Neighbouring Hydroxy-group Participation in the Reductive Elimination of Chlorine from 5α,6β-Dichlorocholestanes with Sodium Borohydride

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Sodium borohydride-promoted, reductive elimination of chlorine from 5α,6β-dichlorocholestane and some of its derivatives has been studied in propan-2-ol. The presence of a 3α-hydroxy-group in the steroidal skeleton strongly accelerates the process, and evidence is given for an intramolecular, electrophilic, assisted reaction. Various mechanisms for the reductive elimination are discussed and an *E*2 mechanism is proposed for the reaction of the 1,2-dichlorides.

ORGANIC reactions involving neighbouring group participation have been known for many years.[1-5] While various intramolecular, nucleophilic, anchimeric processes have been investigated in detail,[1-5] assistance in nucleophilic substitution or elimination by neighbouring electrophiles has received little attention,

[1] B. Capon, *Quart. Rev.*, 1964, **18**, 45.
[2] L. Goodman, *Adv. Carbohydrate Chem.*, 1967, **22**, 109.
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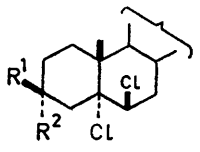
and only a few examples have been observed.[6-12] We have recently reported [13] that epicholesterol (cholest-5-en-3α-ol) is the major product in the reduction of 5α,6β-dibromocholestan-3-one with sodium borohydride in ethanol. It has been suggested [13] that the 3α-hydroxy-group formed in the first step of the reduction, facilitates a consecutive reductive elimination of the two bromine atoms. The aim of the present investigation was to establish the generality of this phenomenon.

1,2-Dibromides can be reduced by various nucleophiles [14-16] including sodium borohydride.[17] However, sodium borohydride has not yet been reported as a reductive eliminating agent for 1,2-dichlorides. To test the possibility of such reaction, 5α,6β-dichlorocholestane and some of its derivatives were chosen as suitable substrates. 5α,6β-Dichlorocholestan-3β-ol (I) was prepared by a known method.[18] Oxidation of (I) with sodium dichromate gave the ketone (II) in almost quantitative yield. Treatment of (II) with a slight excess of sodium borohydride at room temperature gave a mixture of which the main component (63%), isolated by t.l.c., was 5α,6β-dichlorocholestan-3α-ol (III). The minor component in the reduction was (I) (32%). The n.m.r. spectrum of (III) indicated its structure. The proton geminal to the hydroxy-group in (III) gives rise to a multiplet of $W_{\frac{1}{2}}$ 7·2 Hz. This is a characteristic value for an equatorial proton [19] [the multiplet corresponding to the 3α-proton in (I) has $W_{\frac{1}{2}}$ 26·0 Hz]. Oxidation of (III) with sodium dichromate afforded (II) in high yield. Chlorination of epicholesterol (VII) afforded (III) (29%), which was identical with the major component of the reduction of (II). This provided a further chemical proof for the structure of (III). The i.r. spectrum of



(I) $R^1 = OH, R^2 = H$
(II) $R^1 R^2 = O$
(III) $R^1 = H, R^2 = OH$
(IV) $R^1.R^2 = O[CH_2]_2O$
(V) $R^1 = R^2 = H$

(I) in carbon tetrachloride, shows O–H stretching absorption at 3610 cm^{-1}. The corresponding absorption in the spectrum of (III) appears at 3580 cm^{-1}. At high concentration (I) also shows an absorption at 3350 cm^{-1}, which disappears on dilution, but no such absorption is observed in the case of (III). These phenomena indicate that in (III) there is considerable intramolecular hydrogen bonding between the hydroxy-group and the 5α-chlorine atom. Such phenomena have been observed in other compounds having similar structures.[8,20] It is interesting to note that the i.r. spectrum of (III) in Nujol shows a very sharp O–H stretching absorption at 3600 cm^{-1}, whereas in the spectrum of (I) in Nujol the corresponding absorption appears as a very broad peak at 3390 cm^{-1}. Usually, in Nujol, O–H stretching absorptions of hydroxy-steroids appear as broad peaks at the region 3300—3500 cm^{-1}. This suggests that in (III) there is strong intramolecular hydrogen bonding also in the solid state.

