The Stereospecificity of Carbanion Reduction Processes.

By D. H. R. Barton and C. H. Robinson.

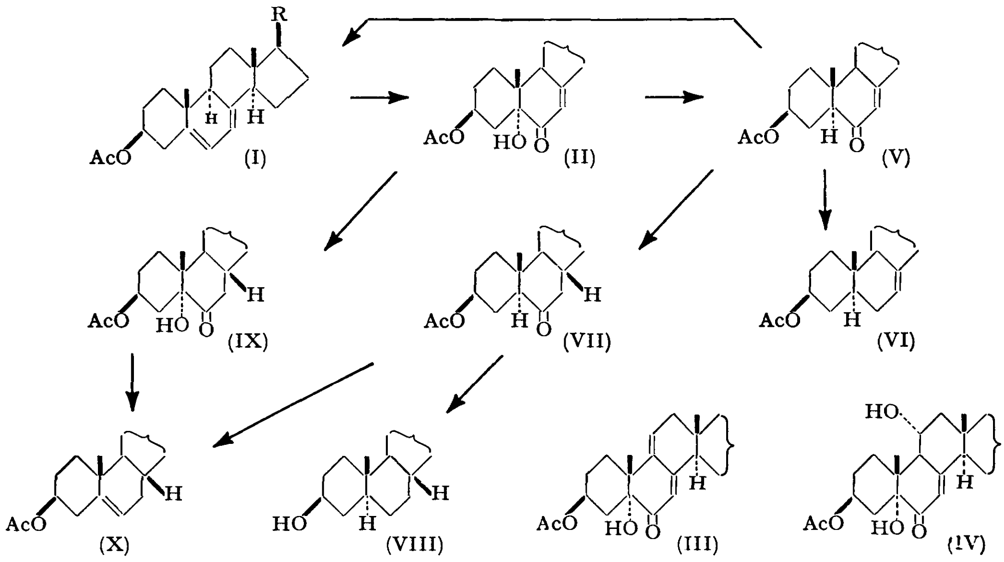
[Reprint Order No. 5326.]

Various transformations based upon 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one are described, including the reduction of this compound and of the derived 3β-acetoxyergosta-7 : 22-dien-6-one by lithium and liquid ammonia to afford products with the β-configuration at $C_{(8)}$. As a result of these and numerous related observations it is concluded that such reductions usually afford the thermodynamically more stable products. This conclusion is, however, only part of a broader generalisation that carbanion reduction processes in alkaline media which involve the creation of asymmetric centres usually appear to afford the stereochemically more stable products. A possible explanation for this is suggested.

A convenient route for the conversion of ergosterol into brassicasterol is reported.

The original objective of the investigations outlined in this paper was the introduction of oxygenated functions at $C_{(11)}$ in derivatives of ergosterol. However, certain theoretical conclusions were drawn from the work and these eventually dictated additional experimentation on the stereospecificity of carbanion reduction processes.

Oxidation of ergosterol acetate (I; $R = C_9H_{17}$) with chromic acid gave 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (II; $R = C_9H_{17}$) (Burawoy, *J.*, 1937, 409), hydrogenated to the 22 : 23-dihydro-derivative (II; $R = C_9H_{19}$). It was originally intended to extend the conjugated system of (II; $R = C_9H_{17}$) to that of (III; $R = C_9H_{17}$); vinylogous β-addition of hydroxyl ion (or its equivalent) to this would afford compounds such as the dihydroxy-ketone (IV; $R = C_9H_{17}$). The oxidising action of bromine was first studied. Treatment of the ergosta-7 : 22-dien-6-one (II; $R = C_9H_{17}$) with bromine gave a dibromide. Since the ergost-7-en-6-one (II; $R = C_9H_{19}$) was inert under the same brominating conditions, this compound must be the side-chain dibromide (II; $R = C_9H_{17}Br_2$). At this

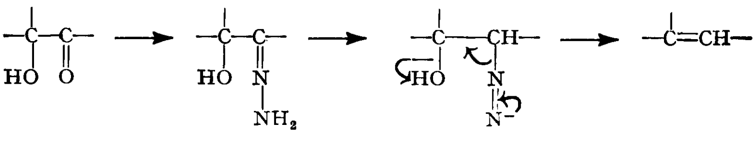


stage in the investigation Professor C. W. Shoppee (Swansea) very kindly informed us of his interest in the same objective and we therefore concentrated on other aspects of the chemistry of 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (II; $R = C_9H_{17}$).

