

Phenanthrene Synthesis: The Synthesis of Juncunone¹ and the Micandrols-A, B, E, and F

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The synthesis of the naturally occurring phenanthrenes micandrol-A (1,7-dimethylphenanthrene-2,6-diol) (1), micandrol-B (9,10-dihydro-1,7-dimethylphenanthrene-2,6-diol) (2), micandrol-E (7-methoxy-1,2-dimethylphenanthren-6-ol) (3), micandrol-F (9,10-dihydro-7-methoxy-1,2-dimethylphenanthren-6-ol) (4), and juncunone [1-(9,10-dihydro-2,6-dihydroxy-1,7-dimethylphenanthren-5-yl)ethan-1-one] (7), by a method involving cyclization of suitable (*Z*)-2-chlorostilbenes with activated magnesium, is described.

In a previous paper² we showed that (*Z*)-2-chlorostilbenes on treatment with activated magnesium, prepared by the method of Rieke and Bales,³ underwent cyclization to phenanthrenes. A homolytic substitution mechanism was proposed for this reaction. We now describe the use of this reaction in the synthesis of a number of naturally occurring phenanthrenes.

Gottlieb and his co-workers^{4,5} have described the isolation and structural elucidation of a number of phenanthrenes from the trunk wood of arboreal Amazonian species of Euphorbiaceae. Micandrol-A (1) and micandrol-B (2) were isolated from *Micandropsis scleroxylon* W. Rodr. They were inter-related by oxidation or reduction, and the location of the methyl groups was fixed by degradation to pimanthrene. The hydroxy

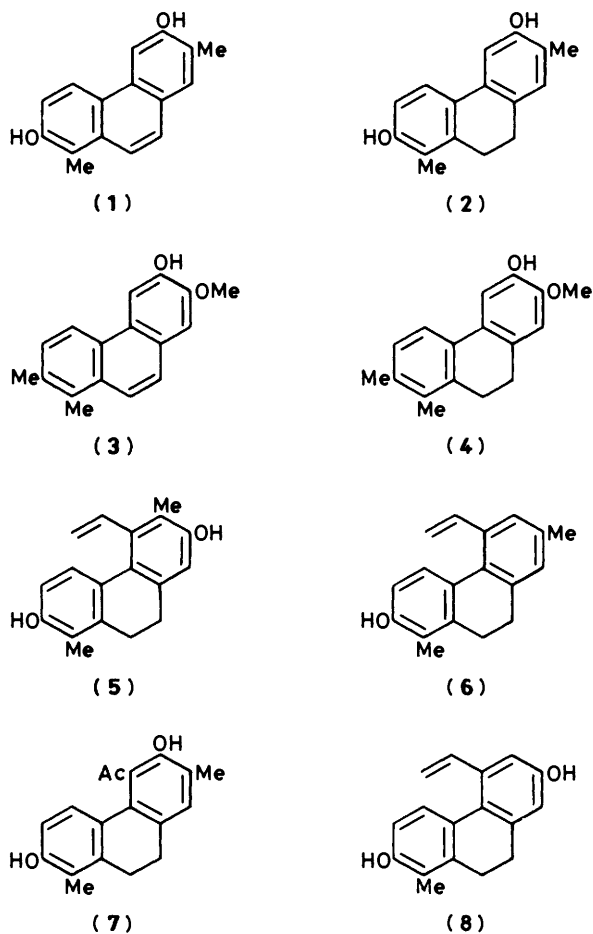
groups were located by ¹H n.m.r. spectroscopy.⁴ Micandrol-E (3) and micandrol-F (4) were isolated from *Sagotia racemosa* Baill. and their structures were determined by spectroscopic methods.⁵ We have verified these structures by synthesis.

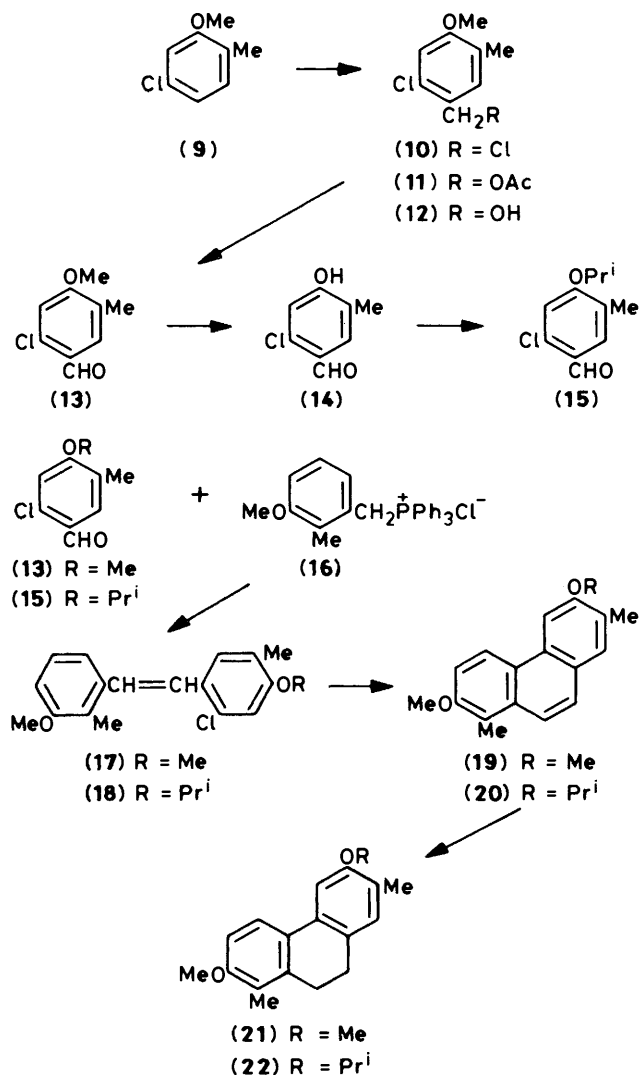
Extracts of the marsh grass, *Juncus roemerianus*, have shown activity against leukaemia and the biogenetically unusual 9,10-dihydrophenanthrenes juncusol (5),⁶ juncunol (6),^{7,8} and juncunone (7)⁹ have been isolated from this source. The related species *Juncus effusus* produces juncusol (5) and effusol (8).¹⁰ The biological activity of juncusol (5) has stimulated synthetic effort in this area.^{8,11} We now report an efficient synthesis of juncunone (7).

