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THE STRUCTURE OF LUMI-4-CHOLESTEN-3-ONE[1]

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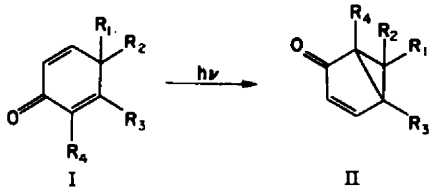
Abstract—UV irradiation of 4-cholesten-3-one has been found to give 1β,5-cyclo-5β,10α-cholestan-2-one, a *lumi* compound of the dihydro*lumi*santonin type. A multiplicity of physical data and chemical transformations is described which points to identical stereochemistry in the photoisomerization of this homoannular enone and analogous dienones.

EXTENSIVE studies on the photochemistry of santonin[4,5] and structurally similar dienones (I)[6] have shown the principal transformation to be that producing the *lumi* (II)[7] compounds. Although the detailed mechanism of this reaction is not known



I II

with certainty,[6] it appears to involve a triplet excited state.[8] The present report is an outgrowth of such a study but is concerned only with the structure of a photoisomerization product of 4-cholesten-3-one. A discussion of reaction mechanism will be presented elsewhere.

The UV irradiation of dilute solutions of 4-cholesten-3-one (III) in t-butyl alcohol afforded a photoisomer in 25% yield. The use of dilute solutions was necessitated by the known facility with which II undergoes photodimerization.[9] Because the quantum

[1] Reported in part in preliminary form; W. W. Kwie, B. A. Shoulders and P. D. Gardner, *J. Amer. Chem. Soc.* **84**, 2268 (1962). B. Nann, D. Gravel, R. Scharta, H. Wehrli, K. Schaffner and O. Jeger, *Helv. Chim. Acta* **46**, 2473 (1963) and O. L. Chapman, T. A. Rettig, A. A. Griswold, A. I Dutton and P. Fitton, *Tetrahedron Letters* 2049 (1963) have reported the photoisomerization of testosterone to a structurally similar compound. This paper forms Part XX of the Westfield College Series on Optical Rotatory Dispersion. For Part XIX see T. R. Emerson, D. F. Ewing, W. Klyne, D. G. Neilson, D. A. V. Peters, L. H. Roach and R. J. Swan, *J. Chem. Soc. submitted.*

[2] Department of Chemistry, University of Texas.

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[4] D. Arigoni, H. Bosshard, H. Bruderer, G. Buchi, O. Jeger and L. K. Krebaum, *Helv. Chim. Acta* **40**, 1732 (1957).

[5] D. H. R. Barton, P. de Mayo and M. Shafiq, *J. Chem. Soc.* 140 (1958).

[6] For leading Ref, see O. L. Chapman, *Photochemical Rearrangements of Organic Molecules* in *Advances in Photochemistry* Vol. II. J. Wiley, New York, N.Y. (1963); G. S. Hammond and N. J. Turro, *Science* **142**, 1541 (1963); H. E. Zimmerman and J. W. Wilson, *J. Amer. Chem. Soc.* **86**, 4036 (1964).

[7] K. Weinberg, E. C. Utzinger, D. Arigoni and O. Jeger, *Helv. Chim. Acta* **43**, 236 (1960).

[8] H. E. Zimmerman and J. S. Swenton, *J. Amer. Chem. Soc.* **86**, 1436 (1964).

[9] A. Butenandt, L. Poschmann, G. Failer, U. Schiedt and E. Biekert, *Liebig Ann.* **575**, 123 (1951).

efficiency of the III → IV conversion is very low, even the use of 0·5 % solutions did not render the dimerization reaction entirely non-competitive. The presentation of physical and chemical data which follows is the basis for the assignment of formulation IV to represent the photoisomer.

The IR spectrum of *lumi*cholestenone (1β,5-cyclo-5β,10α-cholestan-2-one, IV) possesses bands at 3025 and 1714 cm^{-1}. The 3025 cm^{-1} absorption is assigned to cyclopropane C—H stretching.[10] The combination of the two bands is strongly suggestive of a bi-cyclo[3.1.0]hexan-2-one system.[5] This system is also suggested by the UV absorption of IV, λ_{max} 212 mμ (ε 7,900).[11] The NMR spectrum of IV exhibits significant singlets at τ 8·50 and τ 8·84. The former (one proton) is assigned to the lone cyclopropane hydrogen atom at C-1 and the latter (three protons) to the 19-methyl group. This methyl signal is 0·16τ lower field than that of cholestanone, the parent 3-keto steroid. Further confirmation of structure IV was found in the rotatory dispersion curve of this substance. It exhibits a strong positive Cotton effect, a + 238, very much like that found in the spectra of dihydro*lumi*santonin (a + 220) and dihydro*lumi*-1-dehydro-4-methyltestosterone acetate (a + 226).[12,13]

The reaction of IV with hydrochloric acid–acetic acid afforded a chloro ketone (V) no longer possessing a cyclopropane ring. The *lumi* compound (IV) was easily reconstituted from V by brief heating in ethanolic potassium hydroxide.[14]

The IR spectrum of V shows a carbonyl band at 1717 cm^{-1} typical of cyclohexanones. The 19-methyl group gives rise to a three proton NMR signal at τ 8·92. This is 0·08τ lower field than the corresponding signal in the spectrum of cholestan-3-one and therefore establishes the position of the chlorine atom to be at least one atom removed from C-10.[15] The rotatory dispersion curve of V shows a negative Cotton effect, a −30.

