Potentially Carcinogenic Cyclopenta[a]phenanthrenes. Part IX.[1] Characterisation of a 5,10-Epoxybenzocyclodecene as a Major Urinary Metabolite of the Carcinogen 15,16-Dihydro-11-methylcyclopenta[a]-phenanthren-17-one

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The major urinary metabolite of the carcinogen 15,16-dihydro-11-methylcyclopenta[a]phenanthren-17-one (Ib) produced by the rat is shown by chemical and spectral examination to possess the novel structure 8.9-epoxy-1α.2β,15ξ-trihydroxy-11-methyl-8.9-secogona-3.5,7,9.11.13-hexaen-17-one (II).

THERE is a marked difference [2] in the urinary metabolism of 15,16-dihydrocyclopenta[a]phenanthren-17-one (Ia) and its strongly carcinogenic [3] 11-methyl homologue (Ib) in the rat. In both cases, after injection of the [14C]-labelled ketones, 40—50% of the radioactivity present in the urine was extractable by ethyl acetate, and t.l.c. disclosed the presence of ca. 12 metabolites. However,

the extract from the urine of rats which had been administered the carcinogen (Ib) contained a metabolite which accounted for ca. 50% of the radioactivity in this extract, whereas only a trace of material with a similar R_F value, u.v. absorption, and fluorescence was present in the extract from rats which had received the non-
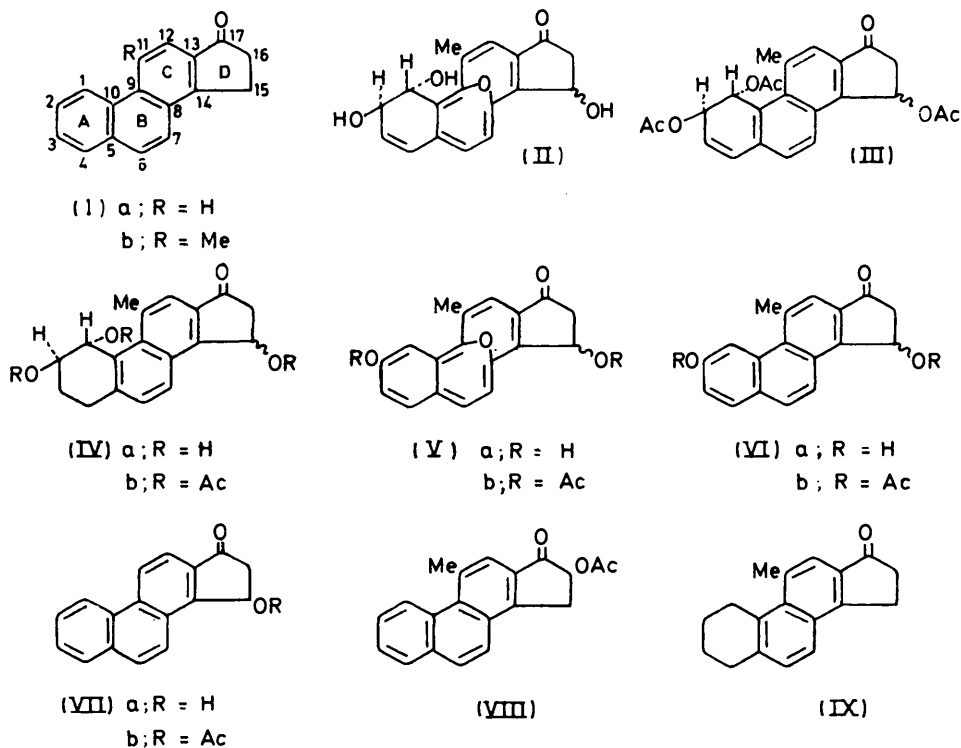
[1] Part VIII, M. M. Coombs, M. Hall, and C. W. Vose, J.C.S. Perkin I, 1973, 2236.

[2] M. M. Coombs and F. E. Crawley, in preparation.

