IV)—To a stirred solution of 8 g. of anhydrous sodium iodide dissolved in 500 cc. of dehydrated methanol, 10 g. of powdered (I) was added during 30 minutes at a room temperature, and the mixture was warmed at 65° for 15 minutes by which the whole became a thick mass. The reaction mixture was cooled to 20°, crystals collected by filtration, and washed with methanol. The crystals do not show any Beilstein reaction. Recrystallization from ether provided pure (IV). Yield was the same as by (3).

5) Preparation of hydroxycholesteryl benzoate A(IV) (Third Method)—A suspension of 10 g. of 7α-bromocholesteryl benzoate (III)[3], m.p. 110° (decomp.), in 500 cc. of dehydrated methanol was boiled for 30 minutes with stirring. The thickened reaction mixture was filtered after cooling and treated as in the foregoing method by which crystals of m.p. 155~156°, giving negative Beilstein reaction, were obtained in approximately the same yield.

6) 7-Dehydrocholesteryl benzoate (VI)—Two g. of either (IV) or (V) was melted at 2-mm. Hg pressure and maintained at around the melting point for about 2 hours, keeping the temperature of the bath at around 160° in the case of (IV) and at around 140° in the case of (V). The cooled reaction product (orange oil) was recrystallized from a mixture of chloroform and acetone to 1 g. of crystals of m.p. 139~140° (melts to a clear liquid at 183°). The products obtained from either of the starting meterials gave no depression of the melting point when admixed with 7-dehydrocholesteryl benzoate, m.p. 137~139°, prepared by heating 7β-bromocholesteryl benzoate (I) with dimethylanilline in a sealed tube for 5 hours in an oil bath of 130°. The 7-dehydrocholesteryl benzoate obtained by dehydrobromination with dimethylaniline showed ultraviolet absorption of $\lambda_{max}^{Et_2O}$ 270 and 282 mμ, $\log \varepsilon = 3.96$ (282 mμ). *Anal.* Calcd. for $C_{34}H_{48}O_3$: C, 83.54; H, 9.91. Found: C, 83.95; H, 10.02. The 7-dehydrocholesteryl benzoate (VI) prepared from (IV) gave $\lambda_{max}^{Et_2O}$ 270 and 282 mμ, $\log \varepsilon = 3.68$(282 mμ). *Anal.* Calcd. for $C_{34}H_{48}O_3$: C, 83.54; H, 9.91. Found: C, 83.95; H, 10.02.

When benzoic acid sublimes during the reaction, the yield becomes less than 50%. In an experiment using around 50 g. of the starting material thermal conduction cannot be made homogeneous that the formation of benzoic acid is unavoidable and the yield consequently becomes low.

Saponification was effected by treating 2.4 g. of (V) as a suspension in 200 cc. of alcohol containing 3 g. potassium hydroxide, in a nitrogen stream, for about 2 hours. The reaction mixture was concentrated under a diminished pressure until some crystals began to separate out and the mixture was allowed to stand. The crystals were collected by filtration and recrystallized from a mixture of ether and methanol to 1.5 g. of 7-dehydrocholesterol, m.p. 142~143°. $\lambda_{max}^{Et_2O}$ 270 and 282 mμ; $\log \varepsilon = 3.250$ (282 mμ), purity, ca. 80%.

7) Hydrocarbon, $C_{54}H_{82}$ (VII)—A suspension of 10 g. of (IV) or (V) in 200 cc. of glacial acetic acid was boiled by which the substance dissolved once but yellow crystals began to precipitate out later. After four hours, the dark brown mass was collected by filtration and washed with ether by which beautiful yellow crystals were obtained. Recrystallization from benzene yielded crystals of m.p. 260~262°. $\lambda_{max}^{Et_2O}$ 352 and 369.5 mμ; $\log \varepsilon = 4.525$ and 4.562. *Anal.* Calcd. for $C_{54}H_{82}$: C, 88.76; H, 11.23. Found: C, 88.86; H, 11.34. This substance is obtained in an average yield of 6% from (V) or (IV).

