956. *Hydroaromatic Steroid Hormones. Part V.** *Some* D-*Homo*-18 : 19-*bisnorsteroids.*

By A. J. Birch and Herchel Smith.

Syntheses of (±)-D-homo-18 : 19-bisnortestosterone † (II; R = H) and (±)-D-homo-18 : 19-bisnorandrostane-3 : 17-dione † (I; R = H) from 1 : 2 : 7 : 8-tetrahydro-3 : 10-dimethoxychrysene [1] are described.

In Part I [2] the reasons were given for believing that steroids lacking one or both of the 18- and 19-methyl groups should be biologically active, provided the stereochemistry is correct. This belief has been strengthened by demonstration of the androgenic activity of 19-nortestosterone,[2,3] which was the first active androgen made by total synthesis, and later of other hormone analogues [4,5] all made by essentially the same process involving the reduction of an aromatic ring by means of metal–ammonia–alcohol reagents.[6] Recent work on the biosynthesis of steroids [7] shows that the angular methyl groups are essentially relics of the isoprene units in precursors, providing further grounds for believing that such groups may not be necessary or even desirable for biological activity. Several 19-norsteroid hormones are in fact more biologically active than are the steroids themselves.[4,5]

Alteration of the skeleton may result not only in alteration of the intensity of biological activity but in alteration in ratios of activities when a hormone possesses more than one type of activity. Male hormones in particular have an anabolic activity which is of great therapeutic interest and would in an ideal anabolic agent be divorced from the typical

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* Part IV, Birch and Harrisson, *Austral. J. Chem.*, 1955, **8**, 519.

† These compounds are given steroid numbering to facilitate comparison with this series; various intermediates are numbered systematically as chrysene derivatives.

[1] Collins and Smith, *J.*, 1956, 4308.

[2] Birch, *J.*, 1950, 367.

[3] Birch, *Ann. Reports*, 1950, **47**, 210.

[4] Miramontes, Rosenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1953, **75**, 4440.

[5] Sandoral, Miramontes, Rosenkranz, Djerassi, and Sondheimer, *ibid.*, p. 4117; 1955, **77**, 148.

[6] Birch, *J.*, 1944, 430, and later papers; Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5355.

[7] *E.g.*, Clayton and Bloch, *J. Biol. Chem.*, 1956, **218**, 305, 309.

androgenic activity. That such a separation of activities is possible can already clearly be seen in the norsteroid series. 19-Nortestosterone has an anabolic : androgenic ratio of about 2·5, compared with testosterone; and the D-homo-19-nortestosterone reported in Part IV * has a ratio of about 6. Recently [8] it has been reported that for 17-ethyl-19-nortestosterone the ratio is 16. We now report further work aimed at examining the effect on biological activity of omitting the 18-methyl group, with retention of the natural steroid stereochemistry.

There seems reason to believe that *cyclo*pentenophenanthrene derivatives would be active in absence of the 18-methyl group, provided the C–D ring junction is *trans*.[2] In view of the difficulty of synthesising such compounds we have initially been concerned with D-homo-18-norsteroids with a readily attainable C–D-*trans* junction. Since this suggestion regarding activity was originally made,[2] some confirmation has been obtained by W. S. Johnson and his collaborators who showed that (±)-D-homo-18-norandrostane-3 : 17-dione [9] (I; R = Me) is as active androgenically as (±)-androstane-3 : 17-dione itself. However, it later appeared that D-homo-18-nortestosterone [10] (II; R = Me) is inactive although the acetate and propionate possess one-tenth of the androgenic activity of the corresponding testosterone derivatives. Our own initial attempts [11] in this field were unsuccessful owing to failure to prepare appropriately substituted chrysene derivatives, but a mixture of steroisomers of what is probably an 11-hydroxy-D-homotestosterone (III) was shown to possess weak androgenic activity.[12]

After the start of our work on the synthesis of the ketone (II; R = H), Johnson, Dehn, and Chinn [13] reported its synthesis by a rather difficult route and stated that it was inactive as an androgen. It appeared to us desirable, however, to examine its biological activity further and to develop methods which could be adapted to the preparation of related compounds carrying the side-chains characteristic of other hormones. In view of the great structural specificity already demonstrated for androgenic activity there is clearly still some possibility that activity will be found in analogues of other hormones. Also, since the diketone (I; R = Me) is androgenic whilst the keto-alcohol (II; R = Me) is not, we have prepared the analogue (I; R = H) for comparison with the compound (II; R = H).