[3] M. M. Coombs and C. J. Croft, Progr. Experimental Tumor Research, 1969, 11, 69.

carcinogenic parent ketone (Ia). This paper describes the chemical identification of this major metabolite.

On acetylation this metabolite ($C_{18}H_{16}O_5$) yielded a triacetate (III), $C_{24}H_{22}O_7$, indicating that acetylation was accompanied by the loss of an oxygen atom. Hydrogenation of the metabolite occurred with the uptake of 2 moles of hydrogen to give the dihydrotriol (IVa), $C_{18}H_{18}O_4$, again with loss of an oxygen atom. Acetylation of (IVa) gave the dihydrotriacetate (IVb) ($C_{24}H_{24}O_7$) identical with the product of hydrogenation of the triacetate (III). Treatment of the metabolite with hot mineral acid did not result in loss of oxygen, but gave

each of these ketones the carbonyl group in conjugated, absorbing at 1690 cm^{-1} in the hydroxy-ketones (II) and (Va) and at 1720 cm^{-1} in the acetates (III) and (Vb). A similar difference in the carbonyl frequency has been observed between the 15-hydroxy-ketone (VIIa) and its acetate (VIIb).[1] That one hydroxy-group in these compounds is at C-15, rather than at C-16, is demonstrated by the very similar chemical shifts and coupling constants of the 15- and 16-protons in the n.m.r. spectra of the acetates (III) and (Vb) when compared with those of the synthetic 15-acetoxy-17-ketone (VIIb), in contrast to those of the 16-acetoxy-17-ketone (VIII) (Table 1).

(1) a; R = H
    b; R = Me

(II)

(III)

(IV) a; R = H
     b; R = Ac

(V) a; R = H
    b; R = Ac

(VI) a; R = H
     b; R = Ac

(VII) a; R = H
      b; R = Ac

(VIII)

(IX)

dehydration to the mono-phenolic diol (Va) ($C_{18}H_{14}O_4$), acetylation of which gave the diacetate (Vb) ($C_{22}H_{18}O_6$). Both (Va) and (Vb) retain a non-funtional oxygen atom, whereas the oxygen atoms in the metabolite triacetate (III) are present in functional groups only. The presence of a thermally labile oxygen atom in both the metabolite (II) and its dehydration product (Va) is clearly demonstrated by the mass spectral fragmentation patterns of these two compounds [(Va), m/e 278 ($M - O$); (II), m/e 278 ($M - H_2O - O$)]. Examination by t.l.c. of material recovered from the mass spectrometer inlet after introduction of (II) showed the presence of only one compound with the same R_F value and colour reactions as the dehydration product (Va). No ions corresponding to loss of oxygen appear in the mass spectrum of the metabolite triacetate (III) or in that of the diol (VIa), formed from (III) by deacetylation and dehydration with acid.

Ring c in the metabolite (II) and in its transformation products (III) and (V) is aromatic because in each the 11-methyl group has an n.m.r. absorption near τ 7, and in

The u.v. spectra of (II) and (III) are very similar, despite the loss of the non-functional oxygen atom in the latter, but they differ from those of the other chromophores so far encountered with these metabolites. The u.v. spectra of the compounds formed on reduction with borohydride resemble that of 3,4-dihydro- (but *not* 1,2-dihydro-)phenanthrene. Thus ring B must also be aromatic and the conjugated ethylenic double bond must be between C-3 and C-4. The second and third OH groups are, therefore, attached at C-1 and C-2. Selective hydrogenation of the 3,4-double bond in (III) and in (II) (accompanied in this case by loss of the extra oxygen atom), gave products with u.v. spectra very similar to that of the synthetic ketone (IX),[4] thus confirming that ring A is partially unsaturated.