The starting material for one of the benzenoid rings in the convergent synthesis of micandrol-A (1), micandrol-B (2), and juncunone (7) was the readily available 4-chloro-2-methoxytoluene (9)¹² (Scheme 1). This on chloromethylation by an adaptation of the method of Kraft¹³ gave the chloromethyl compound (10). This was converted *via* the acetate (11), into the alcohol (12), which on oxidation with manganese dioxide furnished the aldehyde (13). Wittig reaction of the aldehyde (13) with the phosphonium salt (16)² by the *in situ* method with lithium methoxide as base and *N,N*-dimethylformamide as solvent gave the stilbene (17) as a mixture of (*Z*)- and (*E*)-isomers in which the former predominated. When the pure (*Z*)-isomer of the stilbene (17) was treated with activated magnesium in boiling tetrahydrofuran di-*O*-methylmicandrol-A (19) resulted. It was converted into micandrol-A (1), identical with an authentic sample, by demethylation with boron tribromide. Hydrogenation of di-*O*-methylmicandrol-A (19) gave compound (21) which on demethylation with boron tribromide gave micandrol-B (2), identical with an authentic sample.

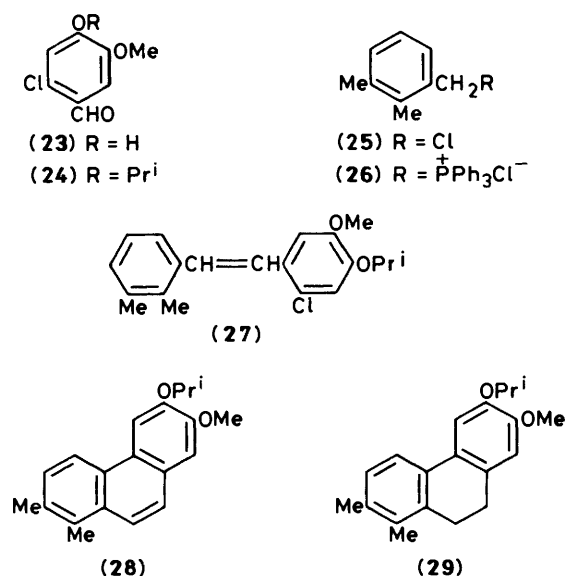
For the synthesis of micandrol-E (3) and micandrol-F (4) the aldehyde (24) and the phosphonium salt (26) were required. The former compound was available by isopropylation of the known chlorovanillin (23).¹⁴ The phosphonium salt (26) was synthesized from the known chloride (25).¹⁵ Wittig reaction between the aldehyde (24) and the phosphonium salt (26) gave the stilbene (27) as a mixture of isomers in which the (*Z*)-isomer predominated. Cyclization of the (*Z*)-isomer of the stilbene (27) with activated magnesium afforded the phenanthrene (28). This was converted into micandrol-E (3) by deisopropylation with boron trichloride. Reduction of the 9,10-double bond of compound (28) gave the dihydrophenanthrene (29) which afforded micandrol-F (4) on deisopropylation.

For the synthesis of juncunone (7) the aldehyde (15) (Scheme 1) was required. It was prepared by boron tribromide-induced demethylation of the aldehyde (13) and isopropylation of the resultant phenol (14). On Wittig reaction of the aldehyde (15) with the phosphonium salt (16) the stilbene (18) was obtained.



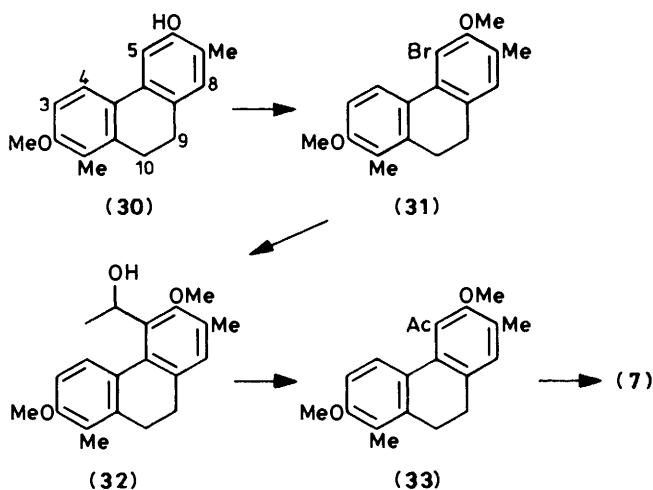


Scheme 1.



Again the (*Z*)-isomer predominated and the mixture was partially enriched in the (*Z*)-isomer by fractional distillation and the mixture was then allowed to react with activated mag-

nesium. The resultant phenanthrene (20) was subjected to catalytic hydrogenation and this reaction afforded the 9,10-dihydrophenanthrene (22). Deisopropylation was achieved with boron trichloride and the resultant phenol (30) (Scheme 2)



Scheme 2.

was brominated and the crude product was *O*-methylated to afford the bromo-compound (31). The position of bromination was convincingly demonstrated by the marked n.m.r. spectral downfield shift (δ 0.68) of the 4-proton on going from the phenol (30) to the bromo compound (31). The bromo compound (31) was subjected to bromine-lithium exchange with butyl-lithium and the lithio-compound thus produced was allowed to react with acetaldehyde thus furnishing the secondary alcohol (32). The alcohol was oxidized with pyridinium chlorochromate and demethylation of the resultant di-*O*-methyljuncunone (33) with boron tribromide yielded juncunone (7), identical with an authentic sample.

Experimental

General directions have been given before.¹⁶ Alumina was Fluka neutral, activity I (Brockmann). Anhydrous magnesium chloride was obtained from the Aldrich Chemical Company. Electronic spectra were determined using a Varian DMS-80 spectrophotometer. Light petroleum refers to the fraction b.p. 40–60 °C.

