Stereochemical Course of the Reduction of 5α-Cholest-8(14)-en-7-one by Metal–Ammonia; a Ready Synthesis of 14β-Steroids

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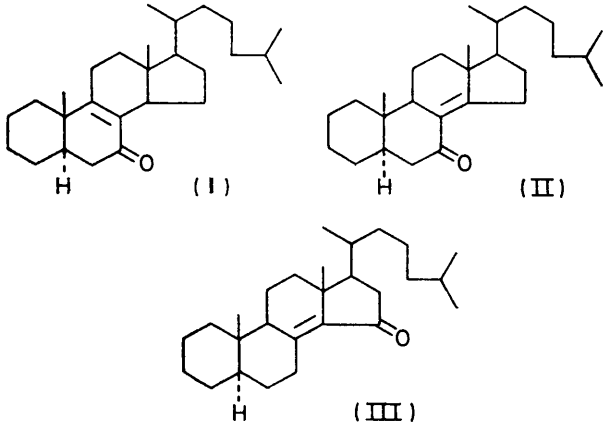
5α-Cholest-8(14)-en-15-one (III) has been isolated as a by-product of an improved synthesis of 5α-cholest-8(14)-en-7-one (II); the previously undescribed n.m.r. and mass spectra of the former compound are discussed since they are of theoretical interest and diagnostic importance. Whereas reduction of steroidal $\Delta^{8(14)}$15-ketones by metal–ammonia has been known for some time to produce saturated ketones of natural stereochemistry, the corresponding reaction of the isomeric $\Delta^{8(14)}$-7-ketone system has now been shown unexpectedly to generate a ketone of unnatural configuration, and so constitutes a novel and simple synthesis of 14β-steroids.

We recently described the preparation of 5α-cholest-8(9)- and -8(14)-en-7-ones [(I) and (II), respectively] [1]



by the route (and mechanism) [2] depicted in Scheme 1, *viz.* treatment of 5α-cholest-7-ene with 2 mol. equiv. of peroxy-acid, chromatographic separation of the resulting epoxy-alcohols (IV) and (V), and acid-catalysed rearrangement of each. Whereas one of these epoxides [the 8α,14α-isomer, (V)] generated an αβ-unsaturated ketone (II), the other afforded a hydroxy-ketone (VI), which suffered dehydration in the presence of alkali to produce the enone (I). We have since found that it is unnecessary—and indeed, less profitable—to isolate and purify these epoxides if they are merely required as intermediates. Instead, the entire crude oxidation product can be treated directly with mineral acid, and only then need purification be effected. In this manner the following fractions (listed in order of increasing polarity) were isolated by chromatography: (i) unchanged cholest-7-ene, (ii) a small quantity of a previously unobserved compound, (iii) 5α-cholest-8(14)-en-7-one (II) (25% overall yield), and (iv) 9α-hydroxy-5α-cholestan-7-one (VI) (10%).

Fraction (ii) gave analytical figures corresponding to a steroidal αβ-unsaturated ketone, and its u.v. absorption maximum (260 nm) indicated the presence of an 8,14-double bond; since this unknown in no way corresponded to the enone (II), it was assigned structure (III) [5α-cholest-8(14)-en-15-one] and this was verified by analysis of its spectral and chemical properties. The wavenumber of its i.r. carbonyl peak (1695 cm^{-1}) is low for such a cyclopentenone derivative † (possibly owing to the exocyclic nature of the double bond), but this is

