10. *Steroids and Related Compounds. Part V. Steroid Diosphenols.*

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Isomeric enolic forms of steroid diosphenols (α-diketones) are theoretically possible. By various methods we have now obtained from Δ^5-cholestene-3 : 4-diol (V; R = H) two distinct modifications (forms *A* and *B*) of the unsaturated diosphenol Δ^5-cholestene-3 : 4-dione. The labile form *A* has been characterised as the *diketo*-modification (I), and form *B* as the stable *mono-enol* form (III). In the case of the saturated diosphenol cholestane-3 : 4-dione, also obtained from the unsaturated diol (V), only one form was found to exist, probably representing the stable *mono-enol* modification (IX).

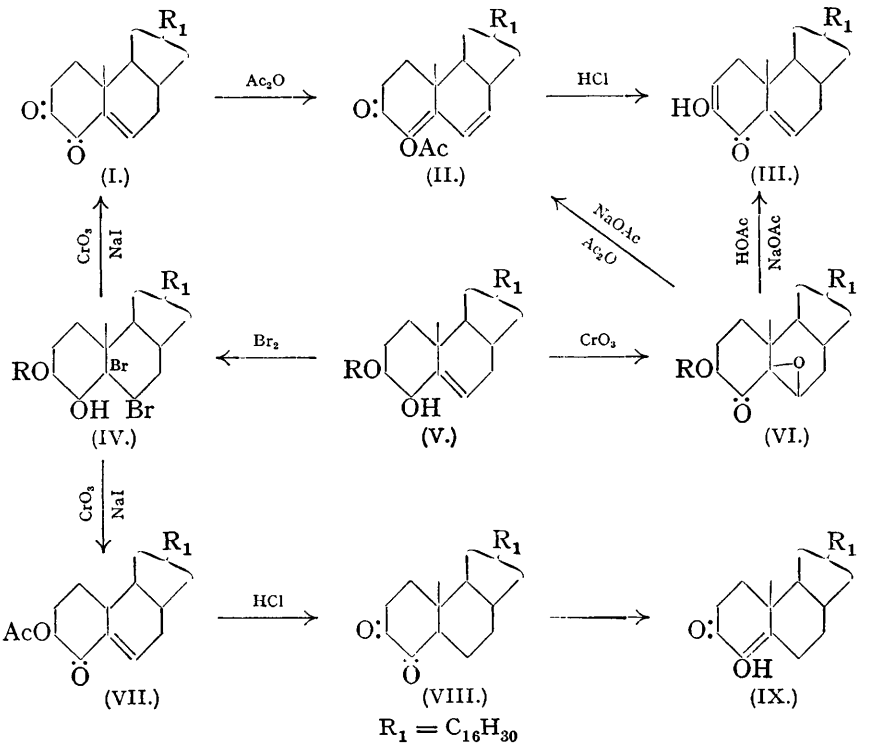
Although steroid α-diketones are to be expected on theoretical grounds to react like diosphenols and to exist in isomeric enolic forms, the existence of such forms has so far been demonstrated only in the case of the saturated cholestane-2 : 3-dione (Stiller and Rosenheim, J., 1938, 353). Starting from Δ^5-cholestene-3 : 4-diol (V; R = H), we have now obtained by different methods two diosphenols, Δ^5-cholestene-3 : 4-dione and cholestane-3 : 4-dione, of which only the former was found to exist in two distinct forms (*A* and *B*). Form *A* is labile and easily convertible into the stable form *B*, the reaction being non-reversible. This unsaturated diosphenol differs therefore characteristically from the saturated diosphenol cholestane-2 : 3-dione, the two enolic forms of which are interconvertible (Stiller and Rosenheim, *loc. cit.*).