2-Chloro-4-methoxy-5-methylbenzyl Chloride (10).—Hydrogen chloride was bubbled through a stirred and cooled (ice-salt) mixture of powdered anhydrous zinc chloride (6.82 g), sodium chloride (0.55 g), aqueous formaldehyde (37%; 48.6 ml), diethyl ether (250 ml), and 1-chloro-3-methoxy-4-methylbenzene (9) (58.75 g)¹² at such a rate that the inner temperature was 22–23 °C. When the mixture was saturated the pale orange solution was allowed to stand for 12 h. The solution was then added to water and extracted with diethyl ether and washed with saturated brine in the usual way. Removal of the solvent gave the *product* (10) (71.1 g) as an amber liquid pure enough for further transformation. A sample had b.p. 95 °C at 0.3 mmHg (Kugelrohr). The distillate crystallized, with time, as needles, m.p. 21–22 °C (Found: C, 52.95; H, 4.9; Cl, 34.4%; M^+ , 204/206/208. C₉H₁₀Cl₂O requires C, 52.7; H, 4.9; Cl, 34.55%; M^+ , 204/206/208); δ (CDCl₃, 90 MHz) 2.15 (3 H, s, Me), 3.79 (3 H, s, OMe), 4.62 (2 H, s, CH₂), 6.81 (1 H, s, 3-H), and 7.16 (1 H, s, 6-H).

2-Chloro-4-methoxy-5-methylbenzyl Acetate (11).—The benzyl chloride (10) (71.1 g) and anhydrous sodium acetate (284 g) were stirred and heated in anhydrous *N,N*-dimethylformamide (340 ml) at 80 °C for 17 h. The cooled mixture was diluted with water. Isolation with ethyl acetate gave the *acetate* (11) (74.0 g) as an oil which crystallized on seeding. A sample had b.p. 110 °C at 0.05 mmHg (Kugelrohr) and formed fine needles from aqueous methanol, m.p. 28–30 °C (Found: C, 57.55; H, 5.5; Cl, 15.2%; M^+ , 228/230. $C_{11}H_{13}ClO_3$ requires C, 57.8; H, 5.75; Cl, 15.5%; M , 228/230); δ ($CDCl_3$, 90 MHz) 2.08 (3 H, s, MeCO), 2.17 (3 H, s, Me), 3.80 (3 H, s, OMe), 5.12 (2 H, s, CH_2), 6.83 (1 H, s, 3-H), and 7.16 (1 H, s, 6-H).

2-Chloro-4-methoxy-5-methylbenzyl Alcohol (12).—The *acetate* (11) (71.8 g) was stirred at 0 °C under nitrogen with sodium hydroxide (26.0 g) in water (60 ml) and methanol (300 ml) for 1.5 h. Acidification with dilute hydrochloric acid and isolation with ethyl acetate gave the *alcohol* (12) (58.1 g), m.p. 80–82 °C. The analytical sample formed needles (from methanol), m.p. 81.5–82.5 °C (Found: C, 58.2; H, 5.95; Cl, 19.1%; M^+ , 186/188. $C_9H_{11}ClO_2$ requires C, 57.9; H, 5.95; Cl, 19.0%; M , 186/188); δ ($CDCl_3$, 90 MHz) 2.16 (3 H, s, Me), 2.25 (1 H, br, OH), 3.79 (3 H, s, OMe), 4.64 (2 H, s, CH_2), 6.79 (1 H, s, 3-H), and 7.16 (1 H, s, 6-H).

2-Chloro-4-methoxy-5-methylbenzaldehyde (13).—The benzyl alcohol (12) (55.95 g) and activated manganese dioxide (261 g) were heated and stirred under reflux in benzene (1 l) in a Dean-Stark apparatus for 17 h. The manganese dioxide was separated by filtration and washed with hot ethyl acetate. Removal of the solvent yielded the pure *aldehyde* (13) (39.5 g). Soxhlet extraction of the manganese dioxide with ethyl acetate afforded less pure aldehyde (12.3 g), m.p. 102–105 °C. The analytical sample formed fine needles (from light petroleum), m.p. 107.5–108.5 °C (Found: C, 58.45; H, 4.9; Cl, 19.4%; M^+ , 184/186. $C_9H_9ClO_2$ requires C, 58.55; H, 4.9; Cl, 19.2%; M , 184/186); δ ($CDCl_3$, 90 MHz) 2.19 (3 H, s, Me), 3.89 (3 H, s, OMe), 6.81 (1 H, s, 3-H), 7.71 (1 H, s, 6-H), and 10.30 (1 H, s, CHO).

2-Chloro-3',4'-dimethoxy-2',5'-dimethylstilbene (17).—A solution of lithium methoxide [from lithium (83 mg)] in dry methanol (50 ml) was added dropwise over 1 h to a stirred solution of the phosphonium salt (16) (5.00 g)² and the aldehyde (13) (2.12 g) in dry *N,N*-dimethylformamide (50 ml) at 90 °C (bath) under dry nitrogen. The solution was stirred and heated at 90 °C for 0.5 h longer and then cooled and poured into water. The crude product, isolated with ethyl acetate, was filtered through a plug of neutral alumina with light petroleum as eluant. This afforded the product (17) (3.23 g) as a mixture of (*Z*)- and (*E*)-isomers in the ratio 3:1 as judged by ¹H n.m.r. spectroscopy. Fractional crystallization from methanol gave the (*Z*)-*isomer* as plates, m.p. 77–78 °C (Found: C, 71.1; H, 6.35; Cl, 11.85%; M^+ , 302/304. $C_{18}H_{19}ClO_2$ requires C, 71.4; H, 6.3; Cl, 11.7%; M , 302/304); λ_{max} (EtOH) 197 and 277 nm (ϵ 40 800 and 15 100); δ ($CDCl_3$, 90 MHz) 1.87 and 2.14 (each 3 H, s, Me), 3.74 and 3.79 (each 3 H, s, OMe), 6.61–7.04 (5 H, m, 5 × ArH), and 6.70 (2 H, s, olefinic H); and the (*E*)-*isomer* as needles, m.p. 112.5–113.5 °C (Found: C, 71.5; H, 6.25; Cl, 11.9%; M^+ , 302/304. $C_{18}H_{19}ClO_2$ requires C, 71.4; H, 6.3; Cl, 11.7%; M , 302/304); λ_{max} (EtOH) 217 and 299 nm (ϵ 27 400 and 25 300); δ ($CDCl_3$, 90 MHz) 2.10 and 2.30 (each 3 H, s, Me), 3.78 and 3.81 (each 3 H, s, OMe), 6.69–7.30 (5 H, m, 5 × ArH), 6.79 (1 H, s, 3-H) and 7.43 (1 H, s, 6-H).

