Potentially Carcinogenic Cyclopenta[*a*]phenanthrenes. Part IV.[1] Synthesis of 17-Ketones by the Stobbe Condensation

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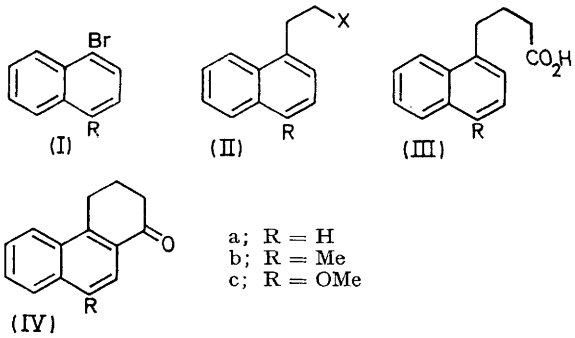
2-, 3-, 4-, and 6-Methyl- and 6-methoxycyclopenta[*a*]phenanthren-17-ones were prepared from appropriately substituted naphthalenes or tetralones, through Stobbe condensation of the corresponding 1,2,3,4-tetrahydrophenanthren-1-ones. The synthesis of ketones labelled with ^{14}C in ring D and in the 11-methyl group is also described.

In Part I [2] we described the use of the intermediate 11,12,13,14,15,16-hexahydrocyclopenta[*a*]phenanthrene-11,17-dione [3] in a simple synthesis of 15,16-dihydrocyclopenta[*a*]phenanthren-17-ones. However, this scheme was not suitable for providing ^{14}C-labelled ketones for biochemical studies, nor did it offer a convenient route to several methyl homologues required to extend our skin-painting experiments.[4] We have therefore used the scheme described by Johnson and Peterson [5] in which an appropriate 1,2,3,4-tetrahydrophenanthren-1-one is condensed by the Stobbe reaction with diethyl sodiosuccinate to provide the extra carbon atoms with which to construct the five-membered ring D. We now describe the synthesis of a number of cyclopenta[*a*]phenanthren-17-ones by this method.

1,2,3,4-Tetrahydrophenanthren-1-ones were prepared by two general routes. In the first, the 1-bromonaphthalenes (Ia—c) were converted into the 1-(2-hydroxyethyl) derivatives (IIa—c; X = OH) by condensation of the derived Grignard reagents with ethylene oxide.[6] The alcohols were treated with phosphorus tribromide to yield the bromides (IIa—c; X = Br) from which the diesters [IIa—c; X = $CH(CO_2Et)_2$] were obtained by condensation with sodiomalonic ester.



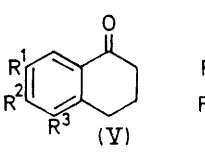
a; R = H
b; R = Me
c; R = OMe

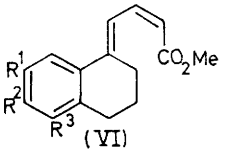
Saponification followed by decarboxylation gave the acids (IIIa—c), which were cyclised with tin(IV) chloride [7] to give the tricyclic ketones (IVa—c).

In the second method the readily available 1-tetralones (Va—d) reacted with methyl γ-bromocrotonate under

[1] Part III, M. M. Coombs, *J. Chem. Soc.*, 1969, 2484.
[2] Part I, M. M. Coombs, *J. Chem. Soc.*, 1966, 955.
[3] A. Koebner and R. Robinson, *J. Chem. Soc.*, 1938, 1994; A. J. Birch, R. Jaeger, and R. Robinson, *ibid.*, 1945, 582.
[4] M. M. Coombs and C. J. Croft, *Progr. Experimental Tumor Research*, 1969, **11**, 69.
[5] W. S. Johnson and J. W. Peterson, *J. Amer. Chem. Soc.*, 1945, **67**, 1366.
[6] W. E. Bachmann and W. L. Wilds, *J. Amer. Chem. Soc.*, 1942, **64**, 1424.
[7] W. E. Bachmann and W. L. Wilds, *J. Amer. Chem. Soc.*, 1940, **62**, 2084.

Reformatsky conditions [8] to yield the 2,4-dienoic esters (VIa—d). Isomerisation of the latter by heating with palladium black followed by saponification gave the acids (VIIa—d), which were cyclised as before to give the ketones (VIIIa—d). The m.p.s of 1,2,3,4-tetrahydro-7-methylphenanthren-1-one (VIIIc) (70·5—71°) and its precursor, the acid (VIIc) (134—135°), differed appreciably from those reported by Orcutt and Bogert [9] (92—94 and 116—118°, respectively), who obtained these compounds from a Friedel–Crafts succinoylation of 2-methylnaphthalene. However, the m.p. of (VIIc) agreed with that quoted by Nasipuri and Roy,[10] who made this compound by the route we used. Since the starting