The ready synthesis of the desired starting material, 1 : 2 : 7 : 8-tetrahydro-3 : 10-dimethoxychrysene (IV) is described elsewhere.[1] * Reduction of this compound with sodium and boiling butan-1-ol gave a mixture of the *cis*- and *trans*-1 : 2 : 7 : 8 : 14 : 17-hexahydro-3 : 10-dimethoxychrysene. The major, higher-melting, and less soluble isomer * was assigned the *trans*-configuration (V) by analogy with the known properties of the *cis*- and *trans*-forms of 1 : 2 : 7 : 8 : 14 : 17-hexahydrochrysene [14] and 1 : 2 : 7 : 8 : 14 : 17-hexahydro-4 : 10-dimethoxychrysene [15] and by taking into account the known results of reducing 1 : 2 : 7 : 8-tetrahydro-4 : 10-dimethoxychrysene with the same reagent.[11] In the sequel this conclusion proved to be correct. The *trans*-isomer could be obtained in a satisfactory state of stereochemical purity by crystallisation of the reaction mixture under controlled conditions. Reduction of the tetrahydro-compound (IV) with potassium in *iso*propyl alcohol, or with sodium or lithium in liquid ammonia,. was less satisfactory as regards both the total yield and stereochemical specificity. Reduction of the hexahydro-compound (V) with lithium (60 g.-atoms) and ethanol in liquid ammonia followed by treatment of the product with mineral acid gave an αβ-unsaturated ketone $C_{19}H_{22}O_2$ produced by reduction of one of the aromatic nuclei. It is known that 1 : 2 : 3 : 4-tetrahydro-6-methoxynaphthalene undergoes reduction with alkali metal and alcohol in liquid ammonia much more readily than the 5-methoxy-isomers,[16] and hence it was taken as

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* We are informed by Dr. J. Walker that he and Dr. P. A. Robins have prepared this compound by an independent route which was reported at a meeting of the Chemical Society on February 16th, 1956.

[8] *Chem. Eng. News*, 1956, **34**, 2134.

[9] Johnson, Lemaire, and Pappo, *J. Amer. Chem. Soc.*, 1953, **75**, 4866.

[10] Johnson, Bannister, Pappo, and Pike, *ibid.*, 1955, **77**, 817.

[11] Birch and Smith, *J.*, 1951, 1882.

[12] Birch and Quartey, *Chem. and Ind.*, 1953, 489.

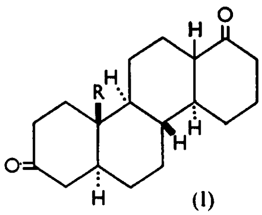
[13] Johnson, Dehn, and Chinn, *J. Org. Chem.*, 1954, **19**, 670.

[14] Ramage and Robinson, *J.*, 1933, 607.

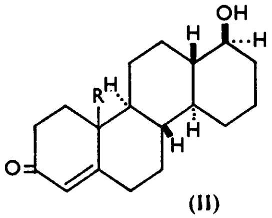
[15] Lewis, Ramage, and Robinson, *J.*, 1935, 1412; Wilds and Sulton, *J. Org. Chem.*, 1951, **16**, 1371.

[16] Birch, Murray, and Smith, *J.*, 1951, 1945.

virtually certain that this ketone has the structure (VI) derived by reduction of the 1 : 2 : 4-substituted benzene ring. The light absorption supported this view. Although the position of the maximal ultraviolet absorption (233 mμ) is at a lower wavelength than would be predicted (244 mμ) on the basis of a modified version of Woodward's rules,[17] certain similarly substituted steroid ketones, *e.g.*, 3 : 12-dioxochol-4-enic acid [18] and 11-deoxy-17-hydroxycorticosterone [19] show deviations of this order. Reduction of the 1 : 2 : 3-substituted benzene ring could lead theoretically to two αβ-unsaturated ketones, (VII) and (VIII), resulting respectively from the 5 : 15- and 4 : 16-dihydro-derivatives. The former should absorb around 249 mμ, the latter around 227 mμ. The infrared absorption spectrum shows bands at 789, 742, and 712 cm.$^{-1}$ which are consistent with the presence of a 1 : 2 : 3-trisubstituted aromatic nuleus; [20] there is no strong band in the 860—800 cm.$^{-1}$ region and hence a 1 : 2 : 4-trisubstituted benzene ring such as would be present in (VII) or (VIII) is contraindicated.[21] These conclusions were later verified. The configuration of the hydrogen atom attached to $C_{(13)}$ is unknown but is established during a bond-migration reaction known to generate the thermodynamically most stable isomer.[11] Therefore the expectation is that the hydrogen atom at $C_{(13)}$ will be ***trans*** to that at $C_{(14)}$, *i.e.*, β as represented in (VI). In this connection it is relevant that rotational evidence as well as the high physiological activity is consistent with the assumption that the β-configuration obtains at $C_{(10)}$ (steroid numbering) in the 19-norhormones similarly formed by reduction of œstrone derivatives.[11, 22]