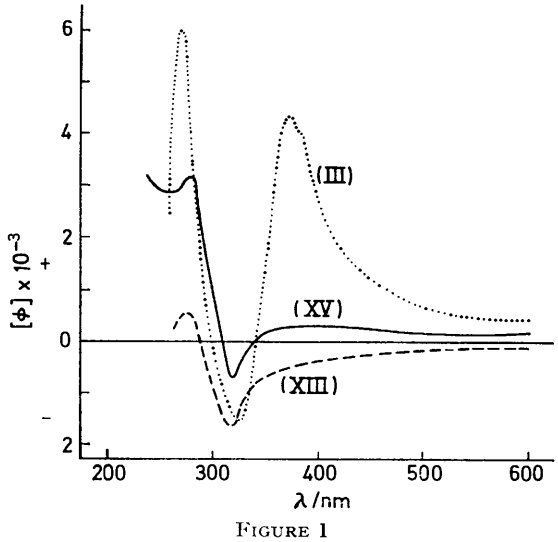


FIGURE 1

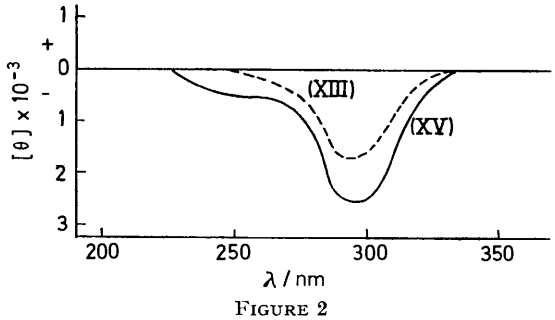


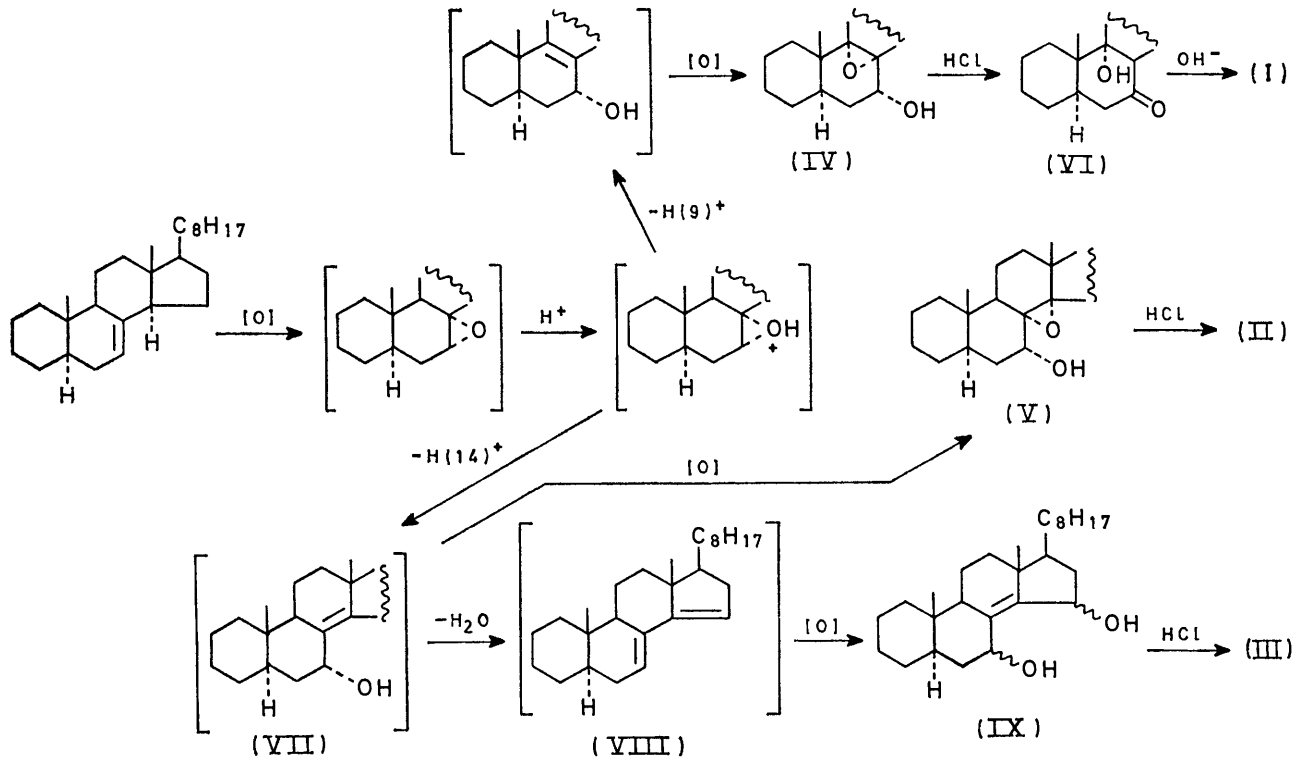
FIGURE 2

shifted to 1740 cm^{-1} upon reduction with metal–ammonia (see later); this behaviour is typical of steroids bearing a carbonyl group in ring D. Although the 'naked' enone was apparently unknown prior to this study, many 3β-oxygenated derivatives of 5α-cholest-8(14)-en-15-one are known, and all are strongly dextrorotatory,‡ so our observed value, $[\alpha]_D^{20}$ +145°, is also

† Barnes *et al.*[3] give $\nu_{C=O}$ 1703 cm^{-1} for their $\Delta^{8(14)}$-15-ketone and 1738 cm^{-1} for the corresponding saturated 15-ketone. See also ref. 4.

‡ For example [5a] 3β-hydroxy-5α-cholest-8(14)-en-15-one has $[\alpha]_D^{20}$ +118° and [5b] 5α-androst-8(14)-en-15-one has $[\alpha]_D^{20}$ +178°.

[1] I. Midgley and C. Djerassi, *J.C.S. Perkin I*, 1972, 2771.
[2] L. F. Fieser, K. Nakanishi, and W.-Y. Huang, *J. Amer. Chem. Soc.*, 1953, **75**, 4719.
[3] C. S. Barnes, D. H. R. Barton, and G. F. Laws, *Chem. and Ind.*, 1953, 616.
[4] D. H. R. Barton and G. F. Laws, *J. Chem. Soc.*, 1953, 52.
[5] (*a*) O. Wintersteiner and M. Moore, *J. Amer. Chem. Soc.*, 1943, **65**, 1513; (*b*) C. Djerassi, J. Fajkos, and A. R. Van Horn, *Steroids*, 1965, **6**, 239.