(V)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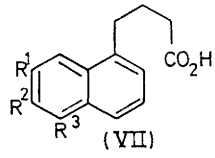
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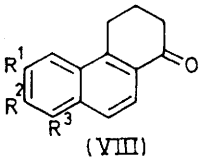
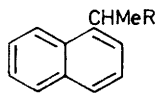

(VIII)

	R^1	R^2	R^3
a;	H	H	H
b;	Me	H	H
c;	H	Me	H
d;	H	H	Me

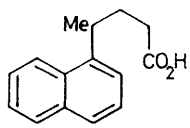
material for this synthesis, 3,4-dihydro-6-methylnaphthalen-1(2*H*)-one (Vc), was prepared by cyclisation of 4-(*m*-tolyl(butyric acid, evidence was sought to demonstrate that cyclisation had not led to the isomeric 8-methyltetralone. The n.m.r. spectra of each of the methyltetralones (Vb—d) in the aromatic proton region exhibited a one-proton signal at τ 2·0—2·2, ascribed to the C-8 proton, downfield from those of the other two aromatic protons (2·8—3·0). Moreover, similar deshielding of the protons of an 8-methyl group is to be expected in view of the magnetic anisotropy induced by the carbonyl group,[11] but the methyl signals of (Vb—d) all had similar τ values (7·66, 7·65, and 7·75, respectively). The structure of (Vc), and thus that of (VIIIc), is therefore assured. Since Friedel–Crafts acetylation of 2-methylnaphthalene gives mixtures of the 6- and 8-acetyl derivatives [12] it seems possible that the minor isomer used by Orcutt and Bogert was 2-methyl-8-succinoylnaphthalene, not the 5-succinoyl compound as claimed. This would have led * to the naphthylbutyric acid (VIIb) and tetrahydrophenanthren-1-one (VIIIb), both of which have been synthesised during the present work and which have m.p.s 125—126 and 89—90°, respectively, similar to those reported by the American workers.

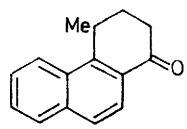
1,2,3,4-Tetrahydro-4-methylphenanthren-1-one (XI), previously prepared [13] from 1-(1-naphthyl)ethyl bromide (IXa) by a procedure involving Arndt–Eistert chain extension of the derived acid (IXb) to (X), was obtained by either of the following routes. Condensation of 2-(1-naphthyl)propionaldehyde (IXc) [14] with malonic acid led to 4-(1-naphthyl)pent-2-enoic acid (IXd) in high yield. Catalytic hydrogenation followed by cyclisation gave the required ketone (XI). Alternatively, 2-(1-naphthyl)propionic acid (IXe) [15] was esterified and reduced to the alcohol (IXf). Conversion into the bromide and chain extension as before yielded the intermediate acid (X).

Condensation of the tricyclic ketones (IVa—c), (VIIIa—d), and (XI) with diethyl succinate was readily accomplished in 40—50% yield by the Stobbe procedure; potassium t-butoxide was used, with a ketone–diester ratio of 1 : 1·5—1·7. Since it was intended to label the


(IX)

a; R = Br
b; R = $CH_2 \cdot CO_2H$
c; R = CHO
d; R = $CH{:}CH \cdot CO_2H$
e; R = CO_2H
f; R = $CH_2 \cdot OH$
g; R = CH_2Br


(X)


(XI)

15,16-dihydrocyclopenta[*a*]phenanthren-17-ones (XIVa and f) at the 15- and 16-positions by use of diethyl-[2,3-$^{14}C_2$]succinate, this reaction was studied in some detail with the unlabelled diester. Based on the amount of the latter employed, the yield of 3-(3,4-dihydro-4-methyl-1-phenanthryl)-3-ethoxycarbonylpropionic acid (XIIf) from (XI) was not appreciably diminished by increasing the ketone–diester ratio to 1 : 1, but an inferior yield was obtained when the ketone was in excess. Cyclisation of the half esters (XIIa—g) with zinc chloride in acetic anhydride–acetic acid proceeded smoothly provided that moisture was carefully excluded; subsequent saponification and decarboxylation then afforded the 11,12,15,16-tetrahydrocyclopenta[*a*]phenanthren-17-ones (XIIIa—g) in good yields.

The final step in this synthesis, dehydrogenation of the 11,12,15,16-tetrahydro-ketones (XIII) to the 15,16-dihydro-derivatives (XIV), was examined in the case of (XIVa) by Dannenberg,[16] who achieved good results by

* We thank a Referee for this suggestion.

[8] K. von Ziegler, A. Spath, E. Schaaf, W. Schumann, and E. Winkelmann, *Annalen*, 1942, **80**, 551; R. C. Fuson, R. I. Arnold, and H. G. Cooke, *J. Amer. Chem. Soc.*, 1938, **60**, 2272; W. Cook and R. Schoental, *J. Chem. Soc.*, 1945, 288; W. C. J. Ross, *ibid.*, 1947, 1364.

