  Bull. Chem. Soc. Jpn., 61, 723—727 (1988)

The Conversion of (+)-Dehydroabietic Acid into Steroidal Hormones

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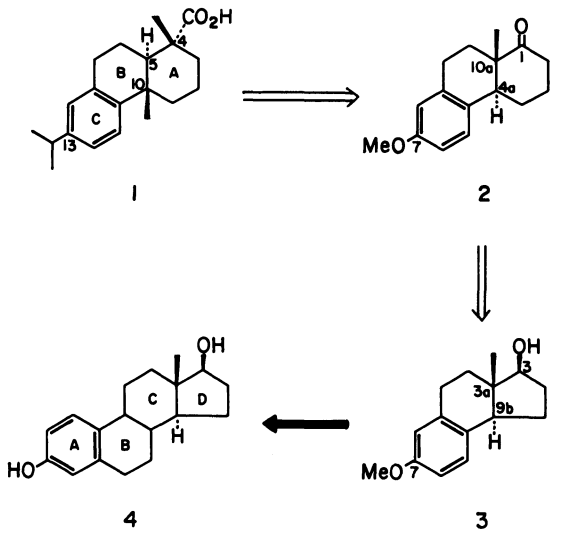
(Received April 24, 1987)

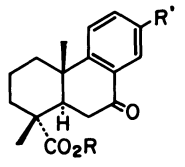
A resin acid, (+)-dehydroabietic acid, was converted into 3,4,4a,9,10,10a-hexahydro-7-methoxy-10aβ-methyl-4aα*H*-phenanthren-1(2*H*)-one (**2**) by the introduction of oxygen functions at the C-4 and C-13 positions, and a rearrangement of the angular methyl group to the C-5 position. The hydrophenanthrene derivative **2** was further transformed into 2,3,3a,4,5,9b-hexahydro-7-methoxy-3aβ-methyl-9bα*H*-1*H*-benz[*e*]inden-3β-ol (**3**). Since the conversion of **3** into steroidal hormones has already been reported, the present synthesis can be regarded as the synthesis of steroidal hormones from (+)-dehydroabietic acid.

The conversion of (+)-dehydroabietic acid (**1**) into steroidal compounds has been attempted by several groups.[1-4] Jeger et al. have reported the transformation of **1** into 3-oxo-17β-acetoxy-14α-methyl-Δ^4-8α,9β,10α,13α-esterene. However, other groups have carried out only partial modifications of **1**, and have not reported the synthesis of natural steroids. We have also investigated the utilization of **1** as a starting material for the syntheses of optically active steroids. In this paper, we describe the transformation of **1** into 2,3,3a,4,5,9b-hexahydro-7-methoxy-3aβ-methyl-9bα*H*-1*H*-benz[*e*]inden-3β-ol (**3**), a useful intermediate for the syntheses of steroidal hormones, which has already been converted into estradiol (**4**), adrenosterone, and so on.[5] Our basic strategy for the synthesis of steroidal hormones is the modification of the A, B, and C rings in the diterpene skeleton to the D, C, and B rings of the steroidal skeleton, as shown in Scheme 1. Namely, (+)-dehydroabietic acid (**1**) was converted into 3,4,4a,9,10,10a-hexahydro-7-methoxy-10aβ-methyl-4aα*H*-phenanthren-1(2*H*)-one (**2**) by the introduction of oxygen functions at the C-4 and C-13 positions, and a rearrangement of the angular methyl group at the C-10 position to the C-5 position. Ring contraction of the cyclohexanone moiety in **2** gave the corresponding cyclopentanol derivative **3**.

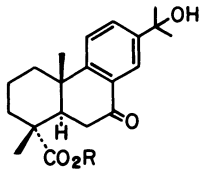


Scheme 1.