(I)



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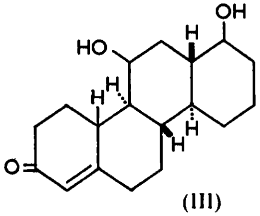

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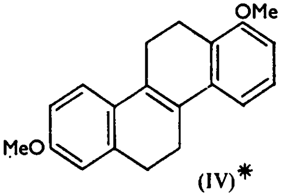
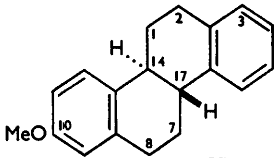
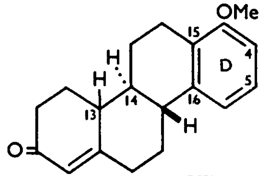


(IV)*



(V)



(VI)

* This and other formulæ for (±)-compounds imply the presence of an equal amount of the enantiomer. For these formulæ, and the resulting names, the hydrogen atom attached to $C_{(9)}$ in the steroid skeleton ($C_{(14)}$ in the hydrochrysene skeleton) has arbitrarily been taken as in the α-configuration.

The reaction of the keto-ether (VI) with ethylene glycol in benzene in the presence of toluene-*p*-sulphonic acid proceeded normally. With αβ-unsaturated ketones dioxolan formation proceeds with a shift of the double bond to the βγ-position [23] which in the case of the substance (VI) can be either the 8(18)- or the 13(18)-position. The infrared absorption spectrum of the ketal which shows bands at 830 and 826 cm.$^{-1}$ is consistent with the

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[17] Fieser and Fieser, " Natural Products Related to Phenanthrene," 3rd edn., Reinhold Publ. Corp., New York, 1949, p. 190.

[18] Sawlewicz and Reichstein, *Helv. Chim. Acta*, 1937, **20**, 949.

[19] Reichstein, *ibid.*, p. 953.

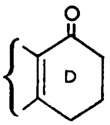
[20] Bellamy, " The Infra-Red Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1954, p. 66.

[21] Ref. 20, p. 67.

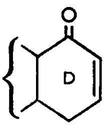
[22] Klyne, *J.*, 1952, 2916; Wilds and Nelson, *J. Amer. Chem. Soc.*, 1953, **75**, 5366.

[23] Fernholz and Stavely, Abs. 102nd Meeting Amer. Chem. Soc., Atlantic City, N.J., 1941; 39M; Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 423.

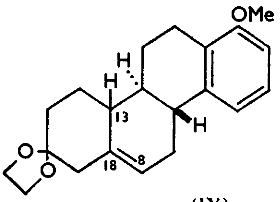
presence of a trisubstituted ethylenic centre [24] and therefore favours the structure (IX), although there is some evidence for inhomogeneity in the product. The point is of no practical importance here, however, since acid hydrolysis will generate the same αβ-unsaturated ketone.



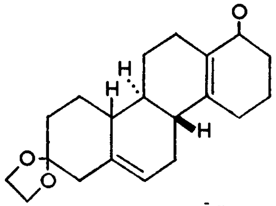
(VII)



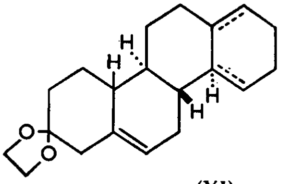
(VIII)



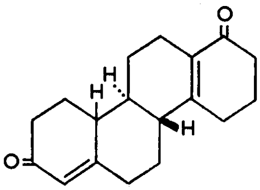
(IX)



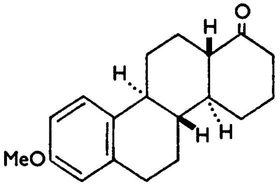
(X)