[9] R. B. Orcutt and M. T. Bogert, *J. Amer. Chem. Soc.*, 1941, **63**, 127.

[10] D. Nasipuri and D. N. Roy, *J. Sci. Ind. Res. India*, 1961, **21***B*, 50.

[11] L. M. Jackman, 'Applications of NMR Spectroscopy in Organic Chemistry,' Pergamon, London, 1959, pp. 112—124.

[12] G. A. R. Kon and W. T. Weller, *J. Chem. Soc.*, 1939, 792.

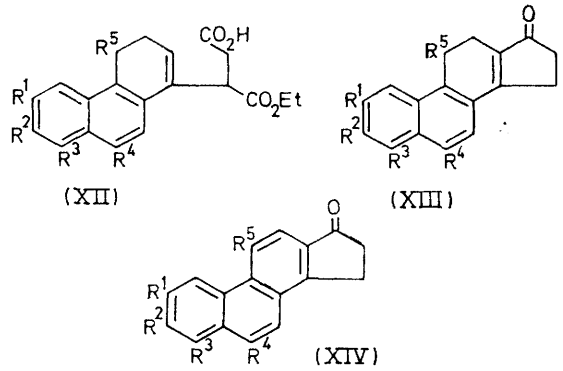
[13] W. E. Bachmann and R. O. Edgerton, *J. Amer. Chem. Soc.*, 1940, **62**, 2221.

[14] L. F. Fieser, L. M. Joshel, and A. M. Seligman, *J. Amer. Chem. Soc.*, 1939, **61**, 2134.

[15] F. F. Bincke and R. F. Feldkamp, *J. Amer. Chem. Soc.*, 1944, **66**, 1087.

[16] H. Dannenberg, *Annalen*, 1950, **568**, 105.

catalytic dehydrogenation under controlled conditions. Hydrogenolysis to the hydrocarbon, 15,16-dihydro-17*H*-cyclopenta[*a*]phenanthrene, was encountered as a side-reaction. Despite considerable experimentation we have been unable to secure satisfactory results with either 20% platinum on charcoal,[17] as used by this author, or with a commercially available 10% sample. Although conditions were varied widely, the reaction at best led to (XIVa) in about 25% yield with considerable recovery of starting material. The 11-methyl homologue (XIVf) was similarly prepared (see Experimental section). Better yields were obtained by dehydrogenation of the tetrahydro-compounds with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), and this method was adopted for the majority of the reactions. The



(XII) (XIII) (XIV)

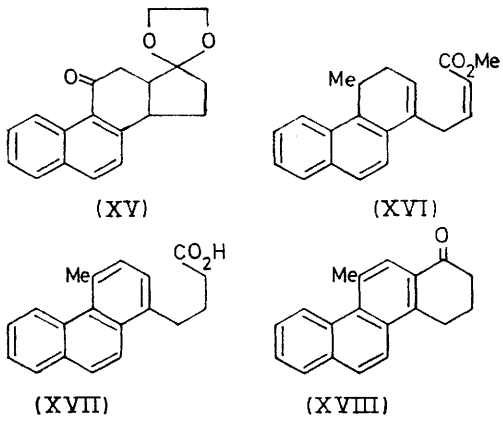
	R^1	R^2	R^3	R^4	R^5
a;	H	H	H	H	H
b;	Me	H	H	H	H
c;	H	Me	H	H	H
d;	H	H	Me	H	H
e;	H	H	H	Me	H
f;	H	H	H	H	Me
g;	H	H	H	OMe	H

11-methyl compound (XIVf) was not obtained from (XIIIf) and DDQ. Presumably steric factors ensure that (XIIIf) exists largely as the isomer in which the 11-methyl group is axial; consequently it does not possess a pair of *trans*-diaxial protons, a stereochemical requirement for quinone dehydrogenation.[18] [15,16-$^{14}C_2$]-Labelled ketones (XIVa and f) were also obtained by slight modifications of the method described, and the 11-[*methyl*-^{14}C] ketone was prepared from the keto-acetal (XV) [2] with [^{14}C]methylmagnesium iodide.

Spectral data for the 15,16-dihydrocyclopenta[*a*]-phenanthren-17-ones (XIVa—g) are collected in Table 4. Introduction of a methyl substituent at position 2, 3, 4, or 6 in the parent ketone (XIVa) caused a bathochromic shift of the main u.v. absorption band of 1—2 nm., but the 11-methyl ketone (XIVf) was anomalous in this respect, as previously observed.[2] The 6-methoxy-ketone (XIVg) was identical with that derived from the acid-catalysed dehydration of 6,7,15,16-tetrahydro-6,7-dihydroxycyclopenta[*a*]phenanthren-17-one.[1]

[17] R. P. Linstead and S. L. S. Thomas, *J. Chem. Soc.*, 1940, 1127.
[18] A. B. Turner and H. J. Ringold, *J. Chem. Soc.*, 1967, 1720.
[19] W. E. Bachmann and R. C. Edgerton, *J. Amer. Chem. Soc.*, 1940, **62**, 2550.