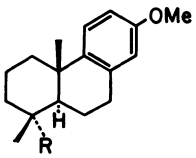
The oxidation of (+)-dehydroabietic acid (**1**) with chromium trioxide and acetic anhydride in acetic acid, followed by alkaline hydrolysis in refluxing diethylene glycol, afforded 13-acetyl-7-oxo-8,11,13-podocarpatrien-18-oic acid[6] (**5**: 8%) and 15-hydroxy-7-oxo-8,11,13-abietatrien-18-oic acid (**6**: 26%). The acid **6** was treated with diazomethane in ether and the resulting ester **7** (97%) was oxidized with *t*-butyl hydroperoxide in acetic acid containing concentrated sulfuric acid to give methyl 13-hydroxy-7-oxo-8,11,13-podocarpatrien-18-oate[6] (**8**: 76%). This compound **8** was also obtained in 32% yield from **5** by a series of reactions: esterification with diazomethane, Baeyer–Villiger oxidation with *m*-chloroperbenzoic acid, and alkaline hydrolysis. The methylation of **8** with methyl iodide and anhydrous potassium carbonate in refluxing ethyl methyl ketone gave a methyl ether **9** (97%), which was converted into methyl 13-methoxy-8,11,13-podocarpatrien-18-oate[7-9] (**10**: 87%) by acidic hydrogenolysis using Pd–C and perchloric acid in ethyl acetate. The Grignard reaction of **10** with phenylmagnesium bromide afforded a diphenylmethanol derivative **11** in 81% yield, which was then treated with lead tetraacetate and calcium carbonate in refluxing benzene to give a mixture of Δ^3, Δ^4, and $\Delta^{4(18)}$-19-nor compounds **12** in 70% yield. Ozonolysis of **12** in dichloromethane afforded 3,4,4a,9,10,10a-hexahydro-7-methoxy-4aβ-methyl-10aα*H*-phenanthren-1(2*H*)-one (**13**) in 60% yield. This ketone **13** was transformed into a tetraene compound **15** (93%) via a mesylate **14** by a series of reactions: lithium aluminium hydride reduction, mesylation, and refluxing with 2,4-lutidine. Subsequently, a rearrangement of the angular methyl group at the C-4a position to the C-10a position was carried out as follows. Epoxidation of **15** with *m*-chloroperbenzoic acid, followed by treatment with boron trifluoride etherate in dichloromethane, afforded a rearranged alcohol (**16**)[10] in 52% yield. This was then hydrogenated over Pd–C in ethanol to give 1,2,3,4,4a,9,10,10a-octahydro-7-methoxy-10aβ-methyl-4aα*H*-phenanthren-1β-ol (**17**: 99%) which gave an acetate **18** (96%). The β-configuration of the hydroxyl group in **17** was



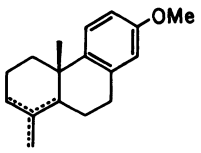
5 R=H, R'=Ac
8 R=Me, R'=OH
9 R=Me, R'=OMe



6 R=H
7 R=Me



10 R=CO_2Me
11 R=C(OH)Ph_2



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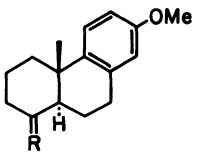
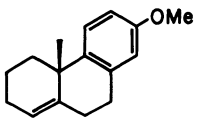


13 R=O
14 R=β-OMs, α-H



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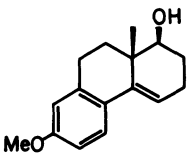

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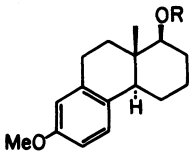
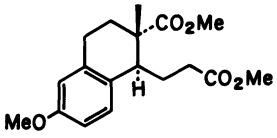


17 R=H
18 R=Ac



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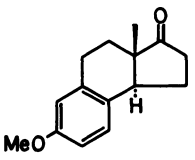

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supported from its ^1H NMR spectrum, which showed a broad signal due to the C-1 proton at δ 3.1—3.5, suggesting the presence of an axial α proton. Oxidation of **17** with pyridinium chlorochromate in dichloromethane afforded the desired ketone **2** in 89% yield.

