Partial Reduction of Steroid Hormones and Related Substances.

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20-Ketones of the pregnane series and 17-ketones of the androstane series were preferentially reduced with sodium borohydride in the presence of the 4-en-3-one grouping. Reduction was stereospecific, giving the 20β- and 17β-hydroxy-epimers. Reduction of the 4-en-3-one grouping, when observed, gave rise to the 4-en-3β-ols, though in one instance reduction of the 4 : 5-olefinic bond occurred also.

Preferential reduction of pregn-4-ene-3 : 20-diones at $C_{(20)}$, though known in biological systems (Caspi, Levy, and Hechter, *Arch. Biochem. Biophys.*, 1953, **45**, 169; Hayano, Wiener, and Lindberg, *Fed. Proc.*, 1953, **12**, 216; Hayano, Lindberg, Wiener, Rosenkrantz, and Dorfman, *Endocrinology*, 1954, **55**, 326), has not been hitherto accomplished by conventional chemical means. The partial reduction at $C_{(20)}$ has been brought about indirectly by protecting the 4-en-3-one grouping (cf. Romo, Romero, Djerassi, and Rosenkranz, *J. Amer. Chem. Soc.*, 1951, **73**, 1528; Sarett, Feurer, and Folkers, *ibid.*, p. 1777; Julian, Meyer, Karpel, and Cole, *ibid.*, p. 1982; Wendler, Huang-Minlon, and Tischler, *ibid.*, p. 3818; Antonucci, Bernstein, Heller, Lenhard, Littel, and Williams, *J. Org. Chem.*, 1953, **18**, 70) or by reducing both carbonyl groups and then oxidising the 4-en-3-ol grouping (Sondheimer, Amandolla, and Rosenkranz, *J. Amer. Chem. Soc.*, 1953, **75**, 5930).

The present work (cf. *Chem. and Ind.*, 1954, 518) concerns the action of sodium borohydride on compounds of the general type (I) and (IV). In exploratory experiments the extent to which cortisone acetate (I*a*) was reduced at $C_{(3)}$ and at $C_{(20)}$ severally was determined analytically. The results (see Table) show preferential reduction at $C_{(20)}$. On this basis a standard preparative method was developed wherein the reduction is performed with *ca.* 1·5 mol. of sodium borohydride in methanol at 0°.

Reduction of cortisone acetate in methanol.

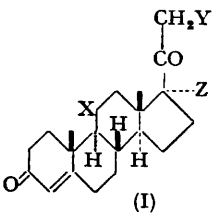
Concn. (mg./c.c.)	Temp.	$NaBH_4$ (mol.)	Reaction (%) at 3-one * 20 min.	at 3-one * 40 min.	at 20-one † 20 min.	at 20-one † 40 min.
2·5	0°	0·4	7	9	51	56
1·7	20	0·7	5	5	56	65
1·2	20	1·4	8	8	78	86
2·5	0	2·1	44	61	100	100
2·5	20	2·1	47	74	100	100

* Based on extinction at 238 mμ. † Measured as chromogen with phenylhydrazine–sulphuric acid (Porter and Silber, *J. Biol. Chem.*, 1950, **185**, 201).

Reduction of cortisone acetate (I*a*) by the standard method and acetylation of the product gave 20β : 21-diacetoxy-17α-hydroxypregn-4-ene-3 : 11-dione (II*a*) (Reichstein's Substance U diacetate) (Reichstein and von Euw, *Helv. Chim. Acta*, 1941, **24**, 247E). Similarly, cortisol acetate (I*b*) gave 20β : 21-diacetoxy-11β : 17α-dihydroxypregn-4-en-3-one (IIb) (Reichstein's Substance E diacetate) (*idem, loc. cit.*).