The six-membered ring D homologue of the carcinogen (XIVf), namely 1,2,3,4-tetrahydro-11-methylchrysen-1-one (XVIII), was readily prepared from the ketone (XI) by application of the Reformatsky reaction with



(XV) (XVI) (XVII) (XVIII)

methyl γ-bromocrotonate, following the method of Cook and Schoental[8] for the unsubstituted ketone. The resulting ester (XVI) was isomerised and saponified to yield the methylphenanthrylbutyric acid (XVII), which on cyclisation gave (XVIII), identical with this ketone previously prepared by a less convenient route.[19]

EXPERIMENTAL

Reagents and apparatus were generally as described in previous Parts of this series. Alumina used for column chromatography was Woelm, grade I, unless otherwise specified. Radioactivity was determined with a Nuclear Chicago Liquid Scintillation System, Mark I, or by counting thin films with a Nuclear Chicago C115 gas-flow counter.

1-(2-*Hydroxyethyl*)*naphthalenes* (IIa—c; X = OH).—These alcohols were prepared by the general method of Bachmann and Wilds:[6] 1-(2-hydroxyethyl)naphthalene (IIa) (85%), m.p. 62°, b.p. 140—141°/2 mm. (lit.,[6] b.p. 140—150°/0·2 mm.); 1-(2-hydroxyethyl)-4-methylnaphthalene (IIb) (80%), b.p. 152—153°/1·6 mm. (lit.,[20] b.p. 135°/0·5 mm.); 1-(2-hydroxyethyl)-4-methoxynaphthalene (IIc) (90%), m.p. 84—86°, b.p. 190°/2 mm. (lit.,[21] m.p. 87°).

1-(2-*Bromoethyl*)*naphthalenes* (IIa—c; X = Br).—The alcohol (25 g.) and redistilled phosphorus tribromide (10 ml.) were heated together on a steam-bath for 2 hr. After dilution with benzene the solutions were washed with 2N-sodium carbonate and with water. Evaporation of the dried solutions gave oils which were distilled under reduced pressure: 1-(2-bromoethyl)naphthalene (IIa) (71·5%), b.p. 160°/5 mm. (lit.,[6] 172°/20 mm.); 1-(2-bromoethyl)-4-methyl-naphthalene (IIb) (42%), b.p. 152—153°/1·6 mm. (lit.,[20] b.p. 142°/0·5 mm.); 1-(2-bromoethyl)-4-methoxynaphthalene (IIc) (43%), b.p. 161°/1·5 mm. (lit.,[21] b.p. 161°/1·2 mm.).

4-(1-*Naphthyl*)*butyric acids* (IIIa—c).—The bromides (IIa—c) were condensed with sodiomalonic ester by the procedure of Bachmann and Wilds[7] to yield the acids (IIIa—c) as follows: 4-(1-naphthyl)butyric acid (IIIa) (77%), m.p. 109—110° (lit.,[7] m.p. 109—110°); 4-(4-*methyl*-1-*naphthyl*)*butyric acid* (IIIb) (63%), m.p. 148—149°

[20] D. J. C. Gamble and G. A. R. Kon, *J. Chem. Soc.*, 1935, 444.
[21] G. A. R. Kon and F. C. J. Ruzicka, *J. Chem. Soc.*, 1936, 187.

(Found: C, 78·7; H, 6·8. $C_{15}H_{16}O_2$ requires C, 78·9; H, 7·05%); 4-(4-methoxy-1-naphthyl)butyric acid (IIIc) (70%), m.p. 129—130° (lit.,[21] m.p. 131°).

4-(1-*Naphthyl*)*butyric acids* (VIIa—d) *from Tetralones* (V).—These compounds were all prepared as described here for (VIIIa).

A mixture of 1-tetralone (9·4 g.), zinc wool (3·5 g.), methyl γ-bromocrotonate (10 g.), absolute ether (40 ml.), and dry benzene (40 ml.), containing a small crystal of iodine, was heated under reflux. Fresh zinc wool (0·5 g.) was added four times during 2 hr.; more methyl γ-bromocrotonate (2 ml.) was then added and heating was continued for 4 hr. The cooled mixture containing much yellow solid was poured into 2N-hydrochloric acid and was shaken with more benzene. The organic layer was evaporated and the residue was hydrolysed by boiling with methanol (50 ml.), potassium hydroxide (5 g.), and water (10 ml.) for 2 hr. After dilution with water the solution was acidified and extracted with benzene. The extract was shaken with saturated sodium hydrogen carbonate solution and the aqueous layer was acidified to give the crude dienoic acid as a gum. This was re-esterified by heating for 1 hr. with methanol (80 ml.) to which acetyl chloride (10 ml.) had been cautiously added. After removal of the solvents under reduced pressure the methyl 2,4-dienoate (VIa) was obtained as a brown syrup (9·68 g.), $\nu_{max.}$ 5·85s (conj. C=O) and 6·2s (conj. diene) μ, $\lambda_{max.}$ (strong, broad) 330 nm.