Δ^5-*Cholestene*-3 : 4-*dione, form* A (I), m. p. 136°, is obtained by means of the following series of reactions : *cis*-Δ^5-Cholestene-3 : 4-diol dibromide (IV; R = H) (Rosenheim and Starling, J., 1937, 377) is oxidised with chromic acid at room temperature, and the oxidation product debrominated with sodium iodide. As a diosphenol the reaction product forms a phenolic potassium salt, which is easily isolated owing to its insolubility in 20% aqueous potassium hydroxide and in ether. The diosphenol is liberated from its potassium salt by acetic acid, and its constitution as Δ^5-cholestene-3 : 4-dione established by the following evidence : The substance gives a purple coloration with ferric chloride and is further characterised as an α-diketone by its ready reaction in alcoholic solution with *o*-phenylenediamine to yield a quinoxaline derivative. On oxidation with hydrogen peroxide the unsaturated dicarboxylic acid $C_{27}H_{44}O_4$ (Diels's acid), m. p. 290°, is obtained. The *mono*-2 : 4-*dinitrophenylhydrazone*, m. p. 255°, is obtained by treatment of form *A* with Brady's reagent. Further, as a diosphenol, the substance can exist in the mono-enol modification and yields a mono-acetate, which must be formulated as 4-acetoxy-$\Delta^{4:6}$-cholestadien-3-one (II), since it is identical with the substance of this constitution which is obtained by debromination of 4 : 5 : 6-tribromocholestan-3-one with potassium acetate (Inhoffen, *Ber.*, 1936, **69**, 1702).

Form *B* of Δ^5-cholestene-3 : 4-dione (III), m. p. 160°, is obtained either by warming an acetic acid solution of form *A* with mineral acid or by hydrolysis of the above-described enol-acetate. An alternative and somewhat simpler route leads in excellent yield from the 3 : 4-diol (V; R = H) directly to form *B*. Mild oxidation of 3-*acetoxy*-Δ^5-*cholesten*-4-*ol* (V; R = Ac) with chromic acid at room temperature gives a neutral compound, $C_{29}H_{46}O_4$, m. p. 174°, which we formulate as 3-*acetoxycholestan*-4-*one*-5 : 6-*oxide* (VI; R = Ac). The function of the newly introduced oxygen atom as a " $C_{5:6}$ oxide " is in accord with the saturated nature of the compound, with the absence of hydroxylic groups (negative Zerewitinoff determination), and with the transparency of the compound to ultra-violet light. Oxidation of 3-benzoyloxy-Δ^5-cholesten-4-ol (V; R = Bz) under the same conditions as described for the monoacetate gives the corresponding 3-*benzoyloxycholestan*-4-*one*-5 : 6-*oxide* (VI; R = Bz), $C_{34}H_{48}O_4$, m. p. 186°. The simultaneous formation of an oxide ring on the ethylenic linkage of an αβ-unsaturated steroid alcohol on oxidation has also been observed in Part III (Petrow, J., 1939, 998). Form *B* of the unsaturated diosphenol is obtained from the oxide either by heating with acetic acid and sodium acetate or by hydrolysis with hydrochloric acid in benzene–alcoholic solution,

the reaction evidently involving opening of the oxide ring, followed by loss of two molecules of water and intramolecular rearrangement.

Form *B* shows an intense ultra-violet absorption at 3200 A., and yields the same *mono-2 : 4-dinitrophenylhydrazone*, m. p. 255°, as form *A* on treatment with Brady's reagent. The potassium salt is obtained on shaking an ethereal solution of the diosphenol with 20% potassium hydroxide solution; form *B* is regenerated on treatment with acetic acid. On oxidation with hydrogen peroxide it yields the known 7-keto-" Diels's acid " (Windaus, *Ber.*, 1908, **41**, 614; Butenandt *et al.*, *Ber.*, 1936, **69**, 2289). Form *B* of the diosphenol is evidently identical with the substance obtained by debromination of 4 : 4′ : 5 : 6-tetrabromocholestan-3-one (Butenandt and Schramm, *loc. cit.*) and previously described by Inhoffen (*loc. cit.*).