According to the method of Rao and Banerjee,[11] the ketone **2** was submitted to oxidative cleavage with potassium hypoiodite and subsequent esterification with diazomethane to afford a dimethyl ester **19** in 49% yield. Dieckmann cyclization of **19** with potassium *t*-butoxide in refluxing benzene, followed by hydrolysis and subsequent decarboxylation, produced 3a,4,5,9b-tetrahydro-7-methoxy-3aβ-methyl-9bαH-1*H*-benz-[*e*]inden-3(2*H*)-one (**20**) in 78% yield. This was reduced with lithium aluminium hydride in ether to give the desired alcohol **3** in 91% yield.

Since the syntheses of steroidal hormones from **3** have already been reported, the present synthesis of **3** can be regarded as the synthesis of steroidal hormones from a resin acid, (+)-dehydroabietic acid (**1**).

Experimental

All melting points are uncorrected. The IR spectra and optical rotations were measured in chloroform, and the ^1H NMR spectra in carbon tetrachloride at 60 MHz, with tetramethylsilane as an internal standard, unless otherwise stated; s: singlet, bs: broad singlet, d: doublet, bd: broad doublet, dd: double doublet, t: triplet, m: multiplet. The column chromatography was performed using Merck silica gel (0.063 mm).

Oxidation of (+)-Dehydroabietic Acid (1) with Chromium Trioxide. Chromium trioxide (43.0 g) was added to a stirred solution of (+)-dehydroabietic acid (**1**) (30.0 g) and acetic anhydride (200 ml) in acetic acid (150 ml) with cooling in a water bath at 15—25 °C over a period of 2 h. After stirring at room temperature for 1 h, methanol (75 ml) was added dropwise to the stirred mixture with cooling in an ice-water bath at 10—15 °C over a period of 1 h. The mixture was concentrated in vacuo, diluted with water, and extracted with benzene. The benzene extract was washed with brine, dried over sodium sulfate, and evaporated in vacuo. The residue was chromatographed on silica gel (Mallinckrodt CC-4, 150 g) using ether–benzene (1:9 and then 3:7) as eluents, to give a mixture (25.1 g) of 15-acetoxy-7-oxo-8,11,13-abietatrien-18-oic acid and 13-acetyl-7-oxo-8,11,13-podocarpatrien-18-oic acid (**5**).[6]

The above mixture (25.1 g) was refluxed with aqueous potassium hydroxide (25%, 30 ml) in diethylene glycol (100 ml) for 2 h. The mixture was cooled, acidified with dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (Mallinckrodt CC-4, 300 g), using ether–benzene (15:85) as the eluent, to give **5** (2.6 g:8.3%). This was recrystallized from a mixture of acetone and hexane, mp 192—193.5 °C, $[\alpha]_D$ +29.7° (*c* 3.61), IR 3600—2300 and 1686 cm^{-1}, ^1H NMR ($CDCl_3$) δ=1.30 (3H, s) and 1.38 (3H, s) (C_4-CH_3 and C_{10}-CH_3), 2.63 (3H, s, -$COCH_3$), 7.48 (1H, d, *J*=8 Hz, C_{11}-H), 8.13 (1H, dd, *J*=8 and 2 Hz, C_{12}-H), 8.52 (1H, d, *J*=2 Hz, C_{14}-H), 9.5 (1H, bs, -CO_2H). Found: C, 72.41; H, 7.35%. Calcd for $C_{19}H_{22}O_4$:C, 72.59; H, 7.05%. Further elution with ether–benzene (35:65) gave 15-hydroxy-7-oxo-8,11,13-abietatrien-18-oic acid (**6**) (8.4 g:25.5%). This was recrystallized from benzene, mp 118—120 °C, $[\alpha]_D$ +10.4° (*c* 5.21), IR 3600—2300, 1698, and 1682 cm^{-1}, ^1H NMR ($CDCl_3$) δ=1.27 (3H, s) and 1.35 (3H, s) (C_4-CH_3 and C_{10}-CH_3), 1.58 (6H, s, -$C(CH_3)_2OH$), 7.34 (1H, d, *J*=9 Hz, C_{11}-H), 7.74 (1H, dd, *J*=9 and 2 Hz, C_{12}-H), 8.06 (1H, d,

J=2 Hz, C_{14}-H). Found: C, 72.40; H, 7.99%. Calcd for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93%.