2,6-Dimethoxy-1,7-dimethylphenanthrene (19).—The (*Z*)-stilbene (17) (1.65 g) in dry tetrahydrofuran (15 ml) was added over 20 min to a suspension of activated magnesium [from anhydrous magnesium chloride (2.10 g), potassium iodide (1.81

g), and potassium (1.71 g)] in dry tetrahydrofuran (50 ml) with stirring and heating under reflux under dry nitrogen. The mixture was heated and stirred under reflux for 17 h and then cooled to 0 °C and treated with an excess of saturated aqueous ammonium chloride under nitrogen. Isolation with ethyl acetate gave the crude product which was filtered through a column of neutral alumina with 0–2% ethyl acetate–light petroleum as eluant. The major fraction crystallized from methanol as plates (420 mg), m.p. 213.5–215 °C (lit.,⁴ 206–207 °C) (Found: C, 80.95; H, 7.0%; M^+ , 266. $C_{18}H_{18}O_2$ requires C, 81.15; H, 6.8%; M , 266); λ_{max} (EtOH) 225, 260, 271, 283, 303infl, 327infl, 343, and 360 nm (ϵ 32 700, 46 200, 39 800, 20 300, 11 000, 1 850, 2 600, and 3 150); δ ($CDCl_3$, 90 MHz) 2.38 and 2.58 (each 3 H, s, Me), 3.93 and 4.01 (each 3 H, s, OMe), 7.25 and 8.42 (2 H, AB, $J_{3,4}$ 9.5 Hz, 3- and 4-H), 7.55 (1 H, s, 8-H), 7.60 and 7.73 (2 H, AB, $J_{9,10}$ 9.5 Hz, 9- and 10-H), and 7.84 (1 H, s, 5-H).

1,7-Dimethylphenanthrene-2,6-diol (Micandrol-A) (1).—A solution of boron tribromide (385 mg) in dry methylene dichloride (5 ml) was added slowly to a stirred solution of the dimethoxy compound (19) (101 mg) in dry methylene dichloride (1 ml) at –10 °C. The solution was stirred for 4 h without further addition of ice to the cooling bath. Water was added and the product was isolated with ethyl acetate. It crystallized from methylene dichloride–light petroleum as very pale yellow needles of the *diol* (1) (97 mg), m.p. 225–227 °C (mixed m.p. 220–225 °C, lit.,⁴ 215–218 °C) identical (i.r. spectrum, R_F values in three solvent systems) with an authentic sample (Found: C, 80.95; H, 5.85%; M^+ , 238. $C_{16}H_{14}O_2$ requires C, 80.65; H, 5.9%; M , 238); λ_{max} (MeOH) 229, 258, 273, 289, 344, and 361 nm (ϵ 31 100, 44 900, 29 800, 15 300, 2 350, and 3 150); m/z 239 (17%), 238 (100, M^+), 237 (17), 223 (15), 209 (17), 195 (18), 194 (24), 189 (11), 179 (10), 178 (20), 166 (12), 165 (38), and 152 (16); δ (CD_3COCD_3 , 90 MHz) 2.38 and 2.54 (each 3 H, s, Me), 7.23 and 8.26 (2 H, AB, $J_{3,4}$ 9.0 Hz, 3- and 4-H), 6.70 (1 H, s, 8-H), 6.72 and 6.79 (2 H, AB, $J_{9,10}$ 9.0 Hz, 9- and 10-H), 8.00 (1 H, s, 5-H), and 8.10 and 8.30 (each 1 H, s, OH).

9,10-Dihydro-2,6-dimethoxy-1,7-dimethylphenanthrene (21).—The phenanthrene (19) (151 mg) and 10% palladized charcoal (100 mg) were stirred in ethyl acetate (15 ml) under an atmosphere of hydrogen until absorption ceased (5 days). Work-up gave the *phenanthrene* (21) (146 mg) as plates (from methanol), m.p. 166–168 °C (lit.,⁴ 169–172 °C) (Found: C, 80.6; H, 7.6%; M^+ , 268. $C_{18}H_{20}O_2$ requires C, 80.55; H, 7.5%; M , 268); λ_{max} (EtOH) 218, 278, 295, and 315 nm (ϵ 36 100, 16 900, 11 200, and 10 100); δ ($CDCl_3$, 90 MHz) 2.27 (6 H, s, 2 × Me), 2.77 (4 H, s, 2 × CH_2), 3.84 and 3.88 (each 3 H, s, OMe), 6.80 and 7.55 (2 H, AB, $J_{3,4}$ 9.0 Hz, 3- and 4-H), 6.97 (1 H, s, 8-H), and 7.13 (1 H, s, 5-H).

9,10-Dihydro-1,7-dimethylphenanthrene-2,6-diol (Micandrol-B) (2).—Demethylation of the phenanthrene (21) (136 mg) with boron tribromide during 2.5 h in a manner similar to that described for compound (19) gave the *diol* (2) (110 mg) as needles (from aqueous methanol), m.p. 168–170 °C (mixed m.p. 166–168 °C, lit.,⁴ 167–170 °C). It was identical (i.r. spectrum, R_F values in three solvent systems) with an authentic sample (Found: C, 79.75; H, 6.7. $C_{16}H_{16}O_2$ requires C, 79.95; H, 6.7%; λ_{max} (MeOH) 218, 277, 297, and 314infl nm (ϵ 28 000, 13 700, 8 700, and 7 500); m/z 241 (20%), 240 (M^+ , 100), 239 (27), 225 (39), 224 (18), 210 (13), 197 (11), 181 (14), 165 (14), and 152 (11); δ (CD_3COCD_3 , 90 MHz) 2.18 (6 H, s, 2 × Me), 2.69 (4 H, s, 2 × CH_2), 6.77 and 7.33 (2 H, AB, $J_{3,4}$ 8.5 Hz, 3- and 4-H), 6.88 (1 H, s, 8-H), 7.13 (1 H, s, 5-H), and 8.10 (2 H, br, 2 × OH).

