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# PHOTOCHEMICAL TRANSFORMATIONS OF DIENES<sup>1</sup> II. THE PHOTOLYSIS OF 3-METHYLCHOLESTA-3,5-DIENE (V)<sup>2</sup>

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#### ABSTRACT

Photolysis of 3-methylcholesta-3,5-diene (V) in ethanol gave 3-methylenecholest-5-ene (VI),  $6\beta$ -ethoxy- $3\alpha$ -methyl- $3\beta$ ,5-cyclo- $5\beta$ -cholestane (VII),  $3\beta$ -ethoxy- $3\alpha$ -methylcholest-5-ene (VIII), and  $3\alpha$ -methylcholesterol (VIIIa) as well as a number of unidentified hydrocarbons and alcohols. A similar photolysis in pentane, followed by reaction of the resulting  $3\beta_{,5};4\alpha_{,6}\alpha_{-}$ bicyclo-5 $\beta$ -cholestane (IIa) with ethanol, gave the cyclo ether VII as the only isolable product.

Recently, Dauben et al. (2) reported that the photolysis of cholesta-3,5-diene (I) in ethanol gave 6-ethoxy- $3\beta$ ,5-cyclo- $5\beta$ -cholestane (III) accompanied by a minor amount of the A-nor ether IV. These two products were also obtained in identical yields by the reaction of ethanol with the bicyclobutane II, itself obtained by irradiation in pentane



of diene I. Since we were interested in obtaining compounds of type III bearing an alkyl group at  $C_3$ , we decided to irradiate 3-methylcholesta-3,5-diene (V).

Cholest-4-en-3-one (3) was treated with methyl magnesium iodide (4). The resulting diene V absorbed in the ultraviolet at 232, 239, and 248 m $\mu$  (log  $\epsilon$  4.26, 4.29, 4.16).

A solution of diene V in ethanol-pentane (1:9)<sup>5</sup> was irradiated with a 450 W mercury arc lamp until the ultraviolet absorption of the reaction mixture between 220 and 400 m $\mu$ was negligible. The solvent was then evaporated and the residue chromatographed on silica gel.

1. Hexane eluted an oil (6.8%) which could not be crystallized. The nuclear magnetic resonance (n.m.r.)<sup>6</sup> indicated the presence of starting material, 3-methylenecholest-5-ene (VI), and other olefins which could not be separated.

- <sup>2</sup>Presented in part at the A.C.F.A.S. meetings in Montreal (1962) and Quebec (1963). <sup>3</sup>From part of the thesis presented by V.D.T. in partial fulfillment of the requirements for the Ph.D. degree. <sup>4</sup>Holder of a National Research Council of Canada Studentship 1962–1963.
- <sup>5</sup> Very similar results were obtained when absolute ethanol was used as solvent.

 $^{6}Tetramethylsilane = 0.$ 

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<sup>&</sup>lt;sup>1</sup>For paper I, see reference 1.

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2. Further elution with hexane gave a crystalline diene,  $\nu$  3030, 1648, and 888 cm<sup>-1</sup> (C=CH<sub>2</sub>),  $\delta$  4.55 p.p.m. (2H, C=CH<sub>2</sub>) and 5.29 p.p.m. (1H, C=CH–), in approximately 15% yield. The diene VI did not absorb in the ultraviolet between 220 and 400 mµ and was hence not conjugated. Catalytic hydrogenation with platinum oxide in acetic acid gave 3-methylcholestane (IX) (5). Treatment with perchloric acid in dioxane at 70° overnight gave a quantitative yield (by ultraviolet) of 3-methylcholesta-3,5-diene (V). Chemical and spectral properties of the diene were compatible with 3-methylene-cholest-5-ene (VI). However, all attempts to prove the proposed structure by degradation reactions or by synthesis were unsuccessful. An indirect proof of structure was therefore sought. Diene VI was treated with slightly less than one equivalent of diborane in diglyme for 1 h (6). Chromatography gave 3-hydroxymethylcholest-5-ene (X), identical in all respects with a sample prepared by reaction of the Grignard reagent from cholesteryl chloride (XI) in tetrahydrofuran with paraformaldehyde.