Removal of the chlorine atom of V was effected by reduction with sodium in ammonia. The reaction product consisted of a mixture of the desired ketone, 5α,10α-cholestan-2-one (VI), and an alcohol (VII) resulting from partial reduction of the carbonyl group. Mild oxidation of VII afforded VI thus establishing the two to have the same configuration at C-5. The IR spectrum of VI shows a carbonyl band at 1712 cm^{-1} which is typical of cyclohexanones. The rotatory dispersion curves of the chloro ketone (V) and ketone (VI) are nearly superimposable suggesting that the two have the same configuration at C-5. An examination of Dreiding models reveals that the only 8β,9α,10α structure which allows all rings to have chair conformations is that with an α configuration at C-5. The octant rule predicts for this structure a negative Cotton effect with a small amplitude such as was found experimentally.[16]

[10] A. R. H. Cole, *J. Chem. Soc.* 3807, 3810 (1954); H. T. Hoffman, Jr., G. E. Evans and G. Glockler, *J. Amer. Chem. Soc.* **73**, 3028 (1951); J. D. Roberts and V. C. Chambers, *Ibid.* **73**, 5030 (1951).

[11] R. H. Eastman, *J. Amer. Chem. Soc.* **76**, 4115 (1954).

[12] These amplitudes were estimated from the published curves.[7]

[13] See also C. Djerassi, W. Klyne, T. Norin, G. Ohloff and E. Klein, *Tetrahedron* **21**, 163 (1965).

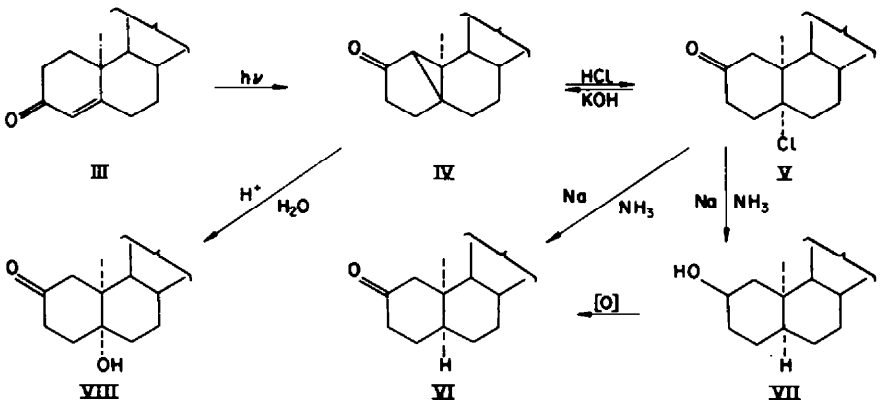
[14] The V → IV conversion is an illustrative example of this mode of synthesis of cyclopropanes, cf., N. A. Nelson and G. A. Mortimer, *J. Org. Chem.* **22**, 1146 (1946).

[15] L. M. Jackman, *Nuclear Magnetic Resonance Spectroscopy* pp. 53–54. Pergamon Press, New York, N.Y. (1959).

[16] W. Klyne in *Advances in Organic Chemistry* Vol. I, p. 239. Interscience, New York, N.Y. (1960); C. Djerassi and W. Klyne, *J. Chem. Soc.* 2949 (1962); 2390 (1963); W. Klyne, *Experientia* **20**, 349 (1964).

Another argument in support of the 5α configuration in VI comes from a consideration of energy-structure relationships in fused ring systems. Because the reduction of V proceeds through a radical and/or carbanion intermediate, its product (VI) is likely to be that which tends to minimize strain energy. The *trans* 5β,10α configuration would force ring B to exist in a boat or twist form and therefore be less stable than the all chair 5α,10α configuration by at least 5·5 kcal.[17]

The NMR spectrum of alcohol VII possesses a very broad multiplet (one proton) at τ 6·1 (W_H = ca. 20 c/s) which is due to the hydrogen atom at C-2. Its half-width leaves no doubt that this hydrogen atom is axial and therefore that the hydroxyl group is equatorial and β.[18]



Acid catalysed hydrolysis of *lumi*cholestenone (IV) afforded a ketol (VIII), ν_{max} 3558 cm^{-1} (hydroxyl) and 1707 cm^{-1} (carbonyl). The 19-methyl appears at τ 8·88 in the NMR spectrum thereby indicating that the hydroxyl is at least one atom removed from this methyl group.[14] The rotatory dispersion curve of VIII is very similar to those of V and VI, exhibiting a negative Cotton effect, *a* −40!. As was expected, VIII failed to form an acetate when submitted to normal acetylation conditions.