This ester was isomerised with palladium black (0·5 g.) at 280—300° for 1 hr. The product was dissolved in methanol, filtered from catalyst, and saponified as before. 4-(1-Naphthyl)butyric acid (VIIa), m.p. 109—110° (47·5% overall yield from 1-tetralone), was identical with the sample prepared by the first route [*i.e.* (IIIa)].

In a similar way 7-methyl-1-tetralone [22] gave 4-(7-*methyl*-1-*naphthyl*)*butyric acid* (VIIb) (70%), m.p. 125—126° (Found: C, 78·4; H, 6·85. $C_{15}H_{16}O_2$ requires C, 78·9; 7·05%); 6-methyl-1-tetralone [10] gave 4-(6-methyl-1-naphthyl)butyric acid (VIIc) (56%), m.p. 134—135° (lit.,[10] 136°); 5-methyl-1-tetralone [23] led to 4-(5-methyl-1-naphthyl)butyric acid (VIId) (50%), m.p. 128—129° (lit.,[24] m.p. 127—129°).

4-(1-*Naphthyl*)*pent-2-enoic Acid* (IXd).—Malonic acid (31 g.), pyridine (64 ml.), and 2-(1-naphthyl)propionaldehyde (25 g.), prepared [14] in three steps from 1-naphthylmagnesium bromide, were heated with piperidine (2 ml.) at 80° for 1 hr., then under reflux for 5 hr. The crystalline solid which separated when the mixture was diluted with water and acidified, gave the *acid* (IXd), m.p. 114—115° (from acetic acid) (Found: C, 79·4; H, 6·25. $C_{15}H_{14}O_2$ requires C, 79·6; H, 6·25%).

4-(1-*Naphthyl*)*valeric Acid* (X).[13]—*From* (IXd). The enoic acid (IXd) (10 g.) was hydrogenated over 5% palladium–charcoal (0·5 g.) in ethanol (200 ml.); the theoretical volume of hydrogen was absorbed in 2 days. After removal of the catalyst the solution was evaporated and the residue was crystallised to yield the saturated acid (X) (9 g.), m.p. 76—77° (lit.,[12] 78—80°).

From ethyl 2-(1-*naphthyl*)*propionate*. This ester [15] (24 g.) was reduced with lithium aluminium hydride (3 g.) in dry ether (100 ml.) to yield the alcohol (IXf) (17 g.), b.p. 160°/5 mm. (lit.,[14] 130—132°/2 mm.). Treatment with phosphorus tribromide as already described gave 2-(1-*naphthyl*)*propyl bromide* (IXg) (72%), b.p. 160—162°/10 mm. (Found: Br, 32·2. $C_{13}H_{13}Br$ requires Br, 32·1%). This bromide (47·5 g.) was condensed with diethyl sodiomalonate and the product was decarboxylated as described before to afford (X) (12·8 g.), m.p. 76°. A Reformatsky reaction between 1-tetralone and methyl 4-bromopent-2-enoate [25] followed by heating with palladium black failed to yield the acid (X).

1,2,3,4-*Tetrahydrophenanthren*-1-*ones* (IVa—c), (VIIIb—d), and (XI).—These ketones were obtained from the corresponding naphthylbutyric acids (IIIa—c), (VIIb—d), and (X) by cyclisation with thionyl chloride and tin(IV) chloride; [13] redistillation of the latter immediately before use improved yields. When necessary the crude product was chromatographed over alumina with toluene–dichloromethane to purify it before recrystallisation from methanol. Yields, m.p.s, and spectroscopic data are collected in Table 1.

3-(3,4-*Dihydro*-1-*phenanthryl*)-3-*ethoxycarbonylpropionic Acids* (XIIa—g) *prepared by the Stobbe Reaction*.—*General procedure*. The ketone (IVa) (17·8 g.) and diethyl succinate (30 g., 1·5 mol.) were heated under reflux for 1 hr. with a solution of potassium (5 g.) in dry t-butanol (80 ml.) under dry nitrogen. The cooled solution was acidified with 2N-hydrochloric acid and extracted with ether, which was then re-extracted with N-ammonium hydroxide. The half-ester which precipitated on acidification of the alkaline extract was collected, washed with water, and dried to give a brown solid (22·7 g., 77% based on the ketone). This yield was raised to 97% by twice recycling the ketone recovered from the original ether extracts. When the

TABLE 1

1,2,3,4-Tetrahydrophenanthren-1-ones

	Yield (%)	M.p.	Lit. m.p.	
(IVa)	85	95—96°	94—96° [a]	
(IVb)	51	76	74—75 [b]	
(IVc)	84	93—94	88—89 [c]	
(VIIIb)	63	89—90		(Found: C, 85·85; H, 6·6%) *
(VIIIc)	78	70·5—71		(Found: C, 85·65; H, 6·6%) *
(VIIId)	82	167—168	166—167 [d]	
(XI)	91	79—81	81—83 [a]	

* $C_{15}H_{14}O$ requires C, 85·7; H, 6·6%.