The two forms of the unsaturated diosphenol show characteristic differences in their behaviour towards *o*-phenylenediamine and on acetylation, which enable a decision to be made as to their constitutional formulæ. Both forms yield the same quinoxaline derivative, m. p. 175°, but whereas form *A* reacts with *o*-phenylenediamine on simple warming of the components in alcoholic solution, form *B* fails to react under these conditions and requires fusion at 135° of the dry mixture of the components. On acetylation form *A* easily yields the enol-acetate (II), but form *B* fails to give an acetate on treatment with acetic anhydride (with or without sodium acetate) (cf. Inhoffen, *loc. cit.*). Further, the two forms yield different enolic potassium salts, which on treatment with acetic acid regenerate the forms *A* and *B* respectively. This behaviour justifies the formulation of form *A* as the *diketo*-modification (I), its enol-acetate as (II), and form *B* as $\Delta^{2:5}$-cholestadien-3-ol-4-one (III), one of the possible mono-enol isomerides of (I).

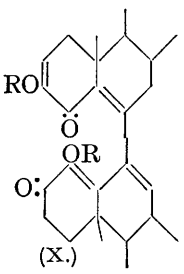
The saturated diosphenol, cholestane-3 : 4-dione, is obtained in excellent yield from the monoacetate of the unsaturated 3 : 4-diol (V; R = Ac) by the following series of reactions: Treatment of (V; R = Ac) in chloroform solution with bromine–acetic acid gives the *dibromide* (IV; R = Ac), m. p. 115°, which passes on oxidation with chromic acid at room temperature, followed by debromination of the intermediate product with

sodium iodide, into 3-*acetoxy*-Δ^5-*cholesten*-4-*one* (VII), $C_{29}H_{46}O_3$, m. p. 124°. This keto-acetate readily enolises on heating with acetic anhydride–sodium acetate to yield the enol-diacetate, 3 : 4-*diacetoxy*-$\Delta^{3:5}$-*cholestadiene*, $C_{31}H_{48}O_4$, m. p. 128°. The constitution (VII) assigned to the monoacetate is in conformity with its ultra-violet absorption spectrum which shows a band at 2800 A. characteristic of $\alpha\beta$-unsaturated ketones. The unsaturated keto-alcohol, liberated on acid or alkaline hydrolysis from its acetate, is unstable and passes smoothly into the saturated diketone, cholestane-3 : 4-dione, m. p. 150° (VIII), or (IX).

We have been unable to obtain an isomeric form of the saturated diosphenol by the methods successful in the case of the unsaturated analogue and of cholestane-2 : 3-dione (Rosenheim and Stiller, *loc. cit.*). Regeneration from the phenolic potassium salt by acetic acid, and alkaline hydrolysis of its enol-acetate or of (VII), yield the same product, m. p. 150°. This fact suggests that only one of the carbonyl groups, presumably the one at C_4, is able to undergo enolisation and that the diosphenol exists in the stable enolic form, Δ^4-cholesten-4-ol-3-one (IX), only. This conclusion is in agreement with the failure of the substance to react with *o*-phenylenediamine in alcoholic solution, fusion of the components at 120° being necessary for the formation of the quinoxaline derivative.

The diosphenol was characterised by a quinoxaline derivative, m. p. 209°, a *mono*-2 : 4-*dinitrophenylhydrazone*, m. p. 252°, and by a mono-enol acetate, m. p. 103°. On oxidation with alkaline hydrogen peroxide it passed into cholestane-C_3 || C_4-diacid (dihydro-Diels's acid), characterised by preparation of the dimethyl ester. Cholestane-3 : 4-dione has previously been obtained in small yield by debromination of 2 : 4-dibromocholestan-3-one with potassium benzoate (Inhoffen, *Ber.*, 1937, **70**, 1695) or with potassium acetate (Butenandt *et al.*, *Ber.*, 1936, **69**, 2779; no experimental details given).

Incidentally some unusual reactions of the above described oxide (VI) may be briefly recorded. On treatment with acetic anhydride in the presence of sodium acetate the enol-acetate (II) is obtained in excellent yield, a reaction which may be explained by assuming that after the initial opening of the oxide ring either a migration of the acetyl group from C_3 to C_4 (cf. Inhoffen, *Ber.*, 1937, **70**, 1695) or an allylic rearrangement has occurred. Alkaline hydrolysis of (VI) leads to the formation of a *dimeric product*, $C_{54}H_{84}O_4$, m. p. 240°, characterised by a *mono*-2 : 4-*dinitrophenylhydrazone*, m. p. 248°. This compound has been assigned the constitution of a $\Delta^{2:5}$-*cholestadien*-3-*ol*-4-*onyl*-6 : 6′-($\Delta^{4':6'}$-*cholestadien*-4′-*ol*-3′-*one*) (X; R = H) on the following evidence : (*a*) the compound contains two active hydrogen atoms, shown both by a Zerewitinoff determination and by the preparation of a *diacetate* (X; R = Ac), $C_{58}H_{88}O_6$, m. p. 206°, and (*b*) molecular-weight determinations of the substance and its diacetate prove them to be dimerides.



