500. *Partial Reduction of Steroid Hormones and Related Substances. Part III.* The Reaction of αβ-Unsaturated Ketones with Zinc in Acetic Acid.*

By JEAN MCKENNA, J. K. NORYMBERSKI, and R. D. STUBBS.

Under appropriate conditions, zinc in acetic acid reduced several 4 : 5-unsaturated 3-oxo-steroids (IV) to the corresponding 3 : 4-unsaturated 5α- and/or 5β-compounds (V and VI respectively). The reaction was selective in the presence of isolated ketone and α-ketol groups. 7-Oxocholesteryl acetate (VII) similarly gave 5α-cholest-6-en-3β-yl acetate (VIII). The steroid 9-en-12-one and the triterpenoid 12-en-11-one systems resisted treatment with zinc.

IT was shown in Part II that treatment of cortisone (I) with a tenfold (w/w) amount of zinc in hot aqueous acetic acid led to 11-dehydrocorticosterone (II) and that the elimination of the 17α-hydroxyl group was to some extent accompanied by the reduction of the 4-en-3-one grouping. Subsequently,[1] it was found that reduction was complete when the amount of zinc was increased 100-fold; the end-product was then not isolated but was tentatively formulated as a pregnene-11 : 20-dione (III). The present work [2] aimed at establishing more rigorously the structures of compounds formed on treatment of αβ-unsaturated ketones, and especially of 4 : 5-unsaturated 3-oxo-steroids, with zinc and acetic acid.

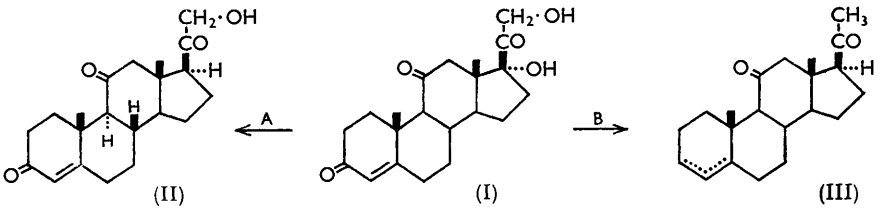
When cortisone (I) or its 21-acetate was treated with a 4000-fold quantity of zinc in acetic acid for an hour at room temperature, reaction in ring A was complete irrespective of the acid concentration, while reaction of the side chain was decreased with increasing acid

* Part II, *J.*, 1956, 517.

[1] Norymberski and Stubbs, *Biochem. J.*, 1956, **64**, 168.

[2] Cf. Norymberski, 16th Internat. Congress Pure & Appl. Chem., Paris, 1957, Handbook, Vol. II, p. 186.

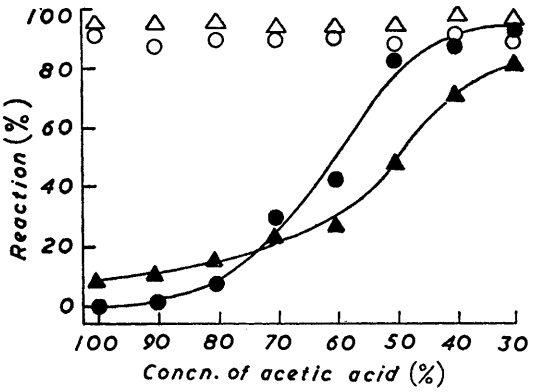
concentration and completely suppressed in glacial acetic acid (Fig. 1). A possible explanation lies in the ability of the 17α-hydroxy-20-oxo-grouping to undergo chelation,[3] the extent of which may be expected to affect the compound's affinity to zinc and to be affected



Zn: (I) = A, 10 : 1; B, ≥1000 : 1.

by the nature of the solvent. In view of the improved selectivity of the reaction in glacial acetic acid at room temperature, these conditions have been adopted in the following experiments.

