Potentially Carcinogenic Cyclopenta[*a*]phenanthrenes. Part 11. Synthesis of the 1-Methyl, 1,11-Methano, and 7,11-Dimethyl Derivatives of 15,16-Dihydrocyclopenta[*a*]phenanthren-17-one

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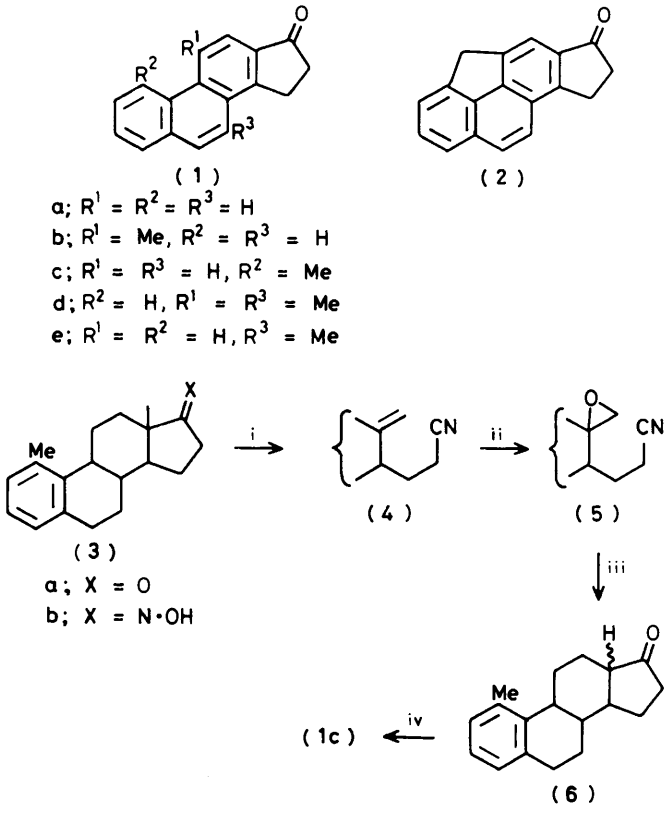
15,16-Dihydro-1-methylcyclopenta[*a*]phenanthren-17-one has been prepared starting from testosterone, and in addition by a multi-stage synthesis from a correctly substituted naphthalene. The latter route has also been employed for the synthesis of the 7,11-dimethyl-17-ketone, and the 1,11-methano-17-ketone containing a bridged bay region.

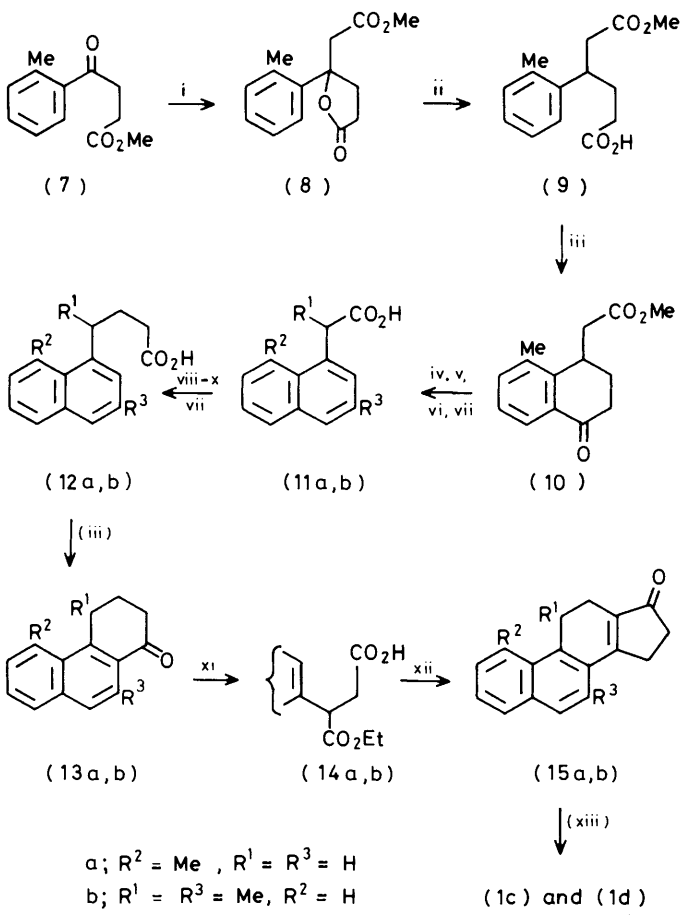
In previous parts of this series we have described the synthesis of the 2-, 3-, 4-, 6-,[1] 7-,[2] 11-, and 12-methyl[3] derivatives of 15,16-dihydrocyclopenta[*a*]phenanthren-17-one (1a), as well as numerous other compounds[4] related to this parent polycyclic ketone. Of these monomethyl derivatives the 11-methyl-17-ketone (1b) is a strong carcinogen,[5] similar in potency to benzo[*a*]pyrene. The 7-methyl isomer is less active and all the other isomers are inactive, as is the parent ketone (1a).[6] The carcinogen (1b) is biologically activated to its *anti*-1,2,3,4-tetrahydro-*trans*-3,4-dihydroxy-1,2-epoxide,[7] and it was therefore anticipated that like the 2-, 3-, and 4-methyl isomers, the unknown 1-methyl-17-ketone would lack carcinogenic activity. The 1,11-methano-derivative (2) was also expected to be inactive since, although it still retains a small electron-releasing substituent at C-11, the bay region is apparently blocked by the 1,11-methylene group. This paper describes the syntheses of these two compounds, the former by two independent routes; a preliminary communication has appeared in connection with the latter (2).[8] Also reported is the synthesis of the 7,11-dimethyl-17-ketone (1d); the potency of this compound was of interest because it bears methyl groups at both positions known to confer carcinogenic activity in this series.