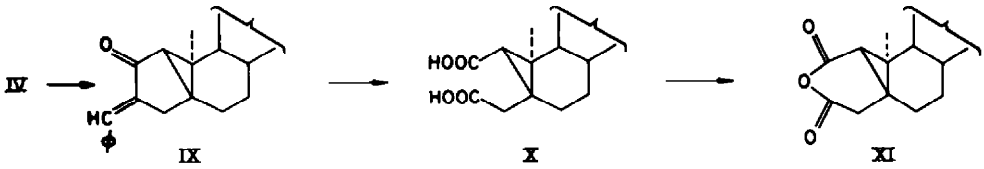
Treatment of IV with benzaldehyde in basic medium afforded the expected benzylidene derivative (IX). Its NMR spectrum has a singlet (one proton) at τ 8·20 due to the hydrogen atom at C-1. The methylene group at C-4 gives rise to an ABX pattern, the AB part of which appears at τ 7·22 and τ 6·85 (J_1 = 18, J_2 = 2·8 and J_3 = 2·0 c/s). This derivative was then converted by ozonolysis to the dicarboxylic acid, 2,3-seco-1β,5-cyclo-5β,10α-cholestan-2,3-dioic acid (X). Reaction of X with acetic anhydride afforded the anhydride (XI), ν_{max} 1787 and 1738 cm^{-1}, or with diazomethane, the desired diester (XII), ν_{max} 1738 and 1725 cm^{-1}.

By analogy with previous literature,[19] it was expected that a Dieckmann reaction with XII would give keto ester XIII. The product of reaction proved to be an unsaturated keto ester, λ_{max} 244 mμ (ε 12,900) but its properties are not at all in agreement with formulation XIII. IR absorption at 1712 and 1626 cm^{-1} for ester and

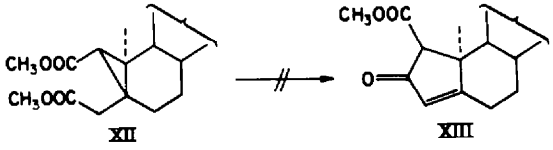
[17] W. S. Johnson, V. J. Bauer, J. L. Margrave, M. A. Frisch, L. H. Dreger and W. N. Hubbard, *J. Amer. Chem. Soc.* **83**, 606 (1961).

[18] R. U. Lemieux, R. K. Kulling, H. J. Bernstein and W. G. Schneider, *J. Amer. Chem. Soc.*, **80**, 6098 (1958). N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry* Chap. 4. Holden-Day, San Francisco (1964).

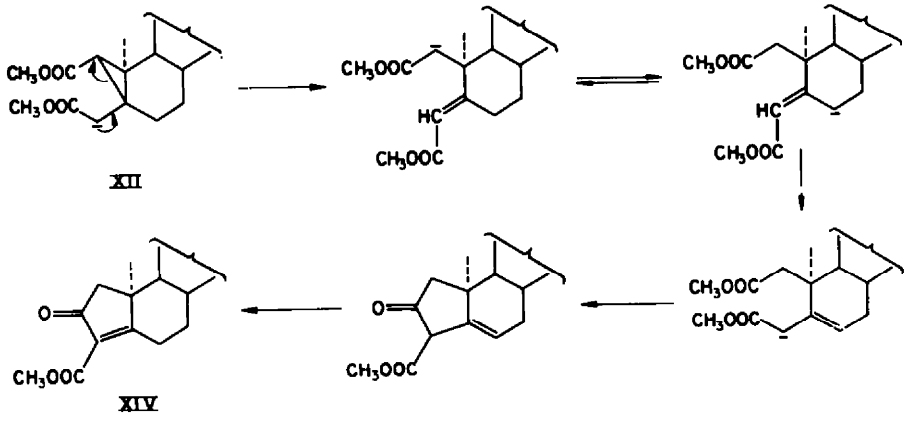
[19] Cf. A. Eschenmoser and A. Furst, *Experientia* **7**, 290 (1951).



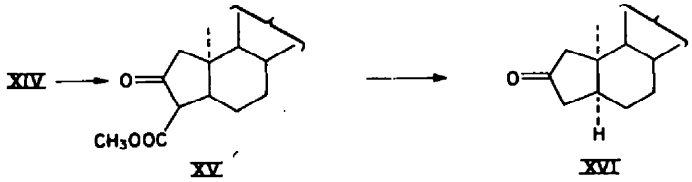
ketone carbonyl groups, respectively, appear at lower frequencies than would be expected for XIII. Moreover, the product failed to produce a colour when treated with ferric chloride solution and gave an NMR spectrum which exhibits no signals in the olefin region. Of the structures which can be written to represent this product, that which best fits the data is the isomeric β-keto ester, methyl A-nor-10α-cholest-3-en-2-one-3-carboxylate (XIV). The failure of XIII to form is best interpreted as shown in the following sequence; the intermediate from initial ring-opening must



have the *anti* structure shown rather than the *syn* configuration required for closure to give XIII.