Reaction at positions 17, 20, 21:
▲ *cortisone*, ● *cortisone acetate.*
Reaction at positions 3, 4, 5:
△ *cortisone*, ○ *cortisone acetate.*



Cholest-4-en-3-one (IVa) with zinc in glacial acetic acid afforded 5α-cholest-3-ene[4] (Va) in *ca.* 40% yield. Testosterone acetate (IVb) gave two isomers, $C_{21}H_{32}O_2$, m. p. 117—118° and 138—141° respectively; both gave positive tests with tetranitromethane and exhibited apparent absorption maxima at 205 mμ (ε ~ 1000), indicating the presence of disubstituted ethylenic bonds.[5] The molecular rotation of the lower-melting isomer is consistent only with a 2 : 3- or 3 : 4-location of the double bond in a 5α-skeleton.[6]* The compound exhibits infrared bands associated with *cis*-ethylenic bonds which coincide with those of 5α-cholest-3-ene but not with those of 5α-cholest-2-ene or of methyl 5β-chol-3-enate[7] (Table 2). Accordingly, it is formulated as 17β-acetoxy-5α-androst-3-ene (Vb). The molecular rotation of the higher-melting isomer requires the presence of a 2 : 3- or 3 : 4-ethylenic bond in a 5β-compound.[6] Absorption in the olefinic C–H out-of-plane region (800—650 cm.$^{-1}$) is closely related to that of methyl 5β-chol-3-enate (Table 2). A 3 : 4-double bond being considered likely, the compound is assigned structure (VIb).

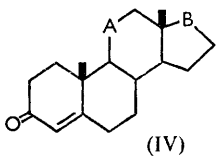
Only one product was isolated on reduction of androst-4-ene-3 : 17-dione (IVc); it is

* Standard tables (ref. 6) record an increment of 194° for the introduction of the 3 : 4-ethylenic bond in the 5α-series. This is a misprint and should read 149° (personal communication from Dr. W. Klyne). The latter value has been used in this paper.

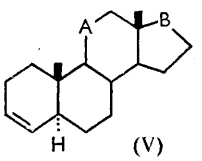
[3] Jones, Humphries, Herling, and Dobriner, *J. Amer. Chem. Soc.*, 1952, **74**, 2820; Norymberski, *J.*, 1954, 762.
[4] Lardelli and Jeger, *Helv. Chim. Acta*, 1949, **32**, 1817.
[5] Bladon, Henbest, and Wood, *J.*, 1952, 2737.
[6] Klyne, in Braude and Nachod's "Determination of Organic Structures by Physical Methods," Academic Press, New York, 1955.
[7] Henbest, Meakins, and Wood, *J.*, 1954, 800.

formulated as 5α-androst-3-en-17-one (Vc) on the basis of its rotational and spectroscopic properties (see Tables 1 and 2). The same product (Vc) was obtained on reduction with zinc in hot aqueous acetic acid. Reduction with sodium borohydride gave 5α-androst-3-en-17β-ol (Vd) which, on acetylation, gave 17β-acetoxy-5α-androst-3-ene (Vb), identical with the product obtained directly from testosterone acetate (IVb).

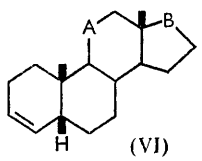
TABLE 1.



(IV)



(V)



(VI)

	A	B	(V) $\varepsilon_{max.}$ [a]	(V) $[M]_D$ Found	(V) $[M]_D$ Calc.[b]	(VI) $\varepsilon_{max.}$ [a]	(VI) $[M]_D$ Found	(VI) $[M]_D$ Calc.[b]
a	CH_2	$CH{\cdot}C_8H_{17}$	1200	+215°	+240°	—	—	+50°
b	CH_2	CH·OAc	1200	+135	+165	900	±0°	−30
c	CH_2	CO	1450	+390	+400	—	—	+210
d	CH_2	CH·OH	—	+145	+135	—	—	−55
e	CH·OH	CO	—	—	+500	1500	+315	+305
f	CO	$C(OH){\cdot}CO{\cdot}CH_2{\cdot}OAc$	2900	+565	—[c]	3100	+470	—[c]
g	CH_2	$CH{\cdot}CO{\cdot}CH_3$	—	—	+460	—	+290[d]	+270

The product from (IVe) is tabulated according to its rotation among 5β-compounds, although its configuration at $C_{(5)}$ has not been established.
[a] $\lambda_{max.}$ 205—206·5 mμ. [b] Calc. from standard tables (ref. 6) and approximated to the nearest 5°. Calculation unreliable (see text). [d] Butenandt and Westphal, ref. 11.