Initially A-ring aromatisation of a suitable steroid *via* the dienone-phenol rearrangement[9] seemed to offer a convenient means of placing the methyl group at C-1 in a cyclopenta[*a*]-phenanthrene. Dannenberg's method[10] was selected, since ring-A aromatisation and removal of the 3-oxygen function are effected simultaneously. Thus testosterone acetate was converted by known methods in four steps into 1-methyloestra-1,3,5(10)-trien-17-one (3a).[11] Several methods were considered for removal of the blocking 18-methyl group, but finally an adaption[12] of the method devised by Pinhey and his co-workers[13] for the removal of a 4-methyl group from a tetracyclic triterpenoid was chosen. An abnormal Beckmann rearrangement of the derived oxime (2b) yielded the methylene nitrile (4). Epoxidation with *m*-chloroperbenzoic acid led to the epimeric epoxynitriles (5) which, without separation, were cyclised with boron trifluoride to give the 18-norketone (6). The yield in the cyclisation step (14%) was much lower than that obtained by Pinhey and his co-workers for recyclisation of the six-membered ring A, and the overall yield of (6) from (2a) was only 8%. Unfortunately, complete dehydrogenation of the 18-norketone (6) to the desired cyclopenta[*a*]phenanthrenone also proved difficult, but as finally achieved, albeit in poor yield, by prolonged reaction with dichlorodicyanobenzoquinone (DDQ) in boiling dioxan to furnish a small sample of 15,16-dihydro-1-methylcyclopenta[*a*]phenanthren-17-one (1c) identical with the material from the second synthesis (see below). Although of no use practically, this route is nevertheless of interest as a new way of converting a natural steroid into a member of the cyclopenta[*a*]phenanthrene series.

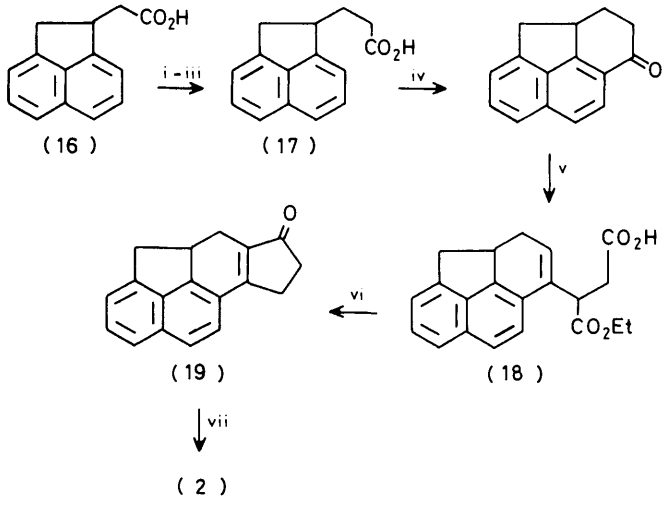
A more practical synthesis of this compound was accomplished by adding rings C and D sequentially to a suitable substituted naphthalene, a strategy previously adopted by us for the synthesis of cyclopenta[*a*]phenanthrenes. Treatment of the keto-ester (7)[14] with methyl bromoacetate in the presence of zinc gave the lactone (8), readily reduced by catalytic hydrogenolysis to the acid-ester (9). Cyclisation of the latter with stannic chloride was followed by borohydride reduction of the resulting tetralone (10); subsequent dehydration, and dehydrogenation of the product by heating with sulphur, yielded 8-methyl-1-naphthylacetic acid (11a). Chain extension was achieved by reduction to the corresponding naphthylethanol, bromination, and application of the malonic acid synthesis. Cyclisation of the resulting naphthylbutyric acid (12a) gave the tricyclic ketone (13a) which was converted, *via* the Stobbe half-ester (14a) and further cyclisation with zinc chloride, into the 11,12-dihydro-compound (15a) by the previously described methods.[1] Catalytic dehydrogenation



Reagents: i, DCC, CF_3CO_2H, Me_2SO; ii, *m*-$ClC_6H_4CO_3H$; iii, BF_3, toluene; iv, DDQ, dioxan



Reagents: i, $BrCH_2CO_2Me$, Zn; ii, Pd/H_2, AcOH, $HClO_4$; iii, PCl_5 $SnCl_4$; iv, $NaBH_4$; v, TosOH; vi, S; vii, NaOH; viii, $LiAlH_4$; ix, Ph_3PBr_2; x, $NaCH(CO_2Et)_2$; xi, Bu^tOK, $(CH_2CO_2Et)_2$; xii, $ZnCl_2$; Ac_2O, HCl; xiii, Pd, boiling *p*-cymene



Reagents: i, $LiAlH_4$; ii, $PhPBr_2$; iii, KCN, then NaOH; iv, PCl_5, $SnCl_4$; v, Bu^tOK, $(CH_2CO_2Et)_2$; vi, Zn, Ac_2O, HCl; vii, Pd, boiling *p*-cymene

with palladium in boiling *p*-cymene then led smoothly to the 1-methyl-17-ketone (1c).