3. Elution with benzene and crystallization from hexane gave a compound,  $C_{30}H_{52}O$ ,<sup>7</sup> in 20–30% yield. Its n.m.r. spectrum showed a pair of one proton doublets (J = 4.5 c.p.s.) at -0.47 and 0.45 p.p.m. characteristic for geminal protons (7) on a cyclopropane ring, and a three proton signal in the 3–3.5 p.p.m. region. This signal was very similar to that shown by photoether III. By analogy with Dauben's work (2) on cholesta-3,5-diene (I), this compound was assigned structure VII. Heating under reflux of photoether VII with perchloric acid in dioxane gave 5% (identified by ultraviolet analysis) of 3-methyl-cholesta-3,5-diene (V) and a mixture of alcohols which could not be separated.

Chromatography of the photoether VII on alumina (activity I) resulted in the loss of the elements of ethanol (2a) and the formation of olefin XIII, similar to that described by Dauben (2) in the 3-unsubstituted series. The signals for the  $C_4$ -cyclopropane protons were now at -0.08 and 0.59 p.p.m. (J = 5 c.p.s.). The olefinic protons at C<sub>6</sub> and C<sub>7</sub> were chemically equivalent and appeared as a singlet at 5.38 p.p.m. Comparison of the n.m.r. spectrum of this olefin with  $3\beta_{0.5}$ -cyclo- $5\beta_{0.5}$ -cholest-6-ene (XIIIa) (2a) and  $3\alpha_{0.5}$ -cyclo- $5\alpha_{0.5}$ -cyclo-5cholest-6-ene (XV) (8, p. 318) supported quite conclusively the stereochemical assignment of the cyclopropane ring (see Table I). In the case of the  $\Delta^6$ -3 $\beta$ ,5-cyclo derivatives, the two olefinic protons appeared essentially as a singlet, whereas in the  $3\alpha$ ,5-cyclo compound, the C<sub>6</sub> and C<sub>7</sub> olefinic protons appeared as an evenly spaced (J = 10 c.p.s.) four line system centered at 5.33 p.p.m. Heating olefin XIII under reflux with perchloric acid in aqueous dioxane gave a 24% yield of 3-methylcholestadiene (V). When ethanol was used as a solvent and the solution refluxed overnight, 21% diene V (identified by ultraviolet analysis) and variable yields (5-30%) of  $3\beta$ -ethoxy- $3\alpha$ -methylcholest-5-ene (VIII) were obtained. Ether VIII was identical in all respects with the photoether described below. These experiments showed that the 3-methyl group influenced markedly the course of the acid-catalyzed reaction of both ether VII and olefin XIII, and probably stabilized a positive charge at C<sub>3</sub> in an intermediate carbonium ion (no formation of cholestadiene or cholesterol was detected in a similar reaction of photoether III).

Catalytic hydrogenation of olefin XIII with platinum oxide in acetic acid at 40° and 60 p.s.i. gave  $3\alpha$ -methyl- $3\beta$ ,5-cyclo- $5\beta$ -cholestane (XIV),  $\delta$  0.44 p.p.m. (1H, doublet, J = 4.45 c.p.s.) and -0.35 p.p.m. (1H, triplet,<sup>8</sup> J = 4.5 c.p.s.).

4. Elution with benzene-ether (4:1) gave an olefinic ether, in 20-30% yield. The n.m.r. spectrum showed low-field signals at 3.45 p.p.m. (2H, quartet, J = 7 c.p.s., OCH<sub>2</sub>CH<sub>3</sub>) and 5.26 p.p.m. (1H, broad, C=C-H) only. Heating ether VIII under reflux with

<sup>7</sup>This compound could also be obtained by direct crystallization of the crude photoylsis mixture. <sup>8</sup>Due probably to long-range coupling, which will be discussed in a forthcoming paper.

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pyridine hydrochloride in acetic acid gave 3-methylcholesta-3,5-diene (V). Catalytic reduction at 60 p.s.i. and 40° in acetic acid gave 3-methylcholestane (IX) (5) (29%) and  $3\beta$ -ethoxy- $3\alpha$ -methylcholestane (XII) (51%). The reduced photoether was obtained in 78% yield as the only crystalline product when sodium nitrite was added to the reaction mixture (9). All attempts to hydrolyze the ether function of either VIII or XII failed and resulted either in recovery of starting material or formation of olefins. The reduced photoether XII was oxidized with ruthenium tetroxide in carbon tetrachloride (10) to a



mixture of  $3\alpha$ -methylcholestan- $3\beta$ -ol (XIIa) and its acetate XIIb. Both compounds were identified by comparison with an authentic sample (5b, 11), and were distinctly different from the C<sub>3</sub>-epimers (5b). This proved the stereochemistry at the C<sub>3</sub>-position.