Similarly, only one product was isolated on reduction of 11β-hydroxyandrost-4-ene-3 : 17-dione (IVe). Its composition ($C_{19}H_{28}O_2$) and spectroscopic characteristics ($\lambda_{max.}$ 205 mμ; $\nu_{max.}$ 3620, 3010, 1745, 1648 cm.$^{-1}$) indicate the structure of an 11β-hydroxyandrost-3-en-17-one (VIe, except for configuration at $C_{(5)}$). Its rotation is in excellent agreement with that calculated for the 5β-epimer (Table 1), and its absorption in the 800—650 cm.$^{-1}$ region with that expected for the 5α-epimer (Table 2). Elucidation of configuration at $C_{(5)}$ therefore awaits further study.

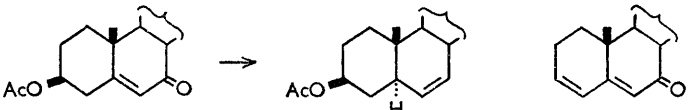
TABLE 2. *Infrared absorption maxima* (cm.$^{-1}$).

Compounds	*cis*-Ethylenic bonds					Oxygen functions
	3100—2950	1700—1600	800—650			
5α-Cholest-2-ene *	3034 †	1653 †	774w		664s	
5α-Cholest-3-ene *	3015 †	1647 †	773s		671s	
Methyl 5β-chol-3-enate *	not reported		783m		678s	
17β-Acetoxy-5α-androst-3-ene (Vb)	3010 ‡	1647	773s	735w	671s	1739 (OAc)
17β-Acetoxy-5β-androst-3-ene (VIb)	3010 ‡	1648	783m	726w	680s 666m	1741 (OAc)
5α-Androst-3-en-17-one (Vc)	3010 ‡	1647	773s	735w 710w	671s	1744 (17-one)
5α-Androst-3-en-17-ol (Vd)	3010 ‡		773s	730w	669s	3640 (OH)
11β-Hydroxy-5β-androst-3-en-17β-one (VIe)	3010 ‡	1648	792w 773s 760w		673s	3620 (OH) 1745 (17-one)
21-Acetoxy-17α-hydroxy-5α-pregn-3-ene-11 : 20-dione (Vf)	3010 ‡	1648	794m 779s 770s	749m 736m	678s 663m	3442 (OH) 1756; 1731 (ketol acetate) 1711 (11-one)
21-Acetoxy-17α-hydroxy-5β-pregn-3-ene-11 : 20-dione (VIf)	3010 ‡	1647	784s 773s	735m	686s 673s 665s	3500 (OH) 1758; 1732 (ketol acetate) 1710 (11-one)

w = weak, m = medium, s = strong. Unless otherwise indicated, measurements in the 1700—1600 cm.$^{-1}$ region were carried out in chloroform, in other regions in carbon disulphide.
* Reported by Henbest *et al.*[7] † In carbon tetrachloride. ‡ Shoulder.

Cortisone acetate (IVf) afforded two isomeric products, $C_{23}H_{32}O_5$, m. p. 175—178° and 211—214° respectively. The lower-melting isomer had the lower rotation, sublimed more readily in a vacuum, and was more readily eluted from alumina. Both compounds gave positive tests with tetranitromethane and with the phenylhydrazine–sulphuric acid reagent of Porter and Silber.[8] They exhibited apparent absorption maxima at 206·5 mμ (ε ~ 3000); this is a strong indication of the presence of disubstituted double bonds when it is considered that the acetylated dihydroxyacetone grouping contributes to the extinction to the extent of 2000—2600.[9] Their infrared spectra confirmed the presence of the grouping $-C(OH)\cdot CO\cdot CH_2\cdot OAc$ and revealed that of the 11-oxo-function; their complexity in the 800—650 cm.$^{-1}$ region did not permit a more detailed characterisation of the ethylenic bonds. The cited properties of the two isomers, in the light of the foregoing examples, led us to formulate the lower-melting isomer as 21-acetoxy-17α-hydroxy-5β- (VIf) and the higher-melting isomer as 21-acetoxy-17α-hydroxy-5α-pregn-3-ene-11 : 20-dione (Vf). Calculation of molecular rotations for structures (Vf) and (VIf) was not attempted, the available data [10] being considered insufficient to determine the rotational contribution of the side chain with reasonable accuracy or to assess any vicinal action between the side chain and the 11-oxo-group.