The position and conformation of the secondary hydroxy-groups at C-1 and C-2 are further established by consideration of the C*H*OH n.m.r. signals for C-1 and C-2 (Table 2). H-2 in metabolite (II) resonates at τ 5·64 and

4 M. M. Coombs and T. S. Bhatt, *J.C.S. Perkin I*, 1973, 1251.

is deshielded by 1·1 p.p.m. in the triacetate (III); it thus behaves as a typical secondary alcohol.[5] H-1 resonates 1·5 p.p.m. lower in (II), at τ 4·15, and is deshielded by 1·26 p.p.m. on passing to (III). The environment of H-1 is similar to that experienced by H-1 in the cyclopenta[a]-phenanthrene (Ib), in which H-1 resonates at 1—1·5

only as an internal epoxy-bridge, since treatment with acid does not open the ring to give a diol, as would be expected if a 1,2-epoxide were present. Several pieces of evidence suggest that (II) contains an internal epoxy-bridge. The presence of ions showing the loss of an oxygen atom in the mass spectrum of (II) is the most

TABLE 1

N.m.r. data (τ values, J in Hz) for compounds (VIIa), (VIII), (III), and (Vb) in $CDCl_3$

Proton	15-Acetoxyketone (VIIa)	16-Acetoxyketone (VIII)	(III)	(Vb)
11-Me		6·97 (3H)	7·02 (3H)	6·84 (3H)
AcO	7·86 (3H)	7·75 (3H)	7·86 (3H)	7·61 (3H)
			7·98 (3H)	7·88 (3H)
			8·01 (3H)	
H-15	3·17 ($J_{15.16}$ 2, $J_{15.16}$ 6)	6·85 ($J_{15.16}$ 4, $J_{15.15}$ 18)	3·22 ($J_{15.16}$ 2, $J_{15.16}$ 6)	3·16 ($J_{15.16}$ 2, $J_{15.16}$ 7)
H-15		6·02 ($J_{15.16}$ 8, $J_{15.15}$ 18)		
H-16	7·29 ($J_{15.16}$ 2, $J_{16.16}$ 18)	4·50 ($J_{15.16}$ 4, $J_{15.16}$ 8)	7·32 ($J_{15.16}$ 2, $J_{15.15}$ 19)	7·30 ($J_{15.16}$ 2, $J_{15.15}$ 19)
H-16	6·65 ($J_{15.16}$ 6, $J_{16.16}$ 18)		6·65 ($J_{15.16}$ 6, $J_{15.15}$ 19)	6·65 ($J_{15.16}$ 7, $J_{15.15}$ 19)
H-1	1·32 (J_o 8, J_m 2)	1·18 (J_o 7, J_m 3)	2·87 ($J_{1.2}$ 2)	1·33 (J_m 2)
H-2			4·52 ($J_{1.2}$ 2, $J_{2.3}$ 6)	
H-11	1·16 ($J_{11.12}$ 9)			
Other protons attached to conjugated C atoms	2·0—2·5 (6H)	2·0—2·6 (6H)	1·92—3·65 (5H)	2·0—2·85 (5H)

p.p.m. to lower field than the rest of the aromatic protons in this molecule. H-1 in (II) and (III) is therefore equatorial, in almost the same plane as the aromatic rings, and within the deshielding zone of the aromatic

TABLE 2

N.m.r. data * (τ values, J in Hz) for compounds (II) and (III) in CD_3OD

Proton	(II)	(III)	$\tau(II) - \tau(III)$ /p.p.m.
H-1	4·15 ($J_{1.2}$ 2)	2·89 ($J_{1.2}$ 2)	1·26
H-2	5·64 ($J_{1.2}$ 2, $J_{2.3}$ 6)	4·53 ($J_{1.2}$ 2, $J_{2.3}$ 5)	1·11
H-3	3·70 ($J_{2.3}$ 6, $J_{3.4}$ 9)	3·72 ($J_{2.3}$ 5, $J_{3.4}$ 9)	−0·02
H-4	3·15 ($J_{3.4}$ 9)	3·05 ($J_{3.4}$ 9)	0·01
H-6	2·48 ($J_{6.7}$ 9)	2·45 ($J_{6.7}$ 9)	0·03
H-7	1·52 ($J_{6.7}$ 9)	1·89 ($J_{6.7}$ 9)	−0·37
H-12	2·48	2·44	0·04
H-15	4·24 ($J_{15.16}$ 2, $J_{15.16}$ 6)	3·30 ($J_{15.16}$ 1·5, $J_{15.16}$ 6)	0·86
H-16	6·81 ($J_{15.16}$ 6, $J_{15.15}$ 19)	6·72 ($J_{15.16}$ 6, $J_{15.15}$ 19)	0·09
H-16	7·40 ($J_{15.16}$ 2, $J_{15.15}$ 19)	7·38 ($J_{15.16}$ 1·5, $J_{15.15}$ 19)	0·02
11-Me	6·78 (3H)	7·07 (3H)	−0·28

