1007. *Stereochemistry of the 3-Hydroxymethyl-A-norcholestanes and Related Compounds*

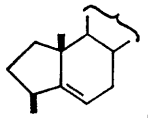
By G. H. WHITHAM and J. A. F. WICKRAMASINGHE

The preparation and assignment of stereochemistry to all four 3-hydroxymethyl-A-norcholestanes is described. From the results it is clear that the products from hydrogenation of both 3β- and 3α-hydroxymethyl-A-norcholest-5-ene have been derived by addition of hydrogen to the β-face of the molecule.

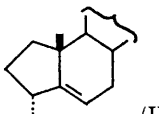
IN the course of studies on the solvolysis of the toluene-*p*-sulphonates of 3β- (I) and 3α-hydroxymethyl-A-norcholest-5-ene (II) [1] we prepared one of the 3-hydroxymethyl-A-norcholestanes (III) by hydrogenation of the homoallylic alcohol (II). This saturated alcohol, which was tentatively assigned A/B-*trans* geometry on the basis of catalyst approach from the α-side of the molecule, was employed for comparison of the rate of acetolysis of its toluene-*p*-sulphonate with those of the two homoallylic alcohols (I) and (II). The toluene-*p*-sulphonates of (I) and (II) were acetolysed appreciably faster than that of the saturated alcohol, as expected on the basis of double-bond assistance to ionisation. However, the difference was not as large as expected, and the saturated toluene-*p*-sulphonate was acetolysed twenty times faster than the toluene-*p*-sulphonate of cyclopentylmethanol at 80°. This suggested that the saturated compound was not a good model for the rate

[1] G. H. Whitham and J. A. F. Wickramasinghe, *J.*, 1964, 1955.

of unassisted ionisation in the acetolysis of the toluene-*p*-sulphonates of (I) and (II). In order to assess the factors responsible for the unusual solvolytic reactivity of the saturated toluene-*p*-sulphonate, a knowledge of its stereochemistry is required. Determination of the latter has involved the preparation and assignment of stereochemistry to all four 3-hydroxymethyl-A-norcholestanes (III).



(I)



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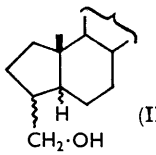
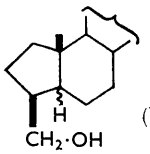


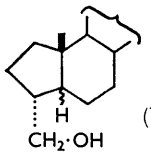
(III)

Two of the stereoisomers of structure (III) were readily obtained by hydrogenation of the homoallylic alcohols (I) and (II) * over platinum in the presence of a trace of perchloric acid. Since the stereochemistry of (I) and (II) is known,[1] the corresponding hydrogenation products must have the structures (IV) and (V), respectively, with the nature of the ring junction undefined. The slight possibility that double-bond migration to C-3,C-5 may have preceded hydrogenation, thereby destroying stereochemical integrity at C-3, was excluded by the demonstration that hydrogenation of 3-hydroxymethyl-A-norcholest-3-ene under the same conditions resulted largely in hydrogenolysis with formation of hydrocarbon. The saturated alcohols derived from (I)and (II) are designated (A) and (B), respectively, for future reference; they were characterised as their *p*-nitrobenzoates.

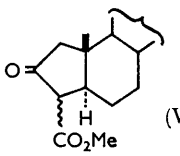
In 1960 Fuchs and Loewenthal [3] described the preparation of a 3-methoxycarbonyl-A-nor-5α-cholestane by the following sequence. The methyl ester of 2,3-seco-5α-cholestane-2,3-dicarboxylic acid [4] was cyclised, with potassium t-butoxide in benzene, to the keto-ester (VI) which was converted into the ethanedithioketal. Desulphurisation of the latter with Raney nickel gave the A-nor ester. These workers assigned the 3β-methoxycarbonyl configuration to this ester on the basis of a rather tenuous argument. We have repeated the preparation, and corroborate the experimental work, although, as will be seen later, we do not agree with the stereochemical assignment. For the present we shall ascribe structure (VII) to the ester since the A/B-*trans* ring junction follows from its method of preparation. Reduction of this ester (VII) with lithium aluminium hydride gave a third alcohol of type (III), alcohol (C), characteristically different from the alcohols (A) and (B) already obtained. Since alcohol (C) possesses a *trans*-A/B fusion it follows that either (A) or (B), or both, must have a *cis*-A/B ring junction.