A similar sequence of reactions was employed in the synthesis of the 7,11-dimethyl-17-ketone (1d). 2-(3-Methyl-1-naphthyl)propionic acid (11b) (obtained *via* Reformatsky reaction between 3-methyltetralone and ethyl 2-bromopropionate) was chain-extended and cyclised as before to yield 4,10-dimethyl-1,2,3,4-tetrahydrophenanthren-1-one (13b) in good yield. Unfortunately the Stobbe reaction with this ketone and the subsequent cyclisation step occurred with difficulty, presumably as a result of steric hindrance by the adjacent methyl group. Similar problems were encountered in the synthesis of 15,16-dihydro-7-methylcyclopenta[*a*]-phenanthren-17-one (1e).[2] The final catalytic dehydrogenation, however, occurred in 85% yield despite the presence of the methyl group at C-11. This dehydrogenation method with palladium in boiling *p*-cymene appears to be superior to the methods previously used (DDQ in boiling benzene, or fusion with palladium at 220 °C).[1]

Originally [8] in the synthesis of the 1,11-methano-compound (2), acenaphthen-1-ylacetic acid (16) was converted into the corresponding propionic acid (17) by the Arndt-Eistert reaction.[15] On a larger scale it was however found preferable to carry out this transformation in several stages, by reduction of the acid (17) and bromination of the resulting alcohol, conversion into the nitrile and hydrolysis to (17). Cyclisation to the tetracyclic ketone (18) followed by elaboration of the five-membered ring *via* the Stobbe half-ester (19) was carried out as before.

The cyclopenta[*a*]phenanthrenones (1c) and (1d) possessed spectral and other properties similar to those of the other positional isomers of this series. Noticeable differences in the u.v. spectrum of the methano-compound (2) probably reflect the considerable distortions of the phenanthrene system induced by bridging the bay region, as disclosed by the previous *X*-ray study.[8] As expected, the 7,11-dimethyl-17-ketone is found to be a potent bacterial mutagen, whilst the 1-methyl-17-ketone is essentially inactive; experiments to evaluate their carcinogenicity are in progress. The methano-ketone (2) proves to be both mutagenic to *Salmonella typhimurium* TA 100 (after biological activation) and a moderately strong skin tumour inducer in mice. An investigation of its metabolism is in hand to attempt to account for this.

Experimental

Unless otherwise stated, m.p.s were determined for samples in open capillary tubes and are uncorrected, as are the b.p.s. I.r. spectra were recorded using either Nujol mulls or liquid films. N.m.r. data are for deuteriochloroform solutions with tetramethylsilane as internal reference and were recorded at 60 MHz. U.v. spectra were recorded for solutions in 98% ethanol. ' Drying ' refers to the use of magnesium sulphate; ' evaporation ' implies the use of reduced pressure.

1-*Methyl*-17-*hydroxyimino-oestra*-1,3,5(10)-*triene* (3b).—1-Methyloestra-1,3,5(10)-trien-17-one [11] (2 g), hydroxylamine hydrochloride (1.04 g), sodium hydrogen carbonate (1.25 g), water (2.5 ml), and methanol (45 ml) were heated together under reflux for 1.5 h, and the mixture then cooled and poured into water (100 ml). The precipitate was collected by filtration, washed with water, and crystallised from ethanol to yield the *oxime* (3b) as needles (2.1 g), m.p. 96—98 °C, $[\alpha]_D$ +178°; $\lambda_{max.}$ 265 nm; $\nu_{max.}$ 3 260, 945, 930, 767, and 740 cm^{-1}; δ 1.02 (3 H, s, 18-Me), 2.36 (3 H, s, ArMe), 2.80 (2 H, m, $ArCH_2$), 7.00 (3 H, s, ArH), and 8.80 (1 H, broad s, NOH) (Found: C, 80.0; H, 8.7; N, 4.8%. M^+, 283.1936. $C_{19}H_{25}NO$ requires C, 80.5; H, 8.9; N, 4.9%; *M*, 283.1938).

1-*Methyl*-13,17-*seco-oestra*-1,3,5(10),13(18)-*tetraene*-17-*carbonitrile* (4).—The oxime (3b) (1.8 g) was added to a mixture of Me_2SO and benzene (54 ml, 1 : 1 v/v) containing

dicyclohexylcasbodi-imide (3.92 g) and trifluoroacetic acid (0.32 ml). After 3 h at room temperature the reaction mixture was added to water, the benzene layer was separated, and the aqueous layer was extracted with more benzene. The combined organic fractions were washed with saturated brine, dried, and evaporated to yield a honey-coloured oil (5 g). Chromatography on silica with benzene elution gave the *seco-nitrile* (4) as an oil (1.2 g) which did not crystallise, $\lambda_{max.}$ 265 nm; $[\alpha]_D$ +235° (EtOH); $\nu_{max.}$ 2 246 (C≡N), 1 645 (>C=CH$_2$), 1 580, 895, 772, and 745 cm^{-1}; δ 2.37 (3 H, s, ArMe), 4.72 (1 H, s, C=CH$_2$), 4.96 (1 H, s, C=CH$_2$), and 7.00 (3 H, s, ArH) (Found: N, 5.1. M^+, 265.1834. $C_{19}H_{23}N$ requires N, 5.3%; *M* 265.1830).

