Introduction of the 11-*Oxo- and the* 11α-*Hydroxy-group into Ring* C *Unsubstituted Steroids. Part IX.* The Epoxides of* $\Delta^{7:9(11)}$-5α-*Hydroxysapogenins.*

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Diosgenin (I) has been converted by known reactions into 9α : 11α-epoxy-22*a*-spirost-7-en-3β : 5α-diol (V*b*) which on oxidation and subsequent combined dehydration-rearrangement afforded 22*a*-spirosta-4 : 8-dien-3 : 11-dione (VIII). The preparation and some transformation products of 7α : 8α : 9α : 11α-diepoxy-22*a*-spirostan-3β : 5α-diol (IX) are described.

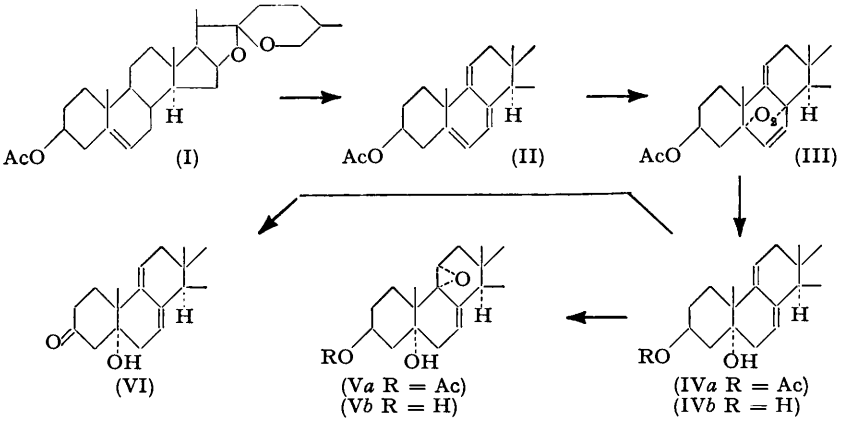
With one exception (Laubach, Schreiber, Agnello, Lightfoot, and Brunings, *J. Amer. Chem. Soc.*, 1953, **75**, 1514) all the chemical methods for the introduction of an 11-oxygen function into steroids unsubstituted in ring C involve oxidation of a 7 : 9(11)-diene (cf. Hems, *J. Pharm. Pharmacol.*, 1953, **5**, 409; Spring, *Progress in Org. Chem.*, 1953, **2**, 104; Djerassi, *Vitamins and Hormones*, 1953, **11**, 205; Rosenkranz and Sondheimer, *Fortschr. Chemie Org. Naturstoffe*, 1953, **10**, 274). Two of these approaches in the ergosterol series proceed through epidioxides (11 : 14, Laubach *et al.*, *loc. cit.*; 5 : 8, Bladon, Clayton, Greenhalgh, Henbest, Jones, Lovell, Silverstone, Wood, and Woods, *J.*, 1952, 4883). The latter method possesses the advantage of retaining a 5α-hydroxyl group until the last step (Bladon, Henbest, Jones, Lovell, and Woods, *J.*, 1954, 125), thus simplifying considerably the ultimate elaboration of the Δ^4-3-oxo-moiety which otherwise has to be performed in a somewhat round-about fashion (Rosenkranz, Djerassi, Yashin, and Pataki, *Nature*, 1951, **168**, 28).

At an early stage of our work on the partial synthesis of adrenal cortical hormones *via* 11-oxygenated sapogenins, we prepared the 5α : 8α-epidioxide (III) of 3β-acetoxy-22*a*-spirosta-5 : 7 : 9(11)-triene (II), itself readily available from diosgenin (I) (Rosenkranz, Romo, Batres, and Djerassi, *J. Org. Chem.*, 1951, **16**, 298). Subsequent manipulations with this substance, however, yielded erratic results and this approach was abandoned in favour of alternative routes (Djerassi and Rosenkranz, *Ciba Foundation Colloquia on Endocrinology*, 1953, **7**, 79; Rosenkranz, Sondheimer, Mancera, Pataki, Ringold, Romo, Djerassi, and Stork, *Recent Progress in Hormone Research*, 1953, **8**, 1). When we were informed by Prof. E. R. H. Jones (cf. Henbest and Jones, *Ciba Foundation Colloquia on Endocrinology*, 1953, **7**, 39) of the smooth reduction of 3β-acetoxy-5α : 8α-epidioxyergosta-6 : 9 : 22-triene by means of a Raney nickel catalyst to the corresponding 5α-hydroxy-7 : 9(11) : 22-triene (Bladon *et al.*, *loc. cit.*) it appeared of interest to apply these conditions to the corresponding epidioxide (III) in the sapogenin series, and the present paper describes its preparation and some subsequent transformation products.