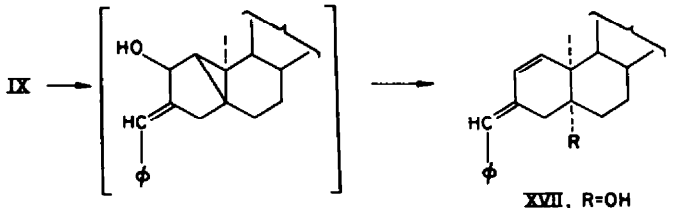


Catalytic reduction of XIV required one mole-equivalent of hydrogen and gave the saturated β-keto ester (XV). This product (positive ferric chloride test) underwent normal decarbomethoxylation in acid medium to yield the parent ketone, A-nor-5α,-10α-cholestan-2-one (XVI). This ketone exhibits carbonyl stretching in the infra-red at 1734 cm^{-1} which is typical of cyclopentanones. A *cis* AB ring fusion in XVI is



suggested by its rotatory dispersion curve which exhibits a strong negative Cotton effect, a −118.[20]

Data presented thus far are felt to establish with a high degree of certainty the structure of *lumi*cholestenone as 1β,5-cyclo-5β,10α-cholestan-2-one. Another avenue of investigation which was initiated early in the study contributed significantly but in a less direct manner. Sodium borohydride reduction of the benzylidene derivative of *lumi*cholestenone (IX) appeared to give a mixture of products although chromatography on silica gel afforded only one substance. Its NMR spectrum exhibits a broad singlet at τ 3·59 (olefin, one proton), a two proton olefin AB pattern at τ 4·05 and τ 3·83 (J = 10 c/s) and a two proton (C-4 methylene) AB part of an ABX pattern at τ 7·15 and τ 7·43 (J_1 = 16·9 c/s, J_2 = 2·2 c/s). The 19-methyl signal is at τ 8·91. The 10 c/s coupling constant for the AB olefin protons suggests the double bond to be in a six-membered ring [21] and free of allylic protons. The presence of a hydroxyl group was established by virtue of a one proton signal which is pH dependent. Unsuccessful attempts to form an acetate derivative or to oxidize the hydroxyl group indicated it to be tertiary. The acetate was finally obtained, however, by the addition of acetic anhydride, rather than water, to a borohydride reduction mixture using IX. The most interesting feature of the NMR spectrum of the acetate—and one which was of value in the preceding interpretation of the spectrum of the alcohol—is the appearance of a doublet (one proton) at τ 6·08 (J = 18·2 c/s). The large coupling constant indicates this doublet to be one-half of an AB quartet due to an isolated methylene group. Thus, the acetoxy group has induced a change in chemical shift (anisotropic effect) of one of the methylene protons at C-4 to lower field. These data leave little doubt that the alcohol is correctly represented as XVII and the acetate as XVIII and that they are formed from a primary reduction product (bracketed alcohol or its salt) on chromatography or acetolysis, respectively. Support for formulation XVII comes



XVII, R=OH
XVIII, R=OAc

from ultra-violet data. Its spectrum has an irregular broad absorption band with a maximum at 283 mμ (ε 32,000) which is virtually identical with that of *trans* 1-phenylbutadiene.[22]

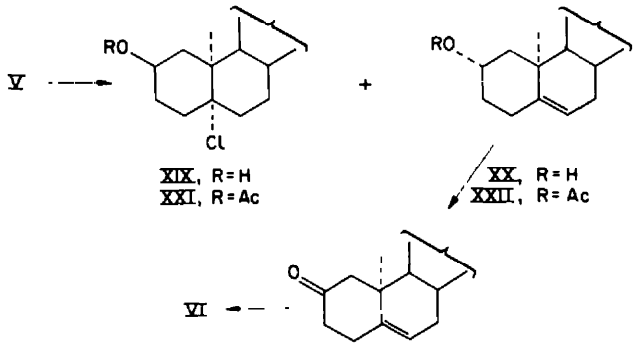
Sodium borohydride reduction of chloro ketone V gave two epimeric alcohols (XIX and XX) but, surprisingly, one of them, 10α-cholest-5-en-2α-ol (XX), proved to be the product of dehydrochlorination as well as reduction. The chloro alcohol (5α-chloro-10α-cholestan-2β-ol, XIX) gave an NMR spectrum having a one proton signal at τ 6·02 (W_H = 22 c/s) which was demonstrated to be due to the proton α to the hydroxyl group (C-2) by conversion to the acetate (XXI) and observing the shift

[20] Cf. W. Klyne, *Tetrahedron* **13**, 29 (1961) for data on other hexahydroindanones.
[21] O. L. Chapman, *J. Amer. Chem. Soc.* **85**, 2014 (1963).
[22] H. M. Walborsky and J. F. Pendleton, *J. Amer. Chem. Soc.*, **82**, 1405 (1960).

of this band to τ 5·08 (W_H = 18 c/s). The large half-width indicates that the proton at C-2 is axial in both XIX and XXI and therefore that the hydroxy and acetoxy functions are equatorial or β. The alcohol (XIX) was readily oxidized to its precursor (V) but was stable to dehydrohalogenation conditions (refluxing ethanolic potassium hydroxide).