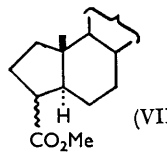
(IV)



(V)



(VI)



(VII)

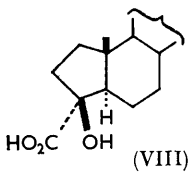
The above route to the saturated ester (VII) is circuitous, and thus we explored alternative ways of preparing such saturated A-nor-esters. A potentially better entry into the series is provided by the ring-contraction of a 3,4-diketone to a hydroxy-acid on treatment with alkali.[5] Although this reaction has been successful in the androstane and pregnane series,[5] it is reported [6] to give a mixture of acids in the case of cholestane-3,4-dione when

* The alcohol derived by hydrogenation of (II) had already been described, without stereochemical implications.[2]

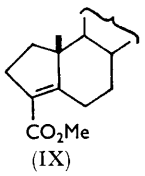
[2] W. G. Dauben and J. A. Ross, *J. Amer. Chem. Soc.*, 1959, **81**, 6521.
[3] B. Fuchs and H. J. E. Loewenthal, *Tetrahedron*, 1960, **11**, 199.
[4] A. Windaus and C. Uibrig, *Ber.*, 1914, **47**, 2384.
[5] B. Camerino and U. Valcavi, *Gazzetta*, 1963, **93**, 723.
[6] J. F. Biellmann and M. Rajic, *Bull. Soc. chim. France*, 1962, 441.

baryta is used as base. However, by a modification of the conditions of Camerino *et al.*,[5] cholestane-3,4-dione was converted into a single hydroxy-acid to which the stereochemistry (VIII) is tentatively assigned on the basis of its mode of formation. Methylation of the acid (VIII) with diazomethane, followed by dehydration with thionyl chloride in pyridine, provides an efficient route to the αβ-unsaturated ester (IX), previously obtained [3] from the keto-ester (VI). The unsaturated ester (IX) can be hydrogenated in ethanol–acetic acid with platinum as catalyst, to give a mixture of two saturated esters in the ratio of about 5 : 1. On the assumption of *cis*-addition of hydrogen, these two esters must have the stereochemistry indicated in formulæ (X) and (XI), although there are no grounds, at this stage, for knowing which is which.

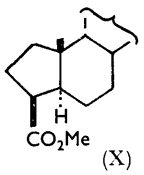
Considering first the predominant isomer from the hydrogenation of ester (IX), proof that it has an A/B-*trans* ring junction was soon forthcoming from the observation that it was smoothly isomerised in high yield to the ester (VII), obtained earlier by the method of Fuchs and Loewenthal, on treatment with sodium methoxide in methanol. The major isomer from hydrogenation of (IX) must therefore have structure (X) which, on base-catalysed epimerisation at C-3, gives the isomeric ester (XII). The 3-methoxycarbonyl-A-nor-5α-cholestane of Fuchs and Loewenthal [3] thus has the structure (XII) which is epimeric at C-3 with the structure originally proposed by them.*



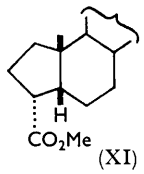
(VIII)



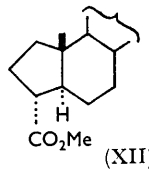
(IX)



(X)



(XI)



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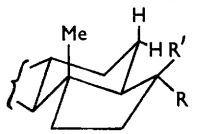

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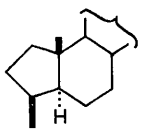

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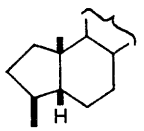
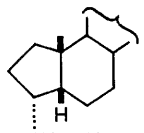


(XV)



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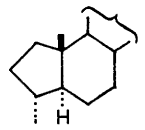


(XVII)

The base-catalysed isomerisation of ester (X) to (XII) may be interpreted as an equilibrium-controlled process involving reversible formation and protonation of an enolate-type ion. The pseudoaxial methoxycarbonyl group in (X), see (XIII; R = H, R′ = CO_2Me), in which a chair conformation for ring B is presumed, suffers destabilising interactions (notably with the C-19 methyl and the 6β-hydrogen), in comparison with the