The epidioxide (III) was prepared essentially according to the method of Windaus and Linsert (*Annalen*, 1928, **465**, 148; cf. Bladon *et al.*, *loc. cit.*). Owing to the high altitude at which the reaction was carried out (7500 feet) no irradiation apart from sunlight was necessary and an alcoholic solution of the triene (II) plus eosin, standing in open vessels, furnished in good yield the desired epidioxide (III). Its structure was adduced from its physical properties (absence of selective absorption in the ulra-violet region), by analogy with the corresponding ergosterol derivative, and by its subsequent reactions. When shaken with Raney nickel in an atmosphere of hydrogen, the epidioxide was smoothly reduced to the 3β-acetoxy-5α-hydroxy-7 : 9(11)-diene (IV*a*); mild hydrolysis then gave the 3 : 5-dihydroxy-diene (IV*b*). The ultra-violet absorption spectra of both compounds (IV*a* and *b*) confirmed their formulation as conjugated dienes. Moreover, since acetylation of the diol (IV*b*) regenerated the original monoacetate (IV*a*), no rearrangement could have taken place during the hydrolysis.

* Part VIII, *J. Amer. Chem. Soc.*, 1953, **75**, 3505.

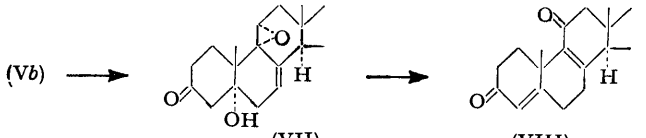
Treatment of the diol (IV*b*) with one mol. of monoperphthalic acid gave (in over 90% yield) the 9α : 11α-monoepoxide (V*b*) which showed no selective ultra-violet absorption. In a similar manner, epoxidation of the 3-acetoxy-5-hydroxy-7 : 9(11)-diene (IV*a*) produced the expected 3-acetoxy-9α : 11α-epoxide (V*a*) which on mild hydrolysis furnished the 3 : 5-dihydroxy-epoxide (V*b*). Completion of the interconversions was accomplished by the acetylation of the 3 : 5-dihydroxy-epoxide (V*b*) back to the corresponding 3-acetoxy-compound (V*a*), again demonstrating that no rearrangement had



taken place during the hydrolysis of the acetoxy-monoepoxide. The formulation of the monoepoxides as the 9α : 11α-isomers is assumed by analogy with the previous work on the oxidations of $\Delta^{9(11)}$-steroids (Bladon, Henbest, Jones, Wood, Eaton, and Wagland, *J.*, 1953, 2916 and references cited therein), and confirmed by their subsequent reactions. Oxidation of the diol (IV*b*) with the pyridine–chromic anhydride complex (Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422) resulted in the formation of the 3-oxo-compound (VI) without concomitant dehydration and this experiment was used as a model for subsequent oxidations in the epoxide series.