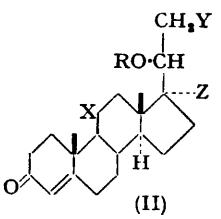
Reduction of 11-deoxycorticosterone (Ic), followed by acetylation, gave 20β : 21-diacetoxypregn-4-en-3-one (II*d*), $[M]_D$ +511°, which was hydrolysed to the diol (IIc), $[M]_D$ +326°, and the latter was converted into its acetonyl derivative. The last two compounds, and their 20-epimers, have been previously prepared by different routes (Steiger and Reichstein, *ibid.*, 1938, **21**, 171; Julian, Meyer, and Printy, *J. Amer. Chem. Soc.*, 1948, **70**, 887) but their configuration at $C_{(20)}$ was not elucidated. This has now been done, as indicated, on the basis of the molecular rotation increment for (IIc ⟶ II*d*) (cf. Sarett, *ibid.*, 1949, **71**, 1175; Klyne and Barton, *ibid.*, p. 1500). 3β : 20β : 21-Triacetoxypregn-4-ene (III*a*), $[M]_D$ +184°, was isolated as a by-product from the reduction of deoxycorticosterone (Ic). The compound is considered to have been formed by way of the ketone (IIc), hence the assignment of 20β-configuration. The configuration at $C_{(3)}$ is indicated by the negative shift of molecular rotation for (II*d* ⟶ III*a*) (cf. Mills, *J.*, 1952, 4976).

Reduction of progesterone (I*d*) afforded a mixture of 20β-hydroxypregn-4-en-3-one (II*e*), $[M]_D$ +280° {acetate (II*f*), $[M]_D$ +502°} (Wieland and Miescher, *Helv. Chim. Acta*, 1949, **32**, 1923), and pregn-4-ene-3β : 20β-diol (III*b*), $[M]_D$ +137°. The latter compound was further characterised by oxidation to the hydroxy-ketone (II*e*) by manganese dioxide (cf. Sondheimer *et al.*, *loc. cit.*). Reduction of 11-oxoprogesterone (I*e*) gave 20β-hydroxypregn-4-ene-3 : 11-dione (II*g*), $[M]_D$ +664° {acetate (II*h*), $[M]_D$ +811°}.



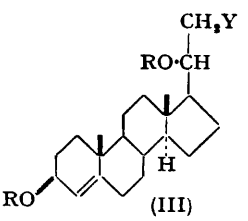
(I)

	X	Y	Z
(Ia) :	O	OAc	OH
(I*b*) :	OH	OAc	OH
(Ic) :	H	OH	H
(I*d*) :	H	H	H
(I*e*) :	O	H	H



(II)

	X	Y	Z	R
(II*a*) :	O	OAc	OH	Ac
(II*b*) :	OH	OAc	OH	Ac
(IIc) :	H	OH	H	H
(II*d*) :	H	OAc	H	Ac
(II*e*) :	H	H	H	H
(II*f*) :	H	H	H	Ac
(II*g*) :	O	H	H	H
(II*h*) :	O	H	H	Ac



(III)