(XI)



(XII)



(XIII)

Reduction of the ketal-ether (IX) with lithium (300 g.-atoms) and ethanol in liquid ammonia followed by hydrolysis with aqueous-ethanolic oxalic acid and treatment of the product with aqueous-ethanolic sodium acetate gave, as the major product, an αβ-unsaturated ketone $C_{20}H_{26}O_3$, the ultraviolet absorption ($\lambda_{max.}$ 248·5 mμ) of which is in good agreement with that predicted for structure (X). A minor product, arising from the reductive removal of the 3-methoxy-group was a diene $C_{20}H_{28}O_2$, in which one double bond is presumably in the 8(18)-position, and the other forms part of ring D. As a point of theoretical interest, we have attempted to obtain further information about the position of this double bond by determining the ultraviolet absorption of the diene in the 200—220 mμ region. From the data given by Bladon, Henbest, and Wood [25] for steroid olefins it appears that the low ε values at 215—220 mμ (10—20) could not have resulted from the addition of the curves for a trisubstituted and tetrasubstituted olefinic centre, and so the 15(16)-position for the second double bond is excluded. The curve corresponds most closely to that produced by the addition of the curves for two trisubstituted olefinic centres, although the presence of a disubstituted double bond cannot with certainty be excluded. It rises smoothly from ε 1500 at 215 mμ through ε 7000 at 210 mμ and flattens to ε 10,000 at 200 mμ. The diene therefore probably has structure (XI).

Reduction of the ketone (X) with lithium and ethanol in liquid ammonia followed by treatment with hydrochloric acid gave a hydroxy-ketone, m. p. 215—218°, $\lambda_{max.}$ 240·5 mμ, which, on the basis of its infrared absorption spectrum and a mixed-melting-point determination, proved to be identical with the compound believed to be have structure (II; R = H) prepared by Johnson and his co-workers.[13] The sample of D-homo-18 : 19-bisnortestosterone prepared by Johnson was obtained from the intermediate (XIII) which has been converted into œstrone.[26] Hence the only elements in the structure (II) remaining unproved are the configurations of the hydrogen atom at $C_{(13)}$ and the 3-hydroxyl group. It is known that the reduction of carbon–carbon multiple-bond systems with dissolving metals in liquid ammonia usually affords the thermodynamically most stable isomer,[11, 27] and on the basis of this rule it would be predicted that reduction of the ketone

[24] Ref. 20, p. 44.

[25] Bladon, Henbest, and Wood, *J.*, 1952, 2737.

[26] Johnson, Banerjee, Schneider, Gutsche, Shelberg, and Chinn, *J. Amer. Chem. Soc.*, 1952, **74**, 2832.

[27] Birch, *Quart. Rev.*, 1950, **4**, 69; Barton and Robinson, *J.*, 1954, 3045.

(X) should give a product having the asymmetric centres in the alternating *trans*-configurations and the 3-hydroxyl group in the β(equatorial)-configuration, and on acid hydrolysis the form (II) should result. Unpublished work has shown that, depending on the conditions, this rule need not be generally valid; it should however apply in this case.

Reduction of the ether (V) with lithium (250 g.-atoms) and ethanol in liquid ammonia and treatment of the product with hydrochloric acid gave a diketone (XII) whose structure follows from its identity with the product obtained by acid hydrolysis of keto-ketal (X). Further reduction of this diketone (XII) with lithium in liquid ammonia gave a saturated diketone which should be [27, 28] the androstane-3 : 17-dione analogue (I; R = H). The same compound was obtained by reducing the unsaturated diketone (XII) with lithium and alcohol in liquid ammonia and oxidising the product in acetic acid solution with chromium trioxide.

Tests on the compounds (I; R = H), (II; R = H), and the propionate of the latter in capons showed no androgenic activity in doses up to 1 mg. Johnson, Dehn, and Chinn [13] showed that the compound (II; R = H) has no androgenic activity but has a high myotrophic activity. Compounds of this type may therefore prove to be useful anabolic agents. Further work is in progress.