In converting 3β-hydroxypregn-5-en-20-one into progesterone (IVg) by the classical reactions—addition of bromine, oxidation with chromic trioxide, and debromination with zinc in acetic acid—Butenandt and Westphal [11] noted that vigorous execution of the last treatment led to the formation of a by-product which they formulated as pregn-4-en-20-one. However, its recorded molecular rotation (+290°) is inconsistent with the proposed structure (calc. $[M]_D$ +500°) but in good agreement with the molecular rotation (+270°) calculated for 5β-pregn-3-en-20-one (VIg), and hence the latter structure is now assigned to the compound. Butenandt and Westphal's finding may now be considered as providing a further example of the general type of reaction here reported, although carried out under conditions different from those used by the present authors.



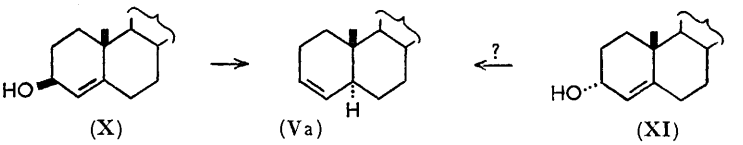
(VII) (VIII) (IX)

Treatment with zinc of 3β-acetoxycholest-5-en-7-one (VII) gave 3β-acetoxy-5α-cholest-6-ene [12] (VIII) and cholest-3 : 5-dien-7-one [13] (IX). Isolation of the latter compound in substantial quantity (35%) is surprising since its direct treatment with zinc resulted in the complete disappearance of the dienone system. In this, as in other preparations, zinc was added portionwise; it is therefore unlikely that the dienone (IX) was formed during the treatment with zinc and that it resisted further reaction owing to the exhaustion of active centres on the zinc surface. More probably elimination of acetic acid occurred during working-up of the reaction mixture.

In working-up of the mixtures obtained from (IVa) and (IVc), a few small, polar chromatographic fractions were isolated which gave a violet colour with trichloroacetic acid in chloroform.[14] This being characteristic of allylic alcohols, the question arose whether they might act as intermediates in the reductive elimination of oxo-groups conjugated with ethylenic bonds. Cholest-4-en-3β-ol (X) and -3α-ol (XI) were therefore

[8] Porter and Silber, *J. Biol. Chem.*, 1950, **185**, 201.
[9] Bird, Norymberski, and Woods, *J.*, 1957, 4149.
[10] Mathieu and Petit, "Pouvoir Rotatoire Naturel, Vol. I, Stéroïdes," Masson, Paris, 1956.
[11] Butenandt and Westphal, *Ber.*, 1934, **67**, 2085.
[12] Plattner, Heusser, Troxler, and Segre, *Helv. Chim. Acta*, 1948, **31**, 852; Barton and Rosenfelder, *J.*, 1949, 2459; Wintersteiner and Moore, *J. Amer. Chem. Soc.*, 1950, **72**, 1923.
[13] Mauthner and Suida, *Monatsh.*, 1896, **17**, 579.
[14] Rosenheim, *Biochem. J.*, 1929, **23**, 47.

treated with zinc. Of the 3β-epimer 60% remained unchanged, 5% was acetylated, and 20% gave an olefinic fraction consisting essentially of 5α-cholest-3-ene (Va); the corresponding fractions from the 3α-epimer amounted to 30, 55, and 10% respectively, the



(X) (Va) (XI)

olefin remaining unidentified. Thus, both epimers reacted with zinc much more sluggishly than the corresponding ketone (IVa), and it is therefore improbable that either acts as an intermediate in the major reaction leading from (IVa) to (Va). This consideration does not rule out the intermediate formation of the allylic structure $C{=}\overset{\curvearrowright}{C}{-}\overset{\curvearrowright}{C}{-}OZn^{+}$ leading to an olefin through the electronic displacement indicated or to the corresponding allylic alcohol through acetolysis of the O–Zn bond. Of incidental interest is the observation that contrary to expectation [15] the quasi-axial 3α-ol was more readily acetylated and less readily hydrogenolysed than the quasi-equatorial 3β-ol. A possible explanation is given by assuming that acetylation proceeds with fission of the $C_{(3)}$–O bond and that hydrogenolysis depends on initial adsorption on the zinc surface.