Treatment of ketone (II) with ethylene glycol in refluxing benzene, with toluene-*p*-sulphonic acid as catalyst, afforded 5α,6β-dichloro-3,3-ethylenedioxy-cholestane (IV). The structure of (IV) was proved by its smooth acidic hydrolysis to regenerate the ketone (II). The n.m.r. and mass spectra provided further evidence for its structure. The major peak in the mass spectrum, *m/e* 99, is a characteristic fragment in the mass spectra of 3,3-ethylenedioxy-steroids.[21] In the n.m.r. spectrum of (IV) the ethylene unit of the acetal appears as an octet, in contrast to the spectrum of 3,3-ethylenedioxycholest-5-ene (VIII) in which the ethylene portion resonates as a singlet. While in (VIII) the two methylene units of the ethylenedioxy-ring have similar chemical environment, in (IV) the two groups are different owing to the non-bonding interaction of the 5α-chlorine and the 3α-oxygen atoms of the acetal ring. Similar phenomena have been observed with 16-substituted 17,17-ethylenedioxy-androstanes.[22]

Reductive eliminations of the dichlorides (I) and (III)—(V) to the corresponding olefins (VI)—(IX) were carried out in refluxing propan-2-ol with a large excess of sodium borohydride. No olefin is formed spontaneously in the absence of the reducing agent, nor in refluxing propan-2-ol containing sodium hydroxide. This indicates that the basicity of the sodium borohydride solution in propan-2-ol is by itself not responsible for the reductive elimination, and that the reaction requires the presence of borohydride ions as nucleophiles. The results (Table) indicate that (III) reacts much faster than any of the other compounds investigated. We have discussed [13] the possibility that the greater reactivity of (III) may be caused by the

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[8] H. B. Henbest and B. J. Lovell, *J. Chem. Soc.*, 1957, 1965.
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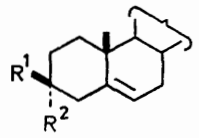
[11] D. H. R. Barton and Y. Houminer, *J.C.S. Chem. Comm.*, 1973, 839.
[12] R. P. Bell and M. I. Page, *J.C.S. Perkin II*, 1973, 1681.
[13] Y. Houminer, *J. Org. Chem.*, in the press.
[14] J. F. King and R. G. Pews, *Canad. J. Chem.*, 1964, **42**, 1294.
[15] E. Baciocchi and A. Schiroli, *J. Chem. Soc.* (*B*), 1969, 554.
[16] E. Baciocchi and C. Lillocci, *J.C.S. Perkin II*, 1973, 38, and references cited therein.
[17] J. F. King, A. D. Allbutt, and R. G. Pews, *Canad. J. Chem.*, 1968, **46**, 805.
[18] D. H. R. Barton and E. Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 370.
[19] L. M. Jackman and S. Sternhell, 'Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, London, 1969, p. 288.
[20] R. Jacquesy and J. Levisalles, *Bull. Soc. chim. France*, 1966, 396; J. C. Jacquesy, R. Jacquesy, and J. Levisalles, *ibid.*, 1967, 1649.
[21] D. H. Williams and I. Howe, ' Principles of Organic Mass Spectrometry,' McGraw-Hill, London, 1972, p. 132.
[22] N. S. Bhacca and D. H. Williams, 'Applications of N.M.R. Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 102.

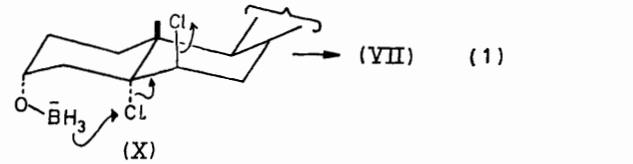
steric interaction of the 3α,5α-groups which raises the energy of its ground state. However, a comparison between the reactivities of (III) and (IV), both of which



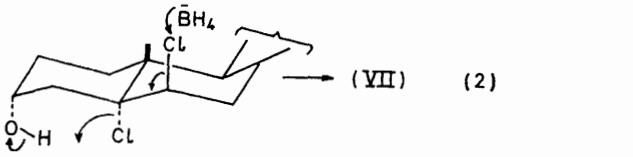
(VI) R^1 = OH, R^2 = H
(VII) R^1 = H, R^2 = OH
(VIII) R^1R^2 = O[CH_2]$_2$O
(IX) R^1 = R^2 = H

have similar non-bonding interaction of the 3α,5α-groups shows clearly that (III) is much more reactive, and therefore this steric interaction factor cannot be important.