Since the reduction of photoether VIII had resulted in hydrogenolysis, when no sodium nitrite had been added, and since molecular rotation increments upon hydrogenation of VIII to XII did not permit unambiguous assignment of the position of the double bond to either the 4- or the 5-position, it was determined in the following way. Reaction with osmium tetroxide gave diol XVI, which was further oxidized to keto acid XVII (3.37 p.p.m., 2H, quartet, J = 7 c.p.s.) by chromic acid in aqueous acetic acid at room temperature. When the chromic acid oxidation was carried out at a higher temperature, the dehydroethoxylated keto acid XVIII was obtained. Keto acid XVIII was also obtained by heating XVII with Fehling's solution or with pyridine hydrochloride in acetic acid. Keto acid XVIII, obtained from the three reactions, was amorphous. Its spectral properties were characteristic of an  $\alpha,\beta$ -unsaturated ketone ( $\lambda C_{max}^{ex12}$  231 m $\mu$ ,  $\lambda_{max}^{EtoH}$  236 m $\mu$ ,

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 $\nu_{\rm CCl_4}$  1675 cm<sup>-1</sup>) and not of an  $\alpha,\beta$ -unsaturated acid. When XVIII was treated with ethereal diazomethane, an amorphous methyl ester was obtained. It absorbed in the ultraviolet at 236 m $\mu$  (ethanol) and in the infrared at 1675 cm<sup>-1</sup> and 1738 cm<sup>-1</sup>, confirming the assignment of the functional groups in XVIII.

The identity of photoether VIII was further proved by comparison with the ethanolysis product of  $3\alpha$ -methylcholesteryl mesylate (5b).

5. Elution with ether gave, in 6.7% yield, an oil from which some  $3\alpha$ -methylcholesterol (5b) was isolated.

When the photolysis of 3-methylcholesta-3,5-diene (V) was carried out in pentane, and the solvent evaporated carefully, an oil,  $[\alpha]_{\rm D} - 85^{\circ}$ ,  $\delta - 0.34$  p.p.m. (J = 2.65 c.p.s.) was obtained (see Fig. 1). The high-field n.m.r. signal of the oil was most likely due to a



FIGS. 1-4. Fig. 1, taken in deuterochloroform; Figs. 2-4, taken in carbon tetrachloride.

proton attached to the bicyclobutane ring system in IIa, which, judging from the intensity of the peak, was present in approximately 30%. Treatment of the oil with boiling ethanol gave photoether VII as the only crystalline product in 20-30% yield. The reaction was repeated a number of times. In no instance was it possible to detect even a trace of VIII either by thin-layer chromatography or by other chromatographic procedures.

The photolysis in ethanol hence gave a different product distribution than the photolysis in pentane, followed by a dark reaction in ethanol. This is in marked contrast to the results described by Dauben for the 3-unsubstituted cholestadiene (I), in which identical products had been obtained in both sets of reactions.

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Further work is in progress to establish the mode of formation of some of the photoproducts described.

## EXPERIMENTAL

All melting points were taken in a melting point tube and were uncorrected. Infrared spectra were taken on a Perkin-Elmer 21 spectrophotometer in carbon tetrachloride unless otherwise stated. Ultraviolet spectra were taken on a Bausch and Lomb Spectronic 505 or Beckman DK 1 spectrophotometer. Nuclear magnetic resonance spectra were taken on a Varian HR 60 spectrometer in carbon tetrachloride (tetramethylsilane = 0 p.p.m.). Optical rotations were measured on a C. Zeiss Photoelectric Precision polarimeter  $(0.005^{\circ})$  in chloroform. The adsorbents used for chromatography were Woelm neutral alumina and Grace No. 923 silica gel. The microanalyses were carried out by Mr. A. Bernhardt, and associates, Mulheim, Germany, and Dr. C. Daessle, 5757 Decelles St., Montreal.