Previously, oxygen was removed from a conjugated enone system with the concomitant shift of the ethylenic bond towards the original carbonyl-carbon atom by the Wolff–Kishner reaction.[4] Effected by zinc in acetic acid, the same reaction has wider scope since it proceeds selectively in the presence of isolated carbonyl and α-ketol groups. In particular, its application to steroidal 4-en-3-ones provides a simple route to otherwise not readily accessible compounds. So far, two examples of unreactive conjugated enones have been found in 22a-bromo-9(11)-dehydrohecogenin acetate (9-en-12-one) and methyl glycyrrhetate acetate (triterpenoid 12-en-11-one).

Reduction with zinc in acetic acid of 16-en-20-ones has been reported to lead to saturated 20-ketones [16] or to 16-en-20-ols.[17] Since these transformations were brought about under conditions different from those used in the present investigation, it is not clear whether the difference is due to structure or experimental design.

Experimental

M. p.s were determined on a Kofler stage. Rotations refer to chloroform solutions at 15—20°, and ultraviolet absorption spectra to ethanol solutions. A Perkin-Elmer Model 21 spectrometer was used for measurement of the infrared spectra recorded in Table 2. Specimens for analyses were dried in a high vacuum for 6—16 hr. at 60—100°. For chromatography Peter Spence's grade H alumina was neutralised and reactivated.

Treatment with Zinc: *General Procedure.*—A 0·005—0·01M-solution of the steroid in acetic acid was shaken at room temperature with 1000 g.-atoms of zinc dust (" AnalaR ") added in four equal portions at intervals of 15 min. Shaking was continued for a further 45 min. Surplus zinc was filtered off and washed with little acetic acid. Ice was added to the filtrate and then enough 3N-sodium hydroxide to neutralise nine-tenths of the acid. The mixture was extracted with ether or with ethyl acetate in the usual manner.

Treatment of Cholest-4-en-3-one (IVa).—This compound (300 mg.), treated with zinc by the general procedure, gave a gum (270 mg.) which on repeated crystallisation from acetone furnished cholest-3-ene (Va) in needles (40 mg.), m. p. and mixed m. p. 74—75°, $[\alpha]_D$ +58° (*c* 0·70), $\lambda_{max.}$ 205·5 mμ (ε 1200) (Found: C, 87·3; H, 12·5. Calc. for $C_{27}H_{46}$: C, 87·5; H, 12·5%). The infrared spectrum in carbon disulphide solution was identical with that of an authentic

[15] Cf. Shoppee, Agashe, and Summers, *J.*, 1957, 3107.
[16] Marker, Crooks, and Wagner, *J. Amer. Chem. Soc.*, 1942, **64**, 210; Marker, Crooks, Wagner, and Wittbecker, *ibid.*, p. 2090.
[17] Nes and Mason, *ibid.*, 1951, **74**, 4756; Ercoli and Ruggieri, *Farm. sci. tec., Pavia*, 1952, **7**, 11, 129.

specimen kindly provided by Dr. J. C. Banerji. The following physical constants were previously reported: [4,18] m. p. 72—73°, 72—72·5°, and 74—75°; $[\alpha]_D$ +65°, +57°, and +55°.

Concentration of the mother-liquors afforded a second crop (80 mg.; m. p. 71—74°) of the same product.

The residue from final mother-liquors was chromatographed on alumina (10 g.). Light petroleum eluted gummy fractions (total 100 mg.) which gave a positive test with tetranitromethane. Elution with mixtures of benzene and light petroleum afforded small quantities of amorphous fractions (total 8 mg.). Finally, benzene containing 2—5% of ethyl acetate eluted a few partly crystalline fractions (total 11 mg.), which gave a positive Rosenheim test and had $[\alpha]_D$ +74° (*c* 0·61).