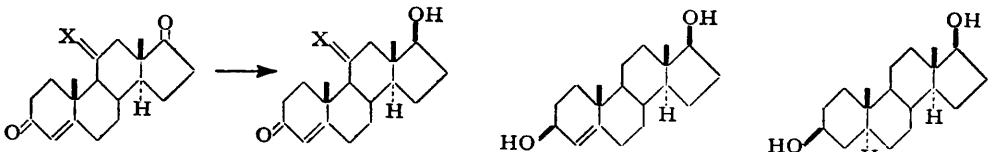
	Y	R
(III*a*) :	OAc	Ac
(III*b*) :	H	H

The results of the foregoing experiments suggested the possibility of partially reducing androst-4-ene-3 : 17-dione (IV*a*) to testosterone (V*a*) with sodium borohydride; owing to its importance, this conversion has received considerable attention: direct conversion has been accomplished by reduction with yeast (Mamoli and Vercellone, *Ber.*, 1937, **70**, 470) and by the Meerwein–Ponndorf method (Miescher and Fischer, *Helv. Chim. Acta*, 1939, **22**, 158) whilst all other preparative routes are indirect (for references see, *inter al.*, Fieser and Fieser, "Natural Products Related to Phenanthrene," 3rd Edn., Reinhold Publ. Corp., 1949, p. 371; Murray and Pederson, *J. Amer. Chem. Soc.*, 1952, **74**, 1239; Sondheimer *et al.*, *loc. cit.*; Dauben, jun., Loken, and Ringold, *ibid.*, 1954, **76**, 1359).

Reduction of the dione (IV*a*) with sodium borohydride, under the same conditions as in the pregnane series, gave testosterone (V*a*) in 60—70% yield. Androst-4-ene-3β : 17β-diol (VI), $[\alpha]_D$ +48° (Butenandt and Heusner, *Ber.*, 1938, **71**, 198), was obtained as a by-product. A further, apparently homogeneous, by-product (m. p. 152—154°, $[\alpha]_D$ +30°) gave with manganese dioxide a mixture of testosterone (V*a*) and androstane-3β : 17β-diol (VII), $[\alpha]_D$ +8°) and so is considered to be a molecular complex of (VI) and (VII). Its alternative composition from androst-4-ene-3α : 17β-diol and (VII) is ruled out on the basis of the former compound's high specific rotation ($[\alpha]_D$ +187°; Butenandt and Heusner, *loc. cit.*). [Reduction of the olefinic bond of androsten-4-ene-3 : 17-dione (IV*a*) by sodium borohydride has been already observed by Sondheimer, Velasco, Batres, and Rosenkranz (*Chem. and Ind.*, 1954, 1482).] The partial reduction of the dione (IV*a*) was also carried

out with potassium borohydride and with sodium trimethoxyborohydride: in both cases testosterone (V*a*) was obtained in good yield. Finally, 11-oxotestosterone (V*b*) (Herzog, Jevnik, Perlman, Nobile, and Hershberg, *J. Amer. Chem. Soc.*, 1953, **75**, 266) was obtained by the partial reduction of androst-4-ene-3 : 11 : 17-trione (IV*b*) with sodium borohydride.

The reactivities of steroid ketones towards sodium borohydride decrease in the order 3-one > 17- and 20-one > 4-en-3-one > 11-one (cf. Elisberg, Vanderhaeghe, and Gallagher,



(IV*a*): X = H_2 (IV*b*): X = O (V*a*): X = H_2 (V*b*): X = O (VI) (VII)

ibid., 1952, **74**, 2814; Oliveto and Hershberg, *ibid.*, 1953, **75**, 488; Mancera, Ringold, Djerassi, Rosenkranz, and Sondheimer, *ibid.*, p. 1286; Soloway, Deutsch, and Gallagher, *ibid.*, p. 2356; Garrett and Lyttle, *ibid.*, p. 6051; this paper). It is worth noting that the sequence of the first four members of the above series is parallelled by that of their simple analogues arranged in order of decreasing oxidation potentials; *cyclo*hexanone (E_0 162 mv), *cyclo*pentanone (E_0 123 mv), *cyclo*hexyl methyl ketone (E_0 116 mv), and *cyclo*hex-2-enone (E_0 85 mv) (Adkins, Elofson, Rossow, and Robinson, *ibid.*, 1949, **71**, 3622); further, only in the case of 11-ketones are steric effects powerful enough to change the sequence of reactivities expected from this analogy. A further point of interest is the stereospecific course of the borohydride reduction of 20-ketones, irrespective of substitution at $C_{(17)}$ and at $C_{(21)}$ (cf. Oliveto and Hershberg, *loc. cit.*) and of 4 : 5-unsaturated 3-ketones (cf. Dauben, Micheli, and Eastham, *ibid.*, 1952, **74**, 3852; Zorbach, *ibid.*, 1953, **75**, 6344).

