Potentially Carcinogenic Cyclopenta[*a*]phenanthrenes. Part III.[1] Oxidation Studies

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Oxidation of 15,16-dihydrocyclopenta[*a*]phenanthren-17-one and of its strongly carcinogenic 11-methyl homologue with chromic acid, osmium tetroxide, lead tetra-acetate, and ammonium cerium(IV) nitrate was studied. The position of attack, either on the phenanthrene nucleus or on the five-membered ring D, depended mainly upon the oxidising agent and only to a minor extent upon the substrate. Both the biologically inactive hydrocarbon, 16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene, and its weakly carcinogenic 11-methyl homologue gave the corresponding 15-ketones as the main products on chromic acid oxidation.

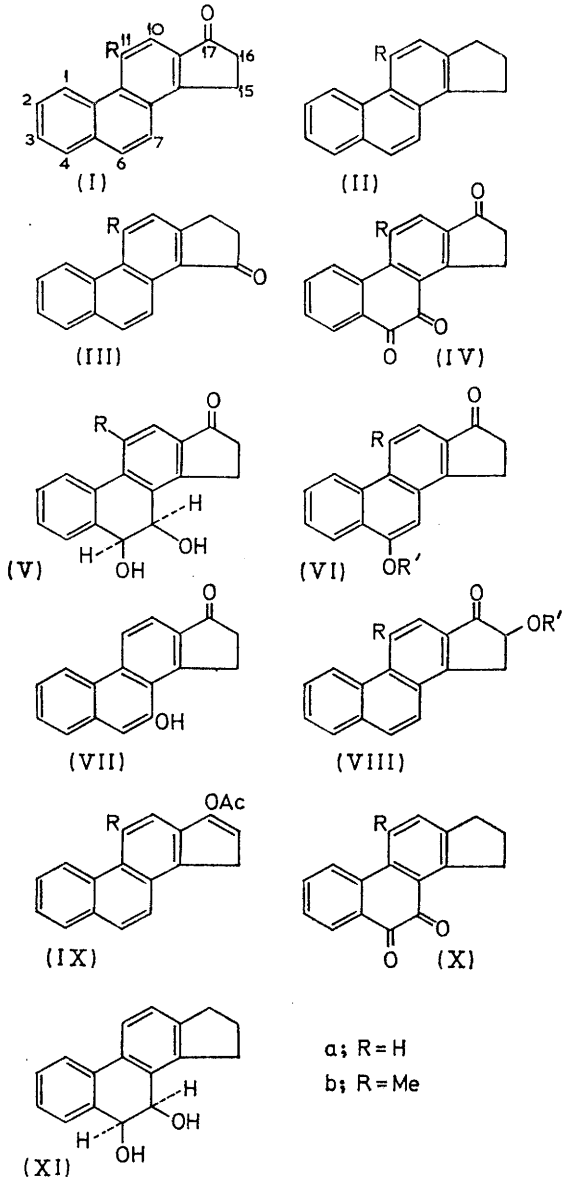
SKIN-PAINTING experiments have revealed the surprising fact that 15,16-dihydro-11-methylcyclopenta[*a*]phenanthren-17-one (Ib) possesses strong carcinogenic properties whereas as expected the unsubstituted ketone (Ia) is devoid of such activity.[2] The chemical reactivities of these two compounds have therefore been compared, and various oxygenated derivatives which might be expected to be encountered in metabolic work now in progress have been synthesised.

Oxidation of the parent hydrocarbon 16,17-dihydro-15*H*-cyclopenta[*a*]phenanthrene (IIa) with chromic acid [3,4] was found to give mainly the 15-ketone (Xa), together with a trace of the 6,7-quinone.[4] The weakly carcinogenic 11-methyl hydrocarbon (IIb),[5] conveniently prepared by hydrogenolysis of the 11-methyl ketone (Ib), on similar oxidation gave the 11-methyl-15-ketone (IIIb) (37%) with recovery of starting material (IIb) (12%). In contrast to these results, similar oxidation of the 17-ketone (Ia) resulted in an almost quantitative yield of the bright yellow 17-oxo-6,7-quinone (IVa), while oxidation of the 11-methyl-17-ketone (Ib) under these conditions gave several products. The major compound (51%) was the 11-methyl-17-oxo-6,7-quinone (IVd), but starting material (16%) was also recovered and t.l.c. disclosed three other minor oxidation products.