2,3-Dimethylbenzyltriphenylphosphonium Chloride (26).—Triphenylphosphine (15.22 g) and 2,3-dimethylbenzyl chloride (25) (8.16g)¹⁵ were heated under reflux under dry nitrogen in dry toluene (50 ml) for 14 h. The hygroscopic salt (26) (19.5 g), m.p. 218.5—219.5 °C, was separated by filtration and washed with a little light petroleum and then with a little dry diethyl ether, and then dried *in vacuo*; δ (CDCl₃, 90 MHz) 1.49 and 2.06 (each 3 H, s, Me), 5.29 (2 H, d, $J_{\text{CH}_2, \text{P}}$ 14 Hz, CH₂), 6.73—7.09 (3 H, m, 3 × ArH), and 7.46—7.87 (15 H, m, 3 × Ph).

2-Chloro-4-isopropoxy-5-methoxybenzaldehyde (24).—2-Chloro-4-hydroxy-5-methoxybenzaldehyde (23) (15.1 g),¹⁴ 2-iodopropane (15.3 g), and anhydrous potassium carbonate (12.5 g) were stirred and heated in dry *N,N*-dimethylformamide (60 ml) at 60 °C for 18 h. The mixture was then poured into water and the product (24) (16.3 g) was separated by filtration, washed with water, and dried *in vacuo*. It crystallized from methylene dichloride–light petroleum as needles, m.p. 99.5—100 °C (Found: C, 57.55; H, 5.65; Cl, 15.7%; M^+ , 228/230. C₁₁H₁₃ClO₃ requires C, 57.8; H, 5.75; Cl, 15.5%; M , 228/230); δ (CDCl₃, 90 MHz) 1.43 (6 H, d, 2 × Me), 3.88 (3 H, s, OMe), 4.65 (1 H, septet, CH), 6.86 (1 H, s, 3-H), 7.38 (1 H, s, 6-H), and 10.30 (1 H, s, CHO).

2-Chloro-4-isopropoxy-5-methoxy-2',3'-dimethylstilbene (27).—Reaction, in a similar manner to that described for the preparation of compound (17), between the phosphonium salt (26) (5.0 g) and the aldehyde (24) (2.63 g) gave a crude product which was filtered through a plug of alumina. Light petroleum eluted the (*Z*)-isomer (1.93 g) which crystallized from methanol as plates, m.p. 66–67 °C (Found: C, 72.55; H, 7.1; Cl, 10.9%; M^+ , 330/332. C₂₀H₂₃ClO₂ requires C, 72.6; H, 7.0; Cl, 10.7%; M , 330/332); λ_{max} (EtOH) 197, 215, and 276 nm (ϵ 38 800, 29 000, and 13 000); δ (CDCl₃, 90 MHz) 1.32 (6 H, d, 2 × Me), 2.14 and 2.24 (each 3 H, s, Me), 3.21 (3 H, s, OMe), 4.45 (1 H, septet, CH), 6.43 (1 H, s, 6-H), 6.77 (2 H, s, 2 × olefinic H), 6.82 (1 H, s, 3-H), and 6.97 (3 H, s, 4', 5', and 6'-H). Elution with 5% ethyl acetate–light petroleum yielded the (*E*)-isomer (1.23 g) which formed needles from methanol, m.p. 94.5—95.5 °C (Found: C, 72.75; H, 7.25; Cl, 10.6%; M^+ , 330/332. C₂₀H₂₃ClO₂ requires C, 72.6; H, 7.0; Cl, 10.7%; M , 330/332); λ_{max} (EtOH) 214, 230, 292, and 323 nm (ϵ 22 800, 17 000, 19 500, and 18 000); δ (CDCl₃, 90 MHz) 1.37 (6 H, d, 2 × Me), 2.30 (3 H, s, Me), 3.89 (3 H, s, OMe), 4.51 (1 H, septet, CH), 6.89 (1 H, s, 6-H), and 7.06—7.48 (6 H, m, 2 × olefinic H and 4 × ArH).

6-Isopropoxy-7-methoxy-1,2-dimethylphenanthrene (28).—The (*Z*)-stilbene (27) (1.0 g) was allowed to react with activated magnesium in a similar manner to that described for compound (19). The crude product was chromatographed over neutral alumina with light petroleum as eluant and crystallization of the major fraction from methanol gave the phenanthrene (28) (430 mg) as plates, m.p. 126—127 °C (Found: C, 81.8; H, 7.65%; M^+ , 294. C₂₀H₂₂O₂ requires C, 81.6; H, 7.55%; M , 294); λ_{max} (EtOH) 221, 259, 281, 303infr, 339, and 356 nm (ϵ 24 300, 66 500, 26 200, 10 100, 3 500, and 4 100); δ (CDCl₃, 90 MHz) 1.46 (6 H, d, 2 × Me), 2.45 (3 H, s, 2-Me), 2.57 (3 H, s, 1-Me), 3.91 (3 H, s, OMe), 4.72 (1 H, septet, CH), 7.20 (1 H, s, 8-H), 7.39 and 8.27 (2 H, AB, $J_{3,4}$ 9.0 Hz, 3- and 4-H), 7.62 and 7.87 (2 H, AB, $J_{9,10}$ 9.0 Hz, 9- and 10-H), and 8.06 (1 H, s, 5-H). Irradiation with 25 dB at δ 2.45 gave a 12% n.O.e. (nuclear Overhauser effect) at the 3-H, and irradiation with 25 dB at δ 2.57 gave a 17% n.O.e. at the 10-H.