Experimental

Specimens for analyses were dried in a high vacuum for 16—24 hr. at 80—100°. M. p.s were determined on a Kofler stage. Unless otherwise specified rotations were measured in $CHCl_3$ (at 15—20°), ultraviolet absorption spectra in EtOH. For chromatography Peter Spence's Grade H alumina was neutralised as previously described (Brooks and Norymberski, *Biochem. J.*, 1953, **55**, 371).

Reductions with Sodium Borohydride. General Procedure.—A solution (0·4—0·6%) of the steroid in methanol (Burroughs' "A.R. quality") was treated with sodium borohydride (1·4—1·6 mol) for 1 hr. at 0°. Unless otherwise stated the mixture was worked up as follows. A few drops of acetic acid were added and the solution brought to dryness *in vacuo*. The residue was extracted with several portions of hot benzene or ethyl acetate. The crude product in benzene was absorbed on a column of alumina (100 parts) and subjected to gradient elution with benzene (50 c.c.)/benzene–ethyl acetate (1 : 1; 150 c.c.); 7-c.c. fractions were collected; finally the column was eluted with ethyl acetate (50—100 c.c.). In the following detailed descriptions the isolated products are recorded, under (i), (ii), &c., in the order of their elution from alumina.

Reduction of Cortisone Acetate (I*a*).—The acetate (200 mg.) was reduced by the general procedure. The mixture was concentrated *in vacuo* to a small volume, diluted with water, acidified with hydrochloric acid, and extracted with chloroform. The dry extract was acetylated with acetic anhydride in pyridine at 18°. The product was crystallised from acetone whereby 20β : 21-diacetoxy-17α-hydroxypregn-4-ene-3 : 11-dione (II*a*) (60 mg.) was obtained, having m. p. 248—251° (undepressed on admixture with material kindly provided by Prof. T. Reichstein), $[\alpha]_D$ +205° (*c*, 1·45), +179° (*c*, 0·86 in $COMe_2$), $\lambda_{max.}$ 237·5 mμ (ε 15,600), $\nu_{max.}$ 1741 [>C(OH)·CH(OAc)·CH_2·OAc], 1701 (11-C=O), 1665 (3-C=O), 1616 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found: C, 67·1; H, 7·6. Calc. for $C_{25}H_{34}O_7$: C, 67·2; H, 7·7%). Chromatography of the mother-liquors over alumina furnished a further 60 mg. of identical material.

Reduction of Cortisol Acetate (I*b*).—The reduction of this ester (200 mg.) was as above. Acetone (5 c.c.) was added, and the mixture concentrated *in vacuo* to a small volume, diluted

with water, and extracted with chloroform. Acetylation followed by chromatography over alumina and crystallisation from acetone furnished 20β : 21-diacetoxy-11β : 17α-dihydroxypregn-4-en-3-one (II*b*) (100 mg.) of m. p. 223—225° undepressed on admixture with material kindly provided by Prof. T. Reichstein. An analytical sample had m. p. 225—226°, $[\alpha]_D$ +169° (*c*, 0·65 in $COMe_2$), $\lambda_{max.}$ 239·5 mμ (ε 16,000), $\nu_{max.}$ 1740 [>C(OH)·CH(OAc)·CH_2·OAc], 1664 (3-C=O), 1619 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found : C, 67·3; H, 8·15. Calc. for $C_{25}H_{36}O_7$: C, 66·9; H, 8·1%).