Reduction of the hydroxyketone (II; R = C_9H_{17}) with zinc dust and acetic acid removed the hydroxyl group. Catalytic hydrogenation of the product (V; R = C_9H_{17}) over platinum gave ergost-8(14)-enyl acetate, but hydrogenation over palladised calcium carbonate furnished 3β-acetoxyergost-7-en-6-one (V; R = C_9H_{19}). Wolff–Kishner reduction of (V; R = C_9H_{17}), followed by reacetylation, gave 5-dihydroergosteryl acetate (VI; R = C_9H_{17}). The infra-red spectrum of the ketone (V; R = C_9H_{17}) showed bands at 1675 and 1620 (αβ-unsaturated ketone), at 1733 and 1234 (acetate), and at 966 cm.$^{-1}$ (*trans*-22 : 23-ethylenic linkage), in agreement with the assigned constitution.

Reduction of the ketone (V; R = C_9H_{17}) with lithium and liquid ammonia (Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5360, 5366), followed by reacetylation, gave 3β-acetoxyergost-22-en-6-one (VII; R = C_9H_{17}). The steric course of the reduction was established by Wolff–Kishner reduction of the product to ergost-22-en-3β-ol (VIII; R = C_9H_{17}) (Barton, Cox, and Holness, *J.*, 1949, 1771). Similar lithium and liquid ammonia reduction of the ergost-7-en-6-one (V; R = C_9H_{19}), followed by reactylation, gave 3β-acetoxyergostan-6-one (VII; R = C_9H_{19}), affording ergostan-3β-ol (VIII; R = C_9H_{19}) on Wolff–Kishner reduction. 3β-Acetoxyergostan-6-one was also available by hydrogenation of (VII; R = C_9H_{17}). The configurations at $C_{(5)}$ in the ketones (VII; R = C_9H_{17} and R = C_9H_{19}), and hence in (V; R = C_9H_{17} and R = C_9H_{19}), are confirmed by molecular-rotation considerations. Thus the observed $[M]_D$'s for (VII; R = C_9H_{17} and R = C_9H_{19}) are −191° and −82° respectively. The calculated values, based on the known molecular rotation of ergost-22-ene (Barton, Cox, and Holness, *loc. cit.*) and computed from the standard tables of Barton and Klyne (*Chem. and Ind.*, 1948, 755), are −182° and −86° respectively.

Reduction of the hydroxy-ketone (II; R = C_9H_{17}) with lithium and liquid ammonia, followed by reacetylation, afforded 3β-acetoxy-5α-hydroxyergost-22-en-6-one (IX; R = C_9H_{17}). Catalytic hydrogenation gave the dihydro-derivative (IX; R = C_9H_{19}), also available by the lithium–ammonia route from the hydroxyergostanone (II; R = C_9H_{19}). Wolff–Kishner reduction of the dihydro-derivatives (IX; R = C_9H_{17} and R = C_9H_{19}) afforded, after reacetylation, 3β-acetoxyergosta-5 : 22-diene (brassicasteryl acetate) (X; R = C_9H_{17}) and 3β-acetoxyergost-5-ene (X; R = C_9H_{19}) respectively. The brassicasteryl acetate was further characterised as the derived sterol and its benzoate. The process reported here represents a convenient partial synthesis of brassicasterol. The conversion of (IX) into (X) is based the observations by Barton, Holness, and Klyne (*J.*, 1949, 2456; see also Ruzicka and Meldahl, *Helv. Chim. Acta*, 1940, **23**, 513; Ames and Bowman, *J.*, 1951, 2752; Leonard and Sentz, *J. Amer. Chem. Soc.*, 1952, **74**, 1704) and especially by Heymann and Fieser (*ibid.*, 1951, **73**, 5252). The theoretical interpretation of this type of reaction advanced by Barton, Holness, and Klyne (*loc. cit.*) was derived from the findings of Jeger and his collaborators (*Helv. Chim. Acta*, 1951, **34**, 1577; and references there cited) on the Wolff–Kishner reduction of αβ-unsaturated ketones. The mechanism of the conversion of (IX) into (X) may be more simply represented by the scheme:



Such a scheme would also encompass satisfactorily the case discussed by Barton, Holness, and Klyne (*loc. cit.*).

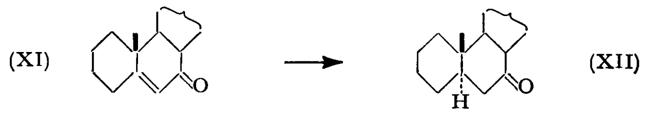
When cholestan-6-one was subjected to the Bamford–Stevens reaction (*J.*, 1952, 4735) it gave cholest-5-ene. Analogous reduction of the ergostenone (VII; R = C_9H_{17}) gave, after recetylation, the ergostadiene (X; R = C_9H_{17}), although in poor yield. Likewise, the dienone (V; R = C_9H_{17}) was reconverted into the triene (I; R = C_9H_{17}).