13,18-ζ-*Epoxy*-1-*methyl*-13,17-*seco*-*oestra*-1,3,5(10)-*triene*-17-*carbonitrile* (5).—An ice-cold solution of *m*-chloroperbenzoic acid (1.45 mmol) in chloroform (3 ml) was added to a vigorously stirred solution of the nitrile (4) (1.32 mmol) in chloroform (9 ml) at 0 °C. The stirred reaction mixture was maintained at this temperature for 15 h, after which it was added to ice-cold water. The chloroform layer was washed with cold aqueous 2M-sodium hydroxide and with water, and then dried and evaporated to yield the *epoxynitrile* as an oil (316 mg) which failed to crystallise, $[\alpha]_D$ +119° (EtOH), $\lambda_{max.}$ 265 nm; $\nu_{max.}$ 2 246 (C≡N), 1 580, 1 220, 840, 772, and 745 cm^{-1}; δ 2.35 (3 H, s, ArMe), 2.70 (4 H, m, ArCH$_2$), and 7.00 (3 H, s, ArH) (Found: C, 80.6; H, 8.5; N, 4.65%; M^+, 281.1774. $C_{19}H_{23}NO$ requires C, 81.1; H, 8.2; N, 5.0%; *M*, 281.1780).

1-*Methyl*-18-*noroestra*-1,3,5(10)-*trien*-17-*one* (6).—The epoxy-nitrile (5) (300 mg) and boron trifluoride–ether (0.75 ml) were heated under reflux in toluene (145 ml) for 54 h. The cooled reaction mixture was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated to give an orange gum (250 mg) which was chromatographed on silica with toluene containing increasing amounts of ethyl acetate. Material eluted with 1% ethyl acetate was crystallised from chloroform to give the *trienone* (6) as yellow needles (38 mg, 14%), m.p. 85—88 °C, $\lambda_{max.}$ 266 nm; $\nu_{max.}$ 1 735 (C=O), 770, and 745 cm^{-1}; δ 2.34 (3 H, s, ArMe), 2.80 (2 H, m, ArCH$_2$), and 7.00 (3 H, s, ArH) (Found: M^+ 254.1665. $C_{18}H_{22}O$ requires *M*, 254.1671).

15,16-*Dihydro*-1-*methylcyclopenta*[a]*phenanthren*-17-*one* (1c).—The trienone (6) (95 mg), DDQ (474 mg), and dioxan (25 ml) were heated under reflux for 3 days after which the mixture was cooled and diluted with ether (25 ml). The hydroquinone was removed by filtration and the filtrate was washed with aqueous sodium hydroxide and with water, dried, and evaporated to give a gum which was chromatographed on alumina. Elution with toluene yielded the 1-methyl-17-ketone (1c) (5 mg) as a semicrystalline material with u.v. and i.r. spectra, fluorescence, and R_F values in several systems identical with those of the pure, analysed sample (see below).

4-*Methoxycarbonylmethyl*-4-(o-*tolyl*)-4-*butanolide* (8).—Methyl 4-oxo-4-*o*-tolylbutyrate (7) [16] (61 g), methyl bromoacetate (52 ml), zinc fillings (36 g), and a small crystal of iodine were heated together in dry ether (200 ml) under reflux. A vigorous reaction took place, after which reflux was maintained for 6 h. The cooled reaction mixture was added to an excess of ice and hydrochloric acid; the organic layer was separated and the aqueous layer was extracted twice with ether. The combined ether solutions were dried and evaporated to yield a mobile golden oil which was heated under reflux for 0.5 h with toluene-*p*-sulphonic acid (100 mg) in benzene (100 ml). The resulting solution was washed with water, dried, evaporated, and distilled to give the *lactone* (8) (52 g) as a viscous lime-coloured liquid, b.p. 188—190 °C/0.6 mmHg, $\nu_{max.}$ 175 (lactone) and 1 730 cm^{-1} (ether); δ 2.44 (3 H, s, ArMe), 2.68 and 3.03 (6 H, 3 × CH$_2$), 3.60 (3 H, s, CO$_2$Me), and 7.0—7.7 (4 H, m, ArH) (Found: C, 67.7; H, 6.5. $C_{14}H_{16}O_4$ requires C, 67.7; H, 6.5%).