Addition of osmium tetroxide across the 6,7-double bond in the hydrocarbon (IIa) was investigated by Dannenberg and his co-workers [5] who isolated the 6,7-diol (XIa) after treatment in benzene solution containing pyridine. The ketones (Ia) and (Ib) under these conditions, or better in pyridine solution without added benzene, gave the corresponding keto-diols (Va) and (Vb) in good yield. These compounds exhibited strong, broad u.v. absorption bands around 310 mμ which shifted on borohydride reduction to maxima around 275 mμ, similar to that of the diol (XIa). A notable feature in the i.r. spectra of the keto-diols (Va and b) was enhanced absorption at 1600 $cm.^{-1}$; this was not observed with the diol (XIa). Oxidation of the keto-diols with chromic acid afforded high yields of the keto-quinones (IVa and b), thus confirming the structure of the latter. The keto-diol (Va) was dehydrated smoothly when heated with sulphuric acid, but the 11-methyl keto-diol (Vb) was dehydrated less readily. The main product from (Va) was the 6-ol (VI; R′ = H); the derived methyl ether (VIa; R^1 = Me) was identical with a specimen synthesised from 1-methoxynaphthalene.[6] A minor phenolic

[1] Part II, M. M. Coombs, *J. Chem. Soc.*, 1966, 963.
[2] M. M. Coombs and C. J. Croft, *Progr. Experimental Tumor Research*, 1969, **11**, 69.
[3] A. Butenandt, H. Dannenberg, and D. von Dresler, *Z. Naturforsch.*, 1946, **1**, 222.
[4] G. M. Badger, W. Carruthers, and J. W. Cook, *J. Chem. Soc.*, 1952, 4996.
[5] A. Butenandt and H. Dannenberg, *Arch. Geschwulstforsch.*, 1953, **6**, 1.
[6] M. M. Coombs and S. B. Jaitly, unpublished work.

product was probably the isomeric 7-hydroxy-17-ketone (VII); it possessed an increased R_F value, as did also the 11-hydroxy-17-ketone in which the hydroxy-group is sterically hindered (see Experimental section). By



analogy, the dehydration product from (Vb) was assumed to be the 6-ol (VIb; R′ = H), and this was supported by its R_F value. Moreover, in the n.m.r. spectrum of the derived acetate (VIb; R′ = Ac) the chemical shift of the multiplet ascribed to the C-15 methylene protons was the same as that of the C-15 methylene protons in the unsubstituted ketone (Ia), whereas distinct alterations in the position of this signal are noted with 7-substituted derivatives.[7]

Oxidation of the ketones (Ia and b) with lead tetra-acetate was also studied, because the potent carcinogen 9,10-dimethylbenzanthracene is oxidised to the 9,10-bis-acetoxymethyl derivative by this reagent,[8] and it was hoped that the 11-acetoxymethyl-17-ketone could be obtained in this way. Little reaction was observed when the unsubstituted ketone (Ia) was stirred with the reagent in glacial acetic acid at room temperature, but irradiation of a boiling mixture gave the 16-acetoxy-ketone (VIIIa; R′ = Ac) in moderate yield. This acetoxy-ketone was better prepared from the enol acetate (IXa), itself obtained in high yield from (Ia) with isopropenyl acetate and toluene-*p*-sulphonic acid, by oxidation with lead tetra-acetate at room temperature. The 17-oxo-group in (VIIIa; R′ = Ac) absorbs at 1720 cm.$^{-1}$, 30 cm.$^{-1}$ to higher frequency than in the parent ketone, probably as a result of interaction with the acetate carbonyl group. Many instances of elevation of normal carbonyl frequencies in 21-acetoxy-20-keto- and 12-acetoxy-11-keto-steroids are recorded.[9] Acid hydrolysis of (VIIIa; R′ = Ac) furnished the 16-hydroxy-17-ketone (VIIIa; R′ = H), which had 'normal' carbonyl absorption at 1690 cm.$^{-1}$. The u.v. spectra of (VIIIa; R′ = H or Ac) were identical and closely resembled that of the ketone (Ia), with the difference that all the maxima were shifted 2—4 mμ to longer wavelengths.