SCHEME 1 Structures in brackets represent suggested intermediates

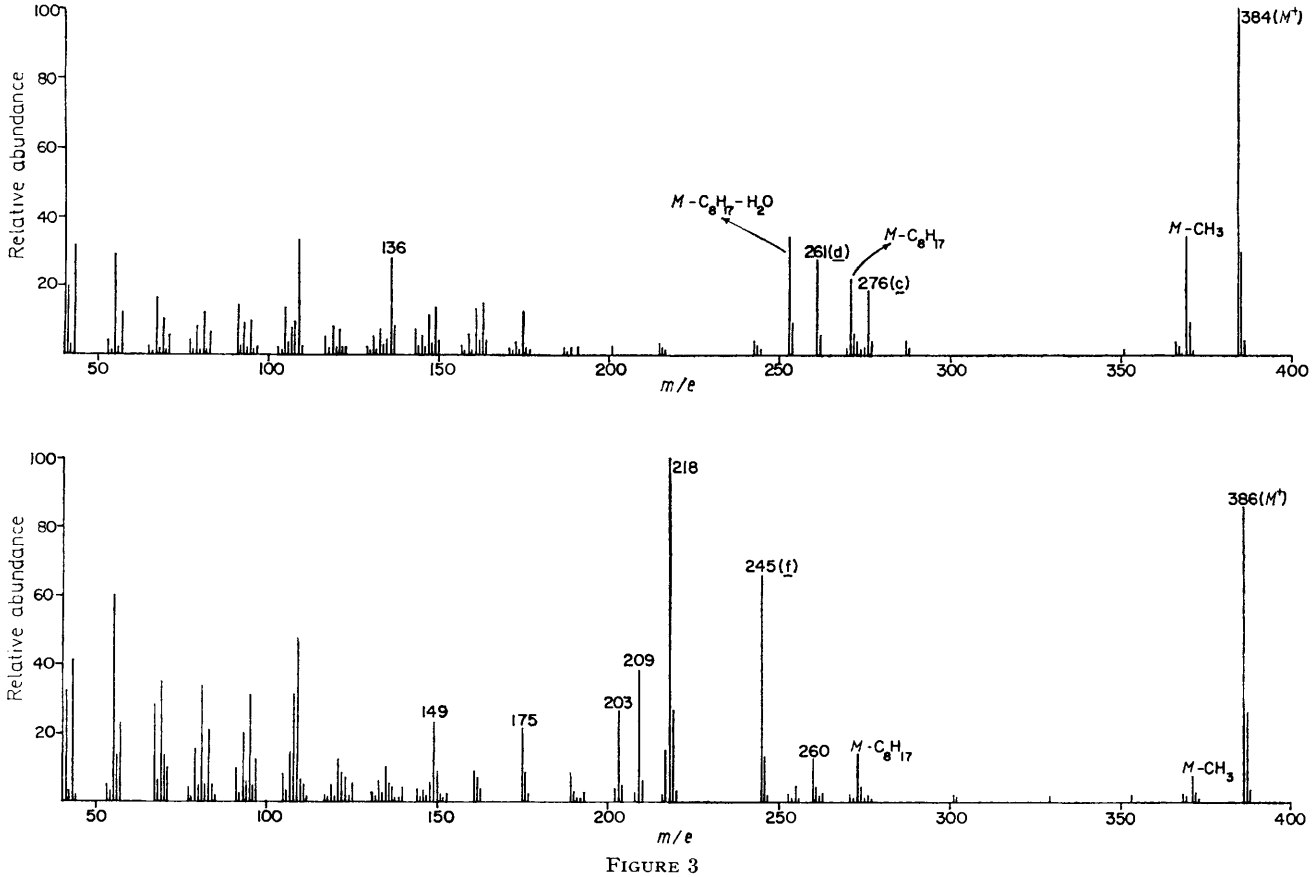
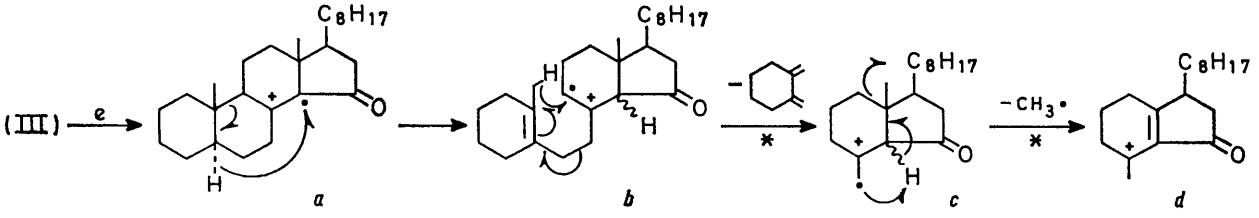


FIGURE 3

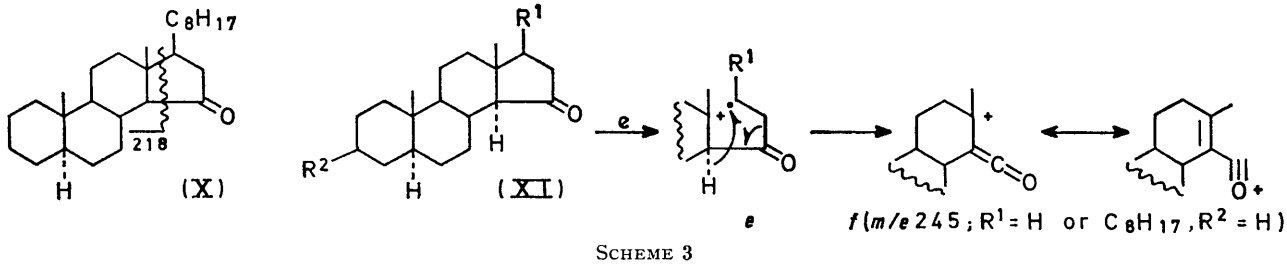
in line with the proposed structure. The o.r.d. curve of this enone (Figure 1) appears to be highly characteristic of the $\Delta^{8(14)}$-15-keto chromophore, when compared to the curves of other steroidal enones.[6] The o.r.d. curve of the corresponding saturated ketone (X) was essentially identical with that of 3β-hydroxy-5α-cholestan-15-one (XI; $R^1 = C_8H_{17}$, $R^2 = OH$) (Scheme 3).[7]