The NMR spectrum of the unsaturated alcohol (XX) is equally informative. The proton at C-2 gives rise to a signal at τ 5·82 (W_H = 7·5 c/s) which was observed to move to τ 4·87 (W_H = 9 c/s) when the substance was converted to its acetate (XXII). These half-widths are in the range expected for equatorial protons[23] and therefore require the assignment of an axial or α configuration to the hydroxyl group and the acetoxy function in XX and XXII.

Evidence for the position of the double bond in XX was obtained by oxidation to the ketone, 10α-cholest-5-en-2-one (XXIII). The carbonyl group gives rise to IR



XXIII

absorption at 1702 cm^{-1} and therefore cannot be α,β-unsaturated. The NMR spectrum of XXIII exhibits a one proton olefinic signal at τ 4·17 as a poorly defined doublet (J = 6 c/s) but possesses no signals in the τ 7·0–7·5 region (—CO—CH$_2$—CH=C—) and thus rules out the possibility that the double bond is β,γ with respect to the carbonyl; the signal for such a vinyl proton would be a clean quartet. The rotatory dispersion curve for this substance shows a negative Cotton effect, a −14. Catalytic hydrogenation of XXIII proceeded smoothly to give VI.

It is concluded from these data that XXIII is 10α-cholest-5-en-2-one and that XX and XXII are therefore 10α-cholest-5-en-2α-ol and its acetate, respectively. This rather astonishing dehydrochlorination concurrent with reduction in the formation of the α-ol but not the β-ol will require additional work before an understanding is forthcoming.

EXPERIMENTAL

Optical rotatory dispersion curves were measured (in London) on a Rudolph spectropolarimeter. Curves for substances IV, XVI and XXIII were obtained with a Bellingham and Stanley-Bendix "Polarmatic 62" instrument. All data were obtained at ca. 20° with MeOH solutions at concentration ca. 0·1 mg/ml. Values are given only for peaks and troughs so labeled only when they are not obvious. NMR data were obtained from $CHCl_3$ or CCl_4 solutions using either a Varian A-60 or DP-60 instrument. Values cited are with reference to tetramethylsilane as the internal standard. IR spectra were measured using KBr wafers.

[23] A good pair of model substances is found in 3β- and 3α-acetoxycholestane. Their spectra exhibit a signal for the C-3 proton with half-widths 22 c/s and 7 c/s, respectively.

1β,5-Cyclo-5β,10α-cholestan-2-one (Lumi*cholestenone*, IV). A solution of 10 g III in 4·0 l. t-butyl alcohol was irradiated with a 200 watt high press. Hg vapour lamp (Hanovia) housed in a water-cooled immersion type thimble for 168 hr or until the conversion of III reached 82%. The radiant energy was filtered through 2 mm Pyrex glass. The reaction mixture was concentrated to a small volume by evaporation of solvent under red. press. and then filtered to remove photodimer[9] (0·1–0·3g). Evaporation of the filtrate to complete dryness and recrystallization of the residue from 50 ml 95% EtOH gave 2·5 g IV, m.p. 162–165°. In some experiments crystallization could not be induced and it was necessary to isolate the product by chromatography over alumina. A sample of IV purified by sublimation (140°, 0·01 mm) and recrystallized from acetone melted at 165–166°, $[\alpha]_D^{25}$ + 70° (12·99 mg/ml $CHCl_3$), λ_{max}^{EtOH} 212 and 285 mμ (ε 7,940 and 69). ORD data: $[\phi]_{303}$ + 4,800, $[\phi]_{364}$ −14,000, *a* +238. (Found: C, 84·22; H, 11·39. Calc. for $C_{27}H_{44}O$: C, 84·31; H, 11·53%.)

Similar results were obtained with a 1,000 watt source (24 hr) or summer sunlight (30 days).

Reaction of lumi*cholestenone* (IV) *with hydrochloric acid.* A 2·5 g sample of IV was dissolved in 5·0 ml hot acetic acid. To the clear solution was added 0·7 ml conc. HCl aq and heating was continued for 5 min. The product was obtained by precipitation with water and suction filtration of the colourless precipitate. Recrystallization from 95% EtOH afforded 2·40 g V as fine colourless needles, m.p. 154·5–155·5°, $[\alpha]_D^{25}$ +53° (10·04 mg/ml $CHCl_3$). ORD data: $[\phi]_{350}$ +600, $[\phi]_{311}$ +50, $[\phi]_{272}$ +3,000, *a* −30!. (Found: C, 77·02; H, 10·45; Cl, 8·50. Calc. for $C_{27}H_{45}OCl$: C, 77·01; H, 10·77; Cl, 8·42.)