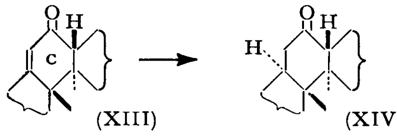
From the theoretical point of view the formation of the thermodynamically more stable 8β-derivatives from unsaturated ketones of the types (II) and (V) is worthy of more extended comment. In Table 1 we have collected examples of the reduction of αβ-unsaturated ketones with lithium and liquid ammonia reported in the literature. To this list we have added the reduction of cholest-5-en-7-one (XI) to cholestan-7-one (XII). Also, in the triterpenoid field, we have found that reduction of 12-oxo-β-amyr-9(11)-en-3β-yl acetate (XIII) gives, after reacetylation, 12-oxo-β-amyran-3β-yl acetate (XIV) and that 11-oxo-β-amyr-12-en-3β-yl benzoate (XV) analogously affords 11-oxo-β-amyran-3β-yl acetate (XVI). In every case so far studied the configuration of the reduction product is the more stable one.*

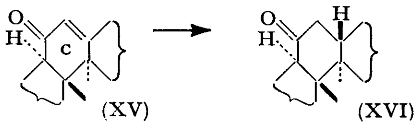
TABLE 1.

System reduced	No. of examples	Confign. of product	Most stable confign.	Refs.
Steroid				
4-en-3-one	5	5α	5α	1, 2
5-en-7-one	1	5α	5α	3
7-en-6-one	4	8β	8β	3
8-en-7-one	1	8β, 9α	8β, 9α	4
8-en-11-one	4	8β, 9α	8β, 9α	5, 6, 7, 8
8(14)-en-15-one	3	8β, 14α	8β, 14α	9
Triterpenoid				
8-en-7-one (lanosterol series)	1	8β, 9α	8β, 9α	10
9(11)-en-12-one	1	9α	9α	3
12-en-11-one	1	13β	13β	3

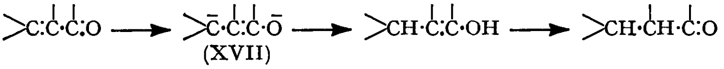
1, Barton, Ives, and Thomas, *Chem. and Ind.*, 1953, 1180; *J.*, 1954, 903. 2, W. S. Johnson, Bannister, Bloom, Kemp, Pappo, Rogier, and Szmuszkovicz, *J. Amer. Chem. Soc.*, 1953, **75**, 2275. 3, This paper. 4, Alt and Barton, *J.*, 1954, 1356. 5, Sondheimer, Yashin, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1952, **74**, 2696; Sondheimer, Mancera, Rosenkranz, and Djerassi, *ibid.*, 1953, **75**, 1282. 6, Schoenewaldt, Turnbull, Chamberlin, Rheinhold, Erickson, Ruyle, Chemerda, and Tishler, *ibid.*, 1952, **74**, 2696. 7, Heusler, Heusser, and Anliker, *Helv. Chim. Acta*, 1953, **36**, 652. 8, Burke, Turnbull, and Wilson, *J.*, 1953, 3237; Bladon, Henbest, Jones, Lovell, and Woods, *J.*, 1954, 125. 9, Barnes, Barton, and Laws, *Chem. and Ind.*, 1953, 616; Barton and Laws, *J.*, 1954, 52. 10, Barton and Thomas, *Chem. and Ind.*, 1953, 172; *J.*, 1953, 1842.


(XI) (XII)


(XIII) (XIV,


(XV) (XVI)

The reduction of αβ-unsaturated ketones by dissolving metals in liquid ammonia can be conveniently represented by the following scheme (cf. Burton and Ingold, *J.*, 1929, 2022; Birch, *Quart. Reviews*, 1950, **4**, 69; Wilds and Nelson, *loc. cit.*) :



$$>C{:}\overset{|}{C}{\cdot}\overset{|}{C}{:}O \longrightarrow \underset{\text{(XVII)}}{>\bar{C}{\cdot}\overset{|}{C}{:}\overset{|}{C}{\cdot}\bar{O}} \longrightarrow >CH{\cdot}\overset{|}{C}{:}\overset{|}{C}{\cdot}OH \longrightarrow >CH{\cdot}\overset{|}{C}H{\cdot}\overset{|}{C}{:}O$$

The formulation of the dianion (XVII) as an intermediate does not, of course, exclude the co-ordination of Li^+ ions with the negative charges to furnish ion-pairs, or even the formation of covalent C–Li bonds (cf. Wilds and Nelson, *loc. cit.*) so long as these dissociate in a reversible manner to give (XVII), which may usually be regarded as the entity protonated. The reduction may, therefore, be classified as a carbanion reduction process and the stereochemistry of the final product (at the β-position) is thus governed by the stereochemistry of the protonation of the carbanion (XVII).