(X.)

Experimental.

Microanalyses were made by Dr. G. Weiler and Dr. F. B. Strauss. All the rotations were measured in chloroform solution in a 4 dm. tube. Melting points are corrected.

Δ^5-*Cholestene*-3 : 4-*dione*, *Form* A (I).—10 G. of *cis*-Δ^5-cholestene-3 : 4-diol dibromide (Rosenheim and Starling, *loc. cit.*) in 60 ml. of benzene were shaken with 2·5 g. of chromic acid in 30 ml. of water and 60 ml. of acetic acid for 3 hours at room temperature. The benzene layer, after being washed twice with water, was treated with a solution of 5 g. of sodium iodide in 40 ml. of alcohol. After 2 minutes the liberated iodine was washed out with 2N-sodium sulphite, ether added, and the acids extracted with 5% sodium carbonate solution. The benzene–ether layer was shaken strongly with 20% aqueous potassium hydroxide, and the separating funnel cooled in ice. The potassium salt of the diosphenol formed a mass of bright yellow crystals at the interface. The aqueous layer was run off, and the ethereal layer decanted from the potassium salt, which was twice washed by decantation with ether. The potassium salt was suspended in 200 ml. of ether, and 2N-acetic acid gradually added until two homogeneous layers were obtained. The ethereal layer was washed with water until neutral, dried over sodium sulphate, and the ether distilled off. Crystallisation of the residue from aqueous acetone (norit) gave faintly yellow, rectangular plates of Δ^5-*cholestene*-3 : 4-*dione*, *form* A, m. p. 135—136° (Found : C, 79·8; H, 10·3. $C_{27}H_{42}O_2,\frac{1}{2}H_2O$ requires C, 79·4; H, 10·4%), $[\alpha]_D^{22°}$ + 30·5°,

$[\alpha]_{5461}^{22°}$ + 41·3° (*c*, 1·156), α_{5461}/α_D = 1·3. Yield, 1 g. The compound gave a yellow coloration with tetranitromethane in chloroform solution.

The quinoxaline derivative was prepared by refluxing 50 mg. of diosphenol and 50 mg. of recrystallised *o*-phenylenediamine in 2 ml. of absolute alcohol for 1½ hours. It (45 mg.) separated on cooling and formed plates from *iso*propyl alcohol, m. p. 175°, not depressed in admixture with the quinoxaline derivative of form *B*.

The *mono*-2 : 4-*dinitrophenylhydrazone* was prepared by treating an alcoholic solution of the diosphenol with Brady's reagent. It formed dark red micro-crystals from benzene–alcohol, m. p. 255° (Found : N, 9·9. $C_{33}H_{46}O_6N_4$ requires N, 9·7%), not depressed in admixture with the dinitrophenylhydrazone derivative of form *B*.

4-Acetoxy-$\Delta^{4:6}$-cholestadien-3-one (II) was prepared by treating 50 mg. of the diosphenol in 1 ml. of pyridine with 5 drops of acetic anhydride for 12 hours at room temperature. The product was treated with water, and the precipitate recrystallised from aqueous acetone; it formed prisms, m. p. 160—161° (Found : C, 78·9; H, 10·0. Calc. for $C_{29}H_{44}O_3$: C, 79·0; H, 10·1%), $[\alpha]_D^{19°}$ + 14·0°, $[\alpha]_{5461}^{19°}$ + 17·4° (*c*, 1·100), α_{5461}/α_D = 1·24. The substance melts to an anisotropic liquid which shows a blue colour on cooling, and does not depress the m. p. of an authentic specimen prepared from 4 : 5 : 6-tribromocholestane (Inhoffen, *loc. cit.*).