* Some assignments were checked by spin–spin decoupling experiments.

ring current. The small magnitude of the coupling between H-1 and H-2 (2 Hz) indicates that these protons are equatorial–equatorial, and the OH groups are thus trans (1α,2β), as expected for a vicinal diol derived metabolically from an aromatic ring A, probably via the 1,2-epoxide. This evidence establishes the structure of the metabolite triacetate as (III).

The similarity of the u.v. spectra of (II) and (III), and of their borohydride reduced derivatives indicates that (II) and (III) have the same overall structure. The 'extra' oxygen atom in (II) can then be accommodated

[5] N. S. Bhacca and D. H. Williams, 'Application of N.m.r. Spectroscopy in Organic Chemistry,' Holden Day, San Francisco, 1964, p. 77.

significant. The valence tautomer (X) of pyrene 15,16-epoxide gave the expected M^+ ion at m/e 218 and an even more intense signal at m/e 202 $(M - O)$.[6] In strong acid this molecule is protonated at oxygen with formation of the stable 3-membered ring. Treatment of 1,6-epoxy-[10]annulene (XI) with acid gave 1-benzoxepin (XII),
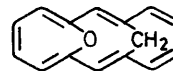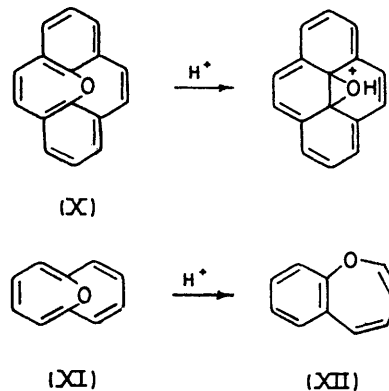

(X)

(XI)   (XII)

(XIII)

while mild hydrogenation led to naphthalene by elimination of the epoxy-bridge.[7] In a similar way treatment of (II) with acid yields (Va) with retention of the 'extra' oxygen atom, while hydrogenation causes its elimination. An n.m.r. study of syn-1,6-epoxy-8,13-methano[14]-annulene (XIII) led to the conclusion that this molecule tolerates compression of the bridges rather than bending

[6] B. A. Hess, A. S. Bailey, and V. Boekelheide, J. Amer. Chem. Soc., 1967, 89, 2746.

[7] A. Shani and F. Sondheimer, J. Amer. Chem. Soc., 1967, 89, 6310.

of the ring.[8] The close similarity of the u.v. spectra of (II) and (III) indicates that here, also, the molecule of (II) is not substantially bent by the oxygen bridge.

Consideration of the n.m.r. spectra of (II) and (III) obtained under identical conditions (Table 2) shows that H-1, -2, and -16 in (III) are deshielded, as expected, by *ca.* 1 p.p.m. The chemical shifts of H-3, -4, -6, -12, and -15 are similar in (II) and (III), indicating that these protons occupy very similar conformations in the two molecules. The slight deshielding of H-4, -6, and -12 probably results from the greater coplanarity, and hence greater ring current, associated with the aromatic rings B and C in (III). By contrast, H-7 and the protons of the 11-methyl group are substantially shielded in (III). This suggests loss of an electronegative substituent from the adjacent 8- and 9-positions on passing from (II) to

