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REACTIONS AND STEREOCHEMISTRY OF SOME 2-OXYGENATED A-HOMO-5α-CHOLESTANE DERIVATIVES

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Aluminum chloride catalyzed reaction of 3α,5-cyclo-5α-cholestan-2-one (*I*) with diazomethane furnishes 4α,5-cyclo-A-homo-5α-cholestan-2-one (*II*). Hydrogenation of *II* over Adams'catalyst in acetic acid followed by reoxidation affords 5-methyl-5β-choletan-2-one (*V*). Treatment of *II* with phenyltrimethylammonium perbromide leads to skeletal rearrangement resulting in formation of the bromine-free ketone *XIV* and its monobromo derivative *XV*. These results are interpreted in terms of the mechanism postulated by King and deMayo for thujone bromination. Hydride reduction of the ketone *II* gives alcohols *VI* and *VII*. The PMR-data and Dreiding model study lead to the postulation of a boat and half-chair conformation for the A-ring of *VI* and *VII*, respectively; in both conformations, the hydroxyl group is equatorial. An analogous study of 4,5-unsaturated 2-hydroxycholestenes *VIII* and *XI* leads to the postulation of half-chair A-ring conformations with equatorial hydroxyl for both epimeric alcohols *VIII* and *XI*.

In a preceding paper[1] we dealt with some reactions of 2-oxygenated 3α,5-cyclo-5α-cholestane derivatives. The present paper extends this study to reactions and stereochemistry of 2-oxygenated derivatives of 4α,5-cyclo-A-homo-5α-cholestane, *i.e.* 4α,5-cyclo-A-homo-5α-cholestan-2-one (*II*) and the respective epimeric 2-hydroxy derivatives *VI* and *VII*. The ketone *II* was prepared starting from the known[1] 3α,5-cyclo-5α-cholestan-2-one (*I*) by reaction with diazomethane catalyzed with aluminum chloride. Two reaction products were isolated from the reaction mixture. The chief product (50%) of molecular weight 398 (mass spectrometry) contains a cyclopropane ring, one proton of which can be detected in the PMR-spectrum as a quartet at 0·470 p.p.m. The keto group of this compound is not conj ugated with the cyclopropane ring. Since four hydrogens can be replaced with deuterium, this substance must be formulated as *II*. Its preponderance in the reaction mixture is in agreement with the expected methylene insertion between the cyclopropane ring and the carbonyl group[2,3]. The by-product, formed in ca 10% yield, was identified as 4α,5-cyclo-A-homo-5α-cholestan-3-one (*III*) on the basis of its spectroscopic properties and physical constants. This compound was prepared in a different manner by other authors[4].

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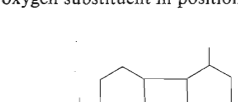
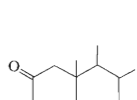
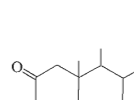
On hydrogenation over Adams'catalyst in acetic acid solution and reoxidation, the ketone *II* affords a new ketone. Spectroscopic data demonstrate the absence of the cyclopropane ring and, instead, presence of an additional tertiary methyl group. This evidence settles the structure *V* for this compound and the above mentioned procedure thus constitutes a preparative route for preparation of 5β-methyl steroids with an oxygen substituent in position 2.



I



II



V

III

IV

VI

VII

VIII, R = H
IX, R = Ac

X

XI

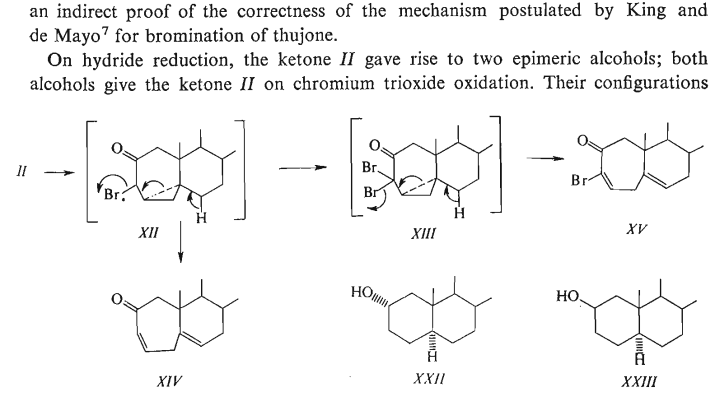
On bromination with phenyltrimethylammonium perbromide[5] the ketone *II* yields two compounds. The first, m.p. 120–121°C, contains no bromine and its elemental analysis is in accordance with the formula $C_{28}H_{44}O$. This composition is also evidenced by the molecular weight of 396 (mass spectrometry). The IR-spectrum discloses the presence of an α,β-unsaturated ketonic system. The PMR-spectrum demonstrates the presence of a —CO—CH=CH—CH_2— moiety and leads to the formula *XIV* for the compound. The multiplet observed at 5·34 p.p.m. indicates the presence of one non-conjugated, trisubstituted double bond and is attributable to the $C_{(6)}$-proton. The UV-spectrum (ethanol, λ_{max} 226 nm, calculated λ_{max} = 227 nm) is also in agreement with the structure *XIV*.