Oxidation of Form A *to Diels's Acid.*—To a warm solution of 200 mg. of diosphenol in 20 ml. of absolute alcohol, 0·5 ml. of perhydrol was added dropwise, followed by 1·5 ml. of 10% aqueous potassium hydroxide. After standing overnight, the mixture was poured into water and extracted with ether. The alkaline fraction was acidified and again extracted with ether. When this ethereal extract was washed free from alcohol, the acid (0·16 g.) separated and collected at the interface. On recrystallisation from glacial acetic acid and finally from methyl ethyl ketone, it was obtained in typical hemihedral crystals, m. p. 290°, not depressed by a sample of Diels's acid prepared from cholesterol.

cis-3-*Acetoxy*-Δ^5-*cholesten*-4-*ol* (V; R = Ac).—A solution of 50 g. of *cis*-Δ^5-cholestene-3 : 4-diol (Rosenheim and Starling, *loc. cit.*) in 150 ml. of dry pyridine was treated with 13 ml. of redistilled acetic anhydride in 150 ml. of dry pyridine. After 12 hours at room temperature the solution was poured into 10% brine, and the precipitated solids collected and recrystallised from 100 ml. of alcohol. cis-3-*Acetoxy*-Δ^5-*cholesten*-4-*ol* formed nacreous plates, m. p. 193—194° (Found : C, 78·1; H, 10·5. $C_{29}H_{48}O_3$ requires C, 78·3; H, 10·9%), $[\alpha]_D^{23°}$ − 64·5°, $[\alpha]_{5461}^{23°}$ − 75·3° (*c*, 0·926), α_{5461}/α_D = 1·15. Yield, 37 g.

3-*Acetoxycholestan*-4-*one*-5 : 6-*oxide* (VI; R = Ac).—20 G. of *cis*-3-acetoxy-Δ^5-cholesten-4-ol in 500 ml. of benzene and 50 ml. of glacial acetic acid were shaken with 15 g. of chromic acid in 20 ml. of water and 200 ml. of glacial acetic acid for 6 hours at room temperature. The benzene layer was washed with water, with 2% sodium hydroxide solution, again with water, and dried over sodium sulphate. The benzene was removed in a vacuum, and the residue (19 g.) crystallised first from absolute alcohol and finally from spirit. 3-*Acetoxycholestan*-4-*one*-5 : 6-*oxide* formed needles, m. p. 173—174° (Found : C, 75·5; H, 9·8. $C_{29}H_{46}O_4$ requires C, 75·9; H, 10·1%), $[\alpha]_D^{20°}$ + 3·8°, $[\alpha]_{5461}^{20°}$ + 4·5° (*c*, 1·116), α_{5461}/α_D = 1·18. Yield, 9·5 g. The compound did not show selective absorption in the ultra-violet region, and did not give a coloration with tetranitromethane. The mother-liquors yielded a compound, m. p. 102—103°, which is being further investigated.

3-*Benzoyloxycholestan*-4-*one*-5 : 6-*oxide* (VI; R = Bz).—This *compound* was prepared from *cis*-3-benzoyloxy-Δ^5-cholesten-4-ol (Rosenheim and Starling, *loc. cit.*) as described for the acetate (above). It formed, from benzene–alcohol (1 : 10), colourless needles which changed into prisms, m. p. 185—186° (Found : C, 78·2; H, 9·1. $C_{34}H_{48}O_4$ requires C, 78·4; H, 9·3%), $[\alpha]_D^{22°}$ + 6·4°, $[\alpha]_{5461}^{22°}$ + 9·3° (*c*, 1·186 in benzene; compound inactive in chloroform solution), α_{5461}/α_D = 1·4.