3) H. Schaltegger: Helv. Chim. Acta, **33**, 2101(1950).

Summary

Two kinds of hydroxycholesteryl benzoate, A and B, were prepared from 7-bromocholesteryl benzoate and their respective dehydration by heating in vacuum provided provitamin D_3. On the other hand, dehydration by boiling in glacial acetic acid gave bicholestatriene, an yellow hydrocarbon, $C_{54}H_{82}$, in a good yield.

(Received May 25, 1953)

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51. Ko Arima and Ryoichi Hayatsu: Studies on Cholestapolyenes. II. Structure of Bicholestatriene A.

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Some reports have been made regarding the formation of a small amount of yellow steroidal hydrocarbon, bicholestatriene, $C_{54}H_{82}$, as a by-product[1]. Its structure, however, still remanins obscure, the assumed structures given in these reports being quite unfounded. Tsuda and others[2] determined the ultraviolet absorption spectrum of this substance and also carried out its titration with perbenzoic acid, proving the presence of six double bonds. In the first paper of this series[3], it was shown that yellow steroidal hydrocarbon was obtained in an average yield of 6% by boiling the two kinds of hydroxycholesteryl benzoate A and B with glacial acetic acid and that the substance was identical with the yellow steroidal hydrocarbon obtained by Tsuda and others.

In the present series of experiments, attempts were made to hydrogenate part or whole of the six double bonds by catalytic reduction. At the present moment, three kinds of colored bicholestatrienes have been isolated by different methods of preparation and these have tentatively been designated A, B, and C. The bicholestatriene reported here and in the previous paper is the one designated as A.

Squire[4] carried out the reduction of cholestenone with sodium amalgam to cholestenone pinacol and obtained 3,3′-bis(3,5-cholestadiene) by its dehydration. The ultraviolet absorption maxima of 3,3′-bis(3,5-cholestadiene) were found to be $\lambda_{max}^{Et_2O}$ 293, 305, and 321 mμ, and log ε=4.73, 4.80, and 4.66. In general, when one double bond conjugates with the double bonds of conjugated diene system, the third double bond is called an extended conjugative double bond, and its maximum absorption is known to shift to a longer wave length range by 30 mμ[5]. Cholestadiene possesses the maxima of $\lambda_{max}^{Et_2O}$ 229, 235, and 244 mμ, and since 3,3′-bis(3,5-cholestadiene) possesses two more extended conjugative double bonds than bicholestadiene, its absorption maxima should shift 60 mμ to the longer wave length range. The calculated values for 3,3′-bis(3,5-cholestadiene) would, therefore, be 289, 295, and 305 mμ. Two of these values coincide with those of 3,3′-bis(3,5-cholestadiene) with less than 2 mμ difference. This fact shows that the foregoing general law is applicable in a certain amount of precision when the increase of the extended conjugative double bond is between 2 and 4. Comparision of the calculated values of $\lambda_{max}^{Et_2O}$

1) Tsuda, *et al.*: J. Pharm. Soc. Japan, 71, 282 (1951) (C.A., 45, 8151 (1951)); Hafez: Nature, 165, 401 (1950); Tsuda, *et al.*: J. Pharm. Soc. Japan, 71, 275 (1951) (C.A., 45, 8150 (1951)); Ottke, Bergmann: Nature, 166, 997 (1950).
2) Tsuda, *et al.*: J. Pharm. Soc. Japan, 72, 182 (1952) (C.A., 47, 2190 (1953)).
3) Part I: This Bulletin, 1, 212 (1953).
4) E. N. Squire: J. Am. Chem. Soc., 73, 2586 (1951).
5) L. Fieser, M. Fieser: "Natural Products Related to Phenanthrene," 3rd Ed., p. 185 (1949).