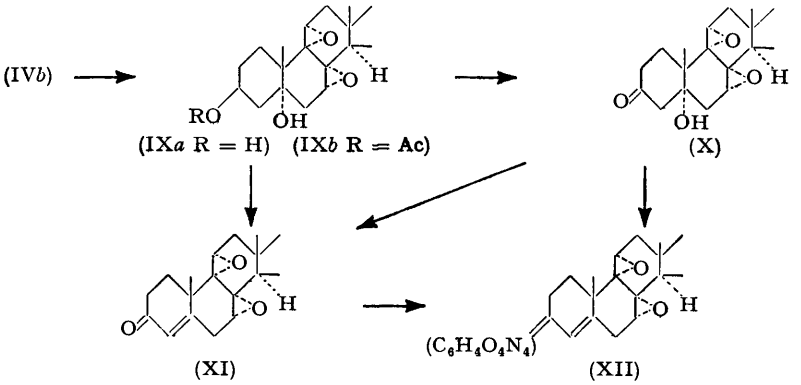
Introduction of the 3-oxo-Δ^4-system was then attempted since it seemed possible that hydrogenation of such an unsaturated 3-oxo-α-epoxide might produce a dihydro-ketone of the 5β-series thus allowing the easy re-introduction of the Δ^4-double bond at a later stage. However, Oppenauer oxidation of the dihydroxy-monoepoxide (V*b*) afforded only highly coloured oils. As it seemed possible that dehydration of the 5α-hydroxy-3-oxo- to the 3-oxo-Δ^4-system could occur under conditions similar to those used in the conversion of Δ^7-9α : 11α-epoxides into the corresponding unsaturated 11-ketones (*i.e.*, treatment with the boron trifluoride–ether complex; Heusser, Eichenberger, Kurath, Dällenbach and Jeger, *Helv. Chim. Acta*, 1951, **34**, 2106), oxidation of the diol monoepoxide (V*b*) to the 5α-hydroxy-3-oxomonoepoxide (VII) was attempted with a view to combining the dehydration and the rearrangement into one operation. The use of boron trifluoride as a dehydrating agent (in acetic acid solution) has been described by Davey, Halsall, Jones, and Meakins (*J.*, 1951, 2696) who, by treatment of 18β-oleanane-3β : 19β : 28-triol 3 : 28-diacetate obtained an unsaturated diacetate indicating that the loss of the axial hydroxyl group had occurred by *trans*-elimination. The required selective oxidation of the 3β-hydroxyl group of the monoepoxy-diol (V*b*) was carried out with the pyridine–chromic anhydride complex as described for the model compound but optimum yields were obtained only when a large excess of pyridine was used. The product, 9α : 11α-epoxy-3-oxo-22*a*-spirost-7-en-5α-ol (VII), on treatment for 2 minutes with two mols. of boron trifluoride–ether complex in refluxing benzene, gave 22*a*-spirosta-4 : 8-dien-3 : 11-dione (VIII), the structure of which was proved as follows. The infra-red absorption spectrum showed only *one* band in the carbonyl region, the position of which (at 1665 cm.$^{-1}$) indicated the presence of one or more αβ-unsaturated ketonic systems. The high intensity of the peak suggested that more than one such system was present, a conclusion confirmed by the

preparation of the 3-mono-2 : 4-dinitrophenylhydrazone which still showed a peak in the absorption spectrum (at 1665 cm.$^{-1}$) though of reduced intensity. The analyses of the diketone and its 3-hydrazone together with their ultra-violet absorption spectra also supported the formulation (VIII). An investigation of the catalytic and chemical reduction products of this compound is under way.



(VII) (VIII)

The preparation of diepoxides from 7 : 9(11)-dienes has been described by two groups (Bladon *et al.*, *loc. cit.*; Chamberlin, Ruyle, Erickson, Chemerda, Aliminosa, Erickson, Sita, and Tishler, *J. Amer. Chem. Soc.*, 1953, **75**, 3477) but subsequent transformations have been few. Since the diepoxides are, in general, more stable to hydrolytic rearrangements than the corresponding monoepoxides it was expected that the 3-oxo-Δ^4-system could be introduced by standard methods. Preparation of the 3 : 5-dihydroxy-7α : 8α-9α : 11α-diepoxide (IX*a*) was accomplished by oxidation of the diene-diol (IV*b*) with two mols. of monoperphthalic acid, and subsequent Oppenauer oxidation gave the required 7α : 8α-9α : 11α-diepoxy-22α-spirost-4-en-3-one (XI). The infra-red and ultra-violet absorption spectra of the unsaturated ketone and its 2 : 4-dinitrophenylhydrazone indicated that only one unsaturated chromophore was present and therefore that the diepoxy-grouping had remained intact.