Treatment of Testosterone Acetate (IVb).—This compound (300 mg.) gave a product (260 mg.) which, crystallised first from methanol and then from ethanol, afforded 17β-*acetoxy*-5α-*androst*-3-*ene* (Vb) in stout prisms (35 mg.), m. p. 117—118°, $[\alpha]_D$ +42° (*c* 0·97), $\lambda_{max.}$ 205 mμ (ε 1200) (Found: C, 79·8; H, 10·2. $C_{21}H_{32}O_2$ requires C, 79·7; H, 10·2%).

The mother-liquors were brought to dryness. Crystallisation of the residue, first from ethanol and then from methanol, furnished 17β-*acetoxy*-5β-*androst*-3-*ene* (VIb) in thick rectangular plates (30 mg.), m. p. 138—141°, $[\alpha]_D$ ±0° (*c* 0·80), $\lambda_{max.}$ 204·5 mμ (ε 900) (Found: C, 80·0; H, 10·2%).

Treatment of Androst-4-*ene*-3 : 17-*dione* (IVc).—(i) *By the general procedure.* This compound (300 mg.) gave a product (260 mg.) which on crystallisation from methanol and then from *n*-hexane furnished 5α-*androst*-3-*en*-17-*one* (Vc) in prisms (105 mg.), m. p. 125—126°, $[\alpha]_D$ +141° (*c* 1·17), $\lambda_{max.}$ 205 mμ (ε 1450) (Found: C, 84·2; H, 10·5. $C_{19}H_{28}O$ requires C, 83·8; H, 10·4%). A second crop (50 mg.; m. p. 122—126°) was obtained from the mother-liquors. (ii) *In hot aqueous acetic acid.* A boiling solution of androst-4-ene-3 : 17-dione (300 mg.) in aqueous acetic acid (50% v/v; 300 ml.) was treated with four portions of zinc dust (4 × 15 g.) at 15-minute intervals. Heating under reflux was continued for 30 min. and the mixture worked up in the usual manner. The crude product (260 mg.) was chromatographed on alumina (20 g.). Elution was effected with light petroleum–benzene containing gradually increasing proportions of the latter; the eluates were collected in fifty 4 ml.-fractions. Fractions 1—14 (60 mg.) failed to crystallise and were not further investigated. Fractions 15—38 crystallised from methanol in prisms, m. p. 124—126° undepressed on admixture with 5α-androst-3-en-17-one obtained in the preceding experiment, $[\alpha]_D$ +145° (*c* 0·64) (Found: C, 83·6; H, 10·65. Calc. for $C_{19}H_{28}O$: C, 83·8; H, 10·4%).

Fractions 39—50 contained only traces of material. Benzene (150 ml.) eluted an amorphous fraction (20 mg.) which gave a positive Rosenheim test but was not further characterised.

Borohydride Reduction of 5α-*Androst*-3-*en*-17-*one* (Vc).—This compound (50 mg.) in methanol (5 ml.) was treated with sodium borohydride (25 mg.) for 1 hr. at room temperature. The usual working up followed by crystallisation from *cyclo*hexane gave 5α-*androst*-3-*en*-17β-*ol* (Vd) in needles, m. p. 147—150°, $[\alpha]_D$ +52° (*c* 0·86) (Found: C, 82·9; H, 10·9. $C_{19}H_{30}O$ requires C, 83·2; H, 11·0%).

This was acetylated with acetic anhydride–pyridine at room temperature. Crystallisation from ethanol gave 17β-acetoxy-5α-androst-3-ene (Vb), m. p. 116—118°, $[\alpha]_D$ +39° (*c* 0·92) (Found: C, 79·8; H, 9·9. Calc. for $C_{21}H_{32}O_2$: C, 79·7; H, 10·2%), identical (mixed m. p.) with the product obtained from testosterone acetate (see above).

Treatment of 11β-*Hydroxyandrost*-4-*ene*-3 : 17-*dione* (IVe).—This compound (600 mg.) was reduced by the general procedure. The crude product (550 mg.) furnished, from methanol, 11β-*hydroxy*-5ξ-*androst*-3-*en*-17-*one* (VIe except for configuration at $C_{(5)}$) in needles (150 mg.), m. p. 145—147°, $[\alpha]_D$ +109° (*c* 1·15), $\lambda_{max.}$ 205 mμ (ε 1500) (Found: C, 78·9; H, 9·7. $C_{19}H_{28}O_2$ requires C, 79·1; H, 9·8%).