[a] Ref. 6. [b] R. D. Haworth and C. R. Mavin, *J. Chem. Soc.*, 1932, 2720. [c] Ref. 21. [d] Ref. 24.

	$\lambda_{max.}$ (nm.) (log ε)
(IVa)	254 (4·82), 289 (3·95), 298 (3·92), 348 (3·30)
(IVb)	257 (4·72), 293 (3·96), 302 (3·92), 350 (3·41)
(IVc)	254 (4·58), 302 (3·77), 360 (3·62)
(VIIIb)	255 (4·84), 289 (3·15), 298 (3·11), 350 (3·37)
(VIIIc)	257 (4·82), 294 (3·95), 302 (3·95), 350 (3·28)
(VIIId)	257 (4·79), 294 (3·94), 302 (3·90), 350 (3·33)
(XI)	255 (4·76), 289 (3·92), 298 (3·91), 350 (3·30)

	$\nu_{max.}$ (μ)
(IVa)	6·0 (C=O), 11·18, 11·40, 11·75, 12·14, 13·3, 13·98, 14·5
(IVb)	6·0 (C=O), 11·06, 11·22, 11·60, 13·05, 13·30, 13·85
(IVc)	6·0 (C=O), 11·0, 11·84, 13·0, 13·84, 14·40
(VIIIb)	5·98 (C=O), 11·24, 11·36, 11·90, 13·44, 14·02, 14·54
(VIIIc)	6·0 (C=O), 11·25, 11·68, 12·20, 12·88, 14·08, 14·5
(VIIId)	5·98 (C=O), 11·32, 12·14, 12·40, 13·50, 14·20
(XI)	5·98 (C=O), 11·42, 12·08, 13·30, 14·40

[22] F. Krollpfeiffer and W. Schäfer, *Ber.*, 1923, **56**, 620.
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ketone–ester ratio was varied the following yields were obtained:

Molar ratio			% Product based on	
ketone		ester	ketone	ester
1·3	:	1	19	25
1	:	1	37	37
1	:	1·4	84	40
1	:	1·9	77	43

Half-esters prepared as described here are shown in Table 2; analytical samples were purified by recrystallisation from methanol.

TABLE 2

Half-esters (XIIa—g) prepared by the Stobbe reaction

Ketone	Half-ester	M.p.	Found (%) C	Found (%) H		Reqd. (%) C	Reqd. (%) H
(IVa)	(XIIa) [a]	148—149°	74·2	6·35	$C_{20}H_{20}O_4$	74·05	6·2
(VIIIb)	(XIIb)	123—125	74·3	6·5			
(VIIIc)	(XIIc)	120—122	74·35	6·4	$C_{21}H_{22}O_4$	74·55	6·55
(VIIId)	(XIId) [b]	154—155	74·4	6·5			
(IVb)	(XIIe)	Not obtained crystalline					
(XI)	(XIIf)	47—50					
(IVc)	(XIIg)	Not obtained crystalline					

[a] Lit.,[5] m.p. 148·2—149·3°. [b] Lit.,[24] m.p. 154·5—155°.

11,12,15,16-*Tetrahydrocyclopenta*[a]*phenanthren*-17-*ones* (XIIIa—g).—The half-ester (XIIa) (6·3 g.), acetic anhydride (64 ml.), and a solution (32 ml.) made by dissolving freshly fused zinc chloride in glacial acetic acid (20 g./l.) without exposure to atmospheric moisture were heated under reflux for 5 hr. under dry nitrogen. After cautious treatment with water (64 ml.) and concentrated hydrochloric acid (38 ml.), boiling was continued for 1 hr.; the solvents were then removed under reduced pressure. The residue was heated on a steam-bath for 30 min. with 5% potassium hydroxide in order to hydrolyse any lactone. The crude product was collected, washed with water, and dried; it formed brown crystals (3·0 g., 63%) which were sufficiently pure for use in the next stage. Purification by chromatography on alumina with toluene–dichloromethane gave analytically pure, pale yellow crystals with little loss.

The compounds (XIIIb—g) were prepared in a similar manner. Analytical and spectroscopic data are collected in Table 3.

15,16-*Dihydrocyclopenta*[a]*phenanthren*-17-*ones* (XIVa—g).—*By dehydrogenation with* 2,3-*dichloro*-5,6-*dicyano*-1,4-*benzoquinone* (*DDQ*). The tetrahydro-ketone (0·5 g.) and DDQ (0·7 g.) were heated under reflux in anhydrous benzene (80 ml.) under dry nitrogen for 70 hr. After removal of the solvent, the residue was chromatographed on alumina as before. The fractions containing the dihydro-ketone gave pale yellow crystals of the pure dihydro-compound. Unchanged tetrahydro-ketones could also be recovered from the appropriate fractions and recycled to increase the total yields, but product thus obtained is not included in the yields given in Table 4.