7-Methoxy-1,2-dimethylphenanthren-6-ol (Micandrol-E) (3).—A solution of boron trichloride (80 mg) in dry methylene dichloride (0.5 ml) was added slowly to a solution of the isopropyl ether (28) (50 mg) in dry methylene dichloride (1 ml)

with stirring at –10 °C. The mixture was stirred for 1.5 h longer during which time a colourless precipitate was thrown down. Addition of water and isolation with diethyl ether gave the product (3) (40.4 mg) which formed glistening plates (from methylene dichloride–light petroleum), m.p. 203—205 °C (lit.⁵ 194—197 °C) identical (KBr disc i.r. spectrum) with an authentic sample (Found: C, 80.75; H, 6.45%; M^+ , 252. C₁₇H₁₆O₂ requires C, 80.95; H, 6.4%; M , 252); λ_{max} (MeOH) 191, 220, 258, 281, 307infr, 339, and 355 nm (ϵ 19 800, 20 700, 54 500, 20 800, 7 200, 2 800, and 3 500); m/z 252 (M^+ , 100%), 237 (45), 209 (53), 194 (11), 178 (10), 165 (29), 152 (12), and 126 (26); δ (CDCl₃, 90 MHz) 2.49 (3 H, s, 2-Me), 2.62 (3 H, s, 1-Me), 4.00 (3 H, s, OMe), 5.89 (1 H, s, OH), 7.17 (1 H, s, 8-H), 7.39 and 8.28 (2 H, AB, $J_{3,4}$ 9.0 Hz, 3- and 4-H), and 7.61 and 7.86 (2 H, AB, $J_{9,10}$ 9.0 Hz, 10- and 9-H).

9,10-Dihydro-6-isopropoxy-7-methoxy-1,2-dimethylphenanthrene (29).—The phenanthrene (28) (177 mg) and 10% palladized charcoal (177 mg) in ethyl acetate (15 ml) were stirred in a hydrogen atmosphere for 3 days. The usual work-up gave the dihydrophenanthrene (29) (168 mg) as needles (from aqueous methanol), m.p. 89—90 °C (Found: C, 81.3; H, 8.3%; M^+ , 296. C₂₀H₂₄O₂ requires C, 81.05; H, 8.15%; M , 296); λ_{max} (EtOH) 219, 278, 290infr, and 311 nm (ϵ 46 000, 20 500, 14 350, and 11 000); δ (CDCl₃, 90 MHz) 1.37 (6 H, d, 2 × Me), 2.24 (3 H, s, 2-Me), 2.31 (3 H, s, 1-Me), 2.80 (4 H, s, 2 × CH₂), 3.86 (3 H, s, OMe), 4.54 (1 H, septet, CH), 6.74 (1 H, s, 8-H), 7.07 and 7.40 (2 H, AB, $J_{3,4}$ 8.0 Hz, 3- and 4-H), and 7.27 (1 H, s, 5-H).

9,10-Dihydro-7-methoxy-1,2-dimethylphenanthren-6-ol (Micandrol-F) (4).—Treatment of the dihydrophenanthrene (29) (99.3 mg) with boron trichloride in a similar manner to that described for compound (28) gave the product (4) (84.8 mg) as needles (from aqueous methanol), m.p. 163—164 °C (lit.⁵ 162—164 °C). It was identical (KBr disc i.r. spectrum) with an authentic sample (Found: C, 80.0; H, 7.15. C₁₇H₁₈O₂ requires C, 80.3; H, 7.15%; λ_{max} (MeOH) 219, 277, 293infr, and 314 nm (ϵ 14 800, 13 700, 8 800, and 9 100); m/z 254 (M^+ , 99%), 240 (18), 239 (100), 211 (23), 196 (32), 195 (14), 193 (11), 181 (16), 165 (16), and 152 (14); δ (CDCl₃, 90 MHz) 2.23 (3 H, s, 2-Me), 2.31 (3 H, s, 1-Me), 2.79 (4 H, s, 2 × CH₂), 3.88 (3 H, s, OMe), 5.48 (1 H, s, OH), 6.70 (1 H, s, 8-H), 7.07 and 7.41 (2 H, AB, $J_{3,4}$ 8.0 Hz, 3- and 4-H), and 7.30 (1 H, s, 5-H).

2-Chloro-4-isopropoxy-5-methylbenzaldehyde (15).—Boron tribromide (54 g) in dry methylene dichloride was added to a stirred solution of the aldehyde (13) (10.0 g) in methylene dichloride (200 ml). The solution was stirred, without further addition of ice to the cooling bath, for 13 h longer. The solution was poured into ice and water and stirred for 12 h. Isolation with ethyl acetate gave 2-chloro-4-hydroxy-5-methylbenzaldehyde (14) (9.24 g) as a solid. A sample formed needles (from methylene dichloride–light petroleum), m.p. 178—179.5 °C; δ (CDCl₃, 90 MHz) 2.18 (3 H, s, Me), 5.57 (1 H, br, OH), 6.90 (1 H, s, 3-H), 7.62 (1 H, q, $J_{\text{Me}, 6-\text{H}}$ 1.5 Hz, 6-H), and 10.20 (1 H, s, CHO). The aldehyde (14) (6.50 g) 2-iodopropane (8.15 g), dry potassium carbonate (6.9 g), and dry *N,N*-dimethylformamide (20 ml) were stirred and heated at 55 °C (bath) under dry nitrogen for 3 days. The mixture was poured into water and isolation with ethyl acetate gave the crude product which was filtered through a plug of silica gel with 2% ethyl acetate–light petroleum as eluant to afford the aldehyde (15) (8.04 g) as a solid. A sample had b.p. 145 °C at 0.25 mmHg (Kugelrohr) and crystallized from cold light petroleum as needles, m.p. 43—45 °C (Found: C, 62.25; H, 6.4; Cl, 16.85%; M^+ , 212/214. C₁₁H₁₃ClO₂ requires C, 62.1; H, 6.15; Cl, 16.65%; M , 212/214); δ (CDCl₃, 90 MHz) 1.38 (6 H, d, 2 × Me), 2.17 (3 H, s, Me), 4.62 (1 H, septet, CH), 6.80 (1 H, s, 3-H), 7.70 (1 H, s, 6-H), and 10.29 (1 H, s, CHO).