The composition of the second substance, m.p. 173–174°C, $C_{28}H_{43}BrO$, is that of a monobromo derivative of *XIV*. The IR-spectrum shows the presence of an α,β-unsaturated keto grouping. The UV-spectrum (ethanol) is consistent with the formula

XV (λ_{max} = 259 nm, calculated 250 nm; *cf.*[6]). Formula *XV* was confirmed by the PMR-spectrum in which the presence of one $C_{(4)}$-olefinic proton appears as a doublet of doublets at 7·42 p.p.m.. and of one $C_{(6)}$-olefinic proton as an unresolved multiplet centered at 5·38 p.p.m.. The signals of $C_{(4a)}$-protons show also the expected pattern as doublet of doublets at 2·91 and 3·15 p.p.m., respectively, $J_{4a,4a} - 16{\cdot}4$, $J_{4a,4} \simeq 9{\cdot}5$ and 3·0 Hz, respectively.

As expected, the relative proportion in the reaction mixture of the brominated ketone increases with the increasing excess of the reagent. The bromo ketone *XV* does not arise from the ketone *XIV* by bromination. This fact was demonstrated by treatment of *XIV* with excess of Jacques'reagent in tetrahydrofuran. Thin-layer chromatography of the reaction mixture showed formation of a variety of compounds but only a trace of a substance identical with *XV* by its R_F. Formation of both compounds *XIV* and *XV* can be plausibly explained by the mechanism depicted in the sequence of formulae *II* → *XII*–*XV*. This mechanism assumes initial formation of the unstable bromo ketone *XII*, splitting off one molecule of hydrogen bromide with skeletal rearrangement resulting in formation of the dienone *XIV*. Analogously, the intermediate dibromo ketone gives rise to the monobromo hetone *XV*. This mechanism was postulated by King and deMayo[7] as operative in the formation of the tribromo derivative *XVI* from thuj one (*XVII*) on bromination with elemental bromine[8]. The view of the latter authors was in conflict with an alternative mechanism postulated by Eastman and coworkers[9] in which addition of bromine to the cyclopropane ring is assumed to be the first step of the reaction: (*XVII* → *XX* → *XXI* → → *XVI*. In our case, it was now possible to isolate the dienone stage of the reaction since the bromination reagent used does not permit further attack of bromine. This, the reaction course in the analogous case described in the present paper constitutes an indirect proof of the correctness of the mechanism postulated by King and de Mayo[7] for bromination of thujone.

On hydride reduction, the ketone *II* gave rise to two epimeric alcohols; both alcohols give the ketone *II* on chromium trioxide oxidation. Their configurations



follow from correlation with the known[10] 2α-hydroxy-4-cholestene. The acetyl derivative of the latter compound was subjected to Simmons–Smith methylenation[11] and the product saponified to furnish, in a low yield, the epimer of m.p. 94–96°C. Thus, the configuration of the hydroxyl in this compound is shown to be 2α. The PMR-spectroscopic measurements of the hydroxy derivatives *VI* and *VII* demonstrated that both compounds differ not only in the configurations of the hydroxyl groups but also in the A-ring conformations. The widths of the $C_{(2)}$-proton multiplets (28·5 and 33·5 Hz in *VI* and *VII*, respectively) demonstrate unambiguously that the $C_{(2)}$-proton assumes the axial conformation in both epimers, *i.e.* that the hydroxyl group is equatorial in both the α- and β-configurations. The observed splitting in the multiplet of the $C_{(2)}$-proton cannot be used directly for obtaining its coupling constants to the protons on adjacent carbons $C_{(1)}$ and $C_{(3)}$ without danger of serious mistakes in the respective values[12]. A study of Dreiding models combined with the results of PMR-measurements lead to the conclusion that the A-ring of the 2β-hydroxy derivative *VII* should exist in the half-chair conformation *A*; on the other hand, the A-ring in the 2α-epimer should assume the twisted boat conformation *D* (Fig. 1). These conclusions are valid on the assumption the B-ring in both epimers has the conventional chair form. In line with these assumptions, both epimers *VI* and *VII* show considerable similarity in the parameters of all attributable protons.