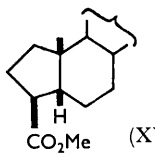
* The 3α-ester (XII) has m. p. 76—77°, $[\alpha]_D$ 0°, and the 3β-ester (X) has m. p. 65—66°, $[\alpha]_D$ +59°. The literature contains a number of references to 3-methoxycarbonyl-A-nor-5α-cholestanes, but the information as to configuration is confused. Shoppee, Winternitz, and co-workers [7] obtained an ester of m. p. 45—46°, $[\alpha]_D$ +1°, as one of the products from the Favorskii rearrangement of 2α-bromocholestan-3-one using sodium methoxide in methanol. This was considered to be 3α-methoxycarbonyl-A-nor-5α-cholestane on the basis of stereochemical considerations of the Favorskii rearrangement. However, the possibility of epimerisation subsequent to the rearrangement was not explicitly considered by these authors. On the basis of our results this material might be a mixture of the 3α- and the 3β-isomers, although the specific rotation quoted does not agree very well with this interpretation. Fuchs and Loewenthal's work [3] has already been discussed. Biellmann and Rajic [6] isolated an ester, m. p. 51°, $[\alpha]_D$ +11°, from the mixture of methyl esters derived by methylation of the product from oxidation of 5α-cholestan-3-one with selenium dioxide and hydrogen peroxide; this ester was considered to be the 3α-methoxycarbonyl isomer on the basis of comparison with the constants quoted by Evans *et al.*,[7] again it may be a mixture of the two epimers. Hellman and Jerussi [8] isolated an ester, identical with that of Fuchs and Loewenthal, from oxidation of 5α-cholestan-3-one with hydrogen peroxide and selenic acid followed by methylation; they accepted the 3β-configuration for this ester although they pointed out that it had not been established unambiguously.

We have considered the possibility that our ester (X) may be a mixture, but we believe it to be pure since its epimerisation to ester (XII) proceeds virtually quantitatively, and mixtures of (X) and (XII) have markedly depressed melting points.

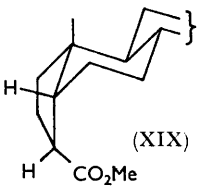
[7] D. E. Evans, A. C. de Paulet, C. W. Shoppee, and F. Winternitz, *J.*, 1957, 1451.
[8] H. M. Hellman and R. A. Jerussi, *Tetrahedron*, 1964, **20**, 741.

relatively unencumbered pseudoequatorial methoxycarbonyl group in (XII) [cf. (XIII; R = CO_2Me, R′ = H)].

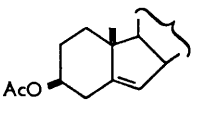
Reduction of the saturated ester (X) with lithium aluminium hydride gave the fourth, and last, of the possible isomers of structure (III). It was readily distinguishable from the isomers (A), (B), and (C) obtained earlier. This last isomer must, on the basis of the structure (X) for its precursor, have the stereochemistry shown in (XIV), and it is therefore the second of the A/B-*trans*-isomers of the series. Isomers (A) and (B), derived by hydrogenation of the homoallylic alcohols (I) and (II), respectively, may thus be assigned structures (XV) and (XVI) with the *cis*-A/B ring fusion. Finally, isomer (C), from lithium aluminium hydride reduction of ester (XII), has the stereochemistry (XVII).



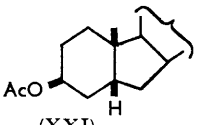
(XVIII)



(XIX)



(XX)



(XXI)

Additional confirmation of the above configurational assignments came from investigation of the minor product obtained on hydrogenation of the unsaturated ester (IX). On the basis of the earlier deductions, this must have the stereochemistry (XI), *i.e.*, it is the ester related to the saturated alcohol (XVI). In agreement, reduction of (XI) with lithium aluminium hydride afforded an alcohol identical with (XVI), alcohol (B) derived from hydrogenation of homoallylic alcohol (II).* Furthermore, the *cis*-fused ester (XI) would be expected to be destabilised relative to the ester (XVIII) with a 3β-methoxycarbonyl group, owing primarily to non-bonded interactions between the ester group and the axial hydrogen at C-7 [see formula (XIX) in which a chair conformation for ring B is presumed]. Consistently, the ester (XI) was converted, on treatment with sodium methoxide in methanol, into an isomeric ester,† and reduction of the latter with lithium aluminium hydride gave a saturated alcohol which was identical with (XV), alcohol (A), derived by hydrogenation of homoallylic alcohol (I).