Methyl 15-Hydroxy-7-oxo-8,11,13-abietatrien-18-oate (7). The acid **6** (3.325 g) was treated with an ethereal diazomethane solution at room temperature for 30 min. After the usual work-up, the crude product was chromatographed on silica gel (0.063—0.200 mm, 120 g), using ether-benzene (3:7) as the eluent, to give an oily **7** (3.355 g:96.8%), $[\alpha]_D$ +15.0° (*c* 6.00), IR 3594, 1720, and 1678 cm^{-1}; ^1H NMR δ=1.23 (3H, s) and 1.30 (3H, s) (C_4-CH_3 and C_{10}-CH_3), 1.51 (6H, s, -C(CH_3)$_2$OH), 3.63 (3H, s, -CO_2CH_3), 7.21 (1H, d, J=8 Hz, C_{11}-H), 7.62 (1H, dd, J=8 and 2 Hz, C_{12}-H), 7.87 (1H, d, J=2 Hz, C_{14}-H). Found: C, 73.43; H, 8.11%. Calcd for $C_{21}H_{28}O_4$: C, 73.22; H, 8.19%.

Methyl 13-Hydroxy-7-oxo-8,11,13-podocarpatrien-18-oate (8). *a*): A stirred mixture of **7** (5.973 g), *t*-butyl hydroperoxide (70%, 5.0 ml), and concentrated sulfuric acid (1.2 ml) in acetic acid (59 ml) was heated at 50 °C for 3 h. The mixture was cooled, poured into aqueous sodium hydrogencarbonate, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (0.063—0.200 mm, 60 g), using ether-benzene (1:9) as the eluent, to give **8** (3.966 g:75.6%). This was recrystallized from benzene, mp 197—198.5 °C, $[\alpha]_D$ −11.4° (*c* 7.47), IR 3325, 1720, and 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.22 (3H, s) and 1.33 (3H, s) (C_4-CH_3 and C_{10}-CH_3), 3.65 (3H, s, -CO_2CH_3), 7.02 (1H, dd, J=9 and 2.5 Hz, C_{12}-H), 7.22 (1H, d, J=9 Hz, C_{11}-H), 7.54 (1H, d, J=2.5 Hz, C_{14}-H), 7.83 (1H, bs, -OH). Found: C, 71.78; H, 7.49%. Calcd for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33%.

b): The acid **5** (1.920 g) was treated with an ethereal diazomethane solution at room temperature for 30 min to give a crude ester (2.003 g), IR 1722 and 1685 cm^{-1}.

The above ester (2.003 g) was refluxed with *m*-chloroperbenzoic acid (85%, 1.218 g) and *p*-toluenesulfonic acid (18 mg) in 1,2-dichloroethane (18 ml) for 4 h. The mixture was cooled, diluted with ether, and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. After removal of the solvent in vacuo, the residue was refluxed with sodium hydrogencarbonate (1.40 g) and water (10 ml) in methanol (40 ml) for 2 h. The mixture was concentrated in vacuo, diluted with water, and extracted with ether. The ether extract was washed with aqueous sodium hydroxide and water, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (0.063—0.200 mm, 30 g), using ether-benzene (1:9) as the eluent, to give the recovered methyl 13-acetyl-7-oxo-8,11,13-podocarpatrien-18-oate (582 mg).

The alkaline washing was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (0.063—0.200 mm, 30 g), using ether-benzene (1:9) as the eluent, to give **8** (581 mg:31.6%), whose IR and ^1H NMR spectra were identical with those of the authentic sample.