(IX*a* R = H) (IX*b* R = Ac) (X)

(XI) (XII)

Oxidation of the diepoxy-diol (IX*a*) with the pyridine–chromic anhydride complex again furnished a 5α-hydroxy-3-oxo-compound (X) which by dehydration with aluminium *iso*propoxide in toluene, or by preparation of the semicarbazone followed by cleavage with pyruvic acid, led to the 7α : 8α-9α : 11α-diepoxy-22a-spirost-4-en-3-one (XI) previously prepared. As was to be expected, both (X) and (XI) reacted with 2 : 4-dinitrophenylhydrazine to give the same hydrazone (XII). The conversion of (XI) into cortisone will be reported elsewhere (Lewis and Djerassi, *J. Amer. Chem. Soc.*, 1954, in the press).

Experimental

M. p.s were determined on a Kofler block, rotations were measured in chloroform solution in a 1-dm. tube at room temperature (20—25°), and ultra-violet light absorption measurements were made in ethanol unless otherwise stated. Infra-red spectra were determined with a Baird Associates model B double-beam recording spectrophotometer with sodium chloride optics.

3β-*Acetoxy*-5α : 8α-*epidioxy*-22a-*spirosta*-6 : 9(11)-*diene* (III).—A solution of 3β-acetoxy-22*a*-spirosta-5 : 7 : 9(11)-triene (II) (20 g.) and eosin (0·044 g.) in dry ethanol (4·4 l.) was allowed to stand in open vessels in direct sunlight for 5 hr., after which the solvent was removed and the

residue crystallised from chloroform–methanol, to give 3β-*acetoxy*-5α : 8α-*epidioxy*-22a-*spirosta*-6 : 9(11)-*diene* (III) (15·1 g.), m. p. 233—235°, $[\alpha]_D$ +15° (Found : C, 71·7; H, 8·4. $C_{29}H_{40}O_6$ requires C, 71·9; H, 8·3%). Only end-absorption was shown in the ultra-violet region.

3β-*Acetoxy*-22a-*spirosta*-7 : 9(11)-*dien*-5α-*ol* (IV*a*).—A solution of the epidioxide acetate (III) (3·0 g.) in dioxan (75 c.c.) was hydrogenated in the presence of Raney nickel (*ca.* 3 c.c. of thick sludge prepared according to Pavlic and Adkins, *J. Amer. Chem. Soc.*, 1946, **68**, 1471, and pre-reduced in dioxan). The uptake of hydrogen was 230 c.c. (corresponding to 2·2 mols. at 570 mm.), after which the catalyst was filtered off, the filtrate diluted with water, and the white precipitate collected, washed, and dried, to yield 2·8 g. of the crude product, $\lambda_{max.}$ 242 mμ (ε 13,800). Crystallisation from chloroform–hexane gave 3β-*acetoxy*-22a-*spirosta*-7 : 9(11)-*dien*-5α-*ol* (IV*a*) (2·41 g.), m. p. 263—265°, $[\alpha]_D$ −6°, $\lambda_{max.}$ 242 mμ (ε 15,200), $\nu_{max.}$ (in $CHCl_3$) 1736 cm.$^{-1}$ (Found : C, 73·7; H, 8·9. $C_{29}H_{42}O_5$ requires C, 74·0; H, 9·0%).

22a-*Spirosta*-7 : 9(11)-*dien*-3β : 5α-*diol* (IV*b*).—To a solution of the diene-acetate (IV*a*) (0·5 g.) in dioxan (30 c.c.) and methanol (200 c.c.) was added a solution of potassium carbonate (0·8 g.) in water (10 c.c.), and the mixture refluxed for 1 hr. Removal of one-half of the solvent under reduced pressure followed by precipitation of the steroid with water led to a crude product (0·47 g.), m. p. 205—210°, which on crystallisation from methanol gave 22a-*spirosta*-7 : 9(11)-*dien*-3β : 5α-*diol* (IV*b*), m. p. 214—216°, $[\alpha]_D$ ±0°, $\lambda_{max.}$ 242 mμ (ε 14,600), $\nu_{max.}$ (in $CHCl_3$) 3470, 3650 cm.$^{-1}$ (Found : C, 75·4; H, 9·5. $C_{27}H_{40}O_4$ requires C, 75·7; H, 9·4%).