The 11-methyl-16-hydroxy-17-ketone (VIIIb; R′ = H) was also readily prepared by oxidation of the enol acetate (IXb) with lead tetra-acetate as already described, and had properties similar to (VIIIa). Treatment of the 11-methyl ketone (Ib) with this reagent at room temperature caused little reaction, but in boiling, irradiated acetic acid it gave as main product the 11-methyl-16-acetoxyketone (VIIIb; R′ = Ac); no evidence for appreciable oxidation of the 11-methyl group was found.

Conversion of the aromatic methyl group in 1-methyl-oestrone methyl ether into a formyl group, by oxidation with cerium(IV) ammonium nitrate in 90% acetic acid at room temperature, has recently been reported [10] to occur smoothly without concomitant attack at the aliphatic (C-18) or *O*-methyl groups, or at the activated methylene groups at C-6 and C-16. However, under these conditions the unsubstituted ketone (Ia) was rapidly oxidised, and the keto-quinone (IVa) was isolated in 28% yield; unchanged (Ia) was also recovered (23%). A third substance (*ca.* 15%) was not obtained pure, but possessed spectral properties suggesting the enolic β-diketone structure, cyclopenta[*a*]phenanthrene-15(16*H*),17-dione. The several minor oxidation products included an acidic fraction (10%) which appeared to consist of a mixture of phenanthrenecarboxylic acids produced by cleavage of the 5-membered ring D. Oxidation of the 11-methyl ketone (Ib) with cerium(IV) ammonium nitrate followed by t.l.c. of the reaction mixture disclosed a similar variety of products, although the amount of quinone was considerably less, as also noted in the chromic acid oxidation of this ketone. The

[7] M. M. Coombs, unpublished work.
[8] G. M. Badger and J. W. Cook, *J. Chem. Soc.*, 1939, 801; E. Boyland and P. Sims, *Biochem. J.*, 1965, **95**, 780.
[9] L. J. Bellamy, 'The Infra-red Spectra of Complex Molecules,' Methuen, London, 2nd edn., 1958, p. 146.
[10] S. B. Laing and P. J. Sykes, *J. Chem. Soc.*, 1968, 2915.

cyclopenta[*a*]phenanthrene ring system is thus markedly more susceptible to oxidation by cerium(IV) ions than is the oestrane system, and these experiments were discontinued.

EXPERIMENTAL

Reagents and apparatus were generally as described in Part I.[11] The medium-to-strong i.r. bands in the 10—15 μ region are quoted in addition to other salient bands of diagnostic relevance.

15,16-*Dihydro*-11-*methylcyclopenta*[a]*phenanthrene* (IIb).—The 11-methyl ketone (Ib),[11] glacial acetic acid (100 ml.) containing conc. hydrochloric acid (4 ml.), and a mixture of Adams catalyst (50 mg.) and 5% palladium–charcoal (100 mg.) were shaken in hydrogen. Absorption of gas ceased when the calculated volume had been consumed (60 hr.). The catalyst was filtered off and the solution furnished an oil which was chromatographed on alumina in benzene–hexane (1 : 1). The hydrocarbon (IIb) was obtained as a colourless oil (1·13 g.) which crystallised and gave needles (510 mg.), m.p. 81—82° (from ethanol) (lit.,[12] 80—81°).

16,17-*Dihydro*-11-*methylcyclopenta*[a]*phenanthren*-15-*one* (IIIb).—The hydrocarbon (IIb) (1·26 g.) was stirred with glacial acetic acid (14 ml.) while a solution of chromium trioxide (0·882 g.) in 80% acetic acid (2·2 ml.) was added during 5 min. Stirring was continued at room temperature for 40 hr., at the end of which the brown suspension was poured into water and extracted with chloroform. The extract was washed with sodium hydrogen carbonate solution and water, and dried. Evaporation left a yellow solid which was redissolved in benzene and chromatographed on a column of alumina. Elution with benzene–cyclohexane (1 : 1) gave the starting material (IIb) (150 mg.). Further elution with benzene yielded the *ketone* (IIIb) 495 mg., 37%), which gave pale yellow needles, m.p. 182—183° (from hot ethanol) (Found: C, 88·0; H, 5·7. $C_{18}H_{14}O$ requires C, 87·8; H, 5·75%), $\lambda_{max.}$ 217 (log ε 4·57), 253 (4·63), 284 (4·15), 323 (4·14), and 363 (3·41) mμ, $\nu_{max.}$ 5·94 (15-CO), 11·60, 11·90, 12·22, 13·28, 13·72, and 14·02 μ.