The 100 MHz n.m.r. spectrum of the enone (III) displays a broad, one-proton doublet (*J ca.* 12 Hz) centred at δ 4·12 p.p.m., which, although at a higher frequency than expected, undoubtedly corresponds to the 7β-proton; a molecular model reveals that this (allylic) proton lies precisely within the plane of the C-15 carbonyl group, and sufficiently close to be considerably deshielded by it. This situation is analogous to the long-range deshielding effects encountered in the case of saturated 7- and 11-oxo-steroids,[8] and the observed (geminal) coupling constant is of similar value. Also in accord with structure (III), mass spectrometry indicated that this compound possesses five enolisable hydrogen atoms (exchanged by deuterium); furthermore, the n.m.r. spectrum of this labelled derivative confirms that one of these protons is responsible for the downfield signal already discussed. The mass spectrum of 5α-cholest-8(14)-en-15-one itself (Figure 3) differs from those of the enones (I) and (II) (which eliminate diagnostic C_{12} fragments involving the side chain and ring B, resulting in the sequential loss of C_8H_{12} and CH_3. Our rationalisation of these latter processes (Scheme 2) involves initial formation of molecular ion *a*, followed by hydrogen rearrangement and fission of the allylic 9,10-bond (⟶*b*); this latter species then undergoes a second hydrogen transfer to the charged part of the ion with concomitant expulsion of a neutral C_8H_{12} molecule, thereby generating ion *c* (*m/e* 276). The mass spectrum of the [$^2H_5$]derivative indicates that the methyl group lost by the labelled counterpart of *c* contains essentially no deuterium. Therefore, the ejected radical must originate from C-18 (or, less likely, from the side chain), possibly in the manner shown (*c* ⟶ *d*):



SCHEME 2

The i.r. and o.r.d. spectra of 5α-cholestan-15-one (X) [derived from (III) by reduction with metal–ammonia (Scheme 4)] have already been shown to support structure (III); further evidence is forthcoming from the mass spectrum of (X) (Figure 4), which corresponds well with published spectra of 5α-androstan-15-one (XI; $R^1 = R^2 = H$)[9] and 3β-hydroxy-5α-cholestan-15-one (XI; $R^1 = C_8H_{17}$, $R^2 = OH$).[10] Thus, the powerful combination of α-fission and ring D cleavage is responsible for production of the base peak (*m/e* 218), whereas initial ionisation of the 13,17-bond and migration of the 14α-hydrogen to the radical site (as in *e*; Scheme 3), followed by homolysis of the 15,16-bond, yields the intense *m/e* 245 peak (*f*). The *m/e* 209 ion in this spectrum is the cholestane analogue



SCHEME 3

portions of rings C and D [1]), in that, with the exception of the $M - CH_3$ (*m/e* 369), $M - C_8H_{17}$ (271), and $M - C_8H_{17} - H_2O$ (253) ions, the only important high-mass peaks owe their origin to fragmentation of of the base peak (*m/e* 97) in the spectrum of 5α-androstan-15-one; the mechanism of this latter process has recently been investigated with the aid of deuterium labelling but is still not completely resolved.[11]

The most reasonable explanation (see Scheme 1) for the formation of the $\Delta^{8(14)}$-15-ketone under our

[6] C. Djerassi, 'Optical Rotatory Dispersion: Applications to Organic Chemistry,' McGraw-Hill, New York, 1960, ch. 4 and references cited therein.

[7] C. Djerassi, W. Closson, and A. E. Lippmann, *J. Amer. Chem. Soc.*, 1956, **78**, 3163.

[8] D. H. Williams, N. S. Bhacca, and C. Djerassi, *J. Amer. Chem. Soc.*, 1963, **85**, 2810.