Δ^5-*Cholestene*-3 : 4-*dione*, *Form* B (III).—(a) A solution of 100 mg. of 3-acetoxycholestan-4-one-5 : 6-oxide in 2 ml. of glacial acetic acid containing 200 mg. of anhydrous sodium acetate was refluxed for 1 hour. The diosphenol crystallised on cooling. It was collected, washed with glacial acetic acid, and recrystallised from 3 ml. of alcohol. Δ^5-Cholestene-3 : 4-dione, form *B*, formed colourless needles, m. p. 162—163° (Found : C, 81·0; H, 10·4. Calc. for $C_{27}H_{42}O_2$: C, 81·3; H, 10·6%), $[\alpha]_D^{22°}$ + 57·3°, $[\alpha]_{5461}^{22°}$ + 85·4° (*c*, 0·726 in benzene), α_{5461}/α_D = 1·5. Yield, 70 mg. The compound gave an intense orange-red colour with tetranitromethane in chloroform solution, and a violet coloration with alcoholic ferric chloride.

(b) 1 G. of 3-acetoxycholestan-4-one-5 : 6-oxide in 3·5 ml. of benzene and 30 ml. of alcohol was refluxed for 1 hour with 2 ml. of concentrated hydrochloric acid. The solvent was removed by an air current on the steam-bath until crystallisation commenced, the flask cooled in ice,

and the product collected and recrystallised from alcohol. Form *B* of the diosphenol formed needles, m. p. 162—163°, not depressed in admixture with a sample prepared by method (a). Yield, 0·5 g.

(c) A warm solution of Δ^5-cholestene-3 : 4-dione, form *A*, in glacial acetic acid was treated with a drop of concentrated hydrochloric acid. Form *B* of the diosphenol slowly crystallised; it was identified by m. p. and mixed m. p. with a sample prepared by method (a).

The mono-2 : 4-dinitrophenylhydrazone was prepared by refluxing an alcoholic solution of form *B* of the diosphenol with excess of Brady's reagent for 3 hours on the steam-bath, and formed microprismatic needles, m. p. 255°, not depressed in admixture with the corresponding derivative from form *A*.

The quinoxaline derivative was prepared by heating 200 mg. of diosphenol and 100 mg. of *o*-phenylenediamine in an oil-bath at 150° for 30 minutes with occasional stirring. The dark red melt was dissolved in 7 ml. of ethyl acetate; on standing overnight, the solution deposited slightly pink leaflets of the quinoxaline derivative, m. p. 175°, not depressed in admixture with the quinoxaline derivative of form *A*.

cis-3-*Acetoxy*-Δ^5-*cholesten*-4-*ol Dibromide* (IV; R = Ac).—A solution of 10 g. of *cis*-3-acetoxy-Δ^5-cholesten-4-ol in 30 ml. of chloroform was treated with a solution of 1·4 ml. of bromine in 40 ml. of glacial acetic acid, the flask being cooled in running water. Absorption of bromine was accompanied by separation of the dibromide. After 5 minutes the solid crystalline mass was diluted with 100 ml. of glacial acetic acid, and the dibromide collected and, after washing with glacial acetic acid, dried over potassium hydroxide in a vacuum desiccator. It was purified by dissolution in 30 ml. of chloroform and addition of 200 ml. of glacial acetic acid, and obtained in colourless needles, m. p. 115°, which decomposed on keeping. Yield, 9·7 g.

3-*Acetoxy*-Δ^5-*cholesten*-4-*one* (VII).—5 G. of the above dibromide in 70 ml. of benzene were shaken with a solution of 3·3 g. of chromic acid in 30 ml. of water and 70 ml. of glacial acetic acid for 6 hours at room temperature. The benzene layer was washed twice with 400 ml. of water and dried over sodium sulphate, and the product debrominated by refluxing with 50 ml. of a 10% solution of sodium iodide in alcohol for 10 minutes. The liberated iodine was removed by shaking with dilute aqueous sodium sulphite. The acidic fraction of the oxidation product was extracted by shaking with sodium hydroxide solution, the benzene layer washed and dried over sodium sulphate, and the solvent removed in a vacuum. The crystalline residue (2·5 g.) gave on crystallisation from alcohol long needles of 3-*acetoxy*-Δ^5-*cholesten*-4-*one*, m. p. 123—124° (Found : C, 79·0; H, 10·7. $C_{29}H_{46}O_3$ requires C, 78·7; H, 10·5%), $[\alpha]_D^{20°}$ — 76·7°, $[\alpha]_{5461}^{20°}$ — 93·8° (*c*, 1·058), $\alpha_{5461}/\alpha_D = 1·22$.