In the PMR-spectra of the epimeric hydroxy derivatives *VI* and *VII*, the $C_{(2)}$-proton and two geminal cyclopropane protons are the only protons of the A-ring which can be assigned. Therefore, we attempted to obtain additional information about the A-ring conformation by measuring the PMR-spectra of both hydroxy derivatives in deuteriochloroform in the presence of tris (dipivalomethanato)europium[13]. In both cases, linear dependence of the chemical shifts of all attributable protons on the amount of the added complex (pursued up to proportion steroid–complex 1 : 1) was observed. However, line broadening and small differences in the chemical shifts of some A-ring protons did not permit complete assignment and extraction of their coupling constants. A comparison of the induced chemical shifts in both hydroxy derivatives *VI* and *VII* demonstrates that the shifts, induced under the same conditions, are generally larger for the 2β-hydroxy derivative. With regard to the fact that Dreiding models show minimal differences in distances and orientation between the hydroxyl oxygen (as a center of complexation) and the individual protons of both epimers, the observed difference can be explained by a larger rigidity of the half-chair conformation of the A-ring in the 2β-hydroxy derivative *VII*. This interpretation is also supported by the observed differences in shapes and widths of the $C_{(2)}$-proton multiplets of both epimers in deuteriochloroform. In both hydroxy derivatives (*VI* and *VII*) a small but significant upfield shift of 21-, 26-, and 27-protons was observed. One case of similar behavior of the steroid side chain has been reported recently[14].

In order to obtain additional information about the factors influencing the conformation of the A-ring in 2-substituted steroids, we also carried out measurements on two epimeric hydroxy derivatives[10] *VIII* and *XI*; these compounds differ from *VI* and *VII* in the presence of the 4,5-double bond instead of a cyclopropane ring at this position. The compound *VIII* was also used as a starting material for the preparation

of its epimer *XI*: the 2α-derivative *VIII* was oxidized with Jones'reagent[15] to the ketone *X* yielding a mixture of *VIII* and *XI* on hydride reduction. The PMR-spectra of the hydroxy derivatives *VIII* and *XI* disclosed analogous peculiarities as found in *VI* and *VII*: the widths of $C_{(2)}$-proton multiplets (30 and 35 Hz for *XI* and *VIII*, respectively) indicated equatorial conformations for both 2α- and 2β-hydroxyl groups and different conformations of the A-rings in both compounds. This conclusion is further supported by different shapes of the signals of the olefinic $C_{(4)}$-protons (a broad triplet at 5·19 p.p.m. and a broad doublet at 5·15 p.p.m. in *XI* and *VIII*, respectively). In view of these results it appeared desirable to compare the above spectra with those of 5α-cholestan-2α-ol[16] (*XXII*), and 5α-cholestan-2β-ol[17] (*XXIII*). As expected, the hydroxyl group in the 2α-epimer (*XXII*) was found to be equatorial (the width of the $C_{(2)}$-proton multiplet = 33 Hz) whereas the 2β-hydroxyl of the second epimer (*XXIII*) assumes the axial conformation (the width of the $C_{(2)}$-proton multiplet 17 Hz). The A-ring assumes thus the normal chair conformation in both epimeric compounds. Pronounced differences in chemical shifts of the $C_{(2)}$-protons (3·75 p.p.m. in *XXII* as compared with 4·13 p.p.m. in *XXIII*) and in shielding of the 19-methyl groups (0·785 p.p.m. in *XXII* and 1·02 p.p.m. in *XXIII*) are perfectly in line with the different conformations of both hydroxyl groups.