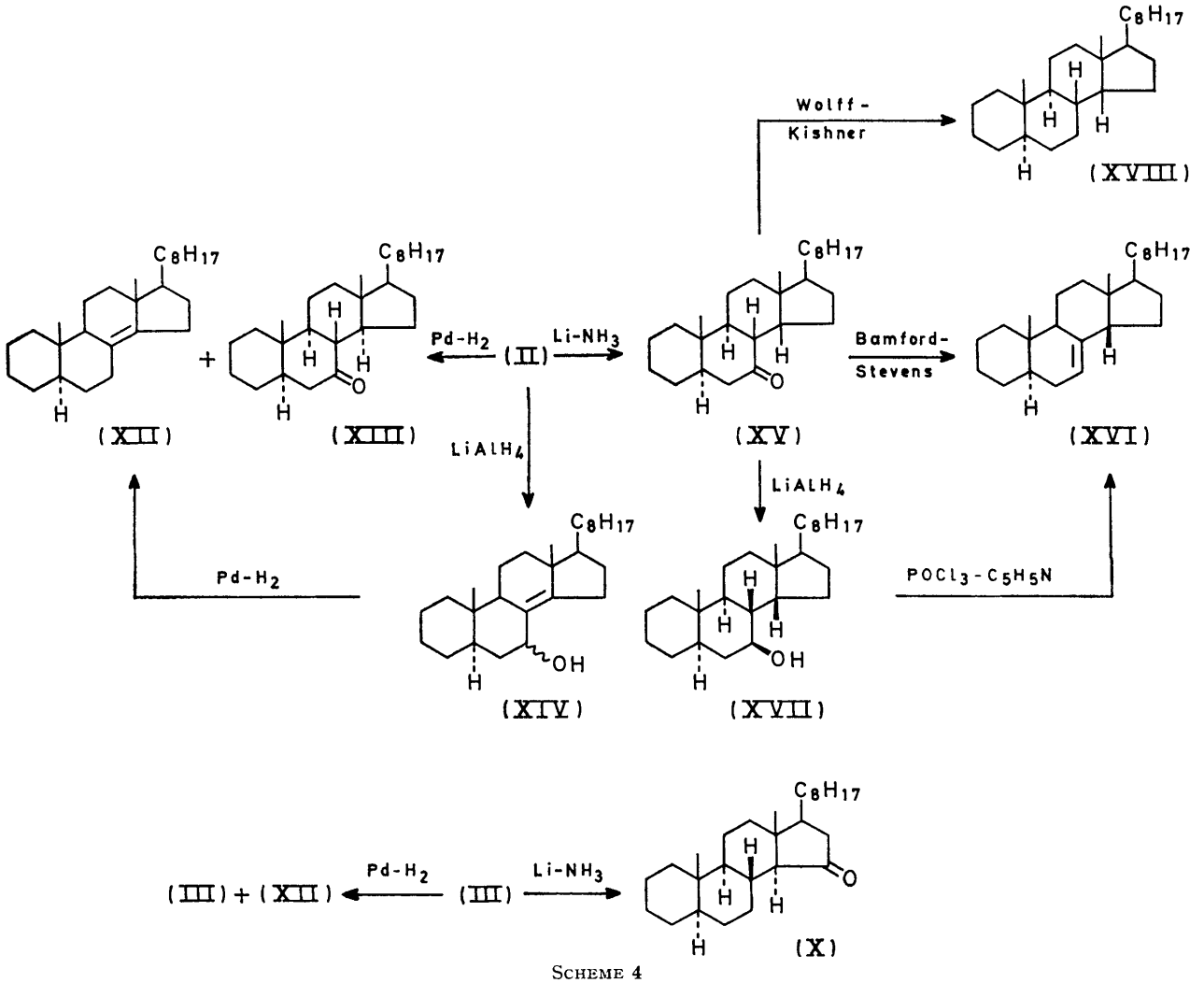
[9] C. Djerassi, G. von Mutzenbecher, J. Fajkos, D. H. Williams, and H. Budzikiewicz, *J. Amer. Chem. Soc.*, 1965, **87**, 817.

[10] H. Budzikiewicz and C. Djerassi, *J. Amer. Chem. Soc.*, 1962, **84**, 1430.

[11] A. R. Van Horn and C. Djerassi, *Steroids*, 1967, **9**, 163.

experimental conditions involves dehydration of the intermediate allylic alcohol (VII) (catalysed by the organic acid present in the oxidation mixture) to form the 7,14-diene (VIII). When such olefins are treated with 2 mol. equiv. of peroxy-acid, the result is a $\Delta^{8(14)}$-7ξ,15ξ-diol (IX);[12] these are known to afford $\Delta^{8(14)}$-15-ketones in the presence of mineral acid.[12]

Catalytic hydrogenation (Scheme 4) of 5α-cholest-8(14)-en-15-one (III) produced a mixture of 5α-cholest-8(14)-ene (XII) and starting material in the ratio 3 : 2, whereas the $\Delta^{8(14)}$-7-ketone (II) under identical conditions gave a mixture of the same olefin and 5α-cholestan-7-one (XIII),[1] this time in the proportions 2 : 3. Both these results have been described previously in the 3β-acetoxy-series,[5a,13] and hence constitute further evidence in support of structure (III). The facts that this enone produces no saturated ketone upon hydrogenation and that more cholest-8(14)-ene is generated from this compound than from enone (II) are both indicative of the greater inaccessibility of the double bond in the former ketone. Formation of the hydrocarbon in these reactions is shown later to be a result of initial reduction of the carbonyl group, rather than the double bond (which is too hindered to approach the catalyst surface), and subsequent hydrogenolysis of the allylic OH group. Thus, reduction with lithium aluminium hydride of the enone (II) yields a crystalline mixture of the epimeric $\Delta^{8(14)}$-7-alcohols (XIV),[14] which, we have found, generates cholest-8(14)-ene in high yield when subjected to the foregoing conditions of catalytic hydrogenation.



SCHEME 4

Reduction of the $\Delta^{8(14)}$-15-ketone (III) with lithium in liquid ammonia produces a saturated ketone [5α-cholestan-15-one (X)] of ' natural ' steroid configuration (*i.e.* 8β,14α); this result also has been described previously for 3β-substituted derivatives.[3,4,12] On the other hand, the saturated ketone resulting from chemical

[12] R. B. Woodward, A. A. Patchett, D. H. R. Barton, D. A. J. Ives, and R. B. Kelly, *J. Chem. Soc.*, 1957, 1131. See also refs. 3 and 4.

[13] O. Wintersteiner and M. Moore, *J. Amer. Chem. Soc.*, 1943, **65**, 1507.

[14] L. F. Fieser and G. Ourisson, *J. Amer. Chem. Soc.*, 1953, **75**, 4404.

reduction (Li–NH_3 or Zn–AcOH) of the $\Delta^{8(14)}$-7-ketone (II) does not possess the natural configuration, a surprising result that has not been observed before. This is most apparent when one compares the o.r.d. curves (Figure 1) of this compound (XV) and 'natural' cholestan-7-one (XIII), but the difference also manifests itself in m.p., optical rotation, and n.m.r. and mass spectra.* Treatment with base has no effect on the properties of this 'iso-ketone'; therefore C-8 is in its thermodynamically most stable configuration. Molecular models indicate that the 8α,14α-configuration is extremely unstable, and even if formed initially, this structure would be expected to rearrange in the presence of base to the more stable natural stereochemistry. Hence we conclude that this ketone has the C/D *cis*-fused conformation, and this is confirmed by the fact that Bamford–Stevens reduction [15] (or $LiAlH_4$ reduction, followed by dehydration with $POCl_3$ in pyridine) produces a steroid olefin whose n.m.r. and mass spectra are different from those of 5α,14α-cholest-7-ene; this new olefin must therefore be 5α,14β-cholest-7-ene (XVI).