#### Preparation of 3-Methylcholesta-3,5-diene (V)

Diene V was prepared by slowly adding 15 g of cholest-4-en-3-one, dissolved in 100 ml of absolute ether, to 20 ml of ethereal methyl magnesium iodide, prepared from 2.66 g of magnesium and 7.35 ml of methyl iodide, and the solution was gently refluxed overnight. Aqueous ammonium chloride was added to the cooled mixture. Ether was added and the organic solution was washed neutral with water. After evaporation of the ether, the oily residue was refluxed overnight in 200 ml of ethanol and 20 ml of concentrated hydrochloric acid, diluted with ether, and washed with aqueous sodium bicarbonate and water until neutral. The solvent was then evaporated until crystals began to form. A slow crystallization gave 11.683 g of diene V, m.p. 82–83° (80° (4a));  $[\alpha]_{\rm D} - 120.4^{\circ}$  (c 1.4);  $\delta$  5.36 p.p.m. (C=C<sub>6</sub>-H), 5.78 p.p.m. (C=C<sub>4</sub>-H). Calc. for C<sub>28</sub>H<sub>46</sub>: C, 87.88; H, 12.12. Found: C, 87.80; H, 12.21.

#### Photolysis of Diene V in Ethanol -n-Pentane<sup>9</sup>

Diene V (10 g) was dissolved in 405 ml of spectrograde *n*-pentane. To the solution was added 45 ml of absolute ethanol. The solution was then irradiated with a 450 W high pressure mercury arc lamp,<sup>10</sup> until there was no absorption in the ultraviolet between 220 and 400 m $\mu$  (67 h). The pentane-ethanol was removed by distillation. The oily residue (14.821 g) was dissolved in 50 ml of warm hexane. After the mixture had cooled and had been allowed to stand at room temperature for a few hours, 1.1 g of 6 $\beta$ -ethoxy-3 $\alpha$ -methyl-3 $\beta$ ,5-cyclo-5 $\beta$ -cholestane (VII), m.p. 129°, was obtained. The mother liquors were chromatographed on 500 g of silica gel.

Elution with 300 ml of hexane gave 0.79 g of a hydrocarbon mixture containing trace amounts of starting material and non-conjugated diene VI, which could not be separated into its components by preparative thin-layer chromatography.

Further elution with 900 ml of hexane gave 1.754 g of crystalline 3-methylenecholest-5-ene (VI), m.p. 109°. Crystallization from ether-acetone raised the melting point to  $109-110^\circ$ ;  $[\alpha]_D -32.4^\circ$  (c 0.344);  $\nu$  3030, 1648, 888 cm<sup>-1</sup> (C=CH<sub>2</sub>);  $\delta$  4.55 p.p.m. (2H, singlet, C=CH<sub>2</sub>), 5.29 p.p.m. (1H, poorly resolved, C=C<sub>6</sub>-H). Calc. for C<sub>28</sub>H<sub>46</sub>: C, 87.88; H, 12.12. Found: C, 87.81; H, 12.03.

Elution with hexane-benzene mixtures gave small amounts (0.138 g) of oil.

Benzene (600 ml) eluted 2.388 g of 6 $\beta$ -ethoxy-3 $\alpha$ -methyl-3 $\beta$ ,5-cyclo-5 $\beta$ -cholestane (VII), m.p. 120–123°. Two crystallizations from hexane gave 1.22 g of VII, m.p. 130–131°; [ $\alpha$ ]<sub>D</sub> 26.1° (*c* 1.5);  $\nu$  3040 cm<sup>-1</sup> (cyclopropane), 1092, 1102, 1128, 1162 cm<sup>-1</sup> (C—O—C);  $\delta$  –0.47 and 0.45 p.p.m. (1H each, doublet, J = 4.5 c.p.s., geminal protons on cyclopropane ring), 3–3.5 p.p.m. (3H, poorly resolved). Calc. for C<sub>30</sub>H<sub>52</sub>O: C, 84.04; H, 12.23. Found: C, 83.91; H, 12.13.

Further elution with 450 ml of benzene-ether (9:1) gave 0.572 g of a colorless oil.

Elution with 150 and 450 ml of benzene-ether (4:1 and 1:1 respectively) gave 3.111 g of VIII, m.p. 120-121°. Two crystallizations from acetone gave long fine needles, m.p. 125-126°;  $[\alpha]_D - 20.7°$  (c, 1.06);  $\nu$  1070, 1110, 1125 cm<sup>-1</sup> (C-O-C);  $\delta$  3.45 p.p.m. (2H, quartet, J = 7 c.p.s. OEt), 5.26 p.p.m. (1H, poorly resolved, C=C<sub>6</sub>-H). Calc. for C<sub>30</sub>H<sub>52</sub>O: C, 84.03; H, 12.22; OEt, 10.5%; molecular weight, 428.7. Found: C, 83.78; H, 11.97; OEt, 9.09%; molecular weight, 411 (Rast).

Elution with ether gave 1.8 g of a yellow oil,  $\nu$  3500, 1000–1100 cm<sup>-1</sup> (broad bands, OH).