It remains to draw attention to the surprising preference for addition to the β-face of the molecule in the hydrogenation of the homoallylic alcohols (I) and (II). This is particularly remarkable in the first case, alcohol (I), where the β-face is shielded by both the C-19 methyl and the hydroxymethyl group. A related example of unexpected β-hydrogenation has been recorded in the case of B-norcholesteryl acetate (XX) which gives mainly (XXI).[9] It is of interest that in both cases the more stable *cis*-hydrindane system is generated, which may indicate that the transition state for such hydrogenations can be influenced by considerations of product stability. However, the observation that hydrogenation of the unsaturated ester (IX) gave mainly the *trans*-A/B-isomer (X) shows that this suggestion should be viewed with caution. Clearly, several subtle factors must be involved.

Discussion of the outcome of acetolysis of the toluene-*p*-sulphonates of the alcohols (III) will be deferred for a later Paper.

[*Note added in Proof.*—Professor Loewenthal has kindly informed us that he has recently obtained nuclear magnetic resonance data on the β-keto-ester (VI) (δH^3, 6·9; $J_{3,5}$ = 13 c./sec.) consistent with the 3α-orientation of the methoxycarbonyl group.]

* This evidence confirms the initial assumption of *cis*-addition of hydrogen in the hydrogenation of (IX).

† Unfortunately, neither of the *cis*-fused esters was obtained crystalline; we were, therefore, unable to make comparisons with earlier literature citations of such compounds.[7]

[9] W. G. Dauben, G. A. Boswell, W. Templeton, J. W. McFarland, and G. H. Berezin, *J. Amer. Chem. Soc.*, 1963, **85**, 1672, and references therein.

Experimental

For general points see ref. 1.

Hydrogenation of 3β-*Hydroxymethyl*-A-*norcholest*-5-*ene*.—A solution of 3β-hydroxymethyl-A-norcholest-5-ene (37 mg.) in chloroform (12 ml.) containing a trace of perchloric acid was shaken under hydrogen in the presence of Adams platinum catalyst for 5 hr. Isolation of the product gave a solid residue which was converted into the *p*-nitrobenzoate by use of *p*-nitrobenzoyl chloride in pyridine. The product was filtered through a short column of silica gel, giving material [27 mg., one spot on thin-layer chromatography, R_F (in benzene) 0·88] which on crystallisation from methanol–ether gave the p-*nitrobenzoate of* 3β-*hydroxymethyl*-A-*nor*-5β-*cholestane* as fine needles, m. p. 141—142·5°, $\nu_{max.}$ (CS_2) 1725 cm.$^{-1}$ (ester CO) (Found: C, 75·95; H, 9·5; N, 2·65. $C_{34}H_{51}NO_4$ requires C, 75·95; H, 9·55; N, 2·6%). The m. p. was markedly depressed on admixture with the *p*-nitrobenzoate of 3β-hydroxymethyl-A-norcholest-5-ene.

3α-*Hydroxymethyl*-A-*nor*-5β-*cholestane*.—3α-Hydroxymethyl-A-norcholest-5-ene (0·54 g.) was converted into the acetate by use of pyridine–acetic anhydride, and the latter was hydrogenated in acetic acid containing a trace of perchloric acid with Adams catalyst. The crude product was hydrolysed with ethanolic potassium hydroxide, giving the saturated alcohol (0·39 g.) which crystallised from aqueous acetone as needles, m. p. 79—80°, $[\alpha]_D^{30}$ −3·5° (lit.,[2] m. p. 89·6—90·2°, $[\alpha]_D^{25}$ −3·6°). The toluene-*p*-sulphonate prepared using toluene-*p*-sulphonyl chloride–pyridine had m. p. 88·5—90° (lit.,[2] m. p. 89—90·5°). The *p*-nitrobenzoate (plates from methanol) had m. p. 79·5—80·5°.

Hydrogenation of 3-*Hydroxymethyl*-A-*norcholest*-3-*ene*.—A solution of the allylic alcohol [1] (20 mg.) in chloroform (20 ml.) containing a trace of perchloric acid was shaken under hydrogen for 5 hr. in the presence of Adams catalyst. The product (19 mg.) was shown by thin-layer chromatography to be largely hydrocarbon in nature, R_F (in light petroleum) 1·0, together with traces of alcohols.