---

* This conclusion was also advanced, on the basis of more limited evidence, by Dr. L. H. Sarett (Merck and Co.) in a lecture at the University of New Brunswick, Canada, in August, 1953. The point was further illustrated by a stereospecific reduction of an αβ-unsaturated ester (see Sarett, Arth, Lukes, Beyler, Poos, Johns, and Constantin, *J. Amer. Chem. Soc.*, 1952, **74**, 4974; Arth, Poos, Lukes, Robinson, Johns, Feurer, and Sarett, *ibid.*, 1954, **76**, 1715).

It is of interest that the stereochemical course of the reduction of conjugated dienes and trienes (in the steroid series) (see Table 2) by dissolving metals is also always such as to afford the thermodynamically more stable product. This is likewise true for the analogous

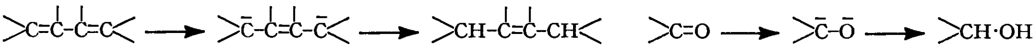
TABLE 2.

System reduced	No. of examples	Products	Confign. of products	Most stable confign.*	Refs.
5 : 7-diene (10-normal) ...	2	7-ene	5α	5α	1, 2, 3, 4
5 : 7-diene (10-*iso*)	1	7-ene	5α	5α	5, 6, 7
6 : 8-diene	1	7-ene	9α	9α	8, 9
5 : 7 : 9(11)-triene	1	7-ene	5α, 9α	5α, 9α	10
		5 : 7-diene	9α	9α	
		7 : 9(11)-diene	5α	5α	
5 : 7 : 14-triene	1	6 : 8(14)-diene	5α	5α	11

* Based on the corresponding saturated structure of normal (*trans-anti-trans*) stereochemistry except as otherwise specified.

1, Windaus and Brunken, *Annalen*, 1928, **460**, 225. 2, von Reichel, *Z. physiol. Chem.*, 1934, **226**, 146. 3, Windaus and Langer, *Annalen*, 1934, **508**, 105. 4, Schenck, Buckholz, and Wiese, *Ber.*, 1936, **69**, 2696. 5, Windaus, Dithmar, and Fernholz, *Annalen*, 1932, **493**, 259. 6, Heilbron, Moffet, and Spring, *J.*, 1937, 411. 7, Cole, *J.*, 1952, 4969. 8, Windaus, Linsert, and Eckhardt, *Annalen*, 1938, **534**, 22. 9, Barton and Cox, *J.*, 1949, 214. 10, Bergmann and Klacsmann, *J. Org. Chem.*, 1948, **13**, 21. 11, Barton and Brunn, *J.*, 1951, 2728.

reductions of ketones to secondary alcohols and of oximes to amines (see Barton, *Experientia*, 1950, **6**, 316; *J.*, 1953, 1027; and references there cited). These three procedures can all be represented as carbanion reduction processes (cf. Birch, *loc. cit.*) :



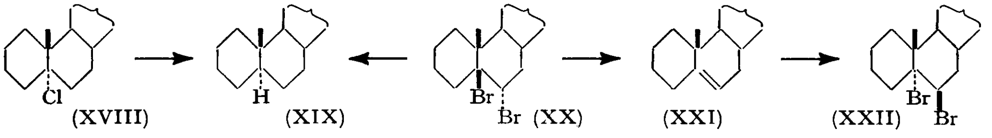
$$>C=\overset{|}{C}-\overset{|}{C}=C< \longrightarrow >\bar{C}-\overset{|}{C}=\overset{|}{C}-\bar{C}< \longrightarrow >CH-\overset{|}{C}=\overset{|}{C}-CH< \qquad >C=O \longrightarrow >\bar{C}-\bar{O} \longrightarrow >CH\cdot OH$$

$$>C=N\cdot OH \longrightarrow >\bar{C}-N^{2-} \longrightarrow >CH\cdot NH_2$$

One may conclude, in general, that reduction of multiple bond systems through intermediate carbanions usually affords the thermodynamically more stable products. A spectacular example of this synthetically useful principle has been given recently by W. S. Johnson *et al.* (*J. Amer. Chem. Soc.*, 1953, **75**, 2275).

It appears that the stereochemical preferences discussed in this paper are most simply rationalised if the carbanion has a preferred tetrahedral configuration. This would be separated from the inverted tetrahedral arrangement by only a low energy barrier (cf. ammonia and tertiary amines) in order to explain the ready racemisation of saturated carbanions (see, for example, Gilman's "Organic Chemistry," Vol. I, p. 383, John Wiley and Sons Inc., New York, 1943). If this is true, the unshared electron pair might be expected to occupy an orbital approximating in size to a C–H bond. Thus the preferred configuration would be that which, on protonation, would afford the more stable arrangement of the asymmetric centre.