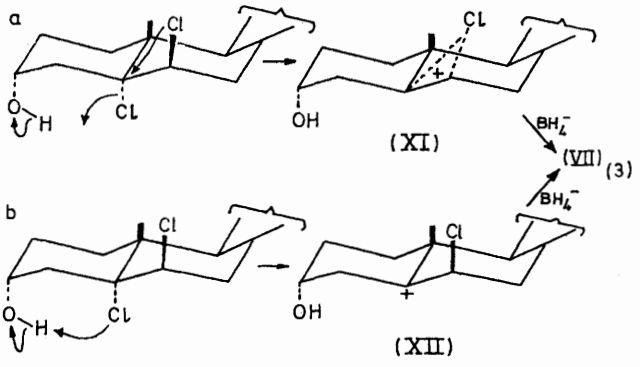
The enhanced reactivity of (III) suggests that in this compound intramolecular catalysis operates, since only in (III) is the neighbouring hydroxy-group in a position to enable such catalysis. There are three possible mechanisms [(1)—(3)] which could explain this phenomenon. In mechanism (1), the sodium



(X) (VII) (1)



(VII) (2)



(XI) (VII) (3) (XII)

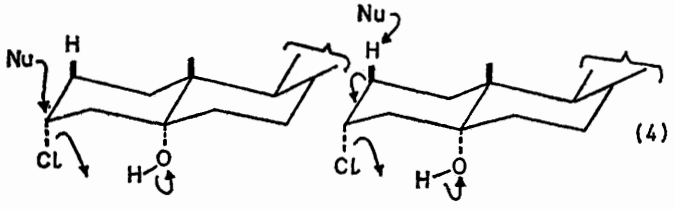
borohydride reacts first with the 3α-hydroxy-group of (III), to give (X), in which the proximity of the reducing agent to the 5α-chlorine atom enables it to react much faster than in an intermolecular reduction process. However, it is doubtful whether compounds such as (X) can exist in alcoholic solutions where the concentration of solvent hydroxy-groups is much higher than that of the substrate. We therefore consider mechanism (1) to be very unlikely.

Mechanisms (2) and (3) are analogues of *E*2 and 'carbonium ion *E*1' or 'heteronium ion *E*1' elimination reactions respectively.[14] The strong intramolecular hydrogen bonding in (III) suggests that both mechanisms may be important. Henbest *et al.*[8] reported that 3α-chlorocholestan-5α-ol undergoes elimination of hydrogen chloride, or substitution, much more rapidly than the corresponding 5α-hydrogen compound [mechanism (4)]. This reaction resembles very much the reductive elimination process, and this phenomenon is explained by an intramolecular catalysis mechanism as shown in mechanism (4).[8] King and Pews[14] discussed the possible mechanisms in the reductive elimination from 1,2-dihalides with lithium aluminium hydride. They found that *trans*-eliminations are faster than *cis*-eliminations and concluded that the 'carbonium ion *E*1' mechanism (3b) is unlikely. However, they could not distinguish between the 'heteronium ion E1' (3a) and the *E*2 (2) mechanisms, and therefore suggested that both are possible. Our results indicate that the rate of the reduction of (III) is strongly dependent on the concentration of sodium borohydride, and moreover, the half-lives of the pseudo-first-order reactions for (III) (Table) are proportional, within the experimental error, to the concentration of the reducing agent (*cf.* runs 3, 5, and 7). Such dependency is in contrast to the first order processes of mechanism (3) and therefore neither (XI) nor (XII) are involved in the rate determining step of the reaction. This is further supported