3α-*Hydroxymethyl*-A-*nor*-5α-*cholestane*.—3α-Methoxycarbonyl-A-nor-5α-cholestane [3] (65 mg.) m. p. 76—77°, $[\alpha]_D$ 0°, in dry ether (20 ml.), was refluxed with lithium aluminium hydride (50 mg.) for 30 min. After addition of 5% hydrochloric acid, the product was isolated in the usual way. Crystallisation from methanol gave the *alcohol* (47 mg.) as short needles, one spot on thin-layer chromatography, R_F (in chloroform–benzene, 1 : 1) 0·33, m. p. 111·5—113°, $[\alpha]_D$ +3·3°, $\nu_{max.}$ (CS_2) 3600, 1030 cm.$^{-1}$ (Found: C, 83·1; H, 12·25. $C_{27}H_{48}O$ requires C, 83·45; H, 12·45%). The p-*nitrobenzoate* (stout needles from ether–methanol) had m. p. 160·5—161·5° (Found: C, 75·9; H, 9·35; N, 3·0. $C_{34}H_{51}NO_4$ requires C, 75·95; H, 9·55; N, 2·6%).

Hydroxylation of Cholest-4-*en*-3-*one*.—Cholest-4-en-3-one (6 g.) in t-butyl alcohol (325 ml.) containing hydrogen peroxide (35%; 68 ml.) and distilled water (24 ml.) was treated with osmium tetroxide (0·9 g.) in t-butyl alcohol (72 ml.), and the solution was stirred at 30° for 3 days. After addition of ether and washing consecutively with aqueous sodium chloride, sodium pyrosulphite, sodium hydrogen carbonate, and water, the dried ethereal layer was evaporated. The solid residue showed $\nu_{max.}$ (CCl_4) 3600, 3495 (OH), and 1720 cm.$^{-1}$ (CO), possessed no selective ultraviolet absorption, and gave two spots on thin-layer chromatography, R_F ($CHCl_3$) 0·45 and 0·35, presumably due to the 4α,5α- and the 4β,5β-glycols.

3-*Hydroxy*-A-*nor*-5α-*cholestane*-3-*carboxylic Acid*.—(*a*) The crude glycols from above (3·5 g.) were heated under reflux (N_2) with potassium hydroxide (4 g.) in methanol (200 ml.) for 1 hr. The solution was neutralised with acetic acid and poured into sodium chloride solution. Isolation with ether followed by crystallisation from acetone gave 4-hydroxycholest-4-en-3-one (0·73 g.), m. p. 148—149·5°, $\lambda_{max.}$ (EtOH) 278 mμ (ε 10,200), $\nu_{max.}$ (CCl_4) 3495 (OH), 1690 (conj. CO), and 1650 cm.$^{-1}$ (C=C), one spot on thin-layer chromatography, R_F ($CHCl_3$) 0·93 [lit., m. p. 149—150°,[10] $\lambda_{max.}$ 278 mμ (ε 13,000) [11]]. A further quantity (0·47 g.) was obtained by chromatography of the mother-liquors. 4-Hydroxycholest-4-en-3-one (0·44 g.) was heated under reflux with potassium hydroxide (4 g.) in n-butanol (40 ml.) for 42 hr. (N_2). After removal of most of the butanol under reduced pressure, water was added and the solution was extracted with ether. The ethereal layer was washed with aqueous potassium hydroxide (10%), and the washings were discarded. Finally, washing with water until neutral followed by acidification of the aqueous layers gave the A-*nor acid* (0·35 g.), needles from light petroleum (b. p. 60—80°), m. p.

[10] V. A. Petrow and W. W. Starling, *J.*, 1940, 60.

[11] L. F. Fieser and M. Fieser, "Steroids," Reinhold, New York, 1959, p. 230.

206·5—207·5°, $[\alpha]_D$ +38°, $\nu_{max.}$ (CCl_4) 3495 (OH), 3200—2700, and 1700 cm.$^{-1}$ (CO_2H) (Found: C, 77·4; H, 10·8. $C_{27}H_{46}O_3$ requires C, 77·5; H, 11·0%).