In support of these ideas we have found that reduction of 5-chlorocholestane (XVIII) (for configuration see Bernal, Crowfoot, and Fankuchen, *Trans. Roy. Soc.*, 1940, *A*, **239**, 135; Crowfoot in " Vitamins and Hormones," Vol. II, p. 409, Academic Press, New York,



(XVIII) (XIX) (XX) (XXI) (XXII)

1944) with lithium and liquid ammonia affords an almost quantitative yield of cholestane (XIX). Cholestane was also the only saturated product from the reduction of 5-chlorocholestane with sodium and alcohol. Likewise in agreement, the reduction of 5 : 6α-dibromocoprostane (XX) (see Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066) by lithium and liquid ammonia gave, along with the (not unexpected) cholest-5-ene (XXI), cholestane as sole saturated product. Similar reduction of the stereoisomeric diaxial

5 : 6β-dibromocholestane (XXII) gave only cholest-5-ene : this is not unexpected from the stereochemical point of view (cf. Barton, *loc. cit.*). Professor C. W. Shoppee (Swansea) has kindly informed us that both 3α- and 3β-bromocholestane afford cholestane-3β-carboxylic acid on carboxylation of their derived Grignard reagent. This important observation is of obvious relevance to the discussion in the present paper.

Dr. Hans Heusser of the Eidg. Technische Höchschule (Zürich) has kindly told us that he has also observed the reduction of 3β-acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one by lithium and liquid ammonia to a 8β-compound. We thank Dr. Heusser cordially for this information.

EXPERIMENTAL

For general experimental detail see *J.*, 1952, 2339. $[\alpha]_D$ were measured in $CHCl_3$, ultra-violet absorption spectra in EtOH. Infra-red spectra were kindly determined by Messrs. Glaxo Laboratories Ltd. in carbon disulphide solution.

3β-*Acetoxy*-5α-*hydroxyergosta*-7 : 22-*dien*-6-*one* (II; $R = C_9H_{17}$) *and* -7-*en*-6-*one* (II; $R = C_9H_{19}$).—The following modification of Burawoy's method (*loc. cit.*) was found to be suitable. To a suspension of ergosteryl acetate (20 g.) in " AnalaR " acetic acid (400 ml.) was added with vigorous stirring chromium trioxide (13·6 g.) in 80% acetic acid (80 ml.) at room temperature. The mixture, after being stirred for a further hour, was left overnight, then, after addition of methanol (3 ml.), diluted with water. The precipitated solid was digested with ethyl acetate (250 ml.) on the steam-bath. Cooling and filtration gave the desired acetoxy-ketone (4·4 g., 20%), m. p. 258—262° (decomp.). Crystallisation from ethyl acetate gave the pure material as plates, m. p. 263—265° (decomp.), $[\alpha]_D$ −5° (*c*, 1·00), $\lambda_{max.}$ 250 mμ (ε 14,000).

Catalytic hydrogenation for 2 hr. in 9 : 1 dioxan–acetic acid with a platinum catalyst gave 3β-*acetoxy*-5α-*hydroxyergost*-7-*en*-6-*one*, m. p. (from ethyl acetate) 252—255° (decomp.), $[\alpha]_D$ +12° (*c*, 1·07), $\lambda_{max.}$ 248 mμ (ε 14,000) (Found : C, 76·05; H, 10·1. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%).

3β-*Acetoxyergosta*-7 : 22-*dien*-6-*one* (V; $R = C_9H_{17}$).—3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (2 g.) in " AnalaR " acetic acid (150 ml.) was refluxed for 1 hr. with portionwise addition of zinc dust (15 g.). Chromatography of the product over alumina and elution with 4 : 1 light petroleum (b. p. 40—60°)–benzene gave 3β-*acetoxyergosta*-7 : 22-*dien*-6-*one*, m. p. (needles from methanol) 184—186°, $[\alpha]_D$ −17° (*c*, 1·49), −16° (*c*, 1·02), $\lambda_{max.}$ 245 mμ (ε 16,000) (Found : C, 79·2; H, 10·05. $C_{30}H_{46}O_3$ requires C, 79·25; H, 10·2%). Hydrogenation of this acetoxy-ketone in acetic acid overnight with a platinum catalyst afforded ergost-8(14)-en-3β-yl acetate, identified by m. p. mixed m. p. and rotation {$[\alpha]_D$ ±0° (*c*, 1·59)}.

Hydrogenation in ethyl acetate for 5 hr. with palladised calcium carbonate gave 3β-*acetoxy-ergost*-7-*en*-6-*one* (V; $R = C_9H_{19}$), m. p. (needles from methanol) 153—155°, $[\alpha]_D$ +5° (*c* 0·63), $\lambda_{max.}$ 245 mμ (ε 14,000) (Found : C, 79·2; H, 10·35. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%). Wolff–Kishner reduction of this ketone (100 mg.) under the normal conditions followed by re-acetylation and chromatography gave 3β-acetoxyergosta-7 : 22-diene (m. p. and mixed m. p.).