15-16-*Dihydrocyclopenta*[a]*phenanthrene*-6,7,17-*trione* (IVa).—The unsubstituted ketone (Ia) (92 mg.) in glacial acetic acid (10 ml.) was stirred with chromium trioxide (150 mg.) at room temperature for 24 hr.; t.l.c. then showed the absence of starting material. The yellow solid which had separated was collected, washed with a little acetic acid, then with water, and dried, giving the *keto-quinone* (IVa) (67 mg.), m.p. 245—247° (decomp.) [m.p. 250° (decomp.) (from toluene)] (Found: C, 77·7; H, 4·2. $C_{17}H_{10}O_3$ requires C, 77·85; H, 3·85%), $\nu_{max.}$ 5·84 (17-CO), 5·97 and 6·30 (quinone), 10·45, 11·63, 11·90, and 12·90 μ. The acetic acid mother liquors were diluted with water and the green solution was extracted with chloroform to yield yellow crystals (20 mg.) shown by t.l.c. to be (IVa) contaminated with traces of four other substances.

This keto-quinone was also obtained by oxidation of the keto-diol (Va) (20 mg.) with chromium trioxide (10 mg.) in acetic acid (4 ml.) for 2 hr. at room temperature. The mixture was treated as before to give yellow crystals (16 mg.), m.p. 246—249°, i.r. spectrum identical with that of the analytical specimen of (IVa).

[11] M. M. Coombs, *J. Chem. Soc.*, 1966, 955.
[12] A. Butenandt, H. Dannenberg, E. Bieneck, and W. Steidle, *Z. Naturforsch.*, 1950, **5b**, 405.

15,16-*Dihydro*-11-*methylcyclopenta*[a]*phenanthrene*-6,7,17-*trione* (IVb).—The 11-methyl ketone (Ib) (492 mg.) was oxidised as already described; after 24 hr. the presence of some unchanged (Ib) together with one major and three minor products was demonstrated by t.l.c. The yellow solution was diluted with water and extracted with chloroform–ethyl acetate to yield an orange gum, trituration of which with a few drops of ethyl acetate gave the 11-*methyl keto-quinone* (IVb) (191 mg.), which yielded small orange prisms, m.p. 230° (decomp.) (from benzene–hexane) (Found: C, 77·95; H, 4·2. $C_{18}H_{12}O_3$ requires C, 78·25; H, 4·4%), $\nu_{max.}$ 5·80 (17-CO), 6·0 and 6·24 (quinone), 10·30, 11·91, 12·80, 13·70, and 13·86 μ.

Column chromatography of the ethyl acetate solution on silica gel in toluene gave the starting material (81 mg.) and a second material (38 mg.). Elution with dichloromethane gave more quinone (IVb) (90 mg.).

Oxidation of the 11-methyl diol (Vb) (100 mg.) with chromium trioxide as before gave the quinone (IVb) as a yellow solid (106 mg.), i.r. spectrum identical with that of the analysed material.

6,7,15,16-*Tetrahydro*-6,7-*dihydroxycyclopenta*[a]*phenanthren*-17-*one* (Va).—The unsubstituted ketone (Ia) (464 mg.), osmium tetroxide (510 mg.), and pyridine (10 ml.) were stirred together in a dry atmosphere at room temperature for 8 days; t.l.c. (ethanol–toluene, 1 : 4) then showed that most of the ketone had been consumed. Water (2 ml.) and sodium pyrosulphite (2 g.) were added and stirring was continued for 5 hr. The dark mixture was poured into water (200 ml.) and the light-coloured solid was collected, washed with water, dried, and stirred with chloroform (10 ml.) to remove unchanged ketone. The residue (438 mg.) was boiled with n-butanol (30 ml.) and the solution, after removal of a small amount of insoluble solid, deposited prisms of the keto-diol (Va), m.p. 232—234° [m.p. 247—249° (from n-butanol)] (Found: C, 76·5; H, 5·1. $C_{17}H_{14}O_4$ requires C, 76·65; H, 5·3%), $\nu_{max.}$ 2·87 and 2·96 (OH), 5·90 (17-CO), 10·28, 12·16, 12·80, and 13·50 μ.