(*b*) A solution of the crude glycol (6·5 g.) in n-butanol (320 ml.) was heated under reflux with potassium hydroxide (30 g.) for 48 hr. (N_2). The product was isolated as under (*a*), giving the A-nor-acid as a crystalline residue (5·0 g.) which, after crystallisation from light petroleum, gave material (2·4 g.) identical with that obtained above. A further quantity (0·65 g.) was obtained by chromatography on silica gel.

3-*Hydroxy*-3-*methoxycarbonyl*-A-*nor*-5α-*cholestane*.—Esterification of the A-nor-hydroxy-acid (2·91 g.) with diazomethane in ether gave the *methyl ester*, plates (2·62 g.) from methanol, m. p. 104—105°, $[\alpha]_D$ +38° $\nu_{max.}$ (CCl_4) 3550 (OH) and 1740 cm.$^{-1}$ (CO_2Me), one spot on thin-layer chromatography, R_F ($CHCl_3$) 0·75 (Found: C, 77·5; H, 11·2. $C_{28}H_{48}O_3$ requires C, 77·7; H, 11·2%).

3-*Methoxycarbonyl*-A-*norcholest*-3-*ene*.—3-Hydroxy-3-methoxycarbonyl-A-nor-5α-cholestane (2·62 g.) in dry pyridine (16 ml.) was treated at 0° with thionyl chloride (4 ml.). After 30 min. at 0°, excess of thionyl chloride was decomposed by water, and the product isolated with ether. Crystallisation from methanol gave the unsaturated ester as needles (2·17 g.), m. p. 83—84°, $[\alpha]_D$ +66, $\lambda_{max.}$ (EtOH) 237 mμ (ε 14,800), $\nu_{max.}$ (CCl_4) 1705 and 1640 cm.$^{-1}$ (conj. CO_2Me), one spot on thin-layer chromatography, R_F ($CHCl_3$–C_6H_6, 1 : 1) 0·85 {lit.,[3] m. p. 84—84·5°, $[\alpha]_D$ +66°, $\lambda_{max.}$ (EtOH) 237 mμ (ε 12,000)}.

Hydrogenation of 3-*Methoxycarbonyl*-A-*norcholest*-3-*ene*.—A solution of the unsaturated ester (1 g.) in ethanol containing acetic acid (25%; 60 ml.) was shaken under hydrogen in the presence of Adams catalyst for 9 hr. Hydrogen (50 ml.) was absorbed. After filtration and evaporation, the residue was chromatographed on neutral alumina (Woelm activity 1). Elution with light petroleum–benzene (2 : 3) gave oily fractions, further elution with light petroleum–benzene (1 : 4) and crystallisation from methanol gave 3β-*methoxycarbonyl*-A-*nor*-5α-*cholestane* (0·4 g.) as needles, m. p. 65—66°, $[\alpha]_D$ +59°, one spot on thin-layer chromatography (appears only on heating for 30 min.), R_F (in C_6H_6) 0·8 (Found: C, 80·9; H, 11·9. $C_{28}H_{48}O_2$ requires C, 80·7; H, 11·6%). Rechromatography of the early fractions on neutral alumina gave 3α-methoxycarbonyl-A-nor-5β-cholestane (90 mg.) as a gum, one spot on thin-layer chromatography, R_F (C_6H_6) 0·9, together with a further quantity (40 mg.) of the crystalline ester.

Lithium Aluminium Hydride Reduction of 3α-*Methoxycarbonyl*-A-*nor*-5β-*cholestane*.—The gummy ester from above (26 mg.) was reduced with lithium aluminium hydride (100 mg.) in ether. Isolation gave 3α-hydroxymethyl-A-nor-5β-cholestane (26 mg.), needles from aqueous acetone, m. p. 78·5—80°, $[\alpha]_D$ −2°. The earlier preparation (see above) had m. p. 79—80°, $[\alpha]_D$ −3·5°. The p-*nitrobenzoate*, plates from methanol, had m. p. 82—83·5° undepressed on admixture with an authentic specimen (Found: C, 75·6; H, 9·3. $C_{34}H_{51}NO_4$ requires C, 75·95; H, 9·55%).