Reduction of 11-*Deoxycorticosterone* (I*c*).—Reduction of this ketone (150 mg.) by the general procedure, followed by acetylation and chromatography gave : (i) 3β : 20β : 21-*Triacetoxypregn-4-ene* (III*a*) (50 mg.; m. p. 125—130°). Crystallisation from acetone–hexane afforded prisms, m. p. 128—131°, $[\alpha]_D$ +40° (*c*, 0·87), no selective absorption between 210 and 280 mμ, $\nu_{max.}$ 1731 (OAc) and 865 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 70·5; H, 8·7. $C_{27}H_{40}O_6$ requires C, 70·4; H, 8·75%). (ii) 20β : 21-*Diacetoxypregn-4-en-3-one* (II*d*) (100 mg.; m. p. 130—152°), blunt needles (from acetone–hexane), m. p. 155—156° (with melting and resolidification at 143—144°), $[\alpha]_D$ +123° (*c*, 0·95), +120° (*c*, 0·97 in $COMe_2$), $\lambda_{max.}$ 240·5 mμ (ε 17,400), $\nu_{max.}$ 1742, 1728 (OAc), 1669 (3-C=O), 865 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 72·25; H, 8·8. $C_{25}H_{36}O_5$ requires C, 72·1; H, 8·7%).

20β : 21-*Dihydroxypregn-4-en-3-one* (II*c*).—The diacetate (II*d*) (210 mg.) in methanol (25 c.c.) was treated with a solution of potassium hydroxide (1·2 g.) in aqueous methanol (25 c.c.; 90%) at 25° for 24 hr. under nitrogen. N-Hydrochloric acid (40 c.c.) was added; overnight crystals (37 mg.; m. p. 157—162°) separated which on recrystallisation from ether gave 20β : 21-dihydroxypregn-4-en-3-one (II*c*), m. p. 163—167°, $[\alpha]_D$ +98° [*c*, 0·86 in $CHCl_3$–EtOH (4 : 1)] (Found : C, 77·1; H, 9·6. Calc. for $C_{21}H_{32}O_3$: C, 75·9; H, 9·7%). Steiger and Reichstein (*loc. cit.*) recorded m. p. 166—167°, $[\alpha]_D$ +92·6° (in EtOH), for one of the epimeric 20 : 21-dihydroxypregn-4-en-3-one; Julian *et al.* (*loc. cit.*) found m. p. 166—168°, $[\alpha]_D$ +98° (in $CHCl_3$). Material (120 mg.) isolated from the aqueous mother-liquors by extraction with ethyl acetate was treated with zinc chloride in acetone (10 c.c.; 5% w/v) overnight at 20°. The crude product was chromatographed as described in the general procedure, except that the system benzene/benzene–ethyl acetate (4 : 1), was used for elution. The main fraction (50 mg.) afforded, on crystallisation from hexane, the *iso*propylidene derivative of the diol (II*c*) as prisms, m. p. 121—123°, $[\alpha]_D$ +94° (*c*, 1·09 in $COMe_2$), $\lambda_{max.}$ 240·5 mμ (ε 18,200) (Found : C, 77·25; H, 10·0. Calc. for $C_{24}H_{36}O_3$: C, 77·35; H, 9·75%). Steiger and Reichstein (*loc. cit.*) recorded m. p. 126°, $[\alpha]_D$ +91·5° (in $COMe_2$).

Reduction of Progesterone (I*d*).—Progesterone (350 mg.) was reduced by the general procedure; the following compounds were isolated. (i) Progesterone (215 mg.; m. p. 126—129°). A sample crystallised from ethanol had m. p. and mixed m. p. 127—129°, $[\alpha]_D$ +199° (*c*, 0·85 in EtOH). (ii) 20β-Hydroxypregn-4-en-3-one (II*e*) (110 mg., m. p. 153—172°), crystallised from acetone–hexane, had m. p. 173—175°, $[\alpha]_D$ +88° (*c*, 0·71), $\lambda_{max.}$ 240·5 mμ (ε 16,000), $\nu_{max.}$ 3480 (OH), 1670 (C=O), 1610, 860 cm.$^{-1}$ (Δ^4) (in Nujol) (Found : C, 79·5; H, 10·15. Calc. for $C_{21}H_{32}O_2$: C, 79·7; H, 10·2%), which with acetic anhydride in pyridine gave, after crystallisation from acetone–hexane, the acetate (II*f*) as leaflets, m. p. 164—165°, $[\alpha]_D$ +140° (*c*, 1·27), $\lambda_{max.}$ 241 mμ (ε 18,400) (Found : C 77·5; H, 9·65. Calc. for $C_{23}H_{34}O_3$: C, 77·05; H, 9·55%). The recorded physical constants of (II*e* and *f*) agree with those reported by Wieland and Miescher (*loc. cit.*), Turner and Voitle (*J. Amer. Chem. Soc.*, 1951, **73**, 2283), and Sondheimer, Amandolla, and Rosenkranz, *ibid.*, 1953, **75**, 5930).