When the 11-methyltetrahydro-ketone (XIIIf) was treated with DDQ only a minute quantity of the dihydro-ketone (XIVf) was isolated.

By dehydrogenation with platinum–charcoal. The ketone (XIIIa) (50 mg.) and catalyst (20% Pt–C [17] or 10% Pt–C; Koch–Light) were heated together in a small hard glass test tube in a metal bath. The cooled mass was dissolved in toluene–dichloromethane, filtered from catalyst, and chromatographed on alumina.

TABLE 3

11,12,15,16-Tetrahydrocyclopenta[*a*]phenanthren-17-ones

	Yield (%)	M.p.	Found (%) C	Found (%) H		Reqd. (%) C	Reqd. (%) H
(XIIIa) [a]	63	218—220°	86·9	6·0	$C_{17}H_{14}O$	87·2	6·0
(XIIIb)	69	139—140	87·5	6·45			
(XIIIc)	61	222—223	86·8	6·4			
(XIIId) [b]	82	245—246			$C_{18}H_{16}O$	87·0	6·5
(XIIIe)	55 *	180·5—181·5	87·1	6·35			
(XIIIf)	87	177—178	87·2	6·3			
(XIIIg)	30 *	175—176	81·45	6·05	$C_{18}H_{16}O_2$	81·8	6·1

[a] Lit.,[6] m.p. 217·5—220·5°. [b] Lit.,[24] m.p. 237·5—241·5°.

* From the crude half-esters.

	$\lambda_{max.}$ (nm.) (log ε)
(XIIIa)	272 (4·61), 282 (4·70), 325 (3·18), 337 (3·21), 367 (2·97)
(XIIIb)	272·5 (4·56), 283 (4·68), 327 (3·29), 338 (3·31), 370 (2·94)
(XIIIc)	272 (4·61), 283 (4·70), 327 (3·25), 340 (3·31), 368 (3·12)
(XIIId)	276 (4·50), 288 (4·59), 327 (3·07), 342 (3·11), 372 (2·89)
(XIIIe)	276 (4·50), 287 (4·65), 327 (3·06), 342 (3·12), 375 (2·99)
(XIIIf)	271 (4·58), 282 (4·68), 327 (3·14), 341 (3·19), 368 (3·00)
(XIIIg)	280 (4·53), 290 (4·64), 327 (2·92), 342 (2·94), 375 (2·99)

	$\nu_{max.}$ (μ)
(XIIIa)	11·50, 11·94, 12·14, 13·24, 13·85
(XIIIb)	10·25, 11·80, 12·10
(XIIIc)	11·16, 12·24, 12·98, 13·78, 14·10
(XIIId)	12·20, 12·44, 13·18
(XIIIe)	11·42, 12·15, 13·10
(XIIIf)	11·52, 12·10, 12·28, 13·26
(XIIIg)	11·70, 12·20, 13·15

TABLE 4

15,16-Dihydrocyclopenta[*a*]phenanthren-17-ones prepared by dehydrogenation of the 11,12,15,16-tetrahydro-ketones with DDQ

	Yield (%)	M.p.	Found (%) C	Found (%) H		Reqd. (%) C	Reqd. (%) H
(XIVa) [a]	34	203—204°	87·8	5·2	$C_{17}H_{12}O$	87·9	5·2
(XIVb)	32	221—222	87·75	5·80			
(XIVc)	30	203—204	87·45	5·65			
(XIVd)	10	265—266	87·55	5·75	$C_{18}H_{14}O$	87·75	5·75
(XIVe)	29	210·5—212	87·7	5·7			
(XIVg)	10	196—197	82·65	5·75	$C_{18}H_{14}O_2$	82·6	5·85

[a] Lit.,[2] m.p. 203—204°.

	$\lambda_{max.}$ (nm.) (log ε)
(XIVa)	265 (4·89), 284 (4·52), 296 (4·38), 334 (3·24), 350 (3·40), 367 (3·44)
(XIVb)	267 (5·05), 284 (4·22), 298 (4·12), 336 (3·11), 352 (3·34), 370 (3·37)
(XIVc)	267 (5·02), 285 (4·67), 298 (4·41), 344 (3·28), 366 (3·25)
(XIVd)	266 (4·98), 284 (4·67), 300 (4·36), 336 (3·06), 352 (3·22), 370 (3·23)
(XIVe)	266 (5·06), 284 (4·69), 298 (4·45), 336 (3·10), 352 (3·32), 370 (3·33)
(XIVf) *	264 (4·83), 288 (4·49), 301 (4·32), 342 (3·11), 358 (3·38), 376 (3·43)
(XIVg)	270 (4·98), 287 (4·69), 302 (4·37), 361 (3·36), 378 (3·33)