Thus, the results of the PMR-study lead to conclusions about conformational preference in compounds *VI*, *VII*, *VIII* and *XI*; the latter compounds differ from 2-hydroxy-5α-cholestanes (*XXII* and *XXIII*) in this respect. The factors determining their conformational behaviour should be briefly discussed now. The A-ring in both epimeric 5α-cholestan-2-ols was found to be present in the preferred chair conformation, the hydroxyl group bein equatorial in the 2α-hydroxy derivative *XXII* and axial in 2β-hydroxy derivative *XXIII*. For 2α-epimer *XXII*, there is no reason for considering any significant presence of the boat form while in the chair form of the 2β-epimer *XXIII* there exists a certain destabilizing influence of 1,3-diaxial interaction between the hydroxyl group and the angular 19-methyl. This interaction (c. 2·2 kcal), however, is too weak to cause flipping of the A-ring into the energetically richer (c. 6 kcal) boat form.

As can be demonstrated on Dreiding models (Fig 1), introduction of the double bonds into the 4,5-position enables the existence of two A-ring conformations represented by the types (*E*, *G*) and (*F*, *H*). Both types can be characterized as half-chair conformations whereby the half-chair (*F*, *H*) is twisted to assume a form with carbon atoms 3, 4, 5, 10, 1 lying almost in one plane so that the half-chair closely resembles a six-membered envelope. The PMR-data of the 2α-hydroxy derivative *VIII* show that the *E*-form with the equatorial hydroxyl group is preferred for this epimer. The preference of the *E*- over the *F*-form appears to be due to the nonbonded interaction of 2α-hydroxyl with 9α-hydrogen and that of 1α-with 11α-hydrogen atom in the alternative form *F*; these interactions are no longer present in the form *E*. In the 2β-hydroxy derivative *XI* the half-chair G is destabilized by nonbonded 1,3-dia-

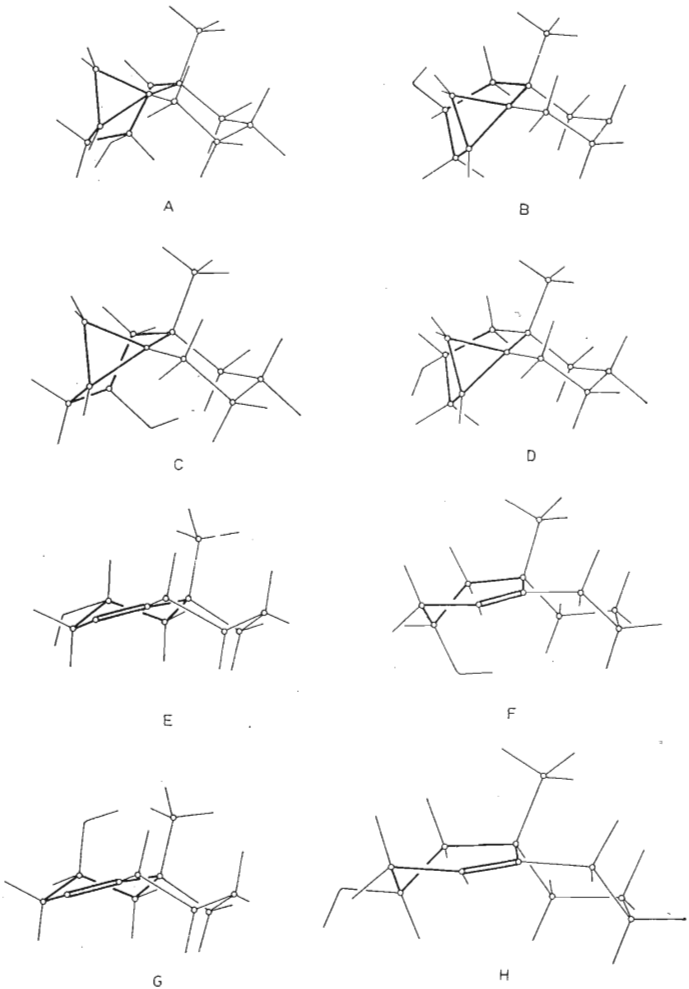


FIG. 1

Alternative Conformations of the Compounds *VI* (*C*, *D*), *VII* (*A*, *B*) *VIII* (*E*, *F*), and *XI* (*G*, *H*).

xial interaction of the hydroxyl and the angular 19-methyl group which results in preference of the half-chair H.

If the 4,5-double bond is replaced by a cyclopropane ring, the 2-hydroxy derivatives *VI* and *VII* are formed and two conformations- (*B*, *D*)-boat and (*A*, *C*)-half-chair may be considered for each epimer. In the *C*-form of the 2α-epimer *VI*, the 2α-hydroxyl is axial and comes into close proximity of 9α-hydrogen; this influence is sufficiently strong to cause preference of the boat form *D* with the equatorial (*be*) hydroxyl group. In the *B*-form of the 2β-hydroxy derivative *VII* the hydroxyl group is axial and in strong nonbonded interaction with the 4aβ-hydrogen atom of the cyclopropane ring. This very strong interaction appears to be the decisive influence leading to preference of the half-chair A.