Acetic anhydride–pyridine (room temperature, overnight) regenerated the diene-acetate (IV*a*), m. p. 261—263°, $[\alpha]$ −8° (infra-red absorption spectrum identical with that of the diene-acetate previously prepared).

3β-*Acetoxy*-9α : 11α-*epoxy*-22a-*spirost*-7-*en*-5α-*ol* (V*a*).—A solution of 3β-acetoxy-22*a*-spirosta-7 : 9(11)-dien-5α-ol (IV*a*) (4·0 g.) in chloroform (30 c.c.) was treated with monoperphthalic acid (1 equiv.) in ether and kept at room temperature for 2 days. The needles which had been deposited were filtered off, washed with aqueous sodium hydrogen carbonate and then water, and dried, yielding the crude monoepoxide acetate (3·1 g.), m. p. 295—298°. The chloroform–ether filtrate was washed with sodium hydrogen carbonate solution and water and on evaporation gave an additional 0·5 g. of crude monoepoxide acetate, m. p. 283—286°. Crystallisation of either product from methanol afforded the same 3β-*acetoxy*-9α : 11α-*epoxy*-22a-*spirost*-7-*en*-5α-*ol* (V*a*), m. p. 299—301°, $[\alpha]_D$ −42°, $\nu_{max.}$ (in $CHCl_3$) 1730 cm.$^{-1}$ having no selective absorption in the ultra-violet region (Found : C, 71·7; H, 9·0. $C_{29}H_{42}O_6$ requires C, 71·6; H, 8·7%).

9α : 11α-*Epoxy*-22a-*spirost*-7-*en*-3β : 5α-*diol* (V*b*).—(a) *By hydrolysis of* 3β-*acetoxy*-9α : 11α-*epoxy*-22a-*spirost*-7-*en*-5α-*ol* (V*a*). The hydrolysis of the monoepoxy-acetate (V*a*) was carried out as described for the preparation of 22*a*-spirosta-7 : 9(11)-dien-3β : 5α-diol (IV*b*) and afforded 9α : 11α-*epoxy*-22a-*spirost*-7-*en*-3β : 5α-*diol* (V*b*) in 85% yield. The analytical sample after crystallisation from acetone had m. p. 226—228°, $[\alpha]_D$ −60° (no selective ultra-violet absorption), $\nu_{max.}$ (in $CHCl_3$) 3510, 3690 cm.$^{-1}$ (Found : C, 72·8; H, 9·2. $C_{27}H_{40}O_5$ requires C, 72·9; H, 9·1%).

(b) *By monoperphthalic acid oxidation of* 22a-*spirosta*-7 : 9(11)-*dien*-3β : 5α-*diol* (IV*b*). A solution of the diene-diol (IV*b*) (3·2 g.) in methylene chloride (50 c.c.) was treated with monoperphthalic acid in ether (10 c.c. of a 1·5N-solution) and kept for 12 hr. at room temperature. Dilution with methylene chloride (100 c.c.), and washing with dilute sodium hydrogen carbonate solution and water, followed by evaporation, gave the crude epoxide (3·1 g.), m. p. 221—225°, which on crystallisation from acetone had m. p. 225—227°, and an infra-red absorption curve identical with that of the mono-epoxy-diol (V*b*) prepared by method (a).

Acetylation with acetic anhydride–pyridine (room temp., overnight) gave the monoepoxy-acetate (V*a*), m. p. 298—300°, with an infra-red absorption curve indistinguishable from that of the sample previously prepared.

9α : 11α-*Epoxy*-3-*oxo*-22a-*spirost*-7-*en*-5α-*ol* (VII).—Chromic anhydride (1·5 g.) was dissolved in pyridine (150 c.c.), cooled in ice-water, and added to a solution of the monoepoxy-diol (V*b*) (1·44 g.) in pyridine, and the whole was set aside for 14 hr. at room temperature. Dilution with much water followed by extraction with ether, washing with very dilute hydrochloric acid and water, evaporation, and crystallisation from acetone–hexane furnished 9α : 11α-*epoxy*-3-*oxo*-22a-*spirost*-7-*en*-5α-*ol* (1·2 g.) (VII), m. p. 236—238°, $[\alpha]_D$ −40°, no selective absorption in the ultra-violet, $\nu_{max.}$ (in $CHCl_3$) 3420, 1702 cm.$^{-1}$ (Found : C, 72·8; H, 8·6. $C_{27}H_{38}O_5$ requires C, 73·3; H, 8·65%).