Bromination of 3β-*Acetoxy*-5α-*hydroxyergosta*-7 : 22-*dien*-6-*one*.—The ketone (500 mg.) in 1 : 1 chloroform–acetic acid (50 ml.) containing anhydrous sodium acetate (880 mg.) was treated with bromine (190 mg.) in " AnalaR " acetic acid (20 ml.) at room temperature for 30 min. Crystallisation of the product from benzene–light petroleum (b. p. 40—60°) afforded 3β-*acetoxy*-5α-*hydroxy*-22 : 23-*dibromoergost*-7-*en*-6-*one* as needles, m. p. 213—215° (decomp.), $[\alpha]_D$ +9° (*c*, 1·08) (Found : C, 57·0; H, 7·6; Br, 25·2. $C_{30}H_{46}O_4Br_2$ requires C, 57·15; H, 7·35; Br, 25·35%). Attempted bromination of 3β-acetoxy-5α-hydroxyergost-7-en-6-one under the same conditions gave back starting material (m. p. and mixed m. p.).

3β-*Acetoxyergost*-22-*en*-6-*one* (VII; $R = C_7H_{17}$).—3β-Acetoxyergosta-7 : 22-dien-6-one (780 mg.) in dry ether (50 ml.) was added with stirring to a solution of lithium (700 mg.) in liquid ammonia (250 ml.). Excess of lithium was destroyed by the addition of ammonium chloride, and the mixture worked up in the usual way. Reacetylation, chromatography over alumina, and elution with light petroleum (b. p. 40—60°) furnished 3β-*acetoxyergost*-22-*en*-6-*one*, m. p. (plates from chloroform–methanol) 162—164°, $[\alpha]_D$ −42° (*c*, 1·18) (Found : C, 78·95; H, 10·35. $C_{30}H_{48}O_3$ requires C, 78·9; H, 10·6%).

Wolff–Kishner reduction of this ketone (100 mg.) in the usual way and crystallisation of the product from methanol gave ergost-22-en-3β-ol (VIII), m. p. 154—156°, $[\alpha]_D$ −11° (*c*, 1·53), undepressed in m. p. on admixture with an authentic specimen (Barton, Cox, and Holness, *J.*, 1949, 1771).

3β-*Acetoxyergostan*-6-*one* (VII; R = C_9H_{19}).—3β-Acetoxyergost-7-en-6-one was subjected to lithium and liquid ammonia reduction under the same conditions to give, after reacetylation, chromatography over alumina, and elution with light petroleum (b. p. 40—60°), 3β-*acetoxyergostan*-6-*one*, m. p. (plates from chloroform–methanol) 142—144°, $[\alpha]_D$ −18° (*c*, 1·23) (Found: C, 79·25, 78·55; H, 10·9, 10·4. $C_{30}H_{50}O_3$ requires C, 78·55; H, 11·0%). This ketone was also obtained (m. p. and mixed m. p.) by catalytic hydrogenation of 3β-acetoxyergost-22-en-6-one in ethyl acetate with a palladised calcium carbonate catalyst. Wolff–Kishner reduction gave ergostan-3β-ol, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ +13° (*c*, 1·09)}.

3β-*Acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one* (IX; R = C_9H_{17}).—3β-Acetoxy-5α-hydroxyergosta-7 : 22-dien-6-one (1·0 g.; dried at 100° for 8 hr.) in suspension in dry ether (200 ml.) was added rapidly to a solution of lithium (300 mg.) in liquid ammonia (200 ml.) with vigorous stirring. The excess of lithium was immediately destroyed with solid ammonium chloride. Reacetylation of the product and crystallisation from ethyl acetate–methanol afforded 3β-*acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one* (500 mg.), m. p. 249—253°, $[\alpha]_D$ −74° (*c*, 0·66) (Found: C, 75·95; H, 10·05. $C_{30}H_{48}O_4$ requires C, 76·2; H, 10·25%).

3β-*Acetoxy*-5α-*hydroxyergostan*-6-*one* (IX; R = C_9H_{19}).—(*a*) 3β-Acetoxy-5α-hydroxyergost-7-en-6-one (300 mg.; dried at 100° for 8 hr.) in suspension in dry ether (60 ml.) was added rapidly with vigorous stirring to a solution of lithium (100 mg.) in liquid ammonia (50 ml.). Working up as in the preceding case afforded 3β-*acetoxy*-5α-*hydroxyergostan*-6-*one* (140 mg.), m. p. 252—256°, $[\alpha]_D$ −53° (*c*, 2·00) (Found: C, 75·5; H, 10·4. $C_{30}H_{50}O_4$ requires C, 75·9; H, 10·6%).