When the photolysis was carried out in *n*-pentane until the ultraviolet was clear between 220 and 400 m $\mu$ , and the pentane was removed by vacuum distillation at room temperature, an oily residue,  $[\alpha]_D - 85^{\circ}$  (c 0.8 in CDCl<sub>3</sub>) was obtained (see Fig. 1 for n.m.r.). The oily residue was refluxed with 100 ml of absolute ethanol for 1 h. The ethanol was distilled off and the semicrystalline residue taken up in hexane. Crystallization gave photoether VII, m.p. 127°. Chromatography of the mother liquors on silica gel gave additional amounts of photoether VII only.

#### Hydrogenation of 3-Methylenecholest-5-ene (VI)

An acetic acid solution of diene VI (0.196 g) was hydrogenated at room temperature for 20 h using

<sup>9</sup>The yields obtained in several runs varied considerably.

<sup>10</sup>The lamp was cooled by running water in a quartz or vycor jacket, supplied by Hanovia Lamp Division, 100 Chestnut St., Newark, N.J., U.S.A.

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0.15 g of platinum oxide as catalyst. The platinum was filtered off and the filtrate diluted with water and ether. A saturated sodium bicarbonate solution (125 ml) was added slowly until the acetic acid was neutralized. The ether layer was then washed neutral, dried over magnesium sulphate, and evaporated. The crystalline residue, m.p.  $91-94^{\circ}$ , melted after two recrystallizations from ether-methanol at  $100-101^{\circ}$  (142 mg), [ $\alpha$ ]<sub>D</sub> 24.8° (c 0.55). The melting point was not depressed upon admixture of an authentic sample of 3-methyl-cholestane (IX) (5b). Calc. for C<sub>28</sub>H<sub>50</sub>: C, 86.97; H, 13.03. Found: C, 87.01; H, 13.11.

## 3-Methylcholesta-3,5-diene from VI

Diene VI (0.18 mg) was dissolved in 10 ml of spectrograde dioxane. To this solution was added 1 drop of 72% perchloric acid. The ultraviolet (u.v.) spectrum was transparent between 220-400 m $\mu$ . Upon standing at 70° for 12 h, the solution absorbed at 232, 239, and 248 m $\mu$  (log  $\epsilon$  4.26, 4.29, and 4.16).

#### 3-Hydroxymethylcholest-5-ene (X)

#### 1. From 3-methylenecholest-5-ene (VI)

Sodium borohydride (18 mg) was added to 383 mg (1 mmole) of diene VI in 25 ml of diglyme. Boron trifluoride etherate (1 ml) was added to the solution. After the mixture was stirred for 1 h, 10 ml of 30% hydrogen peroxide was added slowly. The solution was diluted with 50 ml of ether and 50 ml of water. The ether layer was washed until neutral, dried over magnesium sulphate, and evaporated. The oily residue (350 mg) was chromatographed on 20 g of silica gel. Hexane eluted 63 mg of oil containing 3-methyl-cholesta-3,5-diene (V) (u.v.). Further elution with hexane-benzene and benzene-ether mixtures gave oils which were not investigated. Ether eluted 97 mg of 3-hydroxymethylcholest-5-ene (X) (8, p. 33), m.p. 120°. Recrystallizations from acetone gave pure X, m.p. 129-130°;  $[\alpha]_D - 38.4^\circ$  (c 1.0);  $\nu$  3630, 975-1050 cm<sup>-1</sup> (broad band, OH);  $\delta$  2.96 p.p.m. (1H, singlet, exchanged in D<sub>2</sub>O, OH), 3.4 p.p.m. (2H, poorly resolved signal, C=C<sub>6</sub>—H). Calc. for C<sub>28</sub>H<sub>48</sub>O: C, 83.93; H, 12.08. Found: C, 83.72; H, 12.19.

## 2. From Cholesteryl Magnesium Chloride and Formaldehyde

Cholesteryl chloride (12) was prepared by dissolving cholesterol in thionyl chloride and destroying the excess thionyl chloride by addition to a large excess of water. The water-washed solid residue was recrystallized from ether to give pure cholesteryl chloride, m.p. 97°. Tetrahydrofuran (100 ml) was refluxed over lithium aluminum hydride and distilled directly into a flask containing 2.48 g of magnesium. Methyl iodide (3 ml) was then added and the mixture was heated under reflux for 48 h. After cooling of the mixture, 9.2 g of cholesteryl chloride was added, and the solution was heated under reflux for 48 h. Solid paraformaldehyde (4.6 g) was added to the refluxing solution and the heating continued for another 24 h. A cold aqueous ammonium chloride solution (8 g NH<sub>4</sub>Cl in 50 ml of water) was added drop by drop to the cooled reaction mixture. The mixture was taken up in ether, washed neutral with water, dried over magnesium sulphate, and evaporated. The semicrystalline residue (6.4 g) was chromatographed on alumina (II–III, 200 g).