The *oxime* was prepared by the pyridine–EtOH method[24] and, after several crystallizations from EtOH, melted at 183–184°. (Found: C, 74·62; H, 10·73; N, 3·47. Calc. for $C_{27}H_{46}ONCl$: C, 74·36; H, 10·63; N, 3·21%.)

Regeneration of lumi*cholestenone* (IV) *from 5α-chloro-10α-cholestan-2-one* (V). A solution of 0·150 g V, 25 ml 95% EtOH and one ml 50% KOH aq was heated under reflux for 15 min. The solution was cooled, diluted with water and processed in the usual way by ether extraction. Concentration of the extract to dryness afforded 0·124 g *lumi*cholestenone, m.p. 162–165°, which was identified by mixture m.p. data and a comparison of IR spectra.

Sodium–ammonia reduction of 5α-chloro-10α-cholestan-2-one (V). To the blue solution prepared from 1·0 g Na and 200 ml liquid ammonia was added, dropwise and with vigorous stirring, a solution of 1·00 g V in 100 ml anhydrous ether. The mixture was stirred for 1 hr and then treated with small portions of NH_4Cl until the blue colour disappeared. Ammonia was allowed to evaporate and the residue was dissolved in a mixture of ether and water. The ether layer was combined with two additional ether extracts and washed well with water, Drying the extract and concentration under red. press. left a residue composed of crystalline and amorphous material. It was dissolved in pet. ether and adsorbed on a column of 35 g neutral alumina. Elution with benzene–pet. ether (1:4) gave 0·150 g VI, m.p. 95–98°. Several crystallizations from MeOH gave a pure sample, m.p. 99–100°, $[\alpha]_D^{26}$ +50° (10·75 mg/ml $CHCl_3$). ORD data: $[\Phi]_{340}$ +700, $[\Phi]_{306}$ 0, $[\Phi]_{272}$ +3,300, *a* −33!. (Found: C, 83·85; H, 11·92. Calc, for $C_{27}H_{46}O$: C, 83·87; H, 11·99.)

Further elution of the chromatogram with benzene–pet. ether (2:3) afforded more solid material. Crystallization from MeOH gave 0·260 g VII, m.p. 188–189°, $[\alpha]_D^{25}$ +46° (2·70 mg/ml $CHCl_3$). (Found: C, 83·20; H, 12·29. Calc. for $C_{27}H_{48}O$: C, 83·43; H, 12·45%.)

Oxidation of 5α,10α-cholestan-2β-ol (VII). To a solution of 0·100 g VII in 100 ml dry, purified acetone was added, dropwise and with rapid stirring, a standard solution of chromic acid[25] until an orange tint persisted for more than 3 min. The mixture was diluted with 25 ml water and processed by ether extraction. Evaporation of solvent from the dry, neutral extract gave a viscous oil. Chromatography of this oil as described in the preceding experiment afforded 0·60 g of VI, m.p. 98–100°, which was identified by mixture m.p. and IR data.

Acid-catalysed hydrolysis of lumi*cholestenone* (IV). A solution of 1·00 g *lumi*cholestenone in 100 ml 70% acetic acid was heated under reflux for 10 hr. The product was precipitated by the addition of water and then collected by suction filtration. Chromatography of the residue on 100 g silica gel using benzene–ether (4:1) as the eluting solvent afforded material which was further purified by recrystallization from MeOH, 0·571 g, m.p. 166–167°, $[\alpha]_D^{25}$ +61° (10·69 mg/ml $CHCl_3$). ORD data: $[\Phi]_{318}$ +410, $[\Phi]_{270}$ +3,600, *a* −32!. (Found: C, 80·67; H, 11·58. Calc. for $C_{27}H_{46}O_2$: C, 80·54; H, 11·52%.)

[24] W. E. Bachmann, *J. Amer. Chem. Soc.* **59**, 420 (1937).

[25] K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.* 39 (1946).

This substance, VIII, failed to give an acetate derivative under normal acetylation conditions.

The benzylidene derivative of lumi*cholestenone* (IX). A solution comprised of 1·20 g IV, 4·0 ml freshly distilled benzaldehyde and 1·0 ml 50% KOH aq in 200 ml 95% EtOH was heated under reflux for 20 min in a N_2 atm. On being cooled to room temp, it deposited 1·40 g IX as leaflets, m.p. 195–196°, $[\alpha]_D^{26}$ +97° (10·19 mg/ml $CHCl_3$), λ_{max}^{EtOH} 224, 230 and 300 mμ (ε 9,440, 9,770 and 29,200). (Found: C, 86·08; H, 10·07. Calc. for $C_{34}H_{48}O$: C, 86·38; H, 10·23%.)

The reaction of V under essentially the same conditions afforded IX in the same yield.