In a second experiment a further, less readily eluted product was isolated. It crystallised from acetone–hexane in prisms, m. p. 178—180°, $[\alpha]_D$ +43° (*c*, 1·3). In spite of an unsatisfactory analysis (Found : C, 77·8; H, 10·9. Calc. for $C_{21}H_{34}O_2$: C, 79·2; H, 10·8%) the compound is formulated as pregn-4-ene-3β : 20β-diol (III*b*). Its treatment with manganese dioxide in chloroform (cf. Sondheimer *et al.*, *loc. cit.*) furnished 20β-hydroxypregn-4-en-3-one (II*e*) identified by m. p., mixed m. p., and $[\alpha]_D$ +94° (*c*, 1·08).

Reduction of 11-*Oxoprogesterone* (I*e*).—Reduction of the dione (250 mg.) by the general procedure gave : (i) 11-Oxoprogesterone (I*e*) (15 mg.) identified by m. p., mixed m. p., and $[\alpha]_D$ +250° (*c*, 0·60). (ii) 20β-*Hydroxypregn-4-ene*-3 : 11-*dione* (II*g*) (96 mg.; m. p. 167—187°). Crystallisation from acetone–hexane gave prisms, m. p. 197—200°, $[\alpha]_D$ +201° (*c*, 0·94), $\lambda_{max.}$ 236 mμ (ε 17,300) (Found : C, 76·0; H, 9·1. $C_{21}H_{30}O_3$ requires C, 76·3; H, 9·15%), which gave an *acetate* (II*h*), plates (from acetone–hexane), m. p. 205—207°, $[\alpha]_D$ +218° (*c*, 0·81), $\lambda_{max.}$ 236 mμ (ε 17,800) (Found : C, 74·1; H, 8·55. $C_{23}H_{32}O_4$ requires C, 74·15; H, 8·65%).

Reduction of Androst-4-ene-3 : 17-*dione* (IV*a*).—By the general procedure this dione gave : (i) Testosterone (V*a*) (170 mg.; m. p. 147—154°). A sample crystallised from acetone–hexane