4-o-*Tolyl*-5-*methoxycarbonylpentanoic Acid* (9).—A stirred mixture of the lactone (8) (50 g) and palladium on charcoal (10%, 1 g) in acetic acid (200 ml) containing perchloric acid (10 ml) was hydrogenated at normal pressure for 48 h, during which time 4.8 l of hydrogen were absorbed. The catalyst was removed by filtration and the solution was concentrated by evaporation to *ca.* 50 ml, diluted with water (300 ml), and extracted with ethyl acetate. The dried extract was evaporated to yield the *acid* (9) as a white solid (49 g), m.p. 95—97 °C (benzene–light petroleum), $\nu_{max.}$ 1 735 and 1 710 cm^{-1}; δ 2.1 (4 H, 2 × CH$_2$), 2.35 (3 H, s, ArMe), 2.59 (2 H, CH$_2$), 3.57 (3 H, s, CO$_2$CH$_3$), and 7.14 (4 H, Ar) (Found: C, 67.5; H, 7.4. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.3%).

Methyl 8-*Methyl*-4-*oxo*-1,2,3,4-*tetrahydro*-1-*naphthylacetate* (10).—Phosphorus(v) chloride (30 g) was added in portions to a solution of the acid-ester (9) (25 g) in dichloromethane (200 ml) during 0.5 h at 0 °C. The reaction mixture was heated at 35 °C for a further 0.5 h, cooled to 0 °C, and tin(IV) chloride (50 ml) diluted with dichloromethane (50 ml) was then added dropwise. After being stirred at room temperature for 2 h the reaction mixture was poured onto an excess of ice and hydrochloric acid. Separation of the organic layer was followed by extraction of the aqueous layer with dichloromethane, and the combined extracts were washed with water, dried, evaporated, and distilled to yield *methyl* 8-*methyl*-4-*oxo*-1,2,3,4-*tetrahydro*-1-*naphthylacetate* (10) (15 g) as a mobile oil, b.p. 175 °C/1 mmHg, $\nu_{max.}$ 1 730 (ester) and 1 685 cm^{-1} (unsaturated ketone); δ 2.32 (3 H, s, ArMe), 1.8—2.8 (7 H, m, aliphatic H), 3.68 (3 H, s, CO$_2$Me), 6.75—7.30 (2 H, m, 6-H and 7-H), and 7.75 (1 H, dd, J_{ortho} 7 and J_{meta} 2 Hz, 5-H) (Found: C, 72.2; H, 7.2. $C_{14}H_{16}O_3$ requires C, 72.4; H, 6.9%).

8-*Methyl*-1-*naphthylacetic Acid* (11a).—The tetralone (10) (20 g) was stirred with sodium borohydride (5 g) in ethanol (100 ml) overnight at room temperature. After dilution with water the organic material was extracted with ethyl acetate and the extract washed with water, dried, and evaporated to yield the hydroxy-ester (20 g), $\nu_{max.}$ 3 400v,br, and 1 735 cm^{-1}.

A solution of this hydroxy-ester in benzene (50 ml) containing a small quantity of toluene-*p*-sulphonic acid was heated under reflux for 0.5 h; the cooled solution was then washed with water, dried, and evaporated to leave an oil. Sulphur (3.0 g) was added and the resultant mixture was heated at 230—235 °C for 0.5 h. When cold, the reaction mixture was dissolved in ethanol (20 ml) and heated under reflux for 1 h with sodium hydroxide (10 g) and water (30 ml). After dilution with more water (200 ml), the solution was extracted once with ether and the clear aqueous layer acidified with concentrated hydrochloric acid and extracted several times with ethyl acetate. The combined extracts were dried and evaporated to give the *naphthylacetic acid* (11a) as a slightly greenish solid (12.1 g), m.p. 173—174 °C (ligroin), $\nu_{max.}$ 1 710 cm^{-1}; δ 2.95 (3 H, s, ArMe), 4.38 (2 H, s, CH$_2$), and 7.35—8.20 (6 H, m, ArH) (Found: C, 78.5; H, 6.1. $C_{13}H_{12}O_2$ requires C, 78.0; H, 6.0%).

8-*Methyl*-1-*naphthylbutyric Acid* (12a).—A solution of the acid (11a) (15 g) in dichloromethane (50 ml) was added dropwise to a stirred suspension of lithium aluminium hydride (2 g) in ether (200 ml); when the exothermic addition was com-

plete the reaction mixture was heated under reflux for 1 h and then cooled in ice. Water was added, initially dropwise, followed by concentrated hydrochloric acid; the organic fraction was then separated and the aqueous layer extracted with ether. The combined organic solutions were washed with water, dried, evaporated, and the residue distilled at 130—132 °C/0.9 mmHg to yield 1-(8-*methylnaphthyl*)*ethanol* (12 g) as an oil which slowly crystallised, m.p. 57—58 °C, $\nu_{max.}$ 3 200br cm^{-1}; δ 2.83 (3 H, s, Me), 3.2—3.9 [4 H, m, $(CH_2)_2$], and 6.9—7.8 (6 H, m, ArH) (Found: C, 83.3; H, 7.8. $C_{13}H_{14}O$ requires C, 83.8; H, 7.6%).