Lithium Aluminium Hydride Reduction of 3β-*Methoxycarbonyl*-A-*nor*-5α-*cholestane*.—The ester was reduced as above, giving 3β-*hydroxymethyl*-A-*nor*-5α-*cholestane*, plates (135 mg.) from aqueous acetone, m. p. 128·5—129·5, $[\alpha]_D$ +40°, one spot on thin-layer chromatography, R_F ($CHCl_3$–C_6H_6, 1 : 1) 0·3 (Found: C, 83·65; H, 12·25. $C_{27}H_{48}O$ requires C, 83·45; H, 12·45%). The p-*nitrobenzoate*, needles from acetone, had m. p. 183—184° markedly depressed on admixture with any of the three isomeric p-nitrobenzoates (Found: C, 75·5; H, 9·65%).

Isomerisation of 3β-*Methoxycarbonyl*-A-*nor*-5α-*cholestane*.—The ester (70 mg.) was added to sodium methoxide (from 1 g. of sodium) in dry methanol (20 ml.), and the solution was heated under reflux for 20 min. Distilled water was added, and the mixture was refluxed for a further 10 min. After removal of most of the methanol at the pump the solution was acidified and the product isolated with ether. Esterification with diazomethane followed by isolation of the neutral fraction (70 mg.) and crystallisation from methanol gave 3α-methoxycarbonyl-A-nor-5α-cholestane (50 mg.), m. p. 75—76·5° undepressed on admixture with an authentic sample. The m. p. was depressed to 40—48° on admixture with the parent ester. Two further crops of satisfactory material (13 mg. and 3 mg.) were obtained from the mother liquors, m. p. 74—75·5° and 71—74°, bringing the total yield to 94%.

Isomerisation of 3α-*Methoxycarbonyl*-A-*nor*-5β-*cholestane*.—The gummy ester (90 mg.) from the hydrogenation of 3-methoxycarbonyl-A-norcholest-3-ene was treated with sodium methoxide in methanol and worked up as above, giving 3β-methoxycarbonyl-A-nor-5β-cholestane as a gum (86 mg.) which showed one spot on thin-layer chromatography (appears after heating for 30 min.), R_F (C_6H_6) 0·76.

Lithium Aluminium Hydride Reduction of 3β-*Methoxycarbonyl*-A-*nor*-5β-*cholestane.*—The gummy ester (27 mg.) was reduced with lithium aluminium hydride in the usual way, and the product was chromatographed on a small column of silica gel. Elution with benzene followed by crystallisation from aqueous acetone gave 3β-*hydroxymethyl*-A-*nor*-5β-*cholestane* as needles, m. p. 75·5—77° depressed to 48—59° on admixture with a sample of 3α-hydroxymethyl-A-nor-5β-cholestane (m. p. 79—80°), one spot on thin-layer chromatography, R_F ($CHCl_3$–C_6H_6, 1 : 1) 0·33 (Found: C, 83·55; H, 12·6. $C_{27}H_{48}O$ requires C, 83·45; H, 12·45%). The *p*-nitrobenzoate, after chromatography on a short column of silica gel and crystallisation from ether–methanol, had m. p. 142—143·5° undepressed on admixture with the sample prepared *via* hydrogenation of 3β-hydroxymethyl-A-norcholest-5-ene.

Stability of 3α-*Methoxycarbonyl*-A-*nor*-5α-*cholestane to Sodium Methoxide in Methanol.*—The ester (57 mg.) was treated with sodium methoxide in methanol and worked up as for 3β-methoxycarbonyl-A-nor-5α-cholestane. The crude product (57 mg.) had $[\alpha]_D$ 0°, *i.e.*, no detectable amount of the 3β-ester present, and crystallisation from methanol gave plates, m. p. 73—75° undepressed on admixture with starting material.

Lithium Aluminium Hydride Reduction of 3-*Methoxycarbonyl*-A-*norcholest*-3-*ene.*—The ester (105 mg.) was heated under reflux with lithium aluminium hydride (100 mg.) in dry ether for 30 min. After addition of water and aqueous Rochelle salt, the product was isolated with ether and crystallised from methanol, giving 3-hydroxymethyl-A-norcholest-3-ene (96 mg.) as needles, m. p. 117·5—119°, $[\alpha]_D$ +56° {lit.,[1] m. p. 116—118°, $[\alpha]_D$ +57°}.

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