15,16-*Dihydro*-6-*hydroxycyclopenta*[a]*phenanthren*-17-*one* (VIa; R′ = H).—The keto-diol (Va) (168 mg.) was heated at 100° with 5N-sulphuric acid (10 ml.) in a sealed tube for 1 hr.; the liquid became filled with a flocculent yellow solid. When cold, the solid was collected, washed with water, and dried. This solid (150 mg.), which showed two spots on t.l.c. (see later), gave golden-yellow needles of the *phenol* (VIa; R′ = H) (141 mg.), m.p. 280° [from n-butanol (6 ml.)], which consisted entirely of the slower running material (Found: C, 82·05; H, 4·8. $C_{17}H_{12}O_2$ requires C, 82·25; H, 4·85%), $\nu_{max.}$ 3·20 (OH), 5·96 (17-CO), 11·54, 11·80, 12·18, 12·26, and 13·08 μ.

Relative R_F values and colours developed with Gibbs reagent *

	R_F †	Colour
Dehydration of (Va):		
main product	0·69	Turquoise-green
minor product	0·72	Mauve
Dehydration of (Vb)	0·69	Blue-violet
15,16-Dihydro-3-hydroxycyclopenta-[*a*]phenanthren-17-one	0·69	Fawn
15,16-Dihydro-11-hydroxycyclopenta-[*a*]phenanthren-17-one ‡	0·75	Mauve
9-Phenanthrol		Turquoise-green

* Solution (0·5%) of 2,6-dichloro-*p*-benzoquinone 4-chloroimine in ethanol, followed by 10% aqueous sodium carbonate.
† Silica gel plates; ethanol–toluene, 1 : 5. ‡ R. Robinson, *J. Chem. Soc.*, 1938, 1390.

Methylation of the phenol (VIa; R′ = H) (150 mg.) under nitrogen with 10% aqueous sodium hydroxide (50 ml.) and dimethyl sulphate (10 ml.) gave a solid (125 mg.) which gave pale yellow needles of the *methyl ether* (VIa; R′ = Me) (55 mg.), m.p. 193—195° (from ethanol) (Found: C, 82·7; H, 5·3. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%), $\nu_{max.}$ 5·90 (17-CO), 10·12, 12·22, 12·74, 13·02, and 13·76 μ; mixed m.p. with a sample (m.p. 196—197°) synthesised from 1-methoxynaphthalene showed no depression.

6,7,15,16-*Tetrahydro*-6,7-*dihydroxy*-11-*methylcyclopenta*[a]-*phenanthren*-17-*one* (Vb).—The 11-methyl ketone (Ib) (2·0 g.) was oxidised with osmium tetroxide (2·05 g.) in pyridine (30 ml.) as already described. The crude grey solid was boiled with ethanol (100 ml.), filtered while hot, and concentrated to yield discoloured crystals (1·37 g.); these gave the 11-*methyl keto-diol* (Vb) as prisms, m.p. 244—245° (from ethanol) (Found: C, 76·9; H, 5·7. $C_{18}H_{16}O_3$ requires C, 77·1; H, 5·75%), $\nu_{max.}$ 2·90 and 3·05 (OH), 5·96 (17-CO), 10·20, 10·38, 11·12, 12·04, 12·78, 13·10, 13·40, 13·80, and 14·46 μ.

15,16-*Dihydro*-6-*hydroxy*-11-*methylcyclopenta*[a]*phen-anthren*-17-*one* (VIb; R′ = H).—The diol (Vb) (1·16 g.) was heated in a sealed tube with 5N-sulphuric acid (50 ml.) for 2 hr. The yellow solid was collected and washed with aqueous N-sodium hydroxide, leaving a grey solid (0·73 g.) which proved to be starting material, m.p. 245—247°. The alkaline solution was acidified and the yellow precipitate was collected, washed with water, and dried. The crude solid gave golden-yellow needles (172 mg.), m.p. 335° (decomp.) [from hot octan-2-ol (50 ml.)], of the 11-*methyl phenol* (VIb; R′ = H) (Found: C, 82·0; H, 5·25. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·4%), $\nu_{max.}$ 3·08 (OH), 5·95 (17-CO), 11·46, 12·05, 12·86, 13·04, 13·74, and 14·50 μ.

When the time of heating was extended to 17 hr., the diol (Vb) (0·94 g.) gave the phenol (VIb; R′ = H) (0·76 g.) together with only a trace of alkali-insoluble material. Both this phenol and the crude phenol from the 2 hr. heating gave only one spot on t.l.c.