2-Chloro-4-isopropoxy-3'-methoxy-2',5-dimethylstilbene (18).—The phosphonium salt (16) (5.0 g)² and the aldehyde (15) (2.44 g) were allowed to react in a similar manner to that described for compound (17). The crude product was filtered through a plug of neutral alumina with light petroleum as eluant. This gave the stilbene (18) (3.46 g) as a mixture of (*Z*)- and (*E*)-isomers in the ratio 2:1 as judged by ¹H n.m.r. spectroscopy. A small portion of the mixture was heated under reflux with a trace of iodine in toluene for 18 h. Work-up in the usual way gave the (*E*)-isomer as prisms (from methanol), m.p. 85–86 °C (Found: C, 72.55; H, 6.95; Cl, 10.9%; *M*⁺, 330/332. C₂₀H₂₃ClO₂ requires C, 72.6; H, 7.0; Cl, 10.7%; *M*, 330/332); λ_{max.} (EtOH) 217 and 300 nm (ε 26 400 and 24 400); δ (CDCl₃, 90 MHz) 1.31 (6 H, d, 2 × Me), 2.18 and 2.29 (each 3 H, s, Me), 3.77 (3 H, s, OMe), 4.44 (1 H, septet, CH), 6.67–7.25 (5 H, m, 2 × olefinic H and 3 × ArH), and 6.81 and 7.44 (each 1 H, s, 3- and 6-H). Repeated fractionation of the above mixture under diminished pressure gave a pure sample of the (*Z*)-isomer as an oil, b.p. 120 °C at 0.05 mmHg (Kugelrohr) (Found: C, 72.85; H, 6.8; Cl, 10.65%; *M*⁺, 330/332. C₂₀H₂₃ClO₂ requires C, 72.6; H, 7.0; Cl, 10.7%; *M*, 330/332); λ_{max.} (EtOH) 278 nm (ε 15 700); δ (CDCl₃, 90 MHz) 1.28 (6 H, d, 2 × Me), 1.86 and 2.14 (each 3 H, s, Me), 3.80 (3 H, s, OMe), 4.44 (1 H, septet, CH), and 6.55–7.06 (7 H, m, 2 × olefinic H and 5 × ArH).

6-Isopropoxy-2-methoxy-1,7-dimethylphenanthrene (20).—The stilbene (18) (6.84 g), enriched to 75% (*Z*)-isomer by fractional distillation, was allowed to react with activated magnesium by a similar method to that described above for compound (19). The crude product was filtered through a plug of neutral alumina with light petroleum as eluant. The phenanthrene (20) (3.86 g) formed plates (from methanol), m.p. 118–119 °C (Found: C, 81.55; H, 7.65%; *M*⁺, 294. C₂₀H₂₂O₂ requires C, 81.6; H, 7.55%; *M*, 294); λ_{max.} (EtOH) 228, 259, 272, 286, 327infl, 343, and 360 nm (ε 35 200, 47 000, 38 400, 20 700, 2 250, 2 950, and 3 500); δ (CDCl₃, 90 MHz) 1.43 (6 H, d, 2 × Me), 2.37 and 2.57 (each 3 H, s, Me), 3.91 (3 H, s, OMe), 4.79 (1 H, septet, CH), 7.27 and 8.40 (2 H, AB, *J*_{3,4} 9.5 Hz, 3- and 4-H), 7.55 (1 H, s, 8-H), 7.58 and 7.72 (2 H, AB, *J*_{9,10} 9.5 Hz, 9- and 10-H), and 7.90 (1 H, s, 5-H).

9,10-Dihydro-6-isopropoxy-2-methoxy-1,7-dimethylphenanthrene (22).—The phenanthrene (20) (2.00 g) and 10% palladized charcoal (500 mg) in ethyl acetate (30 ml) were stirred under hydrogen for 7 days. The usual work-up gave the dihydrophenanthrene (22) (2.07 g) which formed plates (from methanol), m.p. 98–99 °C (Found: C, 81.1; H, 8.2%; *M*⁺, 296. C₂₀H₂₄O₂ requires C, 81.05; H, 8.15%; *M*, 296); λ_{max.} (EtOH) 219, 278, 294, and 313 nm (ε 36 400, 18 300, 11 200, and 9 400); δ (CDCl₃, 90 MHz) 1.35 (6 H, d, 2 × Me), 2.21 (6 H, s, 2 × Me), 2.76 (4 H, br, 2 × CH₂), 3.83 (3 H, s, OMe), 4.55 (1 H, septet, CH), 6.79 and 7.52 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), and 6.97 and 7.16 (each 1 H, s, 8- and 5-H).

9,10-Dihydro-2-methoxy-1,7-dimethylphenanthren-6-ol (30).—The dihydrophenanthrene (22) (2.00 g) was allowed to react with boron trichloride for 3 h in a manner similar to that described above for compound (28). The dihydrophenanthrenol (30) (1.70 g) formed stout needles (from methanol), m.p. 198–199 °C (Found: C, 80.4; H, 7.1%; *M*⁺, 254. C₁₇H₁₈O₂ requires C, 80.3; H, 7.15%; *M*, 254); λ_{max.} (EtOH) 218, 277, 296, and 316 nm (ε 36 900, 18 800, 10 700, and 10 500); δ (CDCl₃, CD₃SOCD₃, 90 MHz) 2.19 and 2.22 (each 3 H, s, Me), 2.72 (4 H, br, 2 × CH₂), 3.80 (3 H, s, OMe), 6.73 and 7.47 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), 6.90 (1 H, s, 8-H), and 7.16 (1 H, s, 5-H). The acetate formed plates (from methylene dichloride–light petroleum), m.p. 153–154 °C (Found: C, 77.15; H, 6.8%; *M*⁺, 296. C₁₉H₂₀O₃ requires C, 77.0; H, 6.8%; *M*, 296); λ_{max.} (EtOH)

215, 278, and 287infl nm (ε 37 400, 20 700, and 17 600); δ (CDCl₃, 90 MHz) 2.16 and 2.20 (each 3 H, s, Me), 2.32 (3 H, s, MeCO), 2.79 (4 H, s, 2 × CH₂), 3.82 (3 H, s, OMe), 6.77 and 7.49 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), 7.05 (1 H, s, 8-H), and 7.28 (1 H, s, 5-H).