Reductive elimination from 5α,6β-dichlorocholestane and its derivatives in refluxing propan-2-ol

Steroid [a]	Run no.	10 × [$NaBH_4$] (M)	Refluxing time (h)	Yield of olefin (%) [b]	Unchanged starting material (%) [c]
(I)	1	1·75	24·0	18	50
(III)	2	0	12·0	0	52
	3	0·88	4·5	45	50
	4	1·75	1·0	27	68
	5	1·75	2·5	50	45
	6	1·75	10·0	86	0
	7	3·50	1·5	48	45
(IV)	8	1·75	6·0	0	100
	9	1·75	22·0	Trace	98
	10	3·50	47·0	8	80
(V)	11	1·75	20·0	Trace	95
	12	3·50	45·0	10	85

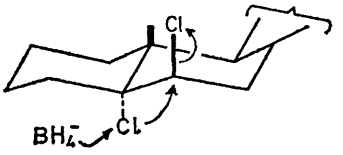
[a] Concentration 7·30 mmol l^{-1}. [b] The errors in these determinations are ±3%.



(4)

by the observation that the rate of decomposition of (III) in refluxing propan-2-ol in the absence of sodium borohydride (run 2) is much lower than the rate of reaction in the presence of the reducing agent. Mechanisms involving either carbonium ion or heteronium ion intermediates in their rate determining step require similar rates for the reactions in the presence or absence of sodium borohydride. It must be pointed out that a unimolecular ionization reaction should be subject to a positive salt effect. However, the contribution of such an effect, for example in the reaction of sodium borohydride with alkyl halides under solvolytic conditions, is small.[23] Therefore, a salt effect cannot be entirely responsible in our case for the strong dependence of the rate on the sodium borohydride concentration. Hence, we conclude that the *E*2 mechanism (2) is the most important one in the reductive elimination from (III) with sodium borohydride.

Mechanism (2) shows that the approach of the reducing agent proceeds from the β-side of the molecule. This is indeed the expected course of the reaction in the case of (III) in which the 3α-hydroxy-group enables delocalization of the negative charge developing on the 5α-chlorine atom in the transition state. The question still remains whether the course of the reaction is the same for the other dichlorides in which neighbouring group participation is impossible, in particular for cases of (I) and (V) in which, owing to the angular 19-methyl group, the 6β-chlorine is sterically more hindered than the 5α-chlorine atom. This could affect the stereochemical course of the reductive elimination, *i.e.* the approach of the reducing agent from the α-side should be easier, thus preferring a reductive elimination route as shown in mechanism (5), for the case of (V). Usually,



(5)

reductive elimination from 5α,6β-dibromocholestane with sodium iodide in acetone is believed to proceed by approach of the iodide anion from the α-side,[24] but no evidence for such pattern had been given. Although the above steric effect is important, other factors may affect the reaction as well. The 5α-chlorine atom, being attached to a tertiary carbon, is less susceptible to nucleophilic attack by the borohydride anion than the 6β-chlorine atom which is bonded to a secondary carbon. This would effect an easier attack on the 6β-chloride, thus giving rise to *E*2 elimination, proceeding as in mechanism (2). Solvation of the transition state, in particular with respect to the negative charge developing on one of the chlorine atoms, may also be important in these reactions.[15] The 5α-chlorine atom is sterically less hindered to the approach of solvent molecules and therefore delocalization of negative charge developing on this atom is easier than in the case of the 6β-chlorine atom. This again will favour a reaction course as in mechanism (2) rather than that shown in mechanism (5). To sum up, each of the above factors may affect the course of the reaction and it is very likely that even in the case of (I), (IV), and (V) the reaction pattern is as in mechanism (2).

[23] H. M. Bell and H. C. Brown, *J. Amer. Chem. Soc.*, 1966, **88**, 1473.

