tion and the filtrate was treated as in the foregoing (i) by which bicholestatriene C was obtained as orange crystals of m.p. 240~243° (decomp.). Ultraviolet absorption: $\lambda_{max}^{Et_2O}$ 308, 326, 379, and 390 mμ, log ε=4.00, 4.06, 4.28, and 4.30. *Anal.* Calcd. for $C_{54}H_{82}$: C, 88.76; H, 11.23. Found: C, 88.20; H, 11.21.

Summary:

For the purpose of structural determination by the synthesis of bicholestatriene A (3,3'-bis(3,5,7-cholestatriene)), 3,3'-bis(3,5,8(9)-cholestatriene) was prepared from cholesta-4,8(9)-dien-3-one and transition of $\Delta^{8(9)}$ was attempted by dry hydrogen chloride. Unexpectedly, however, colored bicholestatriene C was the sole product. The same substance was also obtained when 3,3'-bis(3,5-cholestadiene) was brominated with N-bromosuccinimide. Bicholestatriene C thereby formed was assumed, from its ultraviolet absorption, as 3,3'-bis(2,4,6-cholestatriene) but much is still vague and obscure as to its structure.

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54. **Ko Arima and Ryoichi Hayatsu:** Studies on Cholestapolyenes. V. Synthesis of 3,3'-Bis(3,5,7-cholestatriene) and Bicholestatriene B.

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The preparation of 3,3'-bis(3,5,7-cholestatriene) (II) was described in the first paper of this series⁽¹⁾ but a new method of such synthesis giving a better yield was found by the present experiments. At the same time, a new yellow bicholestatriene B was obtained as a by-product both of which are described in the present paper.

As shown in Fig. 1, both Hafez⁽²⁾ and Ottke and Bergmann⁽³⁾ reported that (II) was formed as a by-product during the bromination of Δ^{5}-isocholestadiene (1) and cholesteryl acetate (III) with N-bromosuccinimide. Tsuda and others⁽⁴⁾ also obtained (II) by the bromination of cholesteryl bromide (VI) and by an N-bromosuccinimide bromination of cholesteryl tosylate (IV). The present authors prepared (II) in a 6% yield by boiling hydroxycholesteryl benzoate (V) with glacial acetic acid⁽¹⁾ but its structure and reaction mechanism of its formation were totally unknown.

By subsequent experiments by Arima⁽⁵⁾, it became almost certain that this yellow steroidal hydrocarbon is 3,3'-bis(3,5,7-cholestatriene) but the reaction mechanism of its formation is still not clear unless the formation of a free radical of cholestatriene as an intermediate can be supposed. It may be assumed that the application of a dehydration agent, such as acids, to compounds that could form such a free radical, would result in the formation of (II). However, attempt at the preparation of a bischolestadiene by the heating of isocholestadiene with glacial acetic acid failed totally.

A new substance (VIII), m.p. 78~80°, yet unknown in literature, was obtained when 7β-bromocholesteryl tosylate (VII) was heated with fused potassium acetate in dehydrated methanol. Analytical values and ultraviolet absorption, $\lambda_{max}^{Et_2O}$ 254 and 272 mμ, indicated that the new substance (VIII) might be a hydrocarbon of a probable structure of $\Delta^{1,8(9)}$ or $\Delta^{6,8(14)}$-isocholestatriene. During this reaction, a small amount of needle crystals, m.p.