22a-*Spirosta*-4 : 8-*dien*-3 : 11-*dione* (VIII).—A solution of the keto-monoepoxide (VII) (0·5 g.) was dissolved in dry benzene (100 c.c.), and solvent (10 c.c.) was distilled off to ensure anhydrous conditions. Boron trifluoride–ether (0·5 c.c.) was then added and the mixture

refluxed for 2 min., whereafter the reaction was immediately stopped by addition of water. The organic layer was diluted with ether, washed with water, and evaporated, to yield a yellow semisolid material (0·46 g.) which on chromatography on deactivated alumina (neutral, Brockmann III) and elution with benzene–ether (9 : 1) followed by crystallisation from acetone–hexane gave 22a-*spirosta*-4 : 8-*dien*-3 : 11-*dione* (VIII) (0·135 g.), m. p. 205—206°, $[\alpha]_D$ +289°; $\lambda_{max.}$ 236—242 mμ (ε 20,800), $\nu_{max.}$ (in $CHCl_3$) 1665 cm.$^{-1}$ (Found: C, 76·25; H, 8·25. $C_{27}H_{36}O_4$ requires C, 76·4; H, 8·55%). The 2 : 4-*dinitrophenylhydrazone* (prepared according to Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003), after crystallisation from chloroform–methanol, had m. p. 258—260°, $\lambda_{max.}$ (in $CHCl_3$) 389 mμ (ε 29,800) $\nu_{max.}$ (in $CHCl_3$) 1665 cm.$^{-1}$ (Found: N, 9·8. $C_{33}H_{40}O_7N_4$ requires N, 10·0%).

5α-*Hydroxy*-22a-*spirosta*-7 : 9(11)-*dien*-3-*one* (VI).—Chromic anhydride–pyridine oxidation of the dien-diol (IV*b*) (1·0 g.) was carried out as described for the preparation of the keto-monoepoxide (VII) and afforded, after crystallisation from acetone–hexane, 5α-*hydroxy*-22a-*spirosta*-7 : 9(11)-*dien*-3-*one* (VI) (0·91 g.), m. p. 248—250°, [α] +10°, $\lambda_{max.}$ 243 mμ (ε 15,900), $\nu_{max.}$ (in $CHCl_3$) 3450, 3640, 1705 cm.$^{-1}$ (Found: C, 75·8; H, 8·8. $C_{27}H_{38}O_4$ requires C, 76·0; H, 9·0%).

7α : 8α-9α : 11α-*Diepoxy*-22a-*spirostan*-3β : 5α-*diol* (IX*a*).—A solution of the dien-diol (IV*b*) (1·0 g.) in methylene chloride (15 c.c.) was treated with ethereal monoperphthalic acid (10 c.c. of a 1·05N-solution) and kept at room temperature overnight. Working up as described for the preparation of the monoepoxy-diol (V*b*) and crystallisation from acetone gave 7α : 8α-9α : 11α-*diepoxy*-22a-*spirostan*-3β : 5α-*diol* (IX*a*) (0·91 g.), m. p. 277—280°, $[\alpha]_D$ −72°, no selective absorption in the ultra-violet, $\nu_{max.}$ (in $CHCl_3$) 3500, 3680 cm.$^{-1}$ (Found: C, 70·4; H, 8·9. $C_{27}H_{40}O_6$ requires C, 70·4; H, 8·75%).

Acetylation by acetic anhydride–pyridine gave 3β-*acetoxy*-7α : 8α-9α : 11α-*diepoxy*-22a-*spirostan*-5α-*ol* (IX*b*), m. p. 340—344°, $[\alpha]_D$ −59°, no selective absorption in the ultra-violet, $\nu_{max.}$ (in $CHCl_3$) 3450, 1730, 1243 cm.$^{-1}$ (Found: C, 69·2; H, 8·1. $C_{29}H_{42}O_7$ requires C, 69·3; H, 8·4%).