to the three protons in rings B and C occur between τ 2·0 and 2·4 as generally observed in cyclopenta[a]phenanthrenes. There is little evidence to suggest the position of the epoxy-bridge (Vb). However, the protons of the 11-methyl group in this compound resonate at a lower field than those in 11-methylcyclopenta[a]phenanthrenes (τ *ca.* 7·0), so that the bridge is probably 8 $\longrightarrow$ 9. If it were 8 $\longrightarrow$ 10, H-1 would not be deshielded to the extent observed. The dehydration product therefore has structure (Va). The product of dehydration and de-acetylation of (III) with acid is similar to (Va) but contains one less oxygen atom, and is therefore probably the corresponding cyclopenta[a]phenanthrene (VIa).

It seems improbable that metabolism of the ketone (Ib) could lead directly to insertion of the 8,9-epoxy-bridge in the metabolite (II). This compound is more

(XIV) (XV) (XVI)
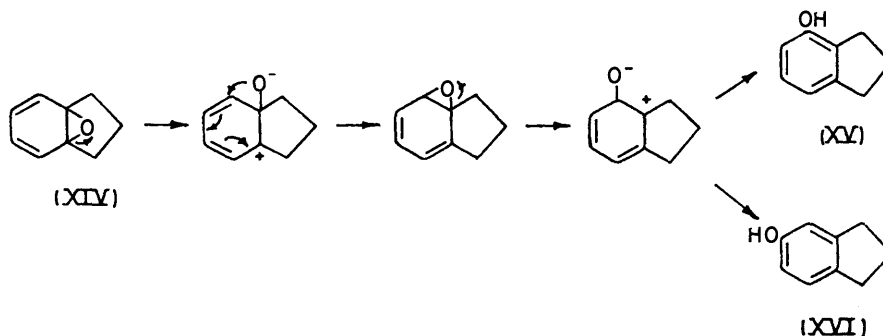
(III), and therefore that the epoxy-bridge is 8 $\longrightarrow$ 9. The structure of the metabolite is therefore as shown in (II).

Since the ready loss of the epoxy-bridge on acetylation under mild conditions was unexpected, the acetylation conditions were investigated. Omission of the acid wash of the ether extract or examination of the reaction mixture before addition of water gave products indistinguishable by t.l.c. from (III); also the metabolite (II) was recovered unchanged after dissolution in dry pyridine. It was therefore concluded that elimination of the oxygen occurred during the acetylation reaction itself. This may involve rear-side attack by the carbonyl oxygen of the C-1 acetyl group at C-9, since a model demonstrates that these two atoms can approach one another closely. Also the 8 $\longrightarrow$ 9 epoxy-bridge in the dehydration product (Va) is stable to acetylation, and the product does not possess a 1α-acetoxy-group. The n.m.r. chemical shifts and coupling constants (Table 1) of H-15 and -16 of this acetate (Vb) are very similar to those of (III). The low field region of this spectrum includes a one-proton doublet at τ 1·33 (J 2 Hz) while the rest of the aromatic protons resonate in the range τ 2·0—2·85. This proton is therefore probably H-1, and in agreement with this it is not *ortho*-coupled since the phenolic OH group must then be at C-2. Two pairs of one-proton quartets at τ 2·58 (J_o 8, J_m 2 Hz) and 2·04 (J_o 8 Hz) can then be assigned to H-3 and -4, respectively. Signals due

likely to have arisen by rearrangement of a reactive intermediate. Chemical oxidation of (Ia) and (Ib) occurs at the K-region, osmium tetraoxide yielding the 6,7-dihydro-6,7-diols and chromic acid giving the 6,7-quinones.[9] It thus seems likely that this region will also be the site of major metabolic attack leading to 6,7-dihydro-6,7-epoxides.[10] Rearrangement of the latter with migration of the oxygen atom at a position bridging C-8 and C-9 seems possible. Recently a rearrangement of this type has been proposed by Bruice [11] to account for the formation of indan-4-ol (XV) and indan-5-ol (XVI) from 3a,7a-epoxy-3a,7a-dihydroindan (XIV). In this rearrangement the arene oxide opens to give a zwitterion which collapses to an isomeric oxide, resulting in movement of the oxygen atom round the ring, finally to yield the two phenols. Possibly the marked difference in urinary metabolism between the carcinogenic 11-methyl-ketone (Ib) which gives (II), and the inactive un-substituted ketone (Ia) which gives only a trace of the unsubstituted homologue, is that the electron-releasing 11-methyl group favours this type of rearrangement, or that oxepin formation allows release of the 1-H–11-Me interaction.