Ozonolysis of the benzylidene derivative of lumi*cholestenone* (IX). A solution of 2·50 g IX in 80 ml $CHCl_3$ and 20 ml MeOH was placed in an ozonation reactor and cooled to −35°. A mixture of O_2 and O_3 was passed through the reactor until the solution turned green. After flushing out excess O_3 with a stream of O_2, the solution was transferred to a flask containing 20 ml 30% H_2O_2 and 60 ml water. Sufficient acetone was added to give a single phase which was then stirred for 12 hr. The bulk of the organic solvents was removed at an aspirator and the concentrate was extracted with ether. The extract was washed several times with $NaHCO_3$ aq. The combined washes were re-extracted with ether and the ethereal solution processed in the usual way. Evaporation to dryness and crystallization of the residue from acetone afforded 1·40 g X, m.p. 198–201°, $[\alpha]_D^{25}$ +68° (4·37 mg/ml $CHCl_3$). (Found: C, 74·88; H, 10·19; Neut. Equiv., 222. Calc. for $C_{27}H_{44}O_4$: C, 74·96; H, 10·25%; Neut. Equiv., 216.)

The *anhydride* (XI) was obtained by heating a solution of 0·200 g X in 10 ml acetic anhydride under reflux for 3 hr followed by removal of all volatile material *in vacuo*. Sublimation of the residue at 125° (0·01 mm) gave 0·114 g XI, m.p. 145–146°, $[\alpha]_D^{26}$ +106° (9·25 mg/ml $CHCl_3$). (Found: C, 78·04; H, 10·26. Calc. for $C_{27}H_{42}O_3$: C, 78·21; H, 10·21%.)

The *dimethyl ester* (XII) was prepared by the addition of ethereal diazomethane to an ethereal solution of X (1·40 g) until the persistence of a yellow colour. The mixture was allowed to stand for 12 hr in the dark and was then freed of solvent under red. press. Recrystallization of the residue from MeOH afforded 1·24 g XII, m.p. 104–105°, $[\alpha]_D^{24}$ −79° (2·60 mg/ml $CHCl_3$). (Found: C, 75·42; H, 10·46. Calc. for $C_{29}H_{48}O_4$: C, 75·60; H, 10·50%.)

Methyl A-*nor*-10α-*cholest*-3-*en*-2-*one*-3-*carboxylate* (XIV). In a 3-neck round bottom flask fitted with a sealed stirrer and reflux condenser was prepared (under N_2) MeONa from 1·0 g Na and 10 ml dry MeOH. Excess MeOH was removed under red. press. While dry N_2 was passed through the assembly, a solution of 1·00 g XII in 25 ml dry toluene was added to the base. Another 25 ml toluene was used to rinse the solution in. The mixture was stirred and heated under reflux for 2 hr, cooled and carefully acidified. Processing of the reaction mixture in the usual way by ether extraction and crystallization of the resulting oily residue from MeOH gave 0·510 g colourless needles (XIV), m.p. 129–131°. Repeated recrystallization afforded a sample, m.p. 130·5–131·5°, $[\alpha]_D^{26}$ −73° (12·60 mg/ml $CHCl_3$), λ_{max}^{EtOH} 244 mμ (ε 12,900). (Found: C, 78·26; H, 10·43. Calc. for $C_{28}H_{44}O_3$: C, 78·45; H, 10·35%.)

Hydrogenation of XIV. To a pre-saturated suspension of 0·10 g 10% Pd–C in 50 ml acetic acid was added 0·200 g XIV. The mixture was stirred under one atmosphere of H_2 and observed to consume one mole-equiv. in 30 min. Removal of catalyst by filtration and evaporation of solvent under red. press. left a solid residue. Recrystallization from MeOH gave 0·170 g of the saturated XV, m.p. 134–136°, $[\alpha]_D^{25}$ −31° (10·91 mg/ml $CHCl_3$). (Found: C, 78·39; H, 10·62. Calc. for $C_{28}H_{46}O_3$: C, 78·09; H, 10·77 %.)

A-*Nor*-5α,10α-*cholestan*-2-*one* (XVI). A mixture of 0·350 g XV, 25 ml acetic acid, 12 ml conc. HCl aq and 3·0 ml water was heated under reflux in a N_2 atm. for 30 min. Dilution with water and extraction with ether, followed by the usual processing of the extract, afforded an oily residue. Crystallization from MeOH yielded 0·190 g XVI, m.p. 93–94°, $[\alpha]_D^{26}$ −44° (10·56 mg/ml $CHCl_3$). ORD data: $[\Phi]_{313}$ −5,360, $[\Phi]_{271}$ +6,450, a −118. (Found: C, 84·05; H, 11·85. Calc. for $C_{26}H_{44}O$: C, 83·80; H, 11·90.%)

Sodium borohydride reduction of IX. A mixture of 1·00 g IX, 1·00 g $NaBH_4$, 50 ml MeOH and 50 ml purified tetrahydrofuran was stirred until the evolution of H_2 ceased (2 hr). Solvent was then removed at an aspirator without heating. The residue was treated with water and then neutralized very carefully with dil. HCl aq. Ether extraction and the usual processing of the extract followed by crystallization of the product from MeOH gave colourless solid, m.p. 132–150°. The solid was redissolved in the mother liquor and the solution was evaporated to dryness *in vacuo*. Chromatography of the residue on 100 g Florex using ether–pet. ether (1:99) gave 0·74 g XVII, m.p. 119–120°. A subsequent preparation yielded a crystalline modification, m.p. 138–139°, which gave NMR and

UV spectra identical with the lower melting form, λ_{max}^{EtOH} 283 mμ (ε 32,000), $[\alpha]_D^{27}$ +154° (84·7 mg/ml $CHCl_3$). (Found: C, 85·53; H, 10·64. Calc. for $C_{34}H_{50}O$: C, 86·01; H, 10·62%.)