A-ring conformations departing from the common chair form have been observed in steroids containing a 3-keto group in the presence of nonbonded interactions in the A-ring[18]. Presence of a distorted conformation of the A-ring was also observed in 2β-acetoxy-5α-cholestan-3-one[19] and in 4,5-unsaturated 3-oxosteroids with 2β-hydroxy- or 2β-acyloxy group[20,21]. Exact molecular shape of several compounds of the latter type was established by X-ray analysis[22] which showed that 2β-acetoxytestosterone exists in the form of inverted half-chair (*i.e.* "with atom $C_{(2)}$ being the tip on the α-side of the general plane of the ring A"). The same characterization as postulated for the compound *VII* in the present paper can be used for the half-chair *A*.

EXPERIMENTAL

Melting points are determined on a Kofler block and are uncorrected. Unless stated otherwise, optical rotations are measured in chloroform. The infrared spectra were measured on a Zeiss UR 10 spectrophotometer, ultraviolet spectra on a CF 4 (Optica Milano) spectrophotometer and ORD measurements on a Jasco Model ORD/UV-5 spectropolarimeter. Unless stated otherwise, the PMR-spectra were measured on a Varian HA-100 instrument in deuteriochloroform using tetramethylsilane as an internal reference. Chemical shifts are expressed in δ-scale with an accuracy of 0·01 p.p.m. The multiplicity of the signals is reported using the following symbols: s singlet, d doublet, dd doublet of doublets, t triplet, m multiplet, b broad, W width of a multiplet, $W_{1/2}$ = halfwidth of a signal. The statement "worked up as usual" stands for: the solution was washed with water, 5% HCl, water, 5% $KHCO_3$, water, dried with potassium sulfate and the solvent evaporated *in vacuo*.

4α,5-Cyclo-A-homo-5α-cholestan-2-one (*II*) and 4α,5-cyclo-A-homo-5α-cholestan-3-one (*III*)

3α,5-Cyclo-5α-cholestan-2-one (*I*, 1·29 g) was dissolved in ether (50 ml) and treated successively with ethereal solution of diazomethane (13 ml) and a trace of aluminum chloride. After five minutes, the colorless solution was washed with water, the solvent evaporated, and the residue chromatographed on silica gel (50 g) in light petroleum–ether (10 : 1). The less polar crystalline fraction (721 mg) was crystallized from ether–methanol to give 630 mg of *II*, m.p. 115—118°C. Analytical sample melts 120—120·5°C, $[\alpha]_D^{20}$ −55° (*c* 1·02). IR-spectrum (tetrachloromethane): 3060, 2995 (cyclopropane ring), 1710 cm^{-1} (CO). Mass spectrum: $M^+ = 398$. PMR spectrum: 0·65, s, 3 H (18-CH_3); 1·04, s, 3 H (19-CH_3); 0·85, d, $J = 6·3$ Hz, 6 H (26, 27-CH_3); 0·87, d, $J = 6·0$, 3 H (21-CH_3); 0·47, dd, $J_{4a\alpha,4a\beta} \simeq 4—4·5$ Hz, $J_{4a\alpha,4} \simeq 8·5—9$ Hz, 1 H ($C_{(4a\alpha)}$—H); 1·83, d + 2·31, d, $J_{1\alpha,1\beta} = 16·5$ Hz, 2 H ($C_{(1)}$—H_2); 2·59, m, 2 H ($C_{(3)}$—H_2). ORD (*c* 0·078, 26°C, chloroform): Φ_{400} −900°, Φ_{350} −2000°, Φ_{317} −6550°, Φ_{297} ±0°, Φ_{276} +6850°, Φ_{250} +4750°; a −134. For $C_{28}H_{46}O$ (398·6) calculated: 84·35% C, 11·63% H; found: 84·24% C, 11·65% H.

Deuterium exchange: Sodium (4 mg) was dissolved in deuterium oxide (0·5 ml)–dioxane (1 ml) solution, the ketone *II* (5 mg) was added and the mixture refluxed for 4 h. The solvent was evaporated under vacuum and the residue taken up in ether. Mass spectrometry shows the presence of c. 85% tetradeuterated and c. 15% trideuterated ketone.