The naphthylethanol (10 g) in acetonitrile (50 ml) was added to a suspension of triphenylphosphine dibromide [17] [from triphenylphosphine (21.12 g) and bromine (12.87 g)] in the same solvent (100 ml), and the mixture was maintained at 60 °C for 2 h. After evaporation of the solvent, the solid residue was triturated with benzene and the solution filtered through a short column of silica. Removal of the benzene left the bromide as a mobile oil which, without further purification, was treated with diethyl sodiomalonate [from diethyl malonate (17 ml) and sodium hydride (50%) (3.8 g) in dry dimethylformamide (100 ml)]; the reaction mixture was stirred at 60 °C for 5 h. After evaporation, the residue was dissolved in ethanol (50 ml) and heated under reflux with sodium hydroxide (12 g) in water (100 ml) for 2 h. The cooled solution was further diluted with water (100 ml) and extracted with ether. The aqueous fraction was acidified with concentrated hydrochloric acid and the organic products were extracted into dichloromethane which was washed with water, dried, and evaporated. The residual gum was dissolved in pyridine (200 ml) and decarboxylation was effected by heating under reflux for 2 h. The pyridine was removed by evaporation to leave an oil, which on treatment with 2M-hydrochloric acid gave the *naphthylbutyric acid* (12a) as a white solid (7.5 g, 61%), m.p. 132—133 °C (toluene), $\nu_{max.}$ 1 705 cm^{-1}; δ 2.05 (2 H, m, CH_2), 2.45 (2 H, t, *J* 6.5 Hz, CH_2CO_2H), 2.90 (3 H, s, Me), 3.32 (2 H, t, *J* 7 Hz, $ArCH_2$), and 7.10—7.85 (6 H, m, ArH) (Found: C, 78.8; H, 7.1. $C_{15}H_{16}O_2$ requires C, 78.9; H, 7.1%).

5-*Methyl*-1,2,3,4-*tetrahydrophenanthren*-1-*one* (13a).—Cyclisation of the acid (12a) (7.0 g) was effected by the method used to prepare the tetralone (10), but employing phosphorus(v) chloride (9.5 g) and tin(IV) chloride (7.0 ml). The *phenanthrenone* (13a) was obtained in 92% yield, m.p. 88—89 °C (benzene–light petroleum), $\nu_{max.}$ 1 675 cm^{-1}; δ 2.50 (2 H, m, CH_2), 3.14 (2 H, t, *J* 6 Hz, CH_2CO), 3.37 (3 H, s, Me), 3.95 (2 H, m, CH_2Ar), 7.48—7.95 (4 H, m, ArH), and 8.37 (1 H, d, $J_{9,10}$ 8 Hz, 10-H) (Found: C, 86.1; H, 7.0. $C_{15}H_{14}O$ requires C, 85.7; H, 6.7%).

3-(3,4-*Dihydro*-5-*methyl*-1-*phenanthryl*)-3-*ethoxycarbonylpropionic Acid* (14a).—To a stirred solution of potassium t-butoxide (1.6 g) in t-butyl alcohol (50 ml) was added the phenanthrenone (13a) (3.0 g) and diethyl succinate (5.0 ml); the mixture was then heated under reflux for 6 h. After dilution with water (200 ml), the solution was acidified with concentrated hydrochloric acid, extracted with ether, and the latter re-extracted with dilute aqueous ammonium hydroxide. Acidification of the alkaline solution was followed by extraction of the organic products into dichloromethane. Evaporation of the dried extract yielded the *half-ester* (14a) as a golden coloured solid (1.5 g), m.p. 163—165 °C (ethanol), $\nu_{max.}$ 1 728 and 1 702 cm^{-1} (Found: C, 74.6; H, 6.6. $C_{21}H_{22}O_4$ requires C, 74.5; H, 6.6%). The n.m.r. spectrum was complex suggesting the presence of more than one isomer.

1-*Methyl*-11,12,15,16-*tetrahydrocyclopenta*[a]*phenanthren*-17-*one* (15a).—A mixture containing the half-ester (14a) (1.5 g), anhydrous zinc chloride (0.2 g), acetic acid (10 ml), and acetic anhydride (20 ml) was heated under reflux for 6 h. While still hot, water (10 ml) was added, initially dropwise, followed by concentrated hydrochloric acid (15 ml); heating under reflux was then continued for a further 2 h. After dilution of the cooled reaction mixture with water (200 ml) the products were extracted with ether, and the extracts were dried and evaporated to leave an oil which was chromatographed on a column of silica gel, with chloroform–light petroleum as eluant. 1-*Methyl*-11,12,15,16-*tetrahydrocyclopenta*[a]*phenanthren*-17-*one* (15a) was isolated as a buff solid (0.8 g), m.p. 138—140 °C (ethanol), $\lambda_{max.}$ 276 (4.55), 286 (4.62), 330 (4.09), 343 (4.11), and 376 (3.87) nm; $\nu_{max.}$ 1 685 (17=CO) and 1 650 cm^{-1} [13(14) double bond] (Found: C, 87.6; H, 6.3. $C_{18}H_{16}O$ requires C, 87.1; H, 6.5%).