(*b*) 3β-Acetoxy-5α-hydroxyergost-22-en-6-one (200 mg.) was hydrogenated in ethyl acetate with palladised calcium carbonate (at 60° owing to the sparing solubility of the unsaturated ketone). Crystallisation of the product from ethyl acetate–methanol afforded 3β-acetoxy-5α-hydroxyergostan-6-one, identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −57° (*c*, 1·19)}.

Wolff–Kishner Reduction of 3β-*Acetoxy*-5α-*hydroxyergost*-22-*en*-6-*one*.—The ketone (300 mg.) and hydrazine hydrate (2 ml.; 100%) in ethanol (2 ml.) were heated in a sealed tube at 180° for 2 hr. Sodium (300 mg.) in ethanol (4 ml.) was then added and heating continued overnight. The products from two such reactions were reacetylated (400 mg.) and chromatographed over alumina. Elution with light petroleum (b. p. 40—60°) afforded 3β-acetoxyergosta-5 : 22-diene (brassicasteryl acetate) (180 mg.) as plates (from chloroform–methanol), m. p. 158—159°, $[\alpha]_D$ −64° (*c*, 1·70), −63° (*c*, 1·00). Hydrolysis with methanolic potassium hydroxide gave ergosta-5 : 22-dien-3β-ol, m. p. (from chloroform–methanol) 150—151°, $[\alpha]_D$ −60° (*c*, 1·28). Benzoyl chloride–pyridine furnished the benzoate, m. p. (from chloroform–methanol) 169—172°, $[\alpha]_D$ −36° (*c*, 1·00). For the corresponding derivatives of brassicasterol Windaus and Welsch (*Ber.*, 1909, **42**, 612) reported m. p. 157—159°, m. p. 148°, $[\alpha]_D$ −64°, and m. p. 167°, respectively.

Wolff–Kishner Reduction of 3β-*Acetoxy*-5α-*hydroxyergostan*-6-*one*.—The ketone (330 mg.) was reduced as above. Re-acetylation of the product, chromatography over alumina, and elution with light petroleum afforded 3β-acetoxyergost-5-ene (X; R = C_9H_{19}) (200 mg.), m. p. (from chloroform–methanol) 152—154°, $[\alpha]_D$ −52° (*c*, 1·42), −50° (*c*, 1·08). The derived sterol had m. p. 146—148°, $[\alpha]_D$ −45° (*c*, 1·65). Fernholz and Ruigh (*J. Amer. Chem. Soc.*, 1940, **62**, 3346) recorded for these substances m. p. 145°, $[\alpha]_D$ −46°, and m. p. 158°, $[\alpha]_D$ −46°, respectively.

Alkaline Decomposition of Some Steroid Toluene-p-*sulphonylhydrazones*.—Cholestan-6-one (386 mg.), prepared from cholest-5-ene according to the directions of Windaus (*Ber.*, 1920, **53**, 488), and toluene-*p*-sulphonhydrazide (Freudenberg and Blümmel, *Annalen*, 1924, **440**, 51) (186 mg.) in hot ethanol (5 ml.) containing one drop of concentrated hydrochloric acid were heated under reflux for 20 min. The solvent was removed *in vacuo* and the residue, in dioxan (5 ml.) and ethylene glycol (5 ml.; redistilled) containing sodium (150 mg.), was refluxed for 45 min. Crystallisation of the product from chloroform–methanol gave cholest-5-ene (60 mg.), identified by m. p., mixed m. p., and rotation {$[\alpha]_D$ −49° (*c*, 1·43)}.

3β-Acetoxyergosta-7 : 22-dien-6-one (228 mg.) (see above), subjected to the same reaction gave, after chromatography of the re-acetylated product over alumina, ergosteryl acetate (74 mg.), identified by m. p., mixed m. p., and absorption spectrum.

3β-Acetoxyergost-22-en-6-one (120 mg.) (see above) treated in the same way afforded, after chromatography of the re-acetylated product over alumina, 3β-acetoxyergosta-5 : 22-diene (40 mg.) identified by m. p., mixed m. p. (see above), and rotation {$[\alpha]_D$ −63° (*c*, 0·70)}.

Reduction of Some αβ-*Unsaturated Ketones with Lithium and Liquid Ammonia*.—Cholest-5-ene was converted into cholest-5-en-7-one, m. p. 128—129°, $[\alpha]_D$ −127° (*c*, 1·71), $\lambda_{max.}$ 238 mμ (ε 11,000) by the method used by Fieser *et al.* (*J. Amer. Chem. Soc.*, 1949, **71**, 2226) for the oxidation of cholesteryl acetate.