Elution with hexane gave 3.6 g of cholest-5-ene, m.p.  $90-91^{\circ}$ . Recrystallization from ether gave pure cholest-5-ene, m.p.  $92-93^{\circ}$ ;  $[\alpha]_{\rm D} -70.5^{\circ}$  (c 2.4);  $\delta$  5.09 p.p.m. (1H, broad signal, C=C<sub>6</sub>—H). Calc. for C<sub>27</sub>H<sub>46</sub>: C, 87.49; H, 12.51. Found: C, 87.38; H, 12.48.

Cholest-5-ene, on hydrogenation in acetic acid with platinum oxide, gave cholestane, m.p. 78-79°, which was depressed upon admixture of 3-methylcholestane and not depressed upon admixture of authentic cholestane.

Further elution with benzene gave 2.153 g of 3-hydroxymethylcholest-5-ene (X), m.p. 110–115°, which, on two crystallizations from acetone, melted at 129–130°. The infrared spectrum of X was identical with that obtained from the hydroboration of 3-methylenecholest-5-ene (VI) described above.

Further elution with the same solvent gave 0.37 g of cholesterol, m.p. 146–148°, which was not depressed upon admixture of an authentic sample. The reaction was carried out in absolute tetrahydrofuran. Use of dioxane or tetrahydrofuran which was not meticulously dried gave only cholest-5-ene and cholesterol. In "absolute" ether, only cholesterol was isolated.

## $\Im_{\alpha}$ -Methyl- $\Im_{\beta}$ ,5-cyclo- $5\beta$ -cholest-6-ene (XIII)

Photoether VII (411 mg) was chromatographed on alumina (1, 20 g). Elution with hexane gave 252 mg of  $3\alpha$ -methyl-3 $\beta$ ,5-cyclo-5 $\beta$ -cholest-6-ene (XIII), m.p. 56–61°. Two crystallizations from ethyl acetate raised the melting point to 67–68°, [ $\alpha$ ]<sub>D</sub> 22.8° (*c* 1.0),  $\delta$  –0.08 and 0.59 p.p.m. (1H each, J = 5 c.p.s., geminal protons on cyclopropane ring), and 5.38 p.p.m. (2H, "singlet"). Calc. for C<sub>28</sub>H<sub>46</sub>: C, 87.88; H, 12.12. Found: C, 87.78; H, 12.01.

#### $3\alpha$ -Methyl- $3\beta$ , 5-cyclo- $5\beta$ -cholestane (XIV)

An acetic acid – ether (4:1, 5 ml) solution of 202 mg of XIII was hydrogenated at atmospheric pressure in the presence of 150 mg of platinum oxide. After 16 h, the platinum was filtered off. The filtrate was diluted with ether and water. The ether layer was washed until neutral, dried over magnesium sulphate, and evaporated. Chromatography of the oily residue on alumina (I, 10 g) gave  $3\alpha$ -methyl- $3\beta$ ,5-cyclo- $5\beta$ -cholestane (XIV), m.p. 72–74°. Two crystallizations from acetic acid raised the melting point to 77–78°,

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 $[\alpha]_{D}$  32.0° (c 1.1),  $\delta$  0.44 p.p.m. (1H, doublet, J = 4.45 c.p.s.), and -0.35 p.p.m. (1H, triplet, J = 4.5 c.p.s.). Calc. for C<sub>28</sub>H<sub>48</sub>: C, 87.42; H, 12.58. Found: C, 87.15; H, 12.75.