15,16-*Dihydro*-1-*methylcyclopenta*[a]*phenanthren*-17-*one* (1c).—The tetrahydro-ketone (15a) (0.7 g), 10% palladium-on-charcoal (0.1 g), and *p*-cymene (50 ml) were vigorously heated under reflux for 0.5 h, filtered whilst hot, and evaporated to leave a light yellow solid. Trituration of the latter with a small volume of benzene gave 15,16-*dihydro*-1-*methylcyclopenta*[a]-*phenanthren*-17-*one* (1c) as a white solid (0.55 g), m.p. 189—190 °C (ethanol), $\lambda_{max.}$ 266 (4.84), 288 (4.53), 303 (4.30), 359 (3.77), and 375 (3.77) nm; $\nu_{max.}$ 1 690 cm^{-1}; δ 2.73 (2 H, t, *J* 6 Hz, 16-CH_2), 3.08 (3 H, s, 1-Me), 3.38 (2 H, t, *J* 6 Hz, 15-CH_2), 7.27—7.84 (6 H, m, ArH), and 8.70 (1 H, d, $J_{11,12}$ 9 Hz, 11-H) (Found: C, 87.8; H, 5.7. $C_{18}H_{14}O$ requires 87.7; H, 5.8%).

4-(3-*Methylnaphthyl*)*pentanoic Acid* (12b).—This acid was prepared by methods similar to those used to convert (11a) into (12a). The intermediate 2-(3-methyl-1-naphthyl)propionic acid (11b) [14] was reduced with lithium aluminium hydride to 4-(3-*methylnaphthyl*)*propanol* in 85% yield, b.p. 155—157 °C/0.9 mmHg, $\nu_{max.}$ 3 560, 3 340, 1 660, and 1 608 cm^{-1}; δ(D_2O) 1.34 (3 H, d, CHMe), 2.44 (ArMe), 3.33—3.92 (3 H, m, CH-CH_2), and 7.05—8.27 (6 H, m, ArH) (Found: C, 83.5; H, 8.2. $C_{13}H_{16}O$ requires C, 84.0; H, 8.1%). This alcohol was readily converted into 4-(3-*methylnaphthyl*)*pentyl bromide* (73%), b.p. 166 °C/2.0 mmHg, $\nu_{max.}$ 1 680 and 1 608 cm^{-1}; δ 1.55 (2 H, d, *J* 6.5 Hz, CHMe), 2.46 (3 H, s, ArMe), 3.2—4.25 (3 H, m, $CHCH_2$), and 7.00—8.23 (6 H, m, ArH) (Found: C, 63.9; H, 6.0. $C_{14}H_{15}Br$ requires C, 63.9; H, 5.8%). Conversion of the latter into the *pentanoic acid* (12b) (70%) was best conducted in absolute ethanol; the product was not obtained crystalline; $\nu_{max.}$ 1 703, 1 660, and 1 608 cm^{-1}; δ 1.40 (3 H, d, *J* 6 Hz, CHMe), 1.90—2.33 [4 H, m; $(CH_2)_2$], 2.98 (3 H, s, ArMe), 3.60 (1 H, m, CH), and 7.10—8.20 (6 H, m, ArH) (Found: C, 79.2; H, 7.8. $C_{16}H_{18}O_2$ requires C, 79.3; H, 7.5%).

4,10-*Dimethyl*-1,2,3,4-*tetrahydrophenanthren*-1-*one* (13b).—Cyclisation with tin(IV) chloride as for (13a) gave the *phenanthrenone* (13b) (65%), m.p. 65 °C (light petroleum), $\nu_{max.}$ 1 670 cm^{-1}; δ 1.45 (3 H, d, *J* 7.5 Hz, CHMe), 1.95—3.00 [4 H, m, $(CH_2)_2$–], 3.92 (1 H, m, CH), and 7.23—8.17 (5 H, m, ArH) (Found: C, 85.3; H, 7.2. $C_{16}H_{16}O$ requires C, 85.7; H, 7.2%).

7,11-*Dimethyl*-11,12,15,16-*tetrahydrocyclopenta*[a]*phenanthren*-17-*one* (15a).—The Stobbe reaction with the ketone (13b), carried out as for (13a), gave the half-ester (14b) (20%), as an oil, $\nu_{max.}$ 1 735 and 1 710 cm^{-1}. Without further purification this material was cyclised with zinc chloride as described for (15a) to yield the *ketone* (15b) (15%), m.p. 145—146 °C (ethanol), $\lambda_{max.}$ 265sh (4.47), 274 (4.75), 285 (4.84), 335br (4.39) nm; $\nu_{max.}$ 1 685, 1 632, and 1 614 cm^{-1}; δ 1.06 (3 H, d, *J* 7 Hz, CHMe), 2.68 (3 H, s, ArMe), and 7.15—8.17 (5 H, m, ArH) (Found: C, 87.2; H, 7.2. $C_{19}H_{18}O$ requires C, 87.0; H, 6.9%).

15,16-*Dihydro*-7,11-*dimethylcyclopenta*[a]*phenanthren*-17-*one* (1d).—Dehydrogenation of (15b) was performed as in the preparation of the 1-methyl compound to yield 15,16-*dihydro*-7,11-*dimethylcyclopenta*[a]*phenanthren*-17-*one* (1d) (85%), m.p. 208—210 °C (ethanol); $\lambda_{max.}$ 275 (4.76), 293 (4.48), 307 (4.29), 368 (3.46), and 389 nm (3.51); $\nu_{max.}$ 1 678 cm^{-1}; δ 2.65 (2 H, t, *J* 5 Hz, 16-CH_2), 2.82 (3 H, s, ArMe), 2.98 (3 H, s, ArMe), 3.63 (2 H, t, *J* 5 Hz, 15-CH_2), and 7.30—8.85 (6 H, m, ArH) (Found: C, 87.6; H, 6.2. $C_{19}H_{16}O$ requires C, 87.7; H, 6.2%).