The unsaturated ketone (200 mg.) in dry ether (25 ml.) was added with vigorous stirring to a solution of lithium (60 mg.) in liquid ammonia (40 ml.). Excess of lithium was destroyed by acetone. Chromatography of the product over alumina and elution with light petroleum gave cholestan-7-one (145 mg.), m. p. (plates from chloroform–methanol) 114—115°, $[\alpha]_D$ −42° (*c*, 1·09), undepressed in m. p. on admixture with an authentic specimen (see Barton and Rosenfelder, *J.*, 1951, 1048).

12-Oxo-β-amyr-9(11)-en-3β-yl acetate (150 mg.) was reduced in the same way and the reacetylated product chromatographed over alumina. Elution with 4 : 1 light petroleum (b. p. 40—60°)–benzene gave 12-oxo-β-amyran-3β-yl acetate (80 mg.), m. p. (from chloroform–methanol) 291—293°, undepressed in m. p. on admixture with an authentic specimen (prepared from β-amyrin acetate according to Spring's directions, *J.*, 1933, 1345).

11-Oxo-β-amyr-12-en-3β-yl benzoate (300 mg.) was reduced in the same way and the product (after hydrolysis with 10% potassium hydroxide in 1 : 1 methanol–dioxan under reflux for 3 hr. and then acetylation) chromatographed over alumina. Elution with 1 : 1 benzene–light petroleum (b. p. 40—60°) gave 11-oxo-β-amyran-3β-yl acetate, m. p. (plates from chloroform–methanol) 330—332° (evacuated capillary), $[\alpha]_D$ +6° (*c*, 1·07). Ruzicka and Jeger (*Helv. Chim. Acta*, 1945, **28**, 209) recorded m. p. 341° (corr.), $[\alpha]_D$ +7°, for this compound.

Reduction of 5-Chlorocholestane.—(*a*) The chloro-compound (300 mg.) in dry ether (30 ml.) was added to a solution of lithium (150 mg.) in liquid ammonia (40 ml.) with stirring. Crystallisation of the product (negative Beilstein test) from chloroform–methanol gave cholestane (18 mg.), m. p. and mixed m. p. 79—80°, $[\alpha]_D$ +24° (*c*, 1·22).

(*b*) The chloro-compound (150 mg.) in *n*-propanol (10 ml.) was heated under reflux with addition of sodium (150 mg.) for 15 min. The product (125 mg.; negative Beilstein test) gave a positive tetranitromethane test due to the presence of cholest-4- and -5-ene (cf. Mauthner, *Monatsh.*, 1907, **28**, 1113; Wettstein *et al.*, *Helv. Chim. Acta*, 1946, **29**, 627). A portion of the product (62 mg.) was treated with ethereal perphthalic acid at 0° for 24 hr. (uptake equiv. to 65% of olefin) and the resulting oil in chloroform (5 ml.) was treated with dry hydrogen chloride at room temperature for 20 min. Chromatography over alumina and elution with light petroleum (b. p. 40—60°) afforded cholestane (18 mg.), identified by m. p. and mixed m. p.

Reduction of the 5 : 6-*Dibromocholestanes.*—(*a*) 5 : 6β-Dibromocholestane (see Barton and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 1066) (300 mg.) was reduced as described above, but with twice the quantity of lithium. Crystallisation of the total product {195 mg., 93%; negative Beilstein test; $[\alpha]_D$ −49° (*c*, 1·64)} from chloroform–methanol gave cholest-5-ene, m. p. and mixed m. p. 90—91°, $[\alpha]_D$ −50° (*c*, 1·47).

(*b*) 5 : 6α-Dibromocoprostane (see Barton and Miller, *loc. cit.*) (200 mg.) was reduced as under (*a*). The total product (129 mg., 92%) gave a negative Beilstein test and had $[\alpha]_D$ −25° (*c*, 1·67). The material (114 mg.) was treated with ethereal perphthalic acid at 0° for 63 hr. The product in chloroform (5 ml.) was treated with dry hydrogen chloride at room temperature for 20 min. and the resulting oil (94 mg.) was chromatographed over alumina. Elution with light petroleum (b. p. 40—60°) afforded cholestane (27 mg.; tetranitromethane test negative), m. p. (from chloroform–methanol) 79—80°, undepressed on admixture with an authentic specimen. The perphthalic acid uptake corresponded to 69% of cholest-5-ene. The observed rotation ($[\alpha]_D$ −25°; see above) for the total product would correspond to 62% of cholest-5-ene and 38% of cholestane.

We thank the Government Grants Committee of the Royal Society, the Central Research Fund of London University, and Imperial Chemical Industries Limited for financial assistance. We are grateful to Messrs. Glaxo Laboratories Limited for generous gifts of chemicals. One of us (C. H. R.) is indebted to the Nuffield Foundation for a maintenance grant.

BIRKBECK COLLEGE, LONDON, W.C.1.

[*Received, April 23rd*, 1954.]