EXPERIMENTAL

Evaporations were carried out under reduced pressure. Light petroleum means the fraction of b. p. 60—80° unless stated otherwise. M. p.s denoted (K) were determined on the Kofler block and are corrected. Absorption spectra were determined by Mr. F. Hastings under the general supervision of Dr. F. B. Strauss. Infrared spectra were determined for Nujol mulls.

trans-1 : 2 : 7 : 8 : 14 : 17-*Hexahydro*-3 : 10-*dimethoxychrysene* (V).—Sodium (9·5 g.) was added to a refluxing solution of 1 : 2 : 7 : 8-tetrahydro-3 : 10-dimethoxychrysene [1] (2 g.) in redistilled butan-1-ol (250 c.c.). After 30 min. sodium (6·5 g.) was added and the refluxing continued until dissolution was complete (1·5 hr.). On cooling, water (200 c.c.) was added and the mixture set aside in the refrigerator. After 48 hr. the precipitate was collected, washed thoroughly with water, dried, and recrystallised from ethanol to give the almost pure *trans*-hexahydrodimethoxychrysene as fine needles (0·81 g.), m. p. 127—130° (sintering at 123°). This preparation was used in all subsequent reductions. After recrystallisation from ethanol and then ethyl acetate it had m. p. 132·5—134·5°. A portion (300 mg.) in benzene was adsorbed on alumina (15 g.), and the column eluted with light petroleum and light petroleum containing increasing amounts of benzene. Light petroleum–benzene (9 : 1) eluted a fraction which, on recrystallisation from light petroleum–ethyl acetate, gave trans-1 : 2 : 7 : 8 : 14 : 17-*hexahydro*-3 : 10-*dimethoxychrysene* (V) as long fine needles, m. p. 133·5—134·5° unchanged on further crystallisation (Found: C, 81·6; H, 7·3. $C_{20}H_{22}O_2$ requires C, 81·6; H, 7·5%). Light absorption in EtOH : $\lambda_{max.}$ 273 (shoulder), 279, and 286 (shoulder) mμ (ε 3100, 3700, and 2100).

Ether (250 c.c.) was added to the mother-liquors after separation of the crude *trans*-compound and the organic layer was separated, dried, and evaporated to an oil which was dissolved in a little ether. Next day the deposited crystals were washed with ether and ethanol and recrystallised from ethanol to give the almost pure *cis*-hexahydrodimethoxychrysene as stout prisms (0·23 g.), m. p. 115·5—116·6°. Purification by chromatography as with the *trans*-isomer gave the cis-1 : 2 : 3 : 4 : 14 : 17-*hexahydro*-3 : 10-*dimethoxychrysene*, m. p. 119·5—120·5° unchanged on further recrystallisation and depressed on admixture with (V) (Found : C, 81·6; H, 7·5%). Light absorption in EtOH : $\lambda_{max.}$ 271 (shoulder), 279, and 287 (shoulder) mμ (ε 2400, 2900, and 1800). The oil (0·54 g.) from the ethereal mother-liquors gave with Brady's reagent a gummy 2 : 4-dinitrophenylhydrazone. The combined oils from a number of similar reductions were hydrolysed with hydrochloric acid in ethanol, and the product chromatographed on Florex. Benzene eluted a small quantity of a ketone, m. p. 208—211°, identical with 1 : 2 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-decahydro-3-methoxy-10-oxochrysene (below) (Found : C, 80·8; H, 7·8. Calc. for $C_{19}H_{22}O_2$: C, 80·6; H, 7·9%).

1 : 2 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-*Decahydro*-3-*methoxy*-10-*oxochrysene* (VI).—*trans*-1 : 2 : 7 : 8 : 14 : 17-Hexahydro-3 : 10-dimethoxychrysene (1 g.) in tetrahydrofuran (70 c.c.) was added with stirring to a solution of lithium (1·45 g.) in liquid ammonia (200 c.c.). Ethanol (18 c.c.) was added dropwise during 20 min. When the blue colour was discharged (5 min.) water (150 c.c.) was added and the mixture was extracted with ether (4 × 100 c.c.). The ether