### Treatment of $3\alpha$ -Methyl- $3\beta$ ,5-cyclo- $5\beta$ -cholest-6-ene (XIII) with Perchloric Acid and Ethanol

Perchloric acid (72%, 30 mg) was added to an ethanolic solution (30 ml) of 141 mg of XIII. The solution was heated under reflux overnight, cooled, and diluted with water and ether. The dried ether layer gave, upon evaporation, 155 mg of an oily residue, which had the characteristic ultraviolet absorption pattern of 3-methylcholesta-3,5-diene (V),  $\lambda_{\rm EtcH}^{\rm EtcH} 230 \, \rm m\mu$  (log  $\epsilon$  3.61, i.e. 21% diene V). The oily residue was chromatographed on alumina (I, 10 g). Elution with hexane gave 43 mg of oils. Further elution gave 25 mg of 3-methylcholesta-3,5-diene (V), m.p. 79°. Benzene eluted 48 mg (34%) 3\beta-ethoxy-3a-methylcholest-5-ene (VIII), m.p. 119-123°. Recrystallization from acetone raised the melting point to 126°. Admixture of an authentic sample did not depress the melting point.

## Treatment of 3a-Methyl-33,5-cyclo-53-cholest-6-ene (XIII) with Perchloric Acid in Aqueous Dioxane

The reaction described above was carried out in 50 ml of 10% aqueous dioxane containing 1 ml of 72% perchloric acid. Evaporation of the ether gave an oily residue which contained 24% of 3-methylcholesta-3,5-diene (V) (by u.v.,  $\lambda_{max}^{E10}$  239 m $\mu$  (log  $\epsilon$  3.65)). Chromatography on alumina (I) gave diene V, m.p. 78°, as the only crystalline compound.

## $\beta$ -Ethoxy- $\beta\alpha$ -methylcholestane (XII)

Photoether VIII (153 mg) in 40 ml of acetic acid was hydrogenated for 14 h at 40° and 60 p.s.i. with 141 mg of platinum oxide catalyst in a Parr apparatus. The reaction mixture was worked up as described above. The oily residue (152 mg) was chromatographed on alumina (I, 5 g). Elution with hexane gave 44 mg of 3-methylcholestane (IX), m.p. 99°. Crystallization raised the melting point to 99–100°. Admixture of an authentic sample did not depress the melting point. Elution with hexane : benzene (1:1) gave 77 mg of  $\beta\beta$ -ethoxy- $3\alpha$ -methylcholestane (XII), m.p. 81–83°. Crystallization from ether-methanol raised the melting point to 89–90°, [ $\alpha$ ]p 2° (c 0.33),  $\nu$  1165, 1100 cm<sup>-1</sup> (OEt). Calc. for C<sub>30</sub>H<sub>34</sub>O: C, 83.65; H, 12.64. Found: C, 83.84; H, 12.79.

As was found out later, the hydrogenolysis reaction could be suppressed by the addition of 10% (based on the weight of VIII) sodium nitrite (5b, 9). In this case, a 78% yield of XII, m.p. 89–90°, was obtained.

## Oxidation of $_{3\beta}$ -Ethoxy- $_{3\alpha}$ -methylcholestane (XII) with Ruthenium Tetroxide

Ether XII (55 mg) in 10 ml of carbon tetrachloride was oxidized with 42 mg of ruthenium tetroxide at room temperature, according to the procedure of Bokowicz and Rylander (10). The oily reaction product (161 mg) was chromatographed on alumina (II–III, 2 g). Elution with hexane gave 16 mg of  $3\beta$ -acetoxy- $3\alpha$ -methylcholestane (XIIb), m.p. 85–95°. The infrared spectrum was identical with that of an authentic sample and different from that of  $3\alpha$ -acetoxy- $3\beta$ -methylcholestane (5b). Elution with benzene gave 32 mg of  $3\alpha$ -methylcholestan- $3\beta$ -ol (XIIa), m.p. 148°. Crystallization from ether-methanol raised the melting point to 149° (150° (11)). Admixture of authentic sample did not depress the melting point. The infrared spectrum was identical with that of an authentic sample and markedly different from its epimer in the 1000–1250 cm<sup>-1</sup> region (5b);  $[\alpha]_D$  36.9° (c 0.34), lit. 28° (c 1.68) (11). Calc. for C<sub>28</sub>H<sub>50</sub>O: C, 83.51; H, 12.52. Found: C, 83.38; H, 12.30.