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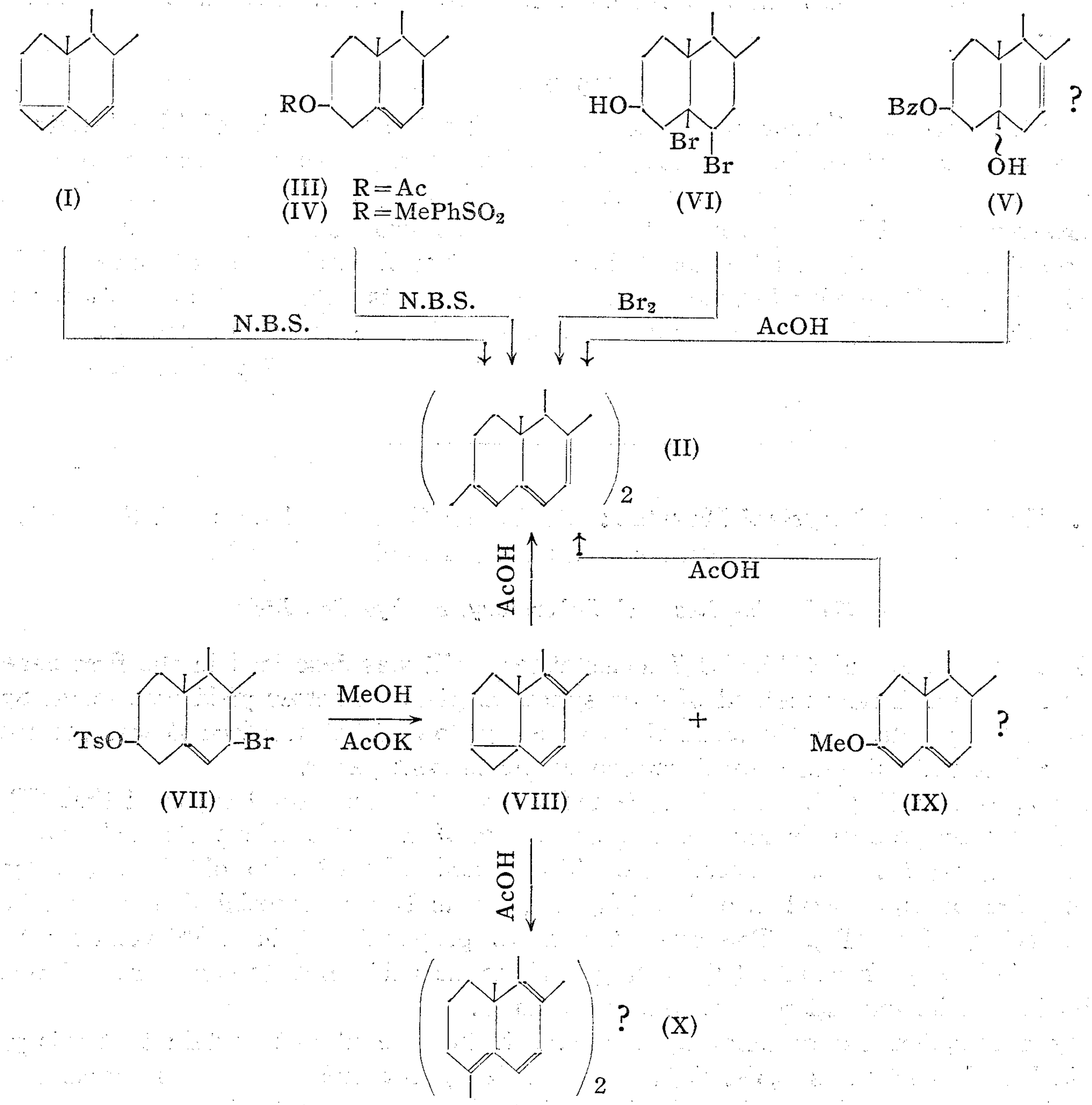
1) Part I: This Bulletin, 1, 212 (1953).
2) Hafez: Nature, 165, 401 (1950).
3) Ottke, Bergman: Nature, 166, 997 (1950).
4) Tsuda, *et al.*: J. Pharm. Soc. Japan, 71, 282(1951) (C. A., 45, 8151 (1951); *ibid.*, 71, 275(1951) (C. A., 45, 8150(1951)); *ibid.*, 72, 182(1952)(C. A. 47, 2190(1953)).
5) Part III: This Bulletin, 1, 220 (1953).

89～92°, were obtained whose analytical values and ultraviolet absorption, $\lambda_{\max}^{Et_2O}$ 235 and 244 mμ, suggested that it might be 3-methoxy-$\Delta^{4,6}$- or -$\Delta^{3,5}$-cholestadiene (IX).