Subsequent fractions (154 mg) were crystallized several times from methanol to give 41 mg, m.p. 115–116°C, of the starting compound *I*. Following fractions (89 mg) were crystallized from aqueous methanol to give the ketone *III* (38 mg), m.p. 88–89°C, $[\alpha]_D^{20}$ +62° (*c* 1·51). Literature reports[4] 89–89·5°C, $[\alpha]_D$ +71°. Mass spectrum: M^+ 398. IR spectrum (tetrachloromethane): 1688 (CO conj. with cyclopropane), 3010, 3075 (cyclopropane ring), 1411 cm^{-1} (CH_2 flanked by CO). For $C_{28}H_{46}O$ (398·6): 84·35% C, 11·63% H; found: 84·29% C, 11·66% H.

4α,5-Cyclo-A-homo-5α-cholestane (*IV*)

The ketone *II* (120 mg), triethylene glycol (10 ml), hydrazine hydrate (1·5 ml) and NaOH (350 mg) were heated to 140°C for 30 min, then at 200°C for 3 h. The mixture was poured in water, extracted with light petroleum, the solution washed with water and filtered through a layer of silica gel to give an oil (101 mg). Crystallization from aqueous acetone gave needles, m.p. 47–48°C, $[\alpha]_D$ +14° (*c* 1·38). PMR-spectrum: 0·08, dd, $J_{4a\alpha,4a\beta} = 4-4·5$ Hz, $J_{4a\alpha',4} = 8·5-9$ Hz, 1 H ($C_{4a\alpha'}$—H); 0·20, t, $J_{4a\beta_4} = J_{4a\beta,4a\alpha} = 4-4·5$ Hz, 1 H ($C_{4a\beta}$—H); 0·67, s, 3 H (18-CH_3); 0·94, s, 3 H (19-CH_3); 0·86, d, $J = 6·5$ Hz, 6 H, (26,27-CH_3); 0·91, d, $J = 6·5$ Hz, 3 H (21-CH_3); no olefinic protons. For $C_{28}H_{48}$ (384·7) calculated: 87·42% C, 12·58% H; found: 87·21% C, 12·55% H.

5-Methyl-5β-cholestan-2-one (*V*)

The ketone *II* (200 mg) in acetic acid (60 ml) was hydrogenated over Adams'catalyst (250 mg) for 15 hours, the catalyst filtered off, the solution poured upon ice, neutralized with ammonia and the product isolated with ether. The resultant mixture of two diols (checked by thin-layer chromatography) was oxidized without separation with chromium trioxide (400 mg) and pyridine (9 ml) overnight, treated with sodium hydrogen carbonate solution and worked up as usual. The product is a single substance *V*, after crystallization from methanol, m.p. 90·5–92°C (104 mg), $[\alpha]_D^{20}$ +40° (*c* 1·08). IR-spectrum: 1718 cm^{-1} (CO), PMR-spectrum (deuteriochloroform): no signals above 0·5 p.p.m.; 0·60, s, 3 H; 0·90, s, 3 H; 1·12, s, 3 H (tertiary methyls). PMR-spectrum (benzene): 0·59, s, 3 H, 0·78, s, 3 H; 0·97, s, 3 H (tertiary methyls). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·22% C, 12·25% H.

A-Homo-3,5-cholestadien-2-one (*XIV*) and A-homo-3-bromo-3,5-cholestadien-2-one (*XV*)

The ketone *II* (200 mg) in tetrahydrofuran (4 ml) was treated with phenyltrimethylammonium perbromide (185 mg) at room temperature. After 10 minutes, the colorless mixture was poured into water and isolated with ether. After usual workup, the crystalline residue was chromatographed on silica gel (6 g) using light petroleum and ether (19 : 1) as eluent. First 150 ml eluted 25 mg of the bromo derivative *XV*. Crystallization from ether–light petroleum gave 10 mg of pure *XV*, m.p. 178–179°C, $[\alpha]_D^{20}$ +28° (*c* 0·65). IR-spectrum (tetrachloromethane): 1690, (CO), 1600, 3030 cm^{-1} (double bond). UV-spectrum (ethanol): $\lambda_{max} = 259$ nm, $\log \varepsilon = 3·54$. PMR-spectrum: 7·42, dd, $J_{4,4a} \simeq 9·5$ and 3·0 Hz, 1 H ($C_{(4)}$—H); 5·38, m, $W_{1/2} \simeq 8·5$ Hz, 1 H ($C_{(6)}$—H); 2·635, d, +2·89, d, $J_{1\alpha,1\beta} \simeq 12·5$ Hz, 2 H ($C_{(1)}$—H_2); 3·15, dd, $J_{4a\alpha,4a\beta} \simeq 16·5$ Hz, $J_{4a,3} \simeq 3·0$ Hz, 1 H ($C_{(4a)}$—H α or β) 2·91, dd, $J_{4a\alpha,4\beta} \simeq 16·5$ Hz, $J_{4\alpha,3} \simeq 9·5$ Hz, 1 H ($C_{(4a)}$—H β or α); 1·05, s, 3 H (19-CH_3); 0·90, d, $J \simeq 6$ Hz, 3 H (21-CH_3); 0·85, d, $J \simeq 6$ Hz, 6 H (26, 27-CH_3),