[28] Barton, *Experientia*, 1950, **6**, 316, and subsequent papers; Johnson, *ibid.*, 1951, **7**, 315

solution was washed with water, dried, and evaporated in a stream of nitrogen to a gum which was dissolved in ethanol (75 c.c.)–6N-hydrochloric acid (18 c.c.) at 60°. The solution was refluxed under nitrogen for 45 min. Water (100 c.c.) was added to the cooled solution, and the mixture was extracted with ethyl acetate–ether (1 : 1; 4 × 50 c.c.). The extract was washed with water, dried, and evaporated to small bulk. The precipitate was recrystallised from ethyl acetate to give 1 : 2 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-*decahydro*-3-*methoxy*-10-*oxochrysene* (VI) as fluffy crystals (0·37 g.), m. p. 208—210°. The analytical sample had m. p. 211—212° (Found : C, 80·8; H, 7·8%). Light absorption in EtOH : $\lambda_{max.}$ 233, 271 (infl.) and 280 (ε 23,900, 2800, and 2300). Infrared absorption : bands at 1669, 1616, 1600, 1580, 789, 742, and 712 cm.$^{-1}$. The mother-liquors from the crude ketone (VI) contained an oil (0·36 g.) which was dissolved in light petroleum–benzene (1 : 1; 20 c.c.) and adsorbed on Florex (15 g.). The column was washed with light petroleum containing increasing proportions of benzene. Benzene (120 c.c.) and benzene–chloroform (4 : 1; 30 c.c.) eluted fractions which on recrystallisation from ethyl acetate gave a further quantity (0·13 g.) of compound (VI), m. p. 208—209°. Recrystallisation of mother-liquors gave a further crop (0·06 g.), m. p. 208—209°.

10-*Ethylenedioxy*-1 : 2 : 7 : 9 : 10 : 11 : 12 : 13 : 14α : 17β-*decahydro*-3-*methoxychrysene* (IX).—The above decahydromethoxyoxochrysene (0·58 g.) was refluxed in benzene (35 c.c.) with ethylene glycol (0·5 c.c.) and toluene-*p*-sulphonic acid (*ca.* 20 mg.) for 4·5 hr. under a Dean–Stark trap. The cooled solution was washed with saturated sodium hydrogen carbonate solution, then water, dried, and evaporated to a crystalline residue which was dissolved in benzene–light petroleum (1 : 3; 15 c.c.) and adsorbed on Florex (12 g.). The same solvent mixture eluted a series of fractions, with m. p.s varying from 115·5—117° to 124—128° (sintering at 120°), the infrared absorption spectra of which were almost identical. The combined fractions were recrystallised from light petroleum, to give 10-*ethylenedioxy*-1 : 2 : 7 : 9 : 10 : 11 : 12 : 13 : 14α : 17β-*decahydro*-3-*methoxychrysene* (IX) (0·45 g.), m. p. 115—118° (Found : C, 77·7; H, 8·1. $C_{21}H_{26}O_3$ requires C, 77·3; H, 8·0%). Infrared absorption : bands at 1597, 1580, 830, and 826 cm.$^{-1}$.

10-*Ethylenedioxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-*tetradecahydro*-3-*oxochrysene* (X).—The foregoing ethylenedioxydecahydromethoxychrysene (0·53 g.) in tetrahydrofuran (50 c.c.) was added with stirring to liquid ammonia (200 c.c.) containing lithium (4 g.) and ethanol (80 c.c.) was run in as quickly as possible. When the blue colour had been discharged (15 min.) water (150 c.c.) was added and the product obtained in the usual way. It was dissolved in ethanol (60 c.c.), and oxalic acid dihydrate (0·92 g.) in water (12 c.c.) was added. The solution was kept at 25° for 45 min. and an excess of saturated sodium hydrogen carbonate solution was added. The mixture was extracted with ether (4 × 75 c.c.), and the ethereal solution was washed with water, dried, and evaporated to a gum. The latter was dissolved in ethanol (40 c.c.), and fused sodium acetate (9 g.) in water (10 c.c.) was added and the solution refluxed under nitrogen for 1 hr. Water (100 c.c.) was added to the cooled solution, and the mixture thoroughly extracted with ether (4 × 75 c.c.). The gummy product was dissolved in light petroleum–benzene (3 : 1; 10 c.c.) and adsorbed on Florex (20 g.). The column was washed with light petroleum (120 c.c.). Elution with light petroleum–benzene (3 : 1; 100 c.c.) gave a fraction which was recrystallised from light petroleum (b. p. 40—60°), to give probably 10-*ethylenedioxy*-1 : 2 : 3 : 4 : 5 : 7 : 9 : 10 : 11 : 12 : 13 : 14α : 15 : 17β(or -1 : 2 : 4 : 5 : 6 : 7 : 9 : 10 : 11 : 12 : 13 : 14α : 16 : 17β)-*tetradecahydrochrysene* (XI) as needles (85 mg.), m. p. 120—122° (Found : C, 80·3; H, 9·2. $C_{20}H_{28}O_2$ requires C, 80·0; H, 9·3%). Infrared absorption : bands at 860 and 831 cm.$^{-1}$. Elution with light petroleum containing increasing proportions of benzene gave a series of oils. Elution with benzene (total 350 c.c.), benzene–ether (19 : 1; 75 c.c.), and benzene–ether (9 : 1; 50 c.c.) gave a series of nine fractions with m. p.s varying from 113—119° to 133—137·5°, the last six all being over 130°. The infrared absorption spectra of all nine fractions were almost identical. The combined fractions were recrystallised from ether at −10° to give 10-*ethylenedioxy*-1 : 2 : 3 : 4 : 5 : 6 : 7 : 9 : 10 : 11 : 12 : 13 : 14α : 17β-*tetradecahydro*-3-*oxochrysene* (X) (0·143 g.), m. p. 132—136° (Found : C, 76·4; H, 8·5. $C_{20}H_{26}O_3$ requires C, 76·4; H, 8·3%). Light absorption in EtOH : $\lambda_{max.}$ 248·5 mμ (ε 12,500). Infrared absorption : bands at 1661, 1618, 829, and 816·5 cm.$^{-1}$.