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EXPERIMENTAL

All m.p.s were determined with a Fisher–Johns apparatus. I.r. spectra were recorded with a Perkin-Elmer 254 spectrophotometer. Optical rotations were determined for solutions in chloroform with a Perkin-Elmer model 141 polarimeter. N.m.r. spectra were taken for solutions in deuteriochloroform with a Varian T 60 spectrometer with tetramethylsilane as internal standard. Mass spectra were recorded on a Varian MAT 311 spectrometer. Both qualitative and preparative t.l.c. were carried out on silica gel G. Plates were eluted with light petroleum (b.p. 60—80°) containing 10—30% acetone.

Solvents and Materials.—Propan-2-ol (Mallinckrodt, spectrophotometric grade) was used. The following compounds were prepared by known methods: 5α,6β-dichlorocholestan-3β-ol (I), m.p. 142—143°, $[\alpha]_D$ −27° (*c* 0·50) (lit.,[18] m.p. 143—144°, $[\alpha]_D$ −27°), $\nu_{max.}$ (Nujol) 3390 and 655 cm^{-1}, $\nu_{max.}$ (CCl_4) 3610 and 655 cm^{-1}, δ 1·35 (s, 19-H_3), 4·35 (m, $W_{\frac{1}{2}}$ 7·0 Hz, 6α-H), and 4·23 (m, $W_{\frac{1}{2}}$ 26·0 Hz, 3α-H), *m/e* 460/458/456 (6, 35, 51%, M^+), 422/420 (12, 38, *M* − HCl), 402 (20) 387 (47), 386 (79), 385 (71), 384 (100, *M* − 2HCl), 369 (47), 368 (75), 367 (43), and 366 (37); 5α,6β-dichlorocholestane (V), m.p. 120—122°, $[\alpha]_D$ −28° (*c* 0·78) (lit.,[18] m.p. 121—122°, $[\alpha]_D$ −28°), $\nu_{max.}$ (Nujol) 660 cm^{-1}, δ 1·33 (s, 19-H_3) and 4·42 (m, $W_{\frac{1}{2}}$ 7·0 Hz, 6α-H), *m/e* 444/442/440 (9, 43, 60%, M^+), 406/404 (11, 27, *M* − HCl), 371 (18), 370 (64), 369 (90), and 368 (100, *M* − 2HCl); epicholesterol (VII), m.p. 141—142°, $[\alpha]_D$ −41° (*c* 0·25) (lit.,[13] m.p. 141—142°, $[\alpha]_D$ −41°); 3,3-ethylenedioxycholest-5-ene (VIII), m.p. 133—134°, $[\alpha]_D$ −30° (*c* 1·02) (lit.,[25] m.p. 134—135°, $[\alpha]_D$ −31°), δ 1·03 (s, 19-H_3), 3·93 (s, OCH_2CH_2O), and 533 (m, 6-H); cholest-5-ene (IX), m.p. 89—92°, $[\alpha]_D$ −53° (*c* 1·20) (lit.,[26] m.p. 92—94°, $[\alpha]_D$ −55°), δ 1·00 (s, 19-H_3) and 5·25 (m, 6-H).

5α,6β-*Dichlorocholestan-3-one* (II).—To a suspension of 5α,6β-dichlorocholestan-3β-ol (2·0 g) in acetic acid (30 ml) at 55° was added a solution of sodium dichromate dihydrate (1·0 g) in acetic acid (10 ml). The mixture was stirred at 55° for 30 min (the solid dissolves after 10 min). A few drops of water were added and the solution was cooled in an ice-bath. To complete crystallization, additional water (50 ml) was added. Filtration afforded almost pure 5α,6β-dichlorocholestan-3-one (1·9 g, 95%), m.p. 108—112°. Recrystallization from ethyl acetate–methanol gave pure (II), m.p. 112—114°, $[\alpha]_D$ −26° (*c* 1·05) (lit.,[18] m.p. 114°, $[\alpha]_D$ −27°), $\nu_{max.}$ (Nujol) 1720 and 650 cm^{-1}, δ 1·49 (s, 19-H_3) and 4·31 (m, $W_{\frac{1}{2}}$ 6·4 Hz, 6α-H), *m/e* 458/456/454 (3, 19, 31%, M^+), 420/418 (21, 53, *M* − HCl), 384 (89), 383 (55), 382 (99, *M* − 2HCl), 299 (35), 269 (59), 247 (66), and 229 (100).