3-*Acenaphthen*-1-*ylpropionic Acid* (17).—Acenaphthen-1-ylacetic acid [5] (16) (10 g) was reduced with $LiAlH_4$ as already described to yield 2-acenaphthen-1-ylethanol (9.0 g) as a yellow oil, $\nu_{max.}$ 3 330br cm^{-1} (OH); δ 1.9 (2 H, m, $CHCH_2$-CH_2), 3.2 (6 H, m, $ArCH_2$ and CH-CH_2-CH_2-OH), and 7.3 (5 H, m, ArH). This alcohol was brominated with triphenylphosphine dibromide in acetonitrile, and the bromide was purified by passage through a column of silica gel to give an oil (9.52 g), δ 2.1 (2 H, m, $CHCH_2CH_2$), 3.2 (5 H, m, $ArCH_2$ and $CHCH_2CH_2$), and 7.3 (5 H, m, ArH).

The bromide was stirred and heated under reflux with potassium cyanide (8.3 g) in methanol (150 ml) for 72 h and the nitrile, isolated as a red oil [$\nu_{max.}$ 2 250 cm^{-1} (C≡N)], was heated under reflux with sodium hydroxide (10 g) in aqueous methanol (100 ml; 9 : 1 v/v) for 24 h. After extraction with ether, the solution was acidified and extracted with ethyl acetate. 3-Acenaphthen-1-ylpropionic acid (17) formed beige needles (6.81 g), m.p. 102—104 °C (lit.,[15] m.p. 102.5—104.5 °C) from ethyl acetate–light petroleum, δ 2.8 (7 H, aliphatic H), 7.55 (6 H, m, ArH), and 10.0br (1 H, s, CO_2H).

3-(3,4-*Dihydro*-4,5-*methylene*-1-*phenanthryl*)-3-*ethoxycarbonylpropionic Acid* (18).—3-Acenaphthen-1-ylpropionic acid (17) (6.64 g) was cyclised with phosphorus(v) chloride and tin(IV) chloride as already described to yield 1,10-methano-1,2-3,4-tetrahydrophenanthren-4-one (4.9 g), m.p. 119—120 °C (lit.,[15] 122—123 °C), $\nu_{max.}$ 1 670 cm^{-1} (C=O); δ 2.85 (7 H, m, alicyclic H), and 7.55 (5 H, m, ArH).

A Stobbe reaction with this ketone (0.7 g) as before gave the *half-ester* (18) as a beige solid (0.9 g), m.p. 160—162 °C (aq. methanol), $\lambda_{max.}$ 251sh, 257 (4.60), 266 (4.64), 295sh, 310 (3.71), 318 (3.75), 331 (3.67), and 347 nm (3.51); $\nu_{max.}$ 1 728 (CO_2Et), 1 702 (CO_2H), 1 175, 1 040, and 1 040 cm^{-1}; δ 1.2 (3 H, t, CH_2Me), 2.9 (8 H, m, aliphatic H), 4.05 (2 H, q, CH_2Me), 5.8 (1 H, m, 2-H, and 7.35 (5 H, m, ArH) (Found: C, 75.3; H, 6.0. $C_{21}H_{20}O_4$ requires C, 75.0; H, 6.0%).

15,16-*Dihydro*-1,11-*methanocyclopenta*[a]*phenanthren*-17-*one* (2).—The above half-ester (18) (0.9 g) was cyclised with zinc chloride and acetic anhydride to give 1,11-*methano*-11,12,15,16-*tetrahydrocyclopenta*[a]*phenanthren*-17-*one* (19) as pale yellow crystals (0.2 g), m.p. 198—200 °C (methanol), $\lambda_{max.}$ 267sh, 277 (4.52), 287 (4.59), 310 (2.83), 322 (3.92), 338 (3.88), and 375 nm (3.92) (Found: C, 88.1; H, 5.9. $C_{18}H_{14}O$ requires C, 87.8; H, 5.7%).

Dehydrogenation of this tetrahydro-compound (0.76 g) with Pd/C in *p*-cymene under reflux for 0.5 h, and recrystallisation of the product from methanol led to 15,16-*dihydro*-1,11-*methanocyclopenta*[a]*phenanthren*-17-*one* (2) as a pale yellow solid (0.64 g), m.p. 195 °C, $\lambda_{max.}$ 266.5 (4.77), 277 (4.76), 303 (3.34), 348 (3.03), and 365.5 nm (2.86); $\nu_{max.}$ 1 685 (CO), 1 634, 1 400, 1 292, 820, and 805 cm^{-1}; δ 2.8 (2 H, m, CH_2C=O), 3.25 (2 H, m, CH_2), 4.2 (2 H, s, $ArCH_2Ar$), and 7.7 (6 H, m, ArH) (Found: C, 88.7; H, 5.1. $C_{18}H_{12}O$ requires C, 88.5; H, 4.95%).

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