7α : 8α-9α : 11α-*Diepoxy*-5α-*hydroxy*-22a-*spirostan*-3-*one* (X).—The diepoxy-diol (IX*a*) (0·5 g.) in pyridine (15 c.c.) was treated with chromic anhydride (0·5 g.) in pyridine (50 c.c.) as described for the preparation of the keto-monoepoxide (VII). The resulting 7α : 8α-9α : 11α-*diepoxy*-5α-*hydroxy*-22a-*spirostan*-3-*one* (X) (0·44 g.) crystallised from methanol, and had m. p. 282—284°, $[\alpha]_D$ −52°, no selective absorption in the ultra-violet, $\nu_{max.}$ (in $CHCl_3$) 3410, 1705 cm.$^{-1}$ (Found: C, 70·4; H, 8·1. $C_{27}H_{38}O_6$ requires C, 70·7; H, 8·35%).

7α : 8α-9α : 11α-*Diepoxy*-22a-*spirost*-4-*en*-3-*one* (XI).—(a) *By Oppenauer oxidation of the diepoxy-diol* (IX*a*). A solution of the diepoxy-diol (IX*a*) (0·17 g.) in toluene (17 c.c.) and *cyclo*hexanone (0·17 c.c.) was distilled until 4 c.c. of distillate had been collected. Aluminium *iso*propoxide (0·4 g.) in toluene (3 c.c.) was added and the mixture slowly distilled for 30 min., 5 c.c. of distillate being then obtained. The inorganic material was taken into solution with sodium potassium tartrate solution, the whole was diluted with ether, and the ethereal layer washed with water and evaporated under reduced pressure. The last traces of solvent were removed azeotropically with water. The resulting sticky solid (0·17 g.) was crystallised from acetone–hexane, to give 0·08 g. of 7α : 8α-9α : 11α-*diepoxy*-22a-*spirost*-4-*en*-3-*one* (XI), m. p. 262—264°, $[\alpha]_D$ +46°, $\lambda_{max.}$ 239 mμ (ε 14,600), $\nu_{max.}$ (in $CHCl_3$) 1665 cm.$^{-1}$ with no hydroxyl band (Found: C, 73·8; H, 8·2. $C_{27}H_{36}O_5$ requires C, 73·6; H, 8·2%).

(b) *By dehydration of the keto-diepoxide* (X) *with aluminium* iso*propoxide in toluene.* A solution of the keto-diepoxide (X) (0·2 g.) in toluene (20 c.c.) was distilled until 2 c.c. of distillate had been collected. A solution of aluminium *iso*propoxide (0·4 g.) in toluene (5 c.c.) was added and distillation continued for 20 min., whereafter sodium potassium tartrate solution was added and the product worked up as described in the Oppenauer oxidation to give the ketone (XI) (0·19 g.), m. p. 261—263°, identical with the previously prepared sample.

(c) *By cleavage of the semicarbazone of the keto-diepoxide* (X). A solution of the keto-diepoxide (X) (0·1 g.) in pyridine (10 c.c.) and ethanol (10 c.c.) was heated on a steam-bath for 1½ hr. with semicarbazide hydrochloride (0·05 g.). Dilution with water and extraction with ether gave a semisolid semicarbazone which was cleaved directly (18 hr., room temperature) by being dissolved in ethanol (10 c.c.), acetic acid (1 c.c.), 50% pyruvic acid (1 c.c.) (cf. Kritchevsky, Garmaise, and Gallagher, *J. Amer. Chem. Soc.*, 1952, **74**, 486). Dilution with water, extraction with ether, washing with dilute sodium hydroxide solution (5%) and water, followed by evaporation and crystallisation from acetone–hexane, gave the ketone (XI) (0·08 g.), m. p. 260—263°.

The 2 : 4-*dinitrophenylhydrazone* (XII) prepared from (XI) crystallised from chloroform–methanol and had m. p. 273—275°, $\lambda_{max.}$ (in $CHCl_3$) 387 mμ (ε 28,900) (Found: N, 9·3.

$C_{33}H_{40}O_8N_4$ requires N, 9·0%). The same hydrazone was obtained from 7α : 8α-9α : 11α-diepoxy-5α-hydroxy-22*a*-spirostan-3-one (X) by the standard acetic acid procedure (Djerassi, *loc. cit.*).

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