5α,6β-*Dichlorocholestan-3α-ol* (III).—(a) *By sodium borohydride reduction of* 5α,6β-*dichlorocholestan-3-one.* The

[25] R. Antonucci, S. Bernstein, R. Littell, K. J. Sax, and J. H. Williams, *J. Org. Chem.*, 1952, **17**, 1341.

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dichloroketone (II) (600 mg) in ethanol (100 ml) was treated with an excess of sodium borohydride (*ca.* 1·5 equiv.) and the solution was stirred at room temperature for 3 h. After dilution with water, the product was extracted with methylene chloride. The extract was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. The residue was separated by t.l.c. to give 5α,6β-*dichlorocholestan*-3α-*ol* (III) (380 mg, 63%), as plates, m.p. 135—136° (from methanol), $[\alpha]_D$ −24° (*c* 0·34), $\nu_{max.}$ (Nujol) 3600vsh and 645 cm^{-1}, $\nu_{max.}$ (CCl_4) 3580 and 645 cm^{-1}, δ 1·30 (s, 18-H_3), 4·08 (m, $W_{\frac{1}{2}}$ 7·2 Hz, 6α-H), and 4·35 (m, $W_{\frac{1}{2}}$ 10·0 Hz, 3β-H), *m/e* 460/458/456 (0·3, 3, 5%, M^+) 442/440/438 (2, 8, 12, $M - H_2O$), 422/420 (4, 10, M — HCl), 402 (57), 387 (35), 386 (35), 385 (100), 384 (82, M — 2HCl), 369 (34), 368 (70), 367 (59), and 366 (75) (Found: C, 71·2; H, 10·25; Cl, 15·15. $C_{27}H_{46}Cl_2O$ requires C, 70·9; H, 10·15; Cl, 15·5%). Also isolated was 5α,6β-dichlorocholestan-3β-ol (I) (190 mg, 32%), m.p. 142—143°, identical with an authentic sample (mixed m.p., i.r., n.m.r., and t.l.c.).

(b) *By chlorination of epicholesterol* (VII). To a solution of epicholesterol (100 mg) in chloroform (10 ml) at −20°, was added a solution of chlorine in chloroform until the yellow colour no longer disappeared. The solution was left at −20° for 15 min, then washed with aqueous sodium carbonate, water, and dried (Na_2SO_4). Evaporation under reduced pressure and separation by t.l.c. gave 5α,6β-dichlorocholestan-3α-ol (40 mg, 29%), m.p. 135—136°, identical with an authentic sample of (III) obtained by method (a) (mixed m.p., i.r., and t.l.c.). The rest of the material was a mixture of unidentified products.

Oxidation of 5α,6β-*Dichlorocholestan*-3α-*ol*.—The steroid (30 mg) in acetic acid (10 ml) was treated with sodium dichromate dihydrate (15 mg) and the mixture was stirred at 55° for 30 min. Water was added and the product extracted with methylene chloride. The extract was washed with aqueous hydrogen carbonate, water, and dried (Na_2SO_4). Evaporation under reduced pressure afforded almost pure 5α,6β-dichlorocholestan-3-one (II) (25 mg, 83%), m.p. 112—113° (from ethyl acetate–methanol), identical with an authentic sample (t.l.c. and i.r.).

5α,6β-*Dichloro*-3,3-*ethylenedioxycholestane* (IV).—A solution of the dichloroketone (II) (2·5 g) in dry benzene (100 ml) containing ethylene glycol (10 ml) and toluene-*p*-sulphonic acid (0·3 g) was refluxed for 36 h with continuous water removal. The mixture was washed with water, aqueous sodium hydrogen carbonate, and again with water, then dried (Na_2SO_4) and evaporated under reduced pressure. Separation by t.l.c. afforded 5α,6β-*dichloro*-3,3-*ethylenedioxycholestane* (1·1 g, 41%), as needles, m.p. 92—94° (from ether–methanol), $[\alpha]_D$ −27° (*c* 0·59), $\nu_{max.}$ (Nujol) 650 cm^{-1}, δ 1·35 (s, 19-H_3), 3·95 (octet, OCH_2-CH_2O), and 4·33 (m, $W_{\frac{1}{2}}$ 7·5 Hz, 6α-H), *m/e* 464/462 (8, 24%, M — HCl) 426 (41, M — 2HCl) and 99 (100) (Found: C, 70·0; H, 9·55; Cl, 13·7. $C_{29}H_{48}Cl_2O_2$ requires C, 69·7; H, 9·7; Cl 14·2%).