Methyl 13-Methoxy-7-oxo-8,11,13-podocarpatrien-18-oate (9). A stirred mixture of **8** (8.778 g), methyl iodide (6.2 ml), and anhydrous potassium carbonate (25.0 g) in ethyl methyl ketone (90 ml) was refluxed for 8 h. The mixture was cooled, diluted with ether, and washed successively with water, aqueous sodium thiosulfate, and brine. The dried solution was evaporated in vacuo. The residue was chromatographed on silica gel (0.063—0.200 mm, 200 g), using ether-benzene (3:97) as the eluent, to give an oily **9** (8.917 g: 97.2%), $[\alpha]_D$ +11.4° (*c* 3.78), IR 1725 and 1676 cm^{-1}, ^1H NMR δ=1.21 (3H, s) and 1.30 (3H, s) (C_4-CH_3 and C_{10}-CH_3), 3.63 (3H, s, -CO_2CH_3), 3.79 (3H, s, -OCH_3), 6.92 (1H, dd, J=9 and 3 Hz, C_{12}-H), 7.19 (1H, d, J=9 Hz, C_{11}-H), 7.33 (1H, d, J=3 Hz, C_{14}-H). Found: C, 72.34; H, 7.69%. Calcd for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65%.

Methyl 13-Methoxy-8,11,13-podocarpatrien-18-oate (10). A mixture of **9** (21.268 g), Pd-C (10%, 4.0 g), and perchloric acid (60%, 4.0 ml) in ethyl acetate (100 ml) was hydrogenated at room temperature under an atmosphere of hydrogen for 9 h. After the usual work-up, the crude product was recrystallized from methanol to give **10** (13.328 g:65.6%), mp 79.5—80 °C, $[\alpha]_D$ +60.7° (*c* 1.52), IR 1720 cm^{-1}, ^1H NMR δ=1.14 (3H, s) and 1.21 (3H, s)(C_4-CH_3 and C_{10}-CH_3), 3.60 (3H, s) and 3.67 (3H, s) (-CO_2CH_3 and -OCH_3), 6.40 (1H, bs, C_{14}-H), 6.50 (1H, dd, J=8 and 2 Hz, C_{12}-H), 6.99 (1H, d, J=8 Hz, C_{11}-H). Found: C, 75.41; H, 8.54%. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67%. The mother liquor of recrystallization was evaporated in vacuo. The residue was chromatographed on silica gel (150 g), using ether-benzene (1:99) as the eluent, to give an additional **10** (4.378 g:21.5%).

Grignard Reaction of 10 with Phenylmagnesium Bromide. A solution of **10** (3.975 g) in dry ether (25 ml) was added to a stirred ether solution of phenylmagnesium bromide prepared from magnesium turnings (1.60 g) and bromobenzene (6.9 ml) in dry ether (15 ml). The mixture was refluxed for 30 min and the ether was removed. The viscous residue was heated at 90—100 °C for 5.5 h. After cooling, the mass was hydrolyzed with a mixture of dilute hydrochloric acid and ice, and then extracted with ether. The ether extract was washed succesively with aqueous sodium thiosulfate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (150 g), using hexane-benzene (1:4) as the eluent, to give a diphenylmethanol derivative **11** (4.555 g:81.2%). This was recrystallized from acetone-hexane, mp 178.5—182 °C, $[\alpha]_D$ +65.8° (*c* 3.71), IR 3580 cm^{-1}, ^1H NMR δ=1.17 (3H, s, C_{10}-CH_3), 1.32 (3H, s, C_4-CH_3), 3.58 (3H, s, -OCH_3), 6.18 (1H, d, J=2.5 Hz, C_{14}-H), 6.43 (1H, dd, J=9 and 2.5 Hz, C_{12}-H), 6.94 (1H, d, J=9 Hz, C_{11}-H), 7.0—7.9 (10H, m, 2-C_6H_5). Found: C, 84.22; H, 8.01%. Calcd for $C_{30}H_{34}O_2$: C, 84.46; H, 8.03%.