The oxo-ketal (X) (60 mg.) was refluxed in ethanol (25 c.c.)–6N-hydrochloric acid (6 c.c.) under nitrogen for 45 min. The partially crystalline product was washed with ether and recrystallised from ethyl acetate to give 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-tetradecahydro-3 : 10-dioxochrysene (XII) (20 mg.), m. p. 147—150° undepressed by the sample prepared as below and possessing the same infrared absorption spectrum.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 15β : 16α : 17β-*Hexadecahydro*-3-*hydroxy*-10-*oxochrysene* (II; R = H).—The above oxo-ketal (X) (143 mg.) in tetrahydrofuran (15 c.c.) was added with stirring to a solution of lithium (250 mg.) in liquid ammonia (100 c.c.). After 3 min. ethanol (5 c.c.) was added dropwise during 15 min. After the blue colour was discharged (15 min.), water (80 c.c.) was added and the mixture extracted with chloroform. The product was dissolved in ethanol (25 c.c.) and refluxed under nitrogen with 6N-hydrochloric acid (6 c.c.) for 40 min. The product was washed with a little ether to give slightly yellow crystals (82 mg.) which were dissolved in benzene (15 c.c.) and adsorbed on Florex (6 g.). The column was first washed with benzene (70 c.c.). Further elution with benzene and benzene containing proportions of chloroform up to 50% eluted a series of crystalline fractions. The first two were rejected and the remainder recrystallised from benzene, to give the 1:2:3:4:5:6:7:8:10:11:12:13:14α:15β:16α:17β-hexadecahydro-3-hydroxy-10-oxochrysene (II; R = H) as long needles (45 mg.), m. p. 208—213°(K) undepressed by the sample prepared by Johnson, Dehn, and Chinn,[18] and possessing the same infrared absorption spectrum (Found: C, 78·6; H, 9·55. Calc. for $C_{18}H_{26}O_2$: C, 78·8; H, 9·4%). Light absorption in ethanol: $\lambda_{max.}$ 240·5 mμ (ε 17·000) [Johnson and his co-workers give m. p. 211·5—213° and $\lambda_{max.}$ 240·5 (ε 17,000)]. Infrared absorption: bands at 3401, 1650, and 1631 cm.$^{-1}$. This compound, purified further by chromatography on deactivated alumina, gave a sample which after two further recrystallisations from benzene had m. p. 215—218°(K).