Determination of the spatial arrangement of the unnatural ketone at C-8, however, is less easy. The c.d. curves (Figure 2) of the new ketone (XV) and the natural 7-ketone (XIII) reveal that the Cotton effect displayed by the former is more negative than that of the latter, but unfortunately, quadrant diagrams imply that this would be expected for both the remaining conformational possibilities (8α,14β and 8β,14β). Construction of models indicates that both could exist in the all-chair form, but that the *trans,syn,cis*-(8β,14β) is considerably less strained than the *cis,syn,cis* (8α,14β) form. These models further reveal that the β-face of the former configuration is much less accessible in the region of the carbonyl group than the latter; therefore if the 'unnatural' ketone possesses the 8β,14β-conformation, reduction with lithium aluminium hydride, for instance, would be expected to proceed predominantly by α-attack, and so produce relatively more of the 7β-alcohol than does natural cholestan-7-one (55% β-, 25% α-cholestan-7-ols [16]). This is what is observed: only one alcohol (by g.l.c., t.l.c., n.m.r., *etc.*) was obtained in crystalline form, although chromatographic analysis indicated that a small amount of the other epimer was present in the mother liquors, but only to the extent of about 15%. A one-proton triplet of doublets (*J ca.* 10·5 and 5 Hz) centred at δ 3·41 p.p.m. in the n.m.r. spectrum of this major reduction product proves that the hydroxy-group is equatorial (*i.e.* β); only by having an axial proton at C-7 could the larger coupling constant arise. Since the individual peaks of this splitting pattern are broadened, it is probable that two diaxial couplings of similar *J* value are contributing, and for the spectrum of a 7β-sterol to exhibit two such interactions, together with one axial–equatorial coupling, the C-8 proton must also be axial; this alcohol is therefore 5α,8β,14β-cholestan-7β-ol (XVII). As final, confirmatory proof of the 8β,14β-configuration, the positions of the C-18 and C-19 proton signals in the n.m.r. spectra of the unnatural ketone (XV), alcohol (XVII), olefin (XVI), and saturated hydrocarbon (XVIII) agree so well with the values calculated by Zürcher's rules [17] (see Experimental section) that any other structure would be inadmissible.

In view of Barton's previous work,[3,4] which concluded that C/D *trans*-fused steroids are more stable than the corresponding *cis*-isomers, the stereochemical results of the present investigation are surprising. Although *cis*-8-methylhydridanes are known to be more stable than their *trans* counterparts,[18] Van Horn and Djerassi [19] have found that the presence of a large 17β-alkyl substituent (*e.g.* C_9H_{19}) in the steroid skeleton causes a complete reversal of this situation, owing to the severe steric interactions between the side chain and the C-13 methyl group. Our results therefore indicate that it is not the thermodynamic stability of the saturated ketone resulting from reduction of its αβ-unsaturated analogue with metal–ammonia that determines its stereochemistry, but the conformation of the transition state which permits maximum orbital overlap.[20] This emphasises previous warnings that attempts to assess the conformational stabilities of polycyclic molecules (especially hydrindanes) on the basis of the stereochemical outcome of reductions with metal–ammonia must always be regarded with circumspection.[21]

EXPERIMENTAL

The instruments (and solvents, where appropriate) used in the determination of m.p.s, optical rotations, and i.r., u.v., n.m.r., and mass spectra have been described previously.[1] Reactions and column chromatographies were monitored by t.l.c.,[1] and the purity of all products was checked by g.l.c. (Hewlett–Packard model 402 High Efficiency Gas Chromatograph; 6 ft column of 3% OV-25 on GasChrom Q support, operating at 250—275°; the same instrument and column were used to isolate pure samples for n.m.r. and mass spectroscopy where necessary).

5α-Cholest-8(14)-en-7- and 15-ones [(II) *and* (III)].—5α-Cholest-7-ene (14 g) was treated with *m*-chloroperbenzoic acid as described previously,[1] but this time the

* The mass spectra of these 14β-steroids [(XV), (XVI), and (XVIII)], together with those of certain deuterium-labelled derivatives, will be published subsequently.

[15] For example, see E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 6269.

[16] R. J. W. Cremlyn and C. W. Shoppee, *J. Chem. Soc.*, 1954, 3515.

[17] R. F. Zürcher, *Helv. Chim. Acta*, 1963, **46**, 2054. See also N. S. Bhacca and D. H. Williams, 'Applications of NMR Spectroscopy in Organic Chemistry,' Holden-Day, San Francisco, 1964, p. 18.

[18] See N. L. Allinger and M. T. Tribble, *Tetrahedron*, 1972, **28**, 1191, for an up to date report on the relative stabilities of hydrindanes and related compounds.

[19] A. R. Van Horn and C. Djerassi, *J. Amer. Chem. Soc.*, 1967, **89**, 651.