Oxidation of 11 with Lead Tetraacetate. A stirred mixture of **11** (8.316 g), lead tetraacetate (91.4%, 12.30 g), and calcium carbonate (10.60 g) in dry benzene (110 ml) was refluxed for 5 h. The mixture was cooled, diluted with ether and water, and then filtered. The filtrate was extracted with ether. The ether extract was washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and brine. The dried solution was evaporated in vacuo. The crude product was chromatographed on silica gel (200 g), using hexane-benzene (9:1) as the eluent, to give 13-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene (**12**) 3.307 g:70.0%) containing small amounts of Δ^3- and Δ^4-isomers. ^1H NMR δ=0.96 (3H, s, C_{10}-CH_3), 3.78 (3H, s, -OCH_3), 4.64 (1H, bs) and 4.79 (1H, bs) (-$\dot{C}$=CH_2), 6.48 (1H, bs, C_{14}-H), 6.55 (1H, dd, J=9 and 3 Hz, C_{12}-H), 7.07 (1H, d, J=9 Hz, C_{11}-H). Found: C, 84.50; H, 9.08%. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15%.

3,4,4a,9,10,10a-Hexahydro-7-methoxy-4aβ-methyl-10aα*H*-phenanthren-1(2*H*)-one (13). A solution of **12** (1.937 g) in dichloromethane (20 ml) was ozonized at −65 °C for 1 h. The solution was evaporated in vacuo. The residue was heated with zinc powder (1.37 g) in aqueous acetic acid (50%, 46 ml) at 80 °C for 1 h and then filtered. The filtrate was concentrated in vacuo and extracted with ether. The ether extract was washed with aqueous sodium hydrogencarbonate and brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (50 g), using ether–benzene (2:98) as the eluent, to give **13** (1.172 g:60.0%). This was recrystallized from hexane, mp 70.5—71 °C, $[\alpha]_D$ +189° (*c* 3.93), IR 1707 cm^{-1}, ^1H NMR δ=0.99 (3H, s, C_{4a}–CH_3), 3.70 (3H, s, -OCH_3), 6.47 (1H, bs, C_8–H), 6.55 (1H, dd, *J*=8 and 2.5 Hz, C_6–H), 7.07 (1H, d, *J*=8 Hz, C_5–H). Found: C, 78.49; H, 8.19%. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.

2,3,4,4a,9,10-Hexahydro-7-methoxy-4aβ-methylphenanthrene (15). A solution of **13** (940 mg) in dry ether (10 ml) was reduced with lithium aluminium hydride (73 mg) at room temperature for 1 h. The mixture was poured into dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was dissolved in pyridine (4.5 ml) and mesylated with methanesulfonyl chloride (0.45 ml) at room temperature for 19 h. The mixture was poured into dilute hydrochloric acid and extracted with ether; the extract was washed successively with aqueous sodium hydrogencarbonate and brine. The dried solution was evaporated in vacuo to give a crude mesylate **14** (1.210 g), IR 1340 and 1175 cm^{-1}, ^1H NMR δ=1.21 (3H, s, C_{4a}–CH_3), 2.92 (3H, s, -OSO_2CH_3), 3.70 (3H, s, -OCH_3), 4.85 (1H, $W_{1/2}$=6 Hz, C_1–H), 6.46 (1H, bs, C_8–H), 6.54 (1H, dd, *J*=9 and 3 Hz, C_6–H), 7.02 (1H, d, *J*=9 Hz, C_5–H).

A solution of the crude mesylate **14** (1.210 g) in 2,4-lutidine (4.0 ml) was refluxed for 2.5 h under a stream of nitrogen. The solution was cooled, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (25 g), using hexane–benzene (1:1) as the eluent, to give **15** (815 mg:92.8% from **13**). This was recrystallized from hexane, mp 69—69.5 °C, $[\alpha]_D$ +233° (*c* 3.41), ^1H NMR δ=1.34 (3H, s, C_{4a}–CH_3), 3.70 (3H, s, -OCH_3), 5.39 (1H, br, C_1–H), 6.40 (1H, d, *J*=3 Hz, C_8–H), 6.60 (1H, dd, *J*=9 and 3 Hz, C_6–H), 7.06 (1H, d, *J*=9 Hz, C_5–H). Found: C, 83.95; H, 9.08%. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.83%.