Hydrolysis of 5α,6β-*Dichloro*-3,3-*ethylenedioxycholestane* (IV).—A solution of (IV) (100 mg) in ethanol (30 ml) containing water (5 ml), ether (10 ml), and 1N-hydrochloric acid (1 ml) was refluxed for 1·5 h. The ether was removed under reduced pressure and after dilution with water, the product was extracted with methylene chloride. The solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Recrystallization from ethyl acetate–methanol afforded 5α,6β-dichlorocholestan-3-one (II) (70 mg, 77%), m.p. 112—114°, identical with authentic (II) (mixed m.p., t.l.c., i.r., and n.m.r.).

Treatment of Compounds (I), (III), (IV), *and* (V) *with Sodium Borohydride*.—The procedure is illustrated for 5α,6β-dichlorocholestan-3α-ol (III). A solution of the dichloride (III) (150 mg, 0·328 mmol) in propan-2-ol (45 ml) containing sodium borohydride (300 mg, 7·90 mmol) was refluxed for 10 h. Acetic acid was added to destroy the excess of sodium borohydride, and after dilution with water, the product was extracted with methylene chloride. The solution was washed with water, dried (Na_2SO_4), and evaporated under reduced pressure. Separation by t.l.c. gave epicholesterol (109 mg, 86%), m.p. 141—142° (from ethanol), $[\alpha]_D$ −41°, δ 0·98 (s, 19-H_3), 4·00 (m, $W_{\frac{1}{2}}$ 7·2 Hz, 3β-H), and 5·38 (m, 6-H), identical with an authentic sample (mixed m.p., i.r., and t.l.c.). When the reaction was carried out for a shorter refluxing time, epicholesterol (VII) could be separated from its dichloride (III) by t.l.c., and the amounts of both (III) and (VII) could be determined by weighing. However, similar t.l.c. separation in the cases of (I), (IV), and (V), was very poor. Therefore, in these compounds the yield of the products as well as the amounts of unchanged starting materials were determined from n.m.r. spectra of the crude reaction mixtures: the signals corresponding to the 6α-proton of the starting material and the 6-vinylic proton of the product were integrated and the yields calculated from the ratio of the integration of each of these signals to that of a signal corresponding to a methyl group at δ 0·69 (this methyl group has the same chemical shift in all compounds studied in this work).

Decomposition of Compound (III) *in Propan*-2-*ol* (*Blank Experiments*).—A solution of (III) (300 mg) in propan-2-ol (100 ml) was refluxed for 12 h. The solvent was evaporated off under reduced pressure. Separation by t.l.c. gave pure (III) (156 mg, 52%), identical with the starting material (mixed m.p., i.r., and n.m.r.). T.l.c. indicated the presence of at least five products, none of which was epicholesterol. These products were also detected in small amounts in the reduction of (III) with sodium borohydride. When the foregoing solution was refluxed for 40 h, most of the starting material decomposed. The crude reaction mixture consisted of many products but again no epicholesterol could be detected. The mixture showed $\lambda_{max.}$ (hexane) 283 nm, δ 2·20 (s), 5·30—6·10 (m), and 7·05—7·45 (m), *m/e* ⩽366.

When (I) was treated as above it decomposed much more slowly, but t.l.c. indicated similar products as in the case of (III).

Decomposition of (III) as well as of (I) (as above) was strongly facilitated in refluxing propan-2-ol which contained sodium hydroxide (50 mg.), and no starting material was left after 3 h in both cases. T.l.c. indicated the formation of similar products as in the reaction in the absence of sodium hydroxide, but again none of the corresponding olefins could be detected.

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