Treatment of Cortisone Acetate (IVf).—The crude product (1·1 g.) obtained from this compound (1·2 g.) was chromatographed on alumina (80 g.). The first 33 fractions (120 mg.), eluted with carbon tetrachloride (3300 ml), consisted of small amounts (<10 mg. per fraction) of mainly amorphous material and were not further investigated. The next 7 fractions (500 mg.) were eluted by the same solvent (1400 ml.); their specific rotations increased in the order of elution from +116° to +143°; each was crystallised from methanol; methanol and acetone–*cyclo*hexane were used for recrystallisations, whereby crystals and mother-liquors of closely agreeing properties (m. p. and rotation) were combined. In this way, two apparently pure

[18] Barton and Rosenfelder, *J.*, 1951, 1053; Alt and Barton, *J.*, 1954, 4284.

compounds (120 mg. and 140 mg. respectively) were isolated and assigned the structures of 21-*acetoxy*-17α-*hydroxy*-5β- (VIf) and 21-*acetoxy*-17α-*hydroxy*-5α-*pregn*-3-*ene*-11 : 20-*dione* (Vf). Both compounds gave a positive test with tetranitromethane and with the phenylhydrazine–sulphuric acid reagent of Porter and Silber. The former compound (VIf) was more readily eluted from alumina and more soluble in methanol. It crystallised from acetone–*cyclo*hexane in needles, m. p. 175—178°, $[\alpha]_D$ +121° (*c* 1·07), $\lambda_{max.}$ 206·5 and 294 mμ (ε 3100 and 110) (Found: C, 70·9; H, 7·85. $C_{23}H_{32}O_5$ requires C, 71·1; H, 8·3%). The latter compound (Vf) crystallised from acetone–*cyclo*hexane in platelets, m. p. 211—214°, $[\alpha]_D$ +145° (*c* 0·78), $\lambda_{max.}$ 206·5 and 294 mμ (ε 2900 and 110) (Found: C, 71·2; H, 8·3%).

Fractions (35 mg.) eluted with benzene (800 ml.) remained unidentified. Ether (700 ml.) eluted a product (80 mg.) which on crystallisation from acetone gave cortisone acetate, m. p. and mixed m. p. 240—242°, $[\alpha]_D$ +220° (*c* 0·82), $\lambda_{max.}$ 238 mμ (ε 14,700). Finally, methanol (700 ml.) eluted a yellowish gum which was not further investigated.

Treatment of 3β-*Acetoxycholest*-5-*en*-7-*one* (VII).—The crude product (280 mg.) obtained from this compound (300 mg.) by the general procedure was chromatographed on alumina (10 g.). Light petroleum (200 ml.) eluted a fraction (80 mg.) which furnished from acetone 3β-acetoxycholest-6-ene (VIII) in long prismatic needles, m. p. 105·5—107° (undepressed on admixture with an authentic specimen kindly provided by Professor C. W. Shoppee, F.R.S.), $[\alpha]_D$ −92° (*c* 1·10) (Found: C, 81·2; H, 11·05. Calc. for $C_{29}H_{48}O_2$: C, 81·3; H, 11·3%). The following physical constants were previously reported: [12] m. p. 104—105°, 103·5—104·5°, 104—106°, and 107—109°; $[\alpha]_D$ −64°, −89°, and −88°.

Elution of the column with more light petroleum (200 ml.) gave a small fraction (18 mg.; m. p. 65—96°) which was not further purified. Light petroleum–benzene (9 : 1 v/v, 200 ml.; and 8 : 2 v/v, 200 ml.) eluted cholesta-3 : 5-dien-7-one (IX) (96 mg.; m. p. 105—113°). Recrystallisation from acetone and then from methanol gave needles, m. p. 113—114° (undepressed on admixture with authentic material kindly provided by Professor C. W. Shoppee, F.R.S.), $[\alpha]_D$ −315° (*c* 0·92), $\lambda_{max.}$ 278 mμ (ε 23,700) (Found: C, 84·7; H, 11·0. Calc. for $C_{27}H_{42}O$: C, 84·75; H, 11·1%). Ruzicka and Prelog [19] reported m. p. 114·5°, $[\alpha]_D$ −305°, $\lambda_{max.}$ 280 mμ (ε 23,800). Treatment of this compound (5·6 mg.) with zinc by the general procedure afforded an amorphous product, $[\alpha]_D$ −3° (*c* 0·51), $\lambda_{max.}$ 240 mμ ($E^{1\%}_{1\,cm.}$ 120).