[20] For the latest review on the metal–ammonia reduction of steroidal enones, see 'Organic Reactions in Steroid Chemistry,' vol. 1, ch. 1, eds. J. Fried and J. A. Edwards, Van Nostrand Reinhold Co., New York, 1972, and references cited therein. Also, G. Stork and S. D. Darling, *J. Amer. Chem. Soc.*, 1960, **82**, 1512, and G. Stork and T. Tsuji, *ibid.*, 1961, **83**, 2783.

[21] C. Djerassi, T. T. Grossnickle, and L. B. High, *J. Amer. Chem. Soc.*, 1956, **78**, 316; C. Djerassi, R. Riniker, and B. Riniker, *ibid.*, p. 6362.

entire crude oxidation product was exposed directly to ethanolic hydrochloric acid. The mixture was evaporated to half volume, then worked up by diluting with water and extracting several times with ether. Conventional treatment of the extracts afforded a golden oil (15 g) which was chromatographed on alumina (800 g; activity II). Elution with n-hexane and 10% benzene–hexane yielded crude, unchanged cholest-7-ene (2·3 g); 75% benzene–hexane eluted first a mixture of enones (II) and (III) (2·8 g), then pure (II) (4·3 g). Elution with ether then produced an oil (3·7 g), which was triturated with hexane; the product was filtered off and washed with the same solvent to yield 9α-hydroxy-5α-cholestan-7-one (VI) (1·5 g) as plates.[1] Rechromatography of the mixture of (II) and (III) on alumina (250 g) in the same fashion afforded, first, pure (III) (0·5 g), then a mixture (0·9 g), and finally pure (II) (1·2 g). Both ' pure ' crops of (II) were combined, then recrystallised twice to yield material (3·5 g) whose properties were identical with those determined previously.[1]

The ' pure ' crop of the enone (III) crystallised from methanol as *needles*, m.p. 103—104°, $[\alpha]_D^{20}$ +145° (*c* 0·6), $\nu_{max.}$ 1695 (C=O) and 1615 cm^{-1} (C=C), $\lambda_{max.}$ 260 nm (ε 15,400), δ 4·12br (d, *J ca* 12 Hz, H-7β), 0·96 (3H, s, 18-H_3; calc.[17] 0·890), and 0·67 p.p.m. (3H, s, 19-H_3; calc.[17] 0·666). [Found: C, 84·1; H, 11·3%; *M* (mass spectrum), 384 $C_{27}H_{44}O$ requires C, 84·4; H, 11·45%; *M*, 384] (see Figure 1 for o.r.d. curve and Figure 3 for mass spectrum).

Reduction of 5α-Cholest-8(14)-en-15-one (III) *by Lithium–Ammonia.*—A solution of the enone (130 mg) in ether (5 ml) was added dropwise to a rapidly stirred solution of lithium (100 mg) in redistilled liquid ammonia (10 ml). The mixture was stirred for a further 1·5 h under reflux, then ammonium chloride was added until the blue colour was discharged. The ammonia was allowed to evaporate, water was added, and the mixture was extracted with ether. The combined extracts were washed successively with water, dil. hydrochloric acid, water, and 5% sodium hydrogen carbonate solution, then dried ($MgSO_4$) and evaporated to dryness. The product was dissolved in acetone and treated with a slight excess of Jones reagent to oxidise any of the alcohol present. After dilution, extraction, *etc.*, a solid product (X) (80 mg, 61%) was obtained which formed long needles, m.p. 144—145° (from methanol) (*cf.* 5α-ergostan-15-one,[19] m.p. 143—144°) $[\alpha]_D^{20}$ +50° (*c* 0·5), $\nu_{max.}$ 1740 cm^{-1} (five-membered cyclic ketone), δ 0·73 (3H, s, 18-H_3; calc.[17] 0·727) and 0·78 p.p.m. (3H, s, 19-H_3; calc.[17] 0·783), *M* (mass spectrum, see Figure 4) 386.

Catalytic Hydrogenation of 5α-Cholest-8(14)-en-15-one (III).—A mixture of the enone (90 mg), 10% palladium–charcoal (45 mg), and ethyl acetate (10 ml) was stirred for 20 h at room temperature under 1 atm of hydrogen. Filtration, evaporation, and chromatography on alumina (8 g; activity II) afforded 5α-cholest-8(14)-ene (XII) (45 mg) (eluted with n-hexane) and starting material (30 mg) (eluted with 20% benzene–hexane). Both products were identified by m.p., mixed m.p., and n.m.r. and mass spectra.*

Reduction of 5α-Cholest-8(14)-en-7-one (II) *with Lithium–Ammonia.*—A solution of the enone (1·0 g) in ether (25 ml) was added to a solution of lithium (0·5 g) in liquid ammonia (60 ml) as already described. After 2 h the mixture was worked up, oxidised with Jones reagent, and chromatographed on alumina (60 g; activity II). n-Hexane eluted a mixture of hydrocarbons (80 mg), but 10 and 15% benzene–hexane produced the saturated ketone (XV) (460 mg), which crystallised from methanol as long needles, m.p. 90—91°, $[\alpha]_D^{20}$ +73·5° (*c* 1·0), $\nu_{max.}$ 1700 cm^{-1}, δ 0·97 (3H, s, 18-H_3; calc.[17] 0·950) and 0·99 p.p.m. (3H, s, 19-H_3; calc.[17] 1·025), *M* 386 (≡ $C_{27}H_{46}O$) (see Figures 1 and 2 for o.r.d. and c.d. curves).