EXPERIMENTAL

Procedures are generally as described in the preceding parts of this series. M.p.s were obtained using a Kofler hot

[8] E. Vogel, U. Haberland, and J. Ick, *Angew. Chem. Internat. Edn.*, 1970, **9**, 517.

[9] M. M. Coombs, *J. Chem. Soc.* (C), 1969, 2484.

[10] E. Boyland, in 'The Jerusalem Symposia on Quantum Chemistry and Biochemistry,' eds. E. D. Bergmann and B. Pullman, vol. 1, Academic Press, Israel, 1969, p. 28.

[11] P. Y. Bruice, G. J. Kasperek, T. C. Bruice, H. Yagi, and D. M. Jerina, *J. Amer. Chem. Soc.*, 1973, **95**, 1673.

stage microscope (RCH, Reichert, Austria), or glass capillary tubes and an Electrothermal electrically heated block. I.r. spectra were recorded as mulls in Nujol on a Perkin-Elmer model 257 spectrometer. N.m.r. spectra were measured on a Varian A60 (60 MHz) or a Perkin-Elmer R32 (90 MHz, Me₄Si lock) spectrometer. Mass spectra were obtained using an A.E.I. MS902 instrument.

Preparation of 15,16-*Dihydro*-11-[³H]*methylcyclopenta*[a]-*phenanthren*-17-*one*.—This compound was prepared from 17,17-ethylenedioxy-12,13,14,16,15,17-hexahydrocyclopenta[a]phenanthren-11-one (588 mg, 2 mmol) and [³H]-methyl iodide (282 mg, 2 mmol, 200 mCi) by a Grignard reaction as previously described [12] for the [¹⁴C]methyl compound. The product (248 mg, 26·5 mCi) obtained after chromatography as fawn needles, m.p. 202°, ran as a single spot on t.l.c. (dichloromethane) and had u.v. and i.r. spectra identical with those of the authentic, unlabelled ketone.

Characterisation of the Metabolite 8,9-*Epoxy*-1α,2β,15ξ-*trihydroxy*-11-*methyl*-8,9-*secogona*-3,5,7,9,11,13-*hexaen*-17-*one* (II).—This material was soluble in ethanol and moderately soluble in water, and was best purified by recrystallisation from ethyl acetate with addition of a little charcoal. After repeated recrystallisation from this solvent the *metabolite* (II) was obtained as pale fawn needles which decomposed without melting at 120° (*in vacuo*), $[\alpha]_D^{26}$ −214° (*c* 0·134, EtOH). For analysis, samples were dried at 40° *in vacuo* after recrystallisation from ethanol (Found: C, 69·3; H, 5·7%), and from ethyl acetate (Found: C, 70·3; H, 5·2%; *m/e* 294·0893. $C_{18}H_{16}O_5$ requires C, 69·2; H, 5·15%. $M^+ − H_2O$ requires *m/e*, 294·0892), *m/e* 294 (6%), 278 ($M − H_2O − O$, 34), 277 (100), 261 (30), 260 (21), 259 (20), 248 (20), 234 (36), and 232 (50), $\lambda_{max.}$ (EtOH) 267 (log ε 4·57), 320 (4·03), 332 (4·04), 352 (3·67), and 370 nm (3·61), unchanged by the addition of aqueous NaOH; treatment of the ethanolic solution with NaBH₄ for 30 min gave $\lambda_{max.}$ (EtOH) 258 (log ε 4·60), 267 (4·67), 3·18 (3·78) nm; $\nu_{max.}$ 3400—3160 (O–H str., probably involving intermolecular hydrogen bonding), 1690 (ArCO), 1605 (conjugated C=C), and 1040 and 1005 cm⁻¹ (possibly C–O–C), τ (CD₃OD, 90 MHz) in Table 2.