Acetylation of the pure phenol (200 mg.) with acetic anhydride–pyridine gave the *acetate* (VIb; R′ = Ac) (158 mg.), m.p. 225—227° [from n-butanol (20 ml.)] (Found: C, 78·85; H, 5·0. $C_{20}H_{16}O_3$ requires C, 78·95; H, 5·3%).

Methylation of the phenol (560 mg.) as before gave the *methyl ether* (VIb; R′ = Me) (564 mg.) which separated from ethanol as prisms, m.p. 203—205° (Found: C, 82·65; H, 5·75. $C_{19}H_{16}O_2$ requires C, 82·6; H, 5·85%), $\nu_{max.}$ 5·86 (17-CO), 12·26, 13·18, and 13·78 μ.

15,16-*Dihydro*-3-*hydroxycyclopenta*[a]*phenanthren*-17-*one*.—15,16-Dihydro-3-methoxycyclopenta[*a*]phenanthren-17-one [11] (0·80 g.) was heated with freshly distilled pyridine hydrochloride (10 g.) at 220° to yield a red liquid. After 3 min. cold water (50 ml.) was added. Trituration gave a yellow powdery solid which was stirred and warmed with 0·1N-sodium hydroxide (600 ml.). After an insoluble orange-coloured solid had been filtered off, the alkaline solution was acidified and the flocculent yellow precipitate was collected, washed with water, and dried (0·25 g.). Recrystallisation from n-butanol gave the *phenol* as small yellow rosettes of needles (Found: C, 81·85; H, 5·1. $C_{17}H_{12}O_2$ requires C, 82·25; H, 4·85%), $\lambda_{max.}$ 270sh (log ε 4·94), 277·5 (5·02), 292infl (4·30), 324 (4·08), 366 (3·28), and 396—403 (2·91) mμ, $\nu_{max.}$ 3·20 (OH), 5·98 (17-CO), 10·50, 11·52, 12·36, 12·60, and 14·15 μ.

Acetylation as before gave 3-*acetoxy*-15,16-*dihydrocyclo-penta*[a]*phenanthren*-17-*one*, pale yellow needles from n-butanol, m.p. 209—213° (Found: C, 78·85; H, 5·2. $C_{19}H_{14}O_2$ requires C, 78·6; H, 4·85%).

17-*Acetoxy*-15H-*cyclopenta*[a]*phenanthrene* (IXa).—The unsubstituted ketone (Ia) (3·30 g.) was heated under reflux with isopropenyl acetate (250 ml.) and toluene-*p*-sulphonic acid (20 mg.) during 6 hr. while the solvent (200 ml.) was slowly distilled off. Dichloromethane (100 ml.) was added and the solution was washed with aqueous sodium hydrogen carbonate and water, and dried. The pale fawn crystals obtained on removal of the solvent yielded the *enol acetate* (IXa) (3·23 g.), m.p. 210—211° [from benzene (30 ml.)] (Found: C, 83·25; H, 5·05. $C_{19}H_{14}O_2$ requires C, 83·2; H, 5·15%), $\lambda_{max.}$ 222 (log ε 4·48), 269 (4·91), 273 (4·92), 291 (4·28), 312 (3·89), 312 (3·89), 329 (2·91), 345 (2·83), and 363 (2·66) mμ, $\nu_{max.}$ 5·72 and 8·24 (enol acetate), 11·00, 12·02, 12·28, 12·85, 13·34, and 13·88 μ.

16-*Acetoxy*-15,16-*dihydrocyclopenta*[a]*phenanthren*-17-*one* (VIIIa; R′ = Ac).—The enol acetate (IXa) (3·53 g.) was stirred in glacial acetic acid (115 ml.) and acetic anhydride (15 ml.) with lead tetra-acetate (6·3 g.; moist with acetic acid), and the flask was irradiated with a 60 w tungsten filament lamp. After 3 hr., more lead tetra-acetate (1·0 g.) was added, and stirring and irradiation were continued overnight (17 hr.). After dilution with dichloromethane (500 ml.) the yellow solution was washed successively with 5% aqueous sodium thiosulphate (2 × 500 ml.), saturated sodium hydrogen carbonate solution (2 × 500 ml.), and water, and was dried. Evaporation left an orange syrup which crystallised; this material had i.r. bands at 5·75m, 5·81s, 8·10s, and 8·23m μ (16,17,17-triacetate?). It crystallised from benzene (20 ml.), after removal of a little insoluble material, as pale yellow leaflets (2·48 g.) of the 16-*acetoxy-ketone* (VIIIa; R′ = Ac), m.p. 178° (Found: C, 78·8; H, 4·65. $C_{19}H_{14}O_3$ requires C, 78·6; H, 4·85%), $\nu_{max.}$ 5·70 and 8·16 (acetate), 5·81 (17-CO), 12·14, 12·40, 12·92, and 13·16 μ.