Reduction of 5α-Cholest-8(14)-en-7-one (II) *with Zinc–Acetic Acid.*—Zinc dust (15 g) was added in four portions during 1 h to a stirred solution of the enone (200 mg) in acetic acid (100 ml) at room temperature. After a further 3 h the mixture was filtered and evaporated to dryness under vacuum. A solution of the residue in ether was washed acid-free with 5% sodium hydrogen carbonate solution, then dried ($MgSO_4$), and evaporated. The product was chromatographed on alumina (15 g; activity II). n-Hexane eluted a mixture of hydrocarbons (80 mg), and 10% benzene–hexane produced 5α,14β-cholestan-7-one (XV) (60 mg, 30%), m.p. and mixed m.p. 90—91°.

Bamford–Stevens Reduction of 5α,14β-Cholestan-7-one (XV).—The ketone (0·46 g), toluene-*p*-sulphonohydrazide (0·46 g), methanol (80 ml), and conc. hydrochloric acid (2 drops) were refluxed for 1 h under nitrogen; the mixture was then evaporated to dryness under vacuum. The residue was partitioned between ether and dil. hydrochloric acid, and the product isolated by standard techniques. Recrystallisation from methanol afforded crystals of the *tosylhydrazone* (0·51 g), m.p. 160—161°, $\nu_{max.}$ 3310 (N–H) and 1605 cm^{-1} (C=N) (Found: C, 73·5; H, 9·65; N, 5·05; S, 5·9. $C_{34}H_{54}N_2O_2S$ requires C, 73·75; 9·75; N, 5·05; S, 5·8%).

The tosylhydrazone (0·5 g) and ethylene glycol (50 ml) were stirred and refluxed under nitrogen while small pieces of sodium (1·5 g) were added during 0·5 h. After a further 2 h under reflux, the mixture was cooled, poured onto ice, and extracted four times with ether. The combined extracts were washed with dil. hydrochloric acid (twice), water, and 5% sodium hydrogen carbonate solution, then dried ($MgSO_4$), and evaporated to dryness. The residue was chromatographed on alumina (12 g; activity II), n-hexane (50 ml) eluting the olefin (XVI) (0·17 g, 52%) as an oil which resisted all efforts at crystallisation. A pure sample obtained by preparative g.l.c. had the correct mol. weight (370 ≡ $C_{27}H_{46}$; mass spectrometry), and exhibited δ 5·35 (1H, m, H-7), 0·89 (3H, s, 18-H_3; calc.[17] 0·825), and 0·73 p.p.m. (3H, s, 19-H_3; calc.[17] 0·742).

Reduction of 5α,14β-Cholestan-7-one (XV) *with Lithium Aluminium Hydride.*—The ketone (160 mg) in anhydrous ether (15 ml) was treated with the hydride (100 mg), then stirred for 5 h under reflux. Excess of hydride was decomposed by dropwise addition of ethyl acetate; dil. sulphuric acid was then added and the mixture was worked up in the usual manner to give an oil which solidified on cooling in ice. This alcohol (XVII) (100 mg, 63%) crystallised from methanol containing a few drops of water as slightly hygroscopic tablets, m.p. 58—61°, $\nu_{max.}$ 3460 cm^{-1} (OH), δ 3·48 (OH, s, removed by adding D_2O), 3·41 (1H, td, *J ca.* 10·5 and 5·0 Hz; 7α-H), 0·99 (3H, s, 18-H_3; calc.[17] 0·975), and 0·78 p.p.m. (3H, s, 19-H_3; calc.[17] 0·775), *M* (mass spectrum) 388 (≡ $C_{27}H_{48}O$).

* Authentic 5α-cholest-8(14)-ene was prepared from the Δ^7-isomer in a similar manner to that described for the ergostene series.[22]

[22] G. M. L. Cragg, C. W. Davey, D. N. Hall, G. D. Meakins, E. E. Richards, and T. L. Whateley, *J. Chem. Soc.* (*C*), 1966, 1266.

Dehydration of 5α,14β-*Cholestan*-7β-*ol* (XVII) *with Phosphoryl Chloride in Pyridine*.—A solution of the alcohol (60 mg) in pyridine (2 ml) at 0° was slowly treated with phosphoryl chloride (0·5 ml; redistilled). The mixture was kept for 60 h at 0—5° in a stoppered flask, then poured onto ice and extracted with ether, *etc.* Preparative g.l.c. afforded a pure sample of olefin, whose n.m.r. and mass spectra were identical with those of the Bamford–Stevens reduction product [*i.e.* 5α,14β-cholest-7-ene (XVI)].

Wolff–Kishner Reduction of 5α,14β-*Cholestan*-7-*one* (XV).—A mixture of the ketone (50 mg), diethylene glycol (10 ml), n-butanol (4 ml), and 97% hydrazine (2 ml) was stirred for 1 h at 150° under nitrogen. After cooling to 100°, potassium hydroxide (0·6 g) was added, and the solution was gradually heated to 210° with the condenser removed. After a further 5 h at this temperature, the mixture was cooled and poured on ice, and the product was isolated by conventional extraction techniques. Chromatography on alumina (4 g; activity II) in n-hexane yielded 5α,14β-cholestane (XVIII) (45 mg, 93%), which was contaminated with 15% of an olefin (g.l.c.). Preparative g.l.c. afforded a sample, which had the correct mol. weight (372 ≡ $C_{27}H_{48}$; mass spectrometry), and displayed δ 0·98 (3H, s, 18-H_3; calc.[17] 0·942) and 0·75 p.p.m. (3H, s, 19-H_3; calc.[17] 0·750).

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