The *propionate* was obtained from light petroleum (b. p. 40—60°) as needles, m. p. 152—155°(K) (Found: C, 75·8; H, 8·95. $C_{21}H_{30}O_3$ requires C, 76·4; H, 9·1%). Infrared absorption: bands at 1733, 1667, 1618, and 1187 cm.$^{-1}$.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-*Tetradecahydro*-3 : 10-*dioxochrysene* (XII).—The hexahydrodimethoxychrysene (V) (1 g.) in tetrahydrofuran (100 c.c.) was added with stirring to liquid ammonia (300 c.c.) containing lithium (6·2 g.). Ethanol (100 c.c.) was run in as quickly as possible and when the blue colour was discharged (30—60 min.) water (300 c.c.) was added and the mixture extracted with ether. The gum obtained by evaporating the ether solution in a stream of nitrogen was dissolved in ethanol (75 c.c.) and refluxed with 6N-hydrochloric acid (18 c.c.) under nitrogen for 45 min. Water (100 c.c.) was added to the cooled solution, and the mixture was extracted with ether–ethyl acetate (1 : 1; 4 × 50 c.c.). The product was dissolved in benzene–light petroleum (1 : 1; 20 c.c.) and adsorbed on Florex (30 g.). The column was eluted with the same solvent mixture, with light petroleum containing increasing amounts of benzene, benzene, and benzene containing increasing amounts of chloroform. Benzene–chloroform (1 : 1) and benzene–chloroform (1 : 3) gave fractions which on recrystallisation from ethyl acetate gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 10 : 11 : 12 : 13 : 14α : 17β-*tetradecahydro*-3 : 10-*dioxochrysene* (XII) (110 mg.), m. p. 145—150°. A sample recrystallised for analysis had m. p. 149—150° (Found: C, 79·5; H, 8·5. $C_{18}H_{22}O_2$ requires C, 80·0; H, 8·15%). Light absorption in EtOH: $\lambda_{max.}$ 244·5 mμ (ε 25,500). Infrared absorption: bands at 1664 and 1626 cm.$^{-1}$.

1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 12 : 13β : 14α : 15β : 16α : 17β : 18α-*Octadecahydro*-3 : 10-*dioxochrysene*.—(*a*) The tetradecahydrodioxochrysene (XII) (272 mg.) in tetrahydrofuran (20 c.c.) was added with stirring to a solution of lithium (55 mg.) in liquid ammonia (50 c.c.). After 10 min. ammonium chloride was added to discharge the blue colour. The product was dissolved in benzene (25 c.c.) and adsorbed on Florex (10 g.). Benzene (125 c.c.) and benzene–chloroform (9 : 1; 25 c.c.) eluted fractions which on recrystallisation from ethyl acetate–light petroleum gave 1 : 2 : 3 : 4 : 5 : 6 : 7 : 8 : 9 : 10 : 11 : 12 : 13β : 14α : 15β : 16α : 17β : 18α-*octadecahydro*-3 : 10-*dioxochrysene* (I; R = H) as slender needles (39 mg.), m. p. 156—157° (Found: C, 78·6; H, 9·6. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·5%). Infrared absorption: band at 1706 cm.$^{-1}$. Benzene–chloroform (9 : 1, 25 c.c.; 4 : 1, 50 c.c.; 3 : 2, 25 c.c.) eluted fractions which on recrystallisation from ethyl acetate gave a hydroxy-ketone, m. p. 200—203°, giving infrared absorption bands at 3367 and 1706 cm.$^{-1}$. Benzene–chloroform (3 : 2; 75 c.c.) next eluted a fraction which after recrystallisation from ethyl acetate had m. p. 257—259° and is probably a diol (infrared absorption band at 3247 cm.$^{-1}$).

In one experiment in which a sample of (XII) having m. p. 140—145° was used, benzene eluted first from Florex a small quantity of a *dione* obtained from light petroleum–ethyl acetate as needles, m. p. 167—168° depressed on admixture with (I; R = H) (Found: C, 79·0; H, 9·6. $C_{18}H_{26}O_2$ requires C, 78·8; H, 9·5%), with infrared absorption bands at 1721 and 1701 cm.$^{-1}$.

(*b*) The tetradecahydrodioxochrysene (XII) (110 mg.) in tetrahydrofuran (10 c.c.) was added with stirring to a solution of lithium (112 mg.) in liquid ammonia (100 c.c.). After 15 min., ethanol (4 c.c.) was added during 10 minutes, and when the blue colour was discharged water

(50 c.c.) was added and the product collected in chloroform. It was dissolved in acetic acid (3 c.c.), and a solution of chromium trioxide (82 mg.) in acetic acid (3·6 c.c.)–water (0·4 c.c.) was added. After 23 hr. at room temperature the mixture was worked up in the known manner, to give an oil which was dissolved in benzene (5 c.c.) and chromatographed on Florex (5 g.) as under (*a*), yielding the perhydrodioxochrysene (I; R = H) (25 mg.), m. p. 158—159° undepressed by the specimen as prepared as under (*a*).

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THE DYSON PERRINS LABORATORY, OXFORD.
CHEMISTRY DEPARTMENT, UNIVERSITY OF MANCHESTER.

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