3 : 4-*Diacetoxy*-$\Delta^{3:5}$-*cholestadiene*.—500 Mg. of 3-acetoxy-Δ^5-cholesten-4-one in 5 ml. of acetic anhydride were refluxed for 1 hour with 500 mg. of anhydrous sodium acetate. The acetic anhydride was removed in a vacuum over potassium hydroxide. The residue was taken up in 85% spirit and, on leaving overnight, colourless crystals (400 mg.) were deposited, which were purified from methyl alcohol. 3 : 4-*Diacetoxy*-$\Delta^{3:5}$-*cholestadiene* formed clusters of needles, m. p. 128° (Found : C, 76·9; H, 9·9. $C_{31}H_{48}O_4$ requires C, 76·8; H, 10·0%).

Cholestane-3 : 4-*dione* (IX).—(a) A boiling solution of 2 g. of 3-acetoxy-Δ^5-cholesten-4-one in 50 ml. of spirit was treated with 5 ml. of concentrated hydrochloric acid, and the mixture refluxed for 15 minutes. The crystals deposited on cooling were collected and purified from spirit. Cholestane-3 : 4-dione formed fine needles, m. p. 149—150° (Found : C, 80·7; H, 10·6. Calc. for $C_{27}H_{44}O_2$: C, 80·9; H, 11·0%), $[\alpha]_D^{18°}$ + 79·7°, $[\alpha]_{5461}^{18°}$ + 94·5° (*c*, 1·208), α_{5461}/α = 1·18. Yield, 1·6 g. A dilute alcoholic solution of the dione gave a violet coloration with ferric chloride.

(b) 500 Mg. of 3-acetoxy-Δ^5-cholesten-4-one in 10 ml. of benzene were treated with 8 ml. of sodium ethoxide solution (prepared from 2·5 g. of sodium and 70 ml. of ethyl alcohol). After 3 minutes at room temperature the yellow-brown solution was poured into water, a little ether added, the non-aqueous layer washed until neutral and dried over sodium sulphate, and the solvent removed in a current of air. The crystalline residue was taken up in ether, and sufficient methyl alcohol added to the filtered solution to produce a turbidity. On standing overnight, clusters of needles of cholestane-3 : 4-dione were deposited, identical in m. p. and mixed m. p. with the product obtained by method (a). Yield, 280 mg.

The quinoxaline derivative, obtained by heating a powdered mixture of equal parts of cholestane-3 : 4-dione and *o*-phenylenediamine for 45 minutes at 102—103°, and extracting the melt with hot alcohol, formed colourless plates from chloroform–alcohol, m. p. 208—209° (Found : N, 6·1. Calc. for $C_{33}H_{48}N_2$: N, 5·9%).

The *mono*-**2** : **4**-*dinitrophenylhydrazone*, obtained by treating an alcoholic solution of cholestane-**3** : **4**-dione with Brady's reagent, formed a dark red, microcrystalline precipitate from benzene–alcohol, m. p. 252—253° (Found : N, 9·4. $C_{33}H_{48}O_6N_4$ requires N, 9·4%).

The enol-acetate was prepared by refluxing 500 mg. of cholestane-**3** : **4**-dione with 5 ml. of acetic anhydride containing 100 mg. of fused sodium acetate for 30 minutes. The acetic anhydride was removed in a vacuum, and the crystalline residue taken up in 4 ml. of hot 85% spirit. The enol-acetate was deposited as clusters of needles on cooling, which were recrystallised once more, m. p. 102—103° (Found : C, 78·6; H, 9·9. Calc. for $C_{29}H_{44}O_3$: C, 79·0; H, 10·1%), $[\alpha]_D^{18°}$ + 92·5°, $[\alpha]_{5461}^{18°}$ + 100·5° (*c*, 1·310), α_{5461}/α_D = 1·2. Yield, 356 mg.