had m. p. and mixed m. p. 154—155°, $[\alpha]_D$ +110° (*c*, 0·7 in EtOH), $\lambda_{max.}$ 240·5 mμ (ε 16,800) (Found: C, 79·3; H, 10·0. Calc. for $C_{19}H_{28}O_2$: C, 79·1; H, 9·8%); the infrared spectrum was identical with that of authentic material. (ii) and (iii) A mixture of diols (35 mg.) which was combined with similar material from replicated preparations: the aggregate (116 mg.) was separated on alumina into two main fractions. The fraction (50 mg.) more readily eluted crystallised from acetone–ethyl acetate in needles, m. p. 162—163°, $[\alpha]_D$ +48° [*c*, 1·14 in $CHCl_3$–EtOH (1 : 1)], no selective absorption above 210 mμ (Found: C, 78·8; H, 10·5. Calc. for $C_{19}H_{30}O_2$: C, 78·55; H, 10·4%), considered to be androst-4-ene-3β : 17β-diol (VI). Butenandt and Heusner (*loc. cit.*) recorded m. p. 153—154°, $[\alpha]_D$ +48·5° (in EtOH). Treatment with manganese dioxide in chloroform (cf. Sondheimer *et al.*, *loc. cit.*) afforded testosterone (V*a*) 90% by spectroscopic evidence), identified by m. p., mixed m. p., $[\alpha]_D$ +108° (*c*, 0·93), $\lambda_{max.}$ 240 mμ (ε 16,500). The fraction (56 mg.) less readily eluted from alumina crystallised from acetone–hexane in prisms, m. p. 152—154°, $[\alpha]_D$ +30·5° [*c*, 0·83 in $CHCl_3$–EtOH (1 : 1)], no selective absorption above 210 mμ [Found: C, 75·95; H, 11·0. $C_{19}H_{30}O_2$,$C_{19}H_{32}O_2$,H_2O (?) requires C, 75·95; H, 10·7%]. Treatment of this material with manganese dioxide in chloroform gave testosterone (V*a*) (50% by spectroscopic evidence). Chromatography over alumina gave, in order of elution, (*a*) testosterone, m. p. and mixed m. p. 152—154°, $[\alpha]_D$ +108° (*c*, 0·88 in EtOH), $\lambda_{max.}$ 240·5 mμ (ε 16,100), and (*b*) androstane-3β : 17β-diol (VII), m. p. 166—167° undepressed on admixture with authentic material (kindly provided by Dr. W. Klyne from the M.R.C. Steroid Reference Collection), $[\alpha]_D$ +8° (*c*, 0·36 in EtOH); the infrared spectrum was identical with that of authentic material. (iv) Sparingly soluble material (10 mg.) which from methanol afforded fine needles, m. p. 217—233°, $[\alpha]_D$ +70° (*c*, 0·3 in dioxan). Further characterisation of this material was not attempted. Repeated reductions of the dione (IV*a*) with sodium borohydride regularly furnished 60—70% of pure testosterone, 15—25% of the diol fraction, and 5—10% of the sparingly soluble material.

Reduction of the dione (IV*a*) (200 mg.) with potassium borohydride (27 mg., 0·7 mol.) at 22° under otherwise unchanged conditions afforded testosterone (135 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +110° (*c*, 0·95 in EtOH).

Reduction of the dione (IV*a*) (200 mg.) with sodium trimethoxyborohydride (360 mg., 4·0 mol.) under otherwise unchanged conditions gave: (i) Androst-4-ene-3 : 17-dione (45 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +191° (*c*, 0·61 in EtOH). (ii) Testosterone (130 mg.), identified by m. p., mixed m. p., and $[\alpha]_D$ +109° (*c*, 0·75 in EtOH).

Reduction of Androst-4-ene-3 : 11 : 17-trione (IV*b*).—Reduction of this trione (100 mg.) by the general procedure gave 11-oxotestosterone (V*b*) (45 mg.; m. p. 182—186°). Crystallisation from acetone–hexane afforded needles, m. p. 186·5—188°, $[\alpha]_D$ +199° (*c*, 0·68 in $COMe_2$), $\lambda_{max.}$ 237·5 mμ (ε 16,500), $\nu_{max.}$ 3460—3420 (OH), 1703 (11-C=O), 1665 (3-C=O), 1618 cm.$^{-1}$ (Δ^4) (in $CHCl_3$) (Found: C, 75·4; H, 8·9. Calc. for $C_{19}H_{26}O_3$: C, 75·45; H, 8·65%). The recorded physical constants are in good agreement with those reported by Herzog *et al.* (*loc. cit.*), Herr and Heyl (*J. Amer. Chem. Soc.*, 1953, **75**, 5927), Bernstein, Lenhard, and Williams (*J. Org. Chem.*, 1953, **18**, 1166), and Mancera, Sondheimer, and Rosenkranz (*J.*, 1953, 2189).

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