Light petroleum–benzene (1 : 1 v/v; 200 ml.) eluted an unidentified fraction (25 mg.; m. p. 70—100°). Benzene (200 ml.) eluted a fraction (22 mg.) which from acetone gave prisms of 3β-acetoxycholest-5-en-7-one (VII), m. p. and mixed m. p. 160—162°, $[\alpha]_D$ −105° (*c* 0·32).

Treatment of Cholest-4-*en*-3β-*ol* (X).—This compound (220 mg.) was treated with zinc by the general procedure. Chromatography of the crude product (195 mg.) on alumina (10 g.) gave, in order of elution, the following three main fractions. (i) Crystals (46 mg.; m. p. 56—68°) eluted by light petroleum (20 ml.); repeated crystallisation from acetone furnished pure cholest-3-ene (Va), m. p. and mixed m. p. 71·5—73°, $[\alpha]_D$ +61° (*c* 0·50) (Found: C, 87·1; H, 12·3. Calc. for $C_{27}H_{46}$: C, 87·5; H, 12·5%), infrared spectrum (in CS_2) identical with that of an authentic specimen. (ii) Gum (10 mg.) eluted by light petroleum; this and the corresponding fraction (8 mg.) from an identical experiment were combined and treated with methanolic sodium hydroxide under reflux; the crude product of hydrolysis was chromatographed on alumina; benzene–ether (9 : 1 v/v) eluted pure cholest-4-en-3β-ol (8 mg.), m. p. and mixed m. p. 128—131°, $[\alpha]_D$ +51° (*c* 0·45). (iii) Benzene–ether (9 : 1 v/v; 100 ml.) eluted cholest-4-en-3β-ol (134 mg.), m. p. and mixed m. p. 131—132°, $[\alpha]_D$ +50° (*c* 0·73).

Treatment of Cholest-4-*en*-3α-*ol* (XI).—This compound (130 mg.) was treated with zinc by the general procedure. Resolution on alumina (5 g.) gave, in order of elution, the following fractions. (i) Gum (13 mg.; $[\alpha]_D$ +27°) eluted by light petroleum (20 ml.); it gave a positive tetranitromethane test and a negative Rosenheim test. (ii) Crystals (76 mg.; m. p. 75—82°) eluted by light petroleum–benzene (9 : 1 to 1 : 1 v/v; 50 ml.); crystallisation from methanol furnished pure 3α-acetoxycholest-4-ene, m. p. and mixed m. p. 79—81°, $[\alpha]_D$ +176° (*c* 0·79) (the authentic specimen had $[\alpha]_D$ +178° in chloroform, +213° in benzene). (iii) Gum (37 mg.) eluted by benzene–ether (9 : 1 to 4 : 1 v/v; 25 ml.); crystallisation from aqueous acetone furnished pure cholest-4-en-3α-ol (XI), m. p. and mixed m. p. 78—81°, $[\alpha]_D$ +119° (*c* 0·60).

Treatment of 23α-*Bromo*-9(11)-*dehydrohecogenin Acetate*.—The crude product from the usual treatment with zinc had $\lambda_{max.}$ 238 mμ ($E^{1\%}_{1\,cm.}$ 215). Crystallisation from chloroform–methanol

[19] Ruzicka and Prelog, *Helv. Chim. Acta*, 1943, **26**, 975.

afforded 9(11)-dehydrohecogenin acetate, m. p. 212—216°, $[\alpha]_D$ −13° (*c* 0·90), $\lambda_{max.}$ 238 mμ (ε 11,400).

Treatment of Methyl Glycyrrhetate Acetate.—Usual treatment with zinc had no effect on the absorption intensity at 248 mμ ($E^{1\%}_{1\,cm.}$ 220). Crystallisation from chloroform–methanol gave starting material, m. p. 302°, $[\alpha]_D$ +135° (*c*, 0·74), $\lambda_{max.}$ 248 mμ (ε 12,400).

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