0·67, s, 3 H (18-CH_3). For $C_{28}H_{43}BrO$ (475·5) calculated: 70·73% C, 9·11% H, 16·81% Br; found: 70·81% C, 9·05% H, 17·33% Br. Further 150 ml eluted 29 mg of intermediate fraction. Subsequent 300 ml of the same solvent mixture eluted the chromatographically pure product (110 mg) furnishing 88 mg of the dienone *XIV*, from aqueous methanol, m.p. 121—122°C, $[\alpha]_D^{20}$ −64° (*c* 0·84). IR-spectrum (tetrachloromethane): 1660, 1620 cm^{-1} (α,β-unsaturated ketone). Mass spectrum: M^+ 396; UV-spectrum (ethanol): λ_{max} 226 nm, log ε 3·85. PMR-spectrum: 0·66, s, 3 H (18-Me); 0·84, d, $J \simeq 6$ Hz, 6 H (26,27-CH_3); 0·89, d, $J \simeq 6$ Hz, 3 H (21-CH_3); 1·05, s, 3 H, (19-CH_3); 2·52—3·25, m, 4 H ($C_{(1\alpha,\beta)}$ + $C_{(4a\alpha,\beta)}H_2$); 6·86, m, $J_{4,3} \simeq 11$ Hz, $J_{4,4a(\alpha \text{ or } \beta)} \simeq 8{\cdot}2$ Hz, $J_{4,4a(\beta \text{ or } \alpha)} \simeq 2{\cdot}7$ Hz, 1 H ($C_{(4)}$—H); 5·92, m, ≃11 Hz, $J_{3,4a(\alpha \text{ or } \beta)} = 2{\cdot}8$ Hz, $J_{3,4a(\beta \text{ or } \alpha)} = 1{\cdot}2$ Hz, 1 H ($C_{(3)}$—H); 5·345, m, 1 H ($C_{(6)}$—H). For $C_{28}H_{44}O$ (396·6) calculated: 84·78% 3, 11·18% H; found: 84·68% C, 11·12% H.

4α,5-Cyclo-A-homo-5α-cholestan-2α-ol (*VI*) and 4α,5-cyclo-A-homo-5α-cholestan-2β-ol (*VII*)