The objective yellow needles precipitate out when (VIII) or (IX) is boiled in glacial acetic acid for two hours. When (IX) is used as the starting material, (II) alone is formed but, when (VIII) is used, some yellow crystals of m.p. 252°(decomp.), more easily soluble in ether than (II) and can be recrystallized from a mixture of ether and methanol, are also obtained besides 3,3′-bis(3,5,7-cholestatriene) (II). The analytical values of these yellow crystals agreed with those of bicholestatriene and, since its ultraviolet absorption maxima appeared at 351, 359, and 370 mμ, the compound was assumed to possess six conjugated double bonds. Though the bonding position is unknown, it is certain that it is not at 3 and 3′, and since 5 and 5′ seems impossible due to steric hindrance, 4 and 4′ bonding is more likely. This compound was tentatively designated as bicholestatriene B and a structure of 4,4′-bis(4,6,8(9)- or 4,6,8(14)-cholestatriene) is assumed for it although there are many points that still remain obscure.

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Experimental

Preparation of isocholestatriene (VIII)—A mixture of 1.2 g. of 7β-bromocholesteryl tosylate, 100 cc. of dehydrated methanol, and 1.2 g. of fused potassium acetate was boiled with reflux for 12 hours by which the mixture became a clear solution. About one-half the total amount of methanol was distilled off, a large amount of water was added, and extracted with ether. The ether layer was washed with water, dried, and the ether removed by low-pressure distillation from which about 300 mg. of pale yellow oil was obtained. Addition of acetone separated a small amount of crystals which were recrystallized from acetone to needles, m.p. 89~92°. *Anal.* Calcd. for $C_{28}H_{46}O$: C, 84.21; H, 11.52. Found: C, 84.31; H, 11.66. Ultraviolet absorption: $\lambda_{max}^{Et_2O}$ 235 and 244 mμ, log ε= 3.49 and 3.65. These values correspond to those of 3-methoxycholestadiene (IX). Yield, 50 mg.

The mother liquor obtained after the separation of above crystals, when allowed to stand in an ice chamber for a long period of time, yielded some crystals of m.p. 78~80° which were assumed to be an isocholesteroidal hydrocarbon from the analytical values and ultraviolet abosorption maxima. Yield, 150 mg. *Anal.* Calcd. for $C_{27}H_{42}$: C, 88.51; H, 11.41. Found: C, 88.26; H, 11.76. Ultraviolet absorption: $\lambda_{max}^{Et_2O}$ 254 and 272 mμ, log ε=3.42 and 3.25.

Preparation of 3,3′-bis(3,5,7-cholestatriene) (II) and bicholestatriene B (X)—A solution of 300 mg. of isocholestatriene (VIII) or 3-methoxycholestadiene (IX) dissolved in 40 cc. of glacial acetic acid was boiled with reflux for 2 hours and yellow crystals began to separate out during the reaction. When cooled, the whole mixture was filtered, the yellowish brown resinous matter on the filter was washed with ether, and the yellow needle crystals that remained were recrystallized from benzene. Such crystals generally melted at 242~244° with decomposition but when determined rapidly by dipping the capillary in a bath of 240°, the crystals melted at 260° without decomposition. The ultraviolet absorption maxima of 352 and 369.5 mμ agreed with those of 3,3′-bis(3,5,7-cholestatriene). *Anal.* Calcd. for $C_{54}H_{82}$: C, 88.76; H, 11.23. Found: C, 88.40; H, 11.77.

When isocholestatriene was used as the starting material, two kinds of bicholestatriene were obtained. The yellow crystals that separate out on the addition of methanol to the ether washing, when recrystallized from a mixture of ether and methol, showed m.p. 252°(decomp.). *Anal.* Calcd. for $C_{54}H_{82}$: C, 88.76; H, 11.23. Found: C, 88.90; H, 11.80. Ultraviolet absorption: $\lambda_{max}^{Et_2O}$ 351, 359, and 370 mμ; log ε=4.23, 4.33, and 4.22. These values agreed with those of bicholestatriene and the compound was designated as bicholestatriene B.

Summary

7β-Bromocholesteryl tosylate was treated with potassium acetate in dehydrated methanol and an unknown hydrocarbon, assumed to be $\Delta^{6,8(9)}$- or $\Delta^{6,8(14)}$-isocholestatriene, was obtained. In this instance, 3-methoxycholestadiene was formed as a by-product. These two compounds, when heated with glacial acetic acid, both formed 3,3′-bis(3,5,7-cholestatriene) but when the isocholestatriene was used as the material, another new hydrocarbon, bicholestatriene B, was formed as a by-product.

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