	$\nu_{max.}$ (μ)
(XIVa)	5·92 (C=O), 11·48, 11·82, 12·40, 12·86, 13·22, 14·18
(XIVb)	5·85 (C=O), 11·72, 11·90, 12·10, 12·50, 12·95, 14·08
(XIVc)	5·88 (C=O), 11·10, 11·60, 11·90, 12·36, 13·05, 13·90, 14·10
(XIVd)	5·92 (C=O), 11·10, 11·88, 12·05, 12·34, 12·60, 13·85, 14·15
(XIVe)	5·86 (C=O), 11·44, 12·12, 13·00, 14·25
(XIVf) *	5·92 (C=O), 11·40, 12·38, 13·26, 14·00
(XIVg)	5·90 (C=O), 11·86, 12·24, 12·76, 13·04, 13·78, 14·12

* Prepared by catalytic dehydrogenation; m.p. 171—172° (lit.,[2] 171—172°).

The experiments listed in Table 5 are representative of a number performed.

TABLE 5

Temp.	Time (min.)	Catalyst (mg.)	Products (%) Dihydro- (XIVa)	Tetrahydro- (XIIIa)
220—225°	3	9 (10%)	10	85
250—255	15	9 (10%)	20	75
250—255	60	10 (10%)	25	65
220—225	3	5 (20%) *	15	70
220—225	3	5 (20%) †	10	85
250—255	15	10 (20%)	20	70

* Heated under dry nitrogen. † Heated under carbon dioxide.

Similar results were obtained with the 11-methyl tetrahydro-ketone (XIIIf).

15,16-*Dihydro*[15,16-$^{14}C_2$]*cyclopenta*[a]*phenanthren*-17-*one*. Diethyl [2,3-$^{14}C_2$]succinate (5·72 g., 1 mCi) was condensed with (VIIIa) (3·92 g.) and the product was cyclised and dehydrogenated with DDQ as already described. The ketone, [15,16-$^{14}C_2$]-(XIVa) (1·54 g., 24 μ Ci/mmole, 33% overall chemical yield), m.p. 205—206°, ran as a single spot on t.l.c. and had u.v. and i.r. spectra identical with those of an authentic specimen. Radiochemical purity determined by dilution analysis was 98·6%.

15,16-*Dihydro*-11-[^{14}C]*methylcyclopenta*[a]*phenanthren*-17-*one*. With use of a vacuum-line technique to exclude atmospheric moisture and oxygen, the Grignard reagent prepared from [^{14}C]methyl iodide (0·71 g., 1 mCi) was treated with the ketoacetal [2] (XV) (1·47 g.), and the product was dehydrated and dehydrogenated by boiling with nitrobenzene and acetic and hydrochloric acids as previously described.[2] After chromatography of the crude product [*methyl*-^{14}C]-(XIVf) (0·66 g., 208 μ Ci/mmole, 55% overall chemical yield) was obtained as pale yellow needles, m.p. 175—177°, the i.r. and u.v. spectra of which were identical with those of an analytical sample. The radiochemical purity was determined by dilution analysis to be 98%.

4-(4-*Methyl*-1-*phenanthryl*)*butyric Acid* (XVII).—1,2,3,4-*Tetrahydro*-4-*methylphenanthren*-1-*one* (XI) (1·72 g.) was treated with zinc wool and methyl γ-bromocrotonate as described for the tetralones. The crude ester (XVI) was isomerised with palladium black (200 mg.) at 240—260° for 2 hr. under dry nitrogen. After separation from the catalyst the saturated ester was saponified to yield 4-(4-methyl-1-phenanthryl)butyric acid (XVII) (800 mg.), m.p. 150—152° (from benzene) (lit.,[13] 152—152·5°).

1,2,3,4-*Tetrahydro*-11-*methylchrysen*-1-*one* (XVIII).—A mixture of the acid (XVII) (500 mg.) and thionyl chloride (0·3 ml.) in anhydrous ether (5 ml.) containing 2 drops of pyridine was left for 1 hr., then evaporated under reduced pressure. The residue was dissolved in dry benzene (10 ml.) and treated with cooling in an ice-bath with redistilled tin(IV) chloride (0·5 ml.). After 20 min. at room temperature the mixture was hydrolysed with ice-cold hydrochloric acid and the benzene layer was washed with aqueous sodium carbonate and water, dried, and evaporated. The residue gave 1,2,3,4-tetrahydro-11-methylchrysen-1-one (XVIII) (195 mg.), m.p. 139·5—140° (from ethanol–acetone) (lit.,[19] 138—140°), $\lambda_{max.}$ 267 (log ε 5·32), 288 (4·84), 302 (4·64), 344 (2·73), 363 (3·06), and 380 (3·10) nm.

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