1,2,3,9,10,10a-Hexahydro-7-methoxy-10aβ-methyl-1β-phenanthrenol (16). A mixture of **15** (303 mg) and *m*-chloroperbenzoic acid (80%, 315 mg) in dichloromethane (10 ml) was stirred at room temperature for 2 h. The mixture was diluted with ether and washed successively with aqueous potassium iodide, aqueous sodium thiosulfate, aqueous sodium hydrogencarbonate, and water. The dried solution was evaporated in vacuo. The residual oil was dissolved in dichloromethane (4.0 ml) and boron trifluoride etherate (0.49 ml) was added at 2—8 °C. After stirring at 2—3 °C for 40 min, the mixture was diluted with ether, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (15 g), using ether–benzene (1:9) as the eluent, to give **16** (168 mg:51.8%). This was recrystallized from acetone–hexane, mp 133.5—135.5 °C, IR 3610 and 3435 cm^{-1}, ^1H NMR ($CDCl_3$) δ=1.01 (3H, s, C_{10a}–CH_3), 3.80 (3H, s, -OCH_3), 5.99 (1H, t, *J*=3.5 Hz, C_4–H), 6.62 (1H, s, C_8–H), 6.71 (1H, dd, *J*=9 and 2 Hz, C_6–H), 7.47 (1H, d, *J*=9 Hz, C_5–H). Found: C, 78.40; H, 8.35%. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.

1,2,3,4 4a,9,10,10a-Octahydro-7-methoxy-10aβ-methyl-4aα*H*-phenanthren-1β-ol (17) and Its Acetate (18). *a*): A mixture of **16** (69.3 mg) and Pd–C (5%, 30 mg) in ethanol (15 ml) was hydrogenated at room temperature under an atmosphere of hydrogen for 3 h. After the usual work-up, the product **17** (69.0 mg:98.8%) was recrystallized from hexane, mp 100—101.5 °C, IR 3610 and 3450 cm^{-1}, ^1H NMR δ=0.69 (3H, s, C_{10a}–CH_3), 3.1—3.5 (1H, m, C_1–H), 3.73 (3H, s, -OCH_3), 6.35—6.65 (2H, m, C_6–H and C_8–H), 6.99 (1H, d, *J*=9 Hz, C_5–H). Found: C, 78.04; H, 9.27%. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00%.

b): A solution of **17** (39.0 mg) and acetic anhydride (0.5 ml) in pyridine (0.5 ml) was heated at 75—80 °C for 2 h. After the usual work-up, the crude product was chromatographed on silica gel (5.0 g), using benzene as the eluent, to give an acetate **18** (44.5 mg:96.2%). This was recrystallized from hexane, mp 141.5—142 °C, IR 1720 cm^{-1}, ^1H NMR (90 MHz) δ=0.75 (3H, s, C_{10a}–CH_3), 1.97 (3H, s, -$OCOCH_3$), 3.69 (3H, s, -OCH_3), 4.45—4.7 (1H, m, C_1–H), 6.49 (1H, s, C_8–H), 6.54 (1H, dd, *J*=9 and 3 Hz, C_6–H), 6.99 (1H, d, *J*=9 Hz, C_5–H). Found: C, 74.81; H, 8.61%. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39%.

Oxidation of 17 into 3,4,4a,9,10,10a-Hexahydro-7-methoxy-10aβ-methyl-4aα*H*-phenanthren-1(2*H*)-one (2). A mixture of **17** (38.0 mg) and pyridinium chlorochromate (56.5 mg) in dichloromethane (3.0 ml) was stirred at 0—5 °C for 5 min and at room temperature for 3 h. After the addition of aqueous sodium hydrogencarbonate, the mixture was extracted with ether. The ether extract was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (5.0 g), using benzene as the eluent, to give **2** (34.1 mg:89.3%). This was recrystallized from hexane, mp 91—92 °C, IR 1701 cm^{-1}, ^1H NMR δ=0.94 (3H, s, C_{10a}–CH_3), 3.73 (3H, s, -OCH_3), 6.51 (1H, s, C_8–H), 6.58 (1H, dd, *J*=9 and 2 Hz, C_6–H), 7.05 (1H, d, *J*=9 Hz, C_5–H). Found: C, 78.48; H, 8.46%. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25%.