An acetate derivative of this substance could not be formed under normal acetylation conditions.

Sodium borohydride reduction of IX *with acetolysis work-up.* A mixture of 0·90 g IX, 1·0 g $NaBH_4$ 50 ml MeOH and 50 ml purified tetrahydrofuran was stirred at 30° until the evolution of H_2 ceased. Solvent was removed, without heating, at an aspirator. The resulting residue was dissolved in 25 ml acetic anhydride containing 2 ml pyridine and stirred for 12 hr. A large volume of water was added and stirring was continued for an additional 4 hr. Extraction with ether and the usual processing of the combined extracts afforded solid material. Chromatography on 120 g Florex with elution by pet. ether gave 0·444 g slightly impure, XVIII m.p. 121–125°, which was purified by crystallization from MeOH, m.p. 128·0–129·5°, λ_{max}^{EtOH} 283 mμ (ε 32,000), $[\alpha]_D^{27}$ +83° (43·40 mg/ml $CHCl_3$). (Found: C, 83·94; H, 10·12. Calc. for $C_{36}H_{52}O_2$: C, 83·66; H, 10·14%.)

Sodium borohydride reduction of 5α-*chloro*-10α-*cholestan*-2-*one* (V). A mixture of 3·00 g V, 50 ml MeOH, 50 ml purified tetrahydrofuran and 3·0 g $NaBH_4$ was stirred at 30° until the evolution of gas ceased. An additional 3·0 g $NaBH_4$ was added and stirring was continued for an additional 12 hr. Solvent was removed, without heating, under aspirator vacuum and the residue was triturated with water. Ether extraction and the usual processing of the combined extracts gave crystalline material. This was dissolved in pet. ether and submitted to chromatography over 400 g Florex with elution by ether–pet. ether mixtures. The 1% ether fractions gave 1·75 g XX which, after crystallization, melted at 142·5–143·5°, $[\alpha]_D^{27}$ −33° (30·51 mg/ml $CHCl_3$). (Found: C, 84·23; H, 12·05. Calc. for $C_{27}H_{46}O$: C, 83·87; H, 11·99%.)

Chromatographic fractions obtained with 3–4% ether afforded 0·94 g XIX which, after recrystallization from MeOH, melted at 168–170°, $[\alpha]_D^{27}$ +44° (35·38 mg/ml $CHCl_3$). (Found: C, 76·90; H, 11·23. Calc. for $C_{27}H_{47}OCl$: C, 76·64; H, 11·20%.)

2α-*Acetoxy*-10α-*cholest*-5-*ene* (XXII), obtained by acetylating XX with acetic anhydride–pyridine, was recrystallized from MeOH, m.p. 85–87°, $[\alpha]_D^{27}$ −28° (93·62 mg/ml $CHCl_3$). (Found: C, 81·21; H, 11·21. Calc. for $C_{29}H_{48}O_2$: C, 81·25; H, 11·29%.)

2β-*Acetoxy*-5α-*chloro*-10α-*cholestane* (XXI) was prepared by the acetylation of XIX with acetic anhydride–pyridine. After recrystallization from MeOH, it melted at 146–147°. (Found: C, 75·05; H, 10·42. Calc. for $C_{29}H_{49}O_2Cl$: C, 74·88; H, 10·62%.)

10α-*Cholest*-5-*en*-2-*one* (XXIII). A solution of 0·50 g sodium dichromate dihydrate in 3·8 ml 10% H_2SO_4 was slowly dropped, with stirring, into a solution of 0·800 g XX dissolved in 15 ml ether. The mixture was stirred at 30° for an additional 2 hr and the layers were separated. The aqueous phase was extracted twice with 5 ml portions of ether and these extracts, combined with the original ethereal layer, were washed with sat. $NaHCO_3$ aq and then with water. Drying with $MgSO_4$ and evaporation to dryness left a solid residue. Recrystallization from MeOH afforded 0·323 g XXIII, m.p. 99·5–100·5°. ORD data: $[\Phi]_{328}$ −1,100(trough), $[\Phi]_{312}$ −1,005(trough), $[\Phi]_{278}$ +300 (peak), a −14. (Found: C, 83·95; H, 11·48. Calc. for $C_{27}H_{44}O$: C, 84·31; H, 11·53%.)

Catalytic hydrogenation of XXIII required one mole-equiv. H_2 and gave VI, m.p. and mixture m.p. 102–103°. An IR spectrum is identical with that of authentic VI.

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