5-Bromo-9,10-dihydro-2,6-dimethoxy-1,7-dimethylphenanthrene (31).—Bromine (770 mg) in methylene dichloride (15 ml) was added dropwise with stirring to a solution of the dihydrophenanthrenol (30) (1.23 g) in methylene dichloride (25 ml) with exclusion of light. After a further 15 min work-up gave the crude product which was methylated at room temperature with iodomethane and potassium carbonate in dry *N,N*-dimethylformamide during 18 h. Work-up gave the crude product which was filtered through a plug of alumina with light petroleum as eluant. The dihydrophenanthrene (31) (1.60 g) formed needles (from methanol), m.p. 113.5–114 °C (Found: C, 62.3; H, 5.55; Br, 22.8%; *M*⁺, 346/348. C₁₈H₁₉BrO₂ requires C, 62.25; H, 5.5; Br, 23.0%; *M*, 346/348); λ_{max.} (EtOH) 216 and 282 nm (ε 36 000 and 19 400); δ (CDCl₃, 90 MHz) 2.22 and 2.33 (each 3 H, s, Me), 2.66 (4 H, s, 2 × CH₂), 3.82 and 3.85 (each 3 H, s, OMe), 6.79 and 8.15 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), and 6.96 (1 H, s, 8-H).

1-(9,10-Dihydro-2,6-dimethoxy-1,7-dimethylphenanthren-5-yl)ethanol (32).—Butyl-lithium (1.35 mmol) in hexane (0.9 ml) was added under dry nitrogen to a stirred solution of the bromo-compound (31) (426.7 mg, 1.23 mmol) in dry diethyl ether (10 ml) at 20 °C. After a further 2 min freshly distilled anhydrous acetaldehyde (10 ml) was added dropwise. The solution was then cooled to 0 °C and an excess of water was added. The crude product, isolated with ethyl acetate, was chromatographed over silica gel with 5% ethyl acetate–light petroleum as eluant. The alcohol (32) (227 mg) crystallized from methylene dichloride–light petroleum as prisms, m.p. 151–152.5 °C (Found: C, 76.85; H, 7.8%; *M*⁺, 312. C₂₀H₂₄O₃ requires C, 76.9; H, 7.75%; *M*, 312); λ_{max.} (MeOH) 215, 275, and 290 nm (ε 41 400, 20 600, and 12 500); δ (CDCl₃, 90 MHz) 1.81 (3 H, d, *J* 6.5 Hz, CH₃CH), 2.23 and 2.32 (each 3 H, s, Me), 2.45–2.82 (4 H, m, 2 × CH₂), 3.78 (1 H, br, OH), 3.89 and 3.92 (each 3 H, s, OMe), 5.29 (1 H, q, *J* 6.5 Hz, CH₃CH), 6.77 and 7.72 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), and 6.97 (1 H, s, 8-H).

1-(9,10-Dihydro-2,6-dimethoxy-1,7-dimethylphenanthren-5-yl)ethan-1-one (33).—A solution of the alcohol (32) (366 mg) in methylene dichloride (1 ml) was added to a stirred suspension of pyridinium chlorochromate (380 mg) in methylene dichloride (5 ml). After 5 h the mixture was diluted with diethyl ether and filtered through Celite. The residue left on removal of the solvents was chromatographed over silica gel with 10% ethyl acetate–light petroleum as eluant. The ketone (33) (320 mg) crystallized from methanol as stout needles, m.p. 133.5–134 °C (Found: C, 77.6; H, 7.35%; *M*⁺, 310. C₂₀H₂₂O₃ requires C, 77.4; H, 7.15%; *M*, 310); λ_{max.} (MeOH) 213, 278, and 300 nm (ε 37 500, 17 200, and 11 200); δ (CDCl₃, 90 MHz) 2.22 (3 H, s, Me), 2.24 (3 H, s, COMe), 2.30 (3 H, s, Me), 2.72 (4 H, s, 2 × CH₂), 3.77 and 3.82 (each 3 H, s, OMe), 6.97 and 7.26 (2 H, AB, *J*_{3,4} 9.0 Hz, 3- and 4-H), and 7.07 (1 H, s, 8-H).

1-(9,10-Dihydro-2,6-dihydroxy-1,7-dimethylphenanthren-5-yl)ethan-1-one (Juncunone) (7).—The ketone (33) (100 mg) was demethylated with boron tribromide during 1 h at –10 °C in a similar manner to that described above for compound (19). Juncunone (7) (68.4 mg) crystallized from methylene dichloride–light petroleum as bright yellow plates, m.p. 191–192 °C (lit.,⁹ 196–197 °C) identical (mixed m.p., i.r., electronic, ¹H n.m.r., and mass spectra) with an authentic sample (Found: C, 76.8; H, 6.5. Calc. for C₁₈H₁₈O₃: C, 76.55; H, 6.45%; λ_{max.} (MeOH) 211,

252, 293infl, and 375 nm (ϵ 34 300, 15 800, 6 200, and 6 500); m/z 282 (M^+ , 100%), 281 (46), 267 (61), 264 (40), 252 (18), 249 (20), 239 (10), and 224 (13); δ ($CDCl_3$, 90 MHz) 2.06 (3 H, s, COMe), 2.27 and 2.30 (each 3 H, s, Me), 2.68 (4 H, m, $2 \times CH_2$), 5.71 (1 H, s, OH), 6.61 and 6.76 (2 H, AB, $J_{3,4}$ 8.0 Hz, 3- and 4-H), 7.15 (1 H, s, 8-H), and 10.52 (1 H, s, OH).

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