a) The ketone *II* (96 mg) was reduced with lithium aluminum hydride (200 mg) in ether (25 ml) at the reflux temperature for 2 h. Excess reagent was then decomposed with ethyl acetate, the mixture poured on ice and HCl (5%) and the product isolated with ether. After usual workup, the residue was chromatographed on silica gel (3 g) in benzene. This solvent eluted the less polar compound *VI* (61 mg) which after repeated crystallization from methanol melted 94—96°C, $[\alpha]_D^{20}$ +40° (*c* 0·89). IR-spectrum (tetrachloromethane): 3610 (OH), 3060 cm^{-1} (cyclopropane ring). PMR-spectrum: 0·03, dd, $J_{4a\alpha,4a\beta} = 4-4{\cdot}5$ Hz, $J_{4a\alpha,4\alpha} = 8{\cdot}5-8$ Hz, 1 H ($C_{(4a\alpha)}$—H); 0·25, t, $J_{4a\beta,4a\alpha} = J_{4a\beta,4\alpha} = 4-4{\cdot}5$ Hz, 1 H ($C_{(4a\beta)}$—H); 0·68, s, 3 H (18-CH_3); 0·86, d, $J = 6{\cdot}2$ Hz, 6 H (26 + 27-CH_3); 0·90, d, $J = 6$, 3 H (21-CH_3); 0·93, s, 3 H (19-CH_3); 3·85, m, $W = 28{\cdot}5$ Hz ($C_{(2)}$—H). For $C_{28}H_{48}O$ (400·6) calculated: 83·93% C, 12·08% H; found: 83·98% C, 12·26% H. Further elution furnished the epimer *VII* (31 mg) which was crystallized repeatedly from methanol giving the pure compound (24 mg), m.p. 131—132°C, $[\alpha]_D^{20}$ −3° (*c* 1·28). IR-spectrum (tetrachloromethane): 3610, 1045, 1036, 1021, 1015 cm^{-1} (OH), 3055 cm^{-1} (cyclopropane ring). PMR-spectrum: 0·20, dd, $J_{4a\alpha,4a\beta} = 4-4{\cdot}5$ Hz, $J_{4a\alpha,4\alpha} = 8{\cdot}5-9{\cdot}0$ Hz, 1 H ($C_{(4a\alpha)}$—H); 0·27, t, $J_{4a\beta,4a\alpha} = J_{4a\beta,4\alpha} = 4-4{\cdot}5$ Hz, 1 H ($C_{(4a\beta)}$—H); 0·67, s, 3 H (18-CH_3); 0·86, d, $J = 6{\cdot}6$ Hz, 6 H (26 + 27 Me); 0·91, d, $J = 6{\cdot}0$, 3 H (21-CH_3); 0·99, s, 3 H (19-CH_3); 3·87, m, $W = 33{\cdot}5$ Hz, 1 H ($C_{(2)}$—H). For $C_{28}H_{48}O$ (400·6) calculated: 83·93% C, 12·08% H; found: 83·88% C, 11·92% H. *b*) A solution of the acetyl derivative *IX* in ether (5 ml) with activated[23] zink (from cupric acetate monohydrate (8·5 mg) and diiodomethane (0·46 ml) was heated in a sealed glass tube at 98—100°C for 5 h. The mixture was then diluted with ether, washed with 5% HCl and worked up as usual. The residue was saponified by standing overnight with 0·2% methanolic potassium hydroxide (50 ml). The solution was concentrated to a small volume, diluted with water and the product taken up in light petroleum. Chromatography on silica gel (6 g) in light petroleum–ether (2%) furnished the desired compound (4 mg) showing R_F identical with that of the compound *VI*. IR-spectrum (KBr) proved identity with *VI*.

4-Cholesten-2-one (*X*)

The hydroxy derivative *VIII* (100 mg) was dissolved in acetone (15 ml) and treated dropwise with Jones'reagent[15] (1 ml) with stirring at 0°C. After 15 min, the solution was poured into $KHCO_3$ solution, extracted with ether and worked up as usual. Crystallization from acetone gave the ketone *X* (60 mg), m.p. 106—108°C, $[\alpha]_D^{20}$ +102° (*c* 2·4). IR-spectrum (tetrachloromethane): 1721 (CO), 1660, 3030 cm^{-1} (double bond). For $C_{27}H_{44}O$ (384·6) calculated: 84·31% C, 11·53% H; found: 83·70% C, 11·48% H.

4-Cholesten-2β-ol (*XI*)

The ketone *X* (100 mg) was reduced with tri-tert-butoxyaluminum hydride (200 mg) in tetrahydrofuran (10 ml) at 35°C for three days. The mixture was then poured upon 5% HCl–ice and extracted with ether (2%). First 250 ml eluted the β-isomer (60 mg), m.p. 95—98°C; recrystallization from methanol raised the m.p. to 105—106°C, $[\alpha]_D^{20}$ ±0°. PMR-spectrum: 0·68, s, 3 H, (18-CH_3): 0·86, d, J = 6·2 Hz, 6 H (26 + 27-CH_3); 0·90, d, J = 5·8 Hz, 3 H (21-CH_3); 1·095, s, 3 H (19-CH_3); 3·95, m, W = 30 Hz, 1 H ($C_{(2)}$—H); 5·19, bt, 1 H ($C_{(4)}$—H). For $C_{27}H_{46}O$ (386·6) calculated: 83·87% C, 11·99% H; found: 83·90% C, 12·21% H. Continued elution with the same solvent furnished a mixture of *XI* and *VIII* (5 mg) followed by pure *VIII* (5 mg), proved to be identical with the authentic sample by thin layer chromatographic migration rate and the IR-spectrum.

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