Oxidation of Cholestane-**3** : **4**-*dione to Cholestane*-$C_3\|C_4$-*diacid*.—To a boiling solution of 500 mg. of cholestane-**3** : **4**-dione in 50 ml. of alcohol were added 3 ml. of perhydrol in 6 ml. of 10% potassium hydroxide solution in three portions at 15-minute intervals, and the mixture refluxed for a further 30 minutes. Water was added to the cooled solution, and the neutral material extracted with ether. The alkaline fraction was acidified with mineral acid, and the liberated acids extracted with ether. The ethereal solution was washed and dried, and the ether removed. Addition of 5 ml. of ethyl acetate to the residue precipitated cholestane-$C_3\|C_4$-diacid (dihydro-Diels's acid) as microscopic hexagonal plates (130 mg.), which were recrystallised from glacial acetic acid; m. p. 247—248° (Found : C, 74·4; H, 10·3. Calc. for $C_{27}H_{46}O_4$: C, 74·6; H, 10·7%).

The dimethyl ester, prepared by treating an ethereal solution of the acid with diazomethane, crystallised from methyl alcohol in long thin prisms, m. p. 126—127°, not depressed in admixture with an authentic specimen.

4-*Acetoxy*-$\Delta^{4:6}$-*cholestadien*-**3**-*one from* **3**-*Acetoxycholestan*-**4**-*one*-**5** : **6**-*oxide*.—100 Mg. of the oxide in 1·1 ml. of acetic anhydride were refluxed with 100 mg. of anhydrous sodium acetate for 1 hour. On cooling, crystals were deposited, which were collected and purified from spirit. 4-Acetoxy-$\Delta^{4:6}$-cholestadien-3-one formed large rhombic plates, m. p. 161—162° (Found : C, 79·1; H, 9·9. Calc. for $C_{29}H_{44}O_3$: C, 79·0; H, 10·1%), not depressed in admixture with an authentic specimen (see above).

$\Delta^{2:5}$-*Cholestadien*-**3**-*ol*-**4**-*onyl*-**6** : **6**′-($\Delta^{4':6'}$-*cholestadien*-**4**′-*ol*-**3**′-*one*) (X; R = H).—To a solution of 1 g. of 3-acetoxycholestan-4-one-5 : 6-oxide in 10 ml. of ether and 10 ml. of alcohol were added 2·5 ml. of N-sodium ethoxide. After 1 minute the resulting yellow viscous solution was acidified (Congo-red) with N-hydrochloric acid. The colourless precipitated material was collected, washed with alcohol and water, and crystallised from ethyl acetate. $\Delta^{2:5}$-*Cholestadien*-**3**-*ol*-**4**-*onyl*-**6** : **6**′-($\Delta^{4':6'}$-*cholestadien*-**4**′-*ol*-**3**′-*one*) formed white needles, m. p. 239—240° (Found : C, 81·6; H, 10·6; *M*, Rast, 725. $C_{54}H_{84}O_4$ requires C, 81·3; H, 10·6%; *M*, 796), $[\alpha]_D^{20°}$ + 23·7°, $[\alpha]_{5461}^{20°}$ + 30·1° (*c*, 1·12), α_{5461}/α_D = 1·27. Active hydrogen (Zerewitinoff) 1·96. The ultra-violet absorption spectrum showed maxima at 2750 A., log ε 3·9, and 3100 A. log ε 3·8.

The *mono*-**2** : **4**-*dinitrophenylhydrazone* formed prismatic needles from benzene–alcohol, m. p. 248° (decomp.) (Found : C, 74·1; H, 9·4; N, 5·8. $C_{60}H_{88}O_7N_4$ requires C, 73·7; H, 9·1; N, 5·7%).

The *diacetate* was prepared by refluxing 0·48 g. of the alcohol with 10 ml. of acetic anhydride for 1 hour. On cooling, rosettes of needles were deposited, which were recrystallised from chloroform–methyl alcohol; m. p. 205—206° (Found : C, 78·6; H, 9·7; *M*, Rast, 845. $C_{58}H_{88}O_6$ requires C, 79·0; H, 10·1%; *M*, 880), $[\alpha]_D^{20°}$ − 52·4°, $[\alpha]_{5461}^{20°}$ − 60·8° (*c*, 1·036), α_{5461}/α_D = 1·16. On hydrolysis the original substance, m. p. 238—239°, was obtained.

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