### Oxidation of $3\beta$ -Ethoxy- $3\alpha$ -methylcholest-5-ene (VIII) with Osmium Tetroxide

Photoether VIII (402 mg) was dissolved in 10 ml of dry ether and 2 ml of pyridine which contained 397 mg of osmium tetroxide (13). The oxidation was carried out in the dark at 33° for 7 days. The solution was worked up according to the procedure given by Woodward *et al.* (13). The oily residue (446 mg) was chromatographed on alumina (IV, 15 g). Elution with hexane gave 315 mg of diol XVI, m.p. 140–141°. Crystallization from hexane raised the melting point to  $141-142^\circ$ ,  $[\alpha]_D 21.6^\circ$  (*c* 0.44),  $\nu$  3475, 3600, 1160 cm<sup>-1</sup> (OH),  $\delta$  2.45 p.p.m. (1H, broad singlet, OH), 3.31 p.p.m. (2H, quartet, J = 6.6 c.p.s., OEt), 4.61 p.p.m. (1H, singlet, OH). It was found that at 18°, 25°, and 33°, the yields of diol XVI were 30, 70, and 74% respectively. Calc. for C<sub>30</sub>H<sub>54</sub>O<sub>3</sub>: C, 77.86; H, 11.76. Found: C, 77.62; H, 11.60.

### 5,6-Seco- $3\beta$ -ethoxy- $3\alpha$ -methylcholestan-5-on-6-oic Acid (XVII)

Chromium trioxide (120 mg) in 50% aqueous acetic acid (12 ml) was added slowly to 158 mg of diol XVI in 10 ml of acetic acid. The reaction mixture was kept at 50° overnight. (Under reflux, dehydroethoxylation occurred.) A few drops of methanol were added to destroy excess chromium trioxide. The solvent was removed at 40° under reduced pressure. The keto acid XVII was extracted with ether, and the organic solution washed until neutral, dried over magnesium sulphate, and evaporated. The oily residue (141 mg) was dissolved in a minimum amount of acetic acid, and a slow (3 days) crystallization was permitted to occur after a few drops of water had been added. Recrystallization of keto acid, m.p. 138–139°, gave 14 mg of keto acid XVII, m.p. 152°, [ $\alpha$ ]p 66° (c 0.46),  $\nu$  3000 cm<sup>-1</sup> and 1705 cm<sup>-1</sup>,  $\delta$  2.26 p.p.m. (2H, poorly resolved peak, CH—CH<sub>2</sub>—COOH), 2.67 p.p.m. (2H, singlet, O—C—CH<sub>2</sub>—C=O), 3.37 p.p.m. (2H, quartet, J = 7 c.p.s., OEt), 10.63 p.p.m. (1H, poorly resolved singlet, COOH). Calc. for C<sub>30</sub>H<sub>52</sub>O<sub>4</sub>: C, 75.60; H, 11.00. Found: C, 75.74; H, 10.86.

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Dehydroethoxylation of Keto Acid XVII

A solution of 182 mg of keto acid XVII in 20 ml acetic acid containing 400 mg of pyridine hydrochloride was refluxed overnight. The solution was diluted with ether and water. The ether layer was washed until neutral, dried over magnesium sulphate, and evaporated. The oily residue was chromatographed on silica gel (7.5 g). Benzene-ether mixtures eluted an oil which could not be crystallized;  $\nu$  1705 cm<sup>-1</sup> (COOH), 1675 cm<sup>-1</sup> (C=C-C=O),  $\lambda_{max}^{cyclohexane}$  230.5 mµ,  $\lambda_{max}^{EtOH}$  236 mµ.

In the presence of Fehling solution, the keto acid XVII was also dehydroethoxylated.

Methyl 5,6-seco-3-methylcholest-3-en-5-on-6-oate (XVIIIa)

Ethereal diazomethane was added to 126 mg of amorphous acid XVIII in cold ether containing a few drops of methanol. After 1 h, the excess diazomethane was destroyed by adding a few drops of acetic acid. The solvent was evaporated and the oily residue chromatographed on alumina (II–III, 5 g). Benzene and benzene-ether (95:5) eluted 66 mg of methylester XVIIIa, which could not be crystallized. The spectral data of XVIIIa were  $\lambda_{\text{max}}^{\text{EtOH}} 236 \text{ m}\mu \text{ (log } \epsilon 3.91), \nu 1738 \text{ cm}^{-1} \text{ (COOCH}_3), 1675 \text{ cm}^{-1} \text{ (C=C=C=O)}, \delta 1.93 \text{ p.p.m.}$  (3H, singlet, C=C-CH<sub>3</sub>), 2.2 p.p.m. (2H, doublet,  $J = 4.1 \text{ c.p.s.}, \text{CH-CH}_2$ -COO), 3.57 p.p.m. (3H, singlet, COOCH<sub>3</sub>), 5.57 p.p.m. (1H, singlet, C=CH-C=O).

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