Hydrolysis of this acetoxy-ketone (500 mg.) in methanol (25 ml.) with 5N-sulphuric acid (10 ml.) under reflux for 2 hr. gave a solution which was cooled to yield pale yellow prisms of the *hydroxy-ketone* (VIIIa; R′ = H) (342 mg.) m.p. 186—187°. Recrystallisation from ethanol–chloroform (2 : 1; 30 ml.) gave a sample, m.p. 195° (decomp.) (Found: C, 82·1; H, 4·55. $C_{17}H_{12}O_2$ requires C, 82·24; H, 4·85%), $\nu_{max.}$ 2·96 (16-OH), 5·92 (17-CO), 12·16, 12·44, and 13·30 μ. Attempted alkaline hydrolysis led to a mixture of products.

16-*Acetoxy*-15,16-*dihydro*-11-*methylcyclopenta*[a]*phen-anthren*-17-*one* (VIIIb; R′ = Ac).—The 11-methyl ketone (Ib) (6·65 g.) was treated with isopropenyl acetate and toluene-*p*-sulphonic acid as already described to give the crude enol acetate (IXb) as a brown crystalline mass. Oxidation of this material with lead tetra-acetate and precipitation from benzene (60 ml.) with hexane (30 ml.) yielded the 11-*methyl* 16-*acetoxy-ketone* (VIIIb; R′ = Ac) (1·94 g.), which (from the same solvent mixture) gave silky needles, m.p. 156—157° (Found: C, 78·9; H, 5·2. $C_{20}H_{16}O_3$ requires C, 78·95; H, 5·35%), $\nu_{max.}$ 5·72 and 8·10 (acetate), 5·81 (17-CO), 12·02, 12·14, 12·90, 13·18, 13·30, and 13·96 μ.

Acid hydrolysis of this acetoxy-ketone (1·79 g.) as before yielded the 11-*methyl* 16-*hydroxy-ketone* (VIIIb; R′ = H) (1·44 g.), which gave pale yellow needles, m.p. 205—207° (from n-butanol) (Found: C, 82·45; H, 5·3. $C_{18}H_{14}O_2$ requires C, 82·4; H, 5·25%), $\nu_{max.}$ 3·00 (16-OH) 5·92 (17-CO), 11·44, 11·62, 12·06, 12·28, 12·55, 12·80, 13·56, and 14·10 μ.

Oxidation of the 17-*Ketones with Lead Tetra-acetate.*—*Unsubstituted ketone* (Ia). This ketone (230 mg.) was boiled under reflux with acetic acid (10 ml.) and lead tetra-acetate (500 mg.) with irradiation for 16 hr. The brown solution was diluted with chloroform and treated as in the similar oxidation of the enol acetate to afford a yellow gum, t.l.c. (dichloromethane) of which disclosed the presence of starting material (Ia), the 16-acetoxy-ketone (VIIIa; R′ = Ac), and small amounts of several other products more polar than the latter. This gum was absorbed on a small column of silica gel. Elution with hexane–dichloromethane (4 : 1) gave material (93 mg.) which yielded (Ia), m.p. 199—201° (30 mg.) (from benzene). Later fractions contained the acetoxy-ketone, m.p. 178—180° (55 mg.). The i.r. and u.v. spectra of this material were identical with those of the sample prepared from the enol acetate.

11-*Methyl ketone* (Ib). Treatment of this ketone (25 mg.) with lead tetra-acetate as already described gave a brown gum, preparative t.l.c. (dichloromethane) of which yielded crystals of the main product with i.r. and u.v. spectra identical with those of the 11-methyl 16-acetoxy-ketone (VIIIb; R′ = Ac) derived from the corresponding enol acetate. The presence of starting material (Ib) was also demonstrated, and the t.l.c. pattern of minor oxidation products was similar to that exhibited by the crude lead tetra-acetate oxidation product of (Ia).