The metabolite (II) gave no immediate colour with Gibb's reagent (not phenolic), nor did it liberate iodine from KI in 2M-H_2SO_4 (not a hydroperoxide).[13] It did not liberate alkali from a solution of $Na_2S_2O_3$ in 50% (v/v) aqueous acetone, a test considered specific for 1,2-dihydro-1,2-epoxides.[14]

1α,2β,15ξ-*Triacetoxy*-1,2,15,16-*tetrahydro*-11-*methylcyclopenta*[a]*phenanthren*-17-*one* (III).—The metabolite (II) (40 mg) was dissolved in a mixture of acetic anhydride (0·5 ml) and dry pyridine (0·5 ml) and kept at room temperature for 18 h. After addition of water (10 ml), the solution was extracted with ether, and the extract was washed successively with 2M-H_2SO_4, saturated aqueous NaHCO₃, and water. Evaporation of the dried solution left an orange gum which crystallised; after repeated recrystallisation from ethanol it gave pale fawn crystals of the *triacetate* (III), m.p. 170—171° (Found: C, 67·95, 68·3; H, 4·9; M^+, 422·1354. $C_{24}H_{22}O_7$ requires C, 68·25; H, 5·25%, *M*, 422·1361), $\lambda_{max.}$ (EtOH) 268 (log ε 4·64), 322 (4·05), 333 (4·07), and 370 nm (3·50), and after treatment with NaBH₄, $\lambda_{max.}$ (EtOH) 264 (log ε 4·62), 269 (4·66), and 323 nm (3·74), $\nu_{max.}$ 1740 (acetate CO) and 1710 (ketone CO), and 1020 cm⁻¹,

τ (CD₃OD) in Table 2, τ (CDCl₃) in Table 1, *m/e* 422 (M^+), no $M − O$ peak.

1,2,3,4,15,16-*Hexahydro*-1α,2β,15ξ-*trihydroxy*-11-*methylcyclopenta*[a]*phenanthren*-17-*one* (IVa).—The metabolite (II) (15 mg), dissolved in ethanol, was stirred in an atmosphere of hydrogen with 10% palladium-on-charcoal (Johnson–Matthey). Uptake of gas ceased after 80 min when 1·95 mol. equiv. of hydrogen had been consumed. The catalyst was removed by filtration and the product was crystallised from ethanol to yield cream needles of the *hydrogenated derivative* (IVa) (Found: M^+, 298·1199. $C_{18}H_{18}O_4$ requires *M*, 298·1205), m.p. 225—227° (from ethanol), $\lambda_{max.}$ (EtOH) 260 (log ε 4·70), 285 (3·89), 295 (3·94), 342 (3·46), and 354 nm (3·49) {cf. 1,2,3,4,15,16-hexahydro-11-methylcyclopenta[a]-phenanthren-17-one (IX),[4] $\lambda_{max.}$ (EtOH) 261 (log ε 4·77), 287 (3·97), 297·5 (4·02), 344 (3·69), and 354 nm (3·74)}. Acetylation of (IVa) as previously described gave a triacetate, m.p 123—124°, identical with the triacetate obtained by hydrogenation of (III) (see below).

Hydrogenation of the Triacetate (III).—Hydrogenation of (III) (5 mg) as already described yielded crystalline 1α,2β,15ξ-*triacetoxy*-1,2,3,4,15,16-*hexahydro*-11-*methylcyclopenta*[a]*phenanthren*-17-*one* (IVb) (Found: M^+, 424·1523. $C_{24}H_{24}O_7$ requires *M*, 424·1522), m.p. and mixed m.p. with the foregoing sample 123—125°, $\lambda_{max.}$ as for (IVa), $\nu_{max.}$ (CHCl₃) as for (III), with increased intensity at 2925 and 2850 cm⁻¹ (aliphatic C–H).

8,9-*Epoxy*-2,15ξ-*dihydroxy*-11-*methyl*-8,9-*secogona*-1,3,5,7,9,11,13-*heptaen*-17-*one* (Va).—The metabolite (II) (20 mg) was heated on a steam-bath with 5M-H_2SO_4 (10 ml); after 1 h the yellow solid was collected, washed with water, and dried to give the *phenol* (Va), homogeneous by t.l.c. [toluene–ethyl acetate–methanol (2:1:1 and 15:5:1, v/v), yellow fluorescence in u.v. light], m.p. 280—282° (Found: C, 73·25; H, 4·4%; *m/e*, 278·0935. $C_{18}H_{14}O_4$ requires C, 73·45; H, 4·8%. $M^+ − O$ requires *m/e*, 278·0943), *m/e* 294 (M^+, 7%), 278 ($M − O$, 22), 277 ($M − OH$, 8), 275 (8), 261 (100), 260 (10), 259 (29), 247 (10), 244 (10), and 232 (14), $\nu_{max.}$ (Nujol) 1690 (conjugated C=O), 3180–3265 (OH), and 1005 cm⁻¹, $\lambda_{max.}$ (EtOH) 278 nm (log ε 4·55), $\lambda_{max.}$ [EtOH soln. (2·5 ml) + 2M-NaOH (0·1 ml)] 255 (4·50) and 299 nm (4·50); after treatment with NaBH₄, $\lambda_{max.}$ (EtOH) 258, 310, 347, and 366 nm, $\lambda_{max.}$ (EtOH + NaOH) 251 and 344 nm. The phenolic nature of (Va) was confirmed by the production of an immediate deep blue colour with Gibb's reagent. Compound (Va) could not be hydrogenated under the conditions described for (II) and (III).

Acetylation of (Va) by the method described previously gave cream crystals of the *diacetate* (Vb), m.p. 208—210° (from ethanol) (Found: C, 70·0; H, 4·6%; M^+, 378·1008. $C_{22}H_{18}O_6$ requires C, 69·85; H, 4·8%; *M*, 378·1103), $\lambda_{max.}$(EtOH), 267, 298sh, 356, and 374 nm, $\nu_{max.}$(Nujol) 1762, 1734, and 1715 cm⁻¹ (C=O str.), no OH absorption, τ (CDCl₃) in Table 1, *m/e* [cf. (Va)] 378 (M^+, 1%) and 362 ($M − O$, 48).

Treatment of the Triacetate (III) *with Acid*.—Compound (III) (5 mg) was heated at 100° with 5M-H_2SO_4 for 2 h, cooled, and extracted with ethyl acetate. Evaporation of the washed and dried extract gave 15,16-dihydro-2,15ξ-dihydroxy-11-methylcyclopenta[a]phenanthren-17-one

[12] M. M. Coombs, S. B. Jaitly, and F. E. H. Crawley, *J. Chem. Soc.* (C), 1970, 1266.

[13] S. N. Lewis, in 'Oxidation,' ed. R. L. Augustine, Marcel Dekker, New York, 1969, p. 213.
[14] W. C. J. Ross, *J. Chem. Soc.*, 1950, 2257.

(VIa) as a yellow solid, $\lambda_{max.}$ (EtOH) 276 nm, $\lambda_{max.}$ (EtOH + NaOH) 250 and 300 nm, $\lambda_{max.}$ (EtOH + $NaBH_4$) 260 and 315 nm. This substance further resembled (Va) in its yellow fluorescence in u.v. light, blue colour with Gibb's reagent, and similar R_F value; m/e 278 (M^+), 277, and 276.

Acetylation of this material in the usual way yielded the *diacetate* (VIb) (Found: M^+, 362·1139. $C_{22}H_{18}O_5$ requires M, 362·1154), $\lambda_{max.}$ (EtOH) 267 nm, $\nu_{max.}$ (Nujol) 1735, 1720, and 1700 cm^{-1}, no OH absorption.