Oxidation of 17-*Ketones with Cerium*(IV) *Ammonium Nitrate.*—*Unsubstituted ketone* (Ia). The ketone (2·32 g.) was stirred at room temperature with acetic acid (50 ml.) while a solution of cerium(IV) ammonium nitrate (22·42 g.) in acetic acid (200 ml.) and water (15 ml.) was added. After a further 3 hr. stirring all the solid had dissolved to give a clear yellow solution which was poured into water (2 l.) and extracted with dichloromethane. The extract was washed with sodium hydrogen carbonate solution and with water, and dried; evaporation left a yellow gum (2·40 g.). The alkaline washings were acidified and extracted to yield a yellow resinous solid (0·26 g.), $\lambda_{max.}$ 265 mμ, $\nu_{max.}$ 2·85 and 3·78, and 5·92—5·78 μ (CO_2H). The neutral material, shown by t.l.c. (dichloromethane) to consist of at least ten compounds, was chromatographed on a column of silica gel, with toluene containing increasing proportions (1—20%) of ethyl acetate as eluant. Later fractions yielded crystalline keto-quinone (IVa) (710 mg.); unchanged ketone (Ia) (609 mg.) was eluted with 3% ethyl acetate. Fractions eluted with 5% ethyl acetate gave a yellow gum (475 mg.) which was rechromatographed to yield an amorphous solid (235 mg.), not obtained crystalline although it appeared to consist of a single substance (t.l.c.). This solid had i.r. bands at 6·10, 5·83, and 5·75 μ (CO), suggesting a partially enolised β-diketone system, and this was confirmed by the production of a green colour when a dilute ethanolic solution of the material was mixed with ethanolic copper(II) acetate. The u.v. spectrum [$\lambda_{max.}$ 268 mμ with broad shoulders at 285 and 295 mμ] altered to $\lambda_{max.}$ 291 mμ on addition of N-sodium hydroxide and to $\lambda_{max.}$ 269—272 mμ on addition of N-hydrochloric acid; these changes were reversible. After addition of sodium borohydride the solution had $\lambda_{max.}$ 260 mμ, similar to both 15- and 17-hydroxy-15,16-dihydrocyclopenta[*a*]phenanthrenes.

U.v. and visible absorption maxima of 15,16-dihydrocyclopenta[*a*]phenanthren-17-one derivatives

		λ max. (mμ) (log ε)
Keto-quinones	(IVa)	271—279 (4·03), 331 (3·31), 406 (3·21)
	(IVb)	263 (4·15), 345 (3·44), 410infl (2·94)
Keto-diols	(Va)	245 (4·02), 309—317 (4·43)
	(Vb)	232infl (4·13), 308—314 (4·22)
Phenols (R′ = H)	(VIa)	274 (4·79), 285sh (4·54), 386 (3·45)
	(VIb)	270 (4·70), 289sh (4·58), 378 (3·32), 3 90 (3·35)
Methyl ethers (R′ = Me)	(VIa)	270 (4·81), 287 (4·48), 302 (4·28), 361 (3·37), 378 (3·42)
	(VIb)	265 (4·76), 289sh (4·51), 306sh (4·27), 368 (3·37), 384 (3·41)
16-Hydroxy-ketones (R′ = H)	(VIIIa)	265 (4·95), 284 (4·49), 296 (4·39), 335 (3·15), 351 (3·32), 369 (3·33)
	(VIIIb)	264 (4·88), 288 (4·52), 301 (4·35), 345 (3·14), 361 (3·36), 379 (3·39)
16-Acetoxy-ketones (R′ = Ac)	(VIIIa)	266 (4·92), 284 (4·50), 297 (4·39), 352 (3·31), 370 (3·32)
	(VIIIb)	263 (4·87), 288 (4·52), 301 (4·35), 342 (3·12), 357 (3·37), 375 (3·42)

The 11-*methyl ketone* (Ib). The ketone (25 mg.) was oxidised as already described. The dichloromethane extract of the mixed oxidation products was noticeably less yellow than that from the similar oxidation of (Ia). T.l.c. disclosed a similar range of products, but the amount of quinone was considerably less.

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