Methyl 1,2,3,4-Tetrahydro-6-methoxy-2α-methoxycarbonyl-2β-methyl-1α*H*-naphthalene-1-propionate (19). A solution of **2** (164.7 mg) in methanol (14 ml) was treated alternately with three drops of a solution of iodine (494.1 mg) in methanol (8.2 ml) and one drop of a solution of potassium hydroxide (889.4 mg) in water (1.8 ml) and methanol (4.9 ml) with vigorous stirring at room temperature under a stream of nitrogen over a period of 1 h. The mixture was allowed to stand at room temperature for 23 h and the methanol was removed in vacuo. The residue was acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed successively with water, aqueous sodium thiosulfate, and water. The dried solution was evaporated in vacuo and the residue was treated with ethereal diazomethane solution at room temperature for 30 min. After the usual work-up, the crude product was chromatographed on silica gel (10 g), using ether–benzene (1:99) as the eluent, to give an oily **19** (104.7 mg:48.5%), IR 1728 cm^{-1}, ^1H NMR δ=1.22 (3H, s, C_2–CH_3), 3.45 (3H, s) and 3.58 (3H, s) (2-CO_2CH_3), 3.69 (3H, s, -OCH_3), 6.43 (1H, bs),

6.51 (1H , dd, J=9 and 3 Hz), and 6.82 (1H, d, J=9 Hz) (aromatic protons). Found: C, 67.65; H, 7.79%. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55%.

3a,4,5,9b-Tetrahydro-7-methoxy-3aβ-methyl-9bα*H*-1*H*-benz[*e*]inden-3(2*H*)-one (20). A stirred mixture of **19** (63.0 mg) and potassium *t*-butoxide (220.6 mg) in dry benzene (4.5 ml) was refluxed for 5 h under a stream of nitrogen. The mixture was cooled, poured into dilute hydrochloric acid, and extracted with ether. The ether extract was washed with water, dried, and evaporated in vacuo to give an oil (60 mg).

A mixture of the above oil (60 mg), concentrated hydrochloric acid (1.5 ml), and water (0.4 ml) in acetic acid (3.0 ml) was refluxed for 1.5 h under a stream of nitrogen. The mixture was evaporated in vacuo. The residue was dissolved in methanol (5.5 ml) and aqueous sodium hydroxide (5%, 4.0 ml), and then refluxed for 1 h under a stream of nitrogen. After removal of the methanol in vacuo, the residue was extracted with ether. The ether extract was washed with water, dried, and evaporated in vacuo. The crude product was chromatographed on silica gel (10 g), using ether–benzene (2:98) as the eluent, to give **20** (35.2 mg:77.7%). This was recrystallized from hexane, mp 115.5—116.5 °C, $[\alpha]_D$ +5° (*c* 1.2), IR 1734 cm^{-1}, ^1H NMR δ=0.68 (3H, s, C_{3a}-CH_3), 3.73 (3H, s, -OCH_3), 6.4—6.7 (2H, m) and 6.90 (1H, d, J=9 Hz) (aromatic protons). Found:C, 78.19; H, 7.92%. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88%.

2,3,3a,4,5,9b-Hexahydro-7-methoxy-3aβ-methyl-9bα*H*-1*H*-benz[*e*]inden-3β-ol (3). A mixture of **20** (24.0 mg) and lithium aluminium hydride (10.0 mg) in dry ether (2.0 ml) was stirred at room temperature for 1 h. The mixture was poured into dilute hydrochloric acid and extracted with ether. The ether extract was washed with brine, dried, and evaporated in vacuo. The residue was chromatographed on silica gel (6.0 g), using ether–benzene (5:95) as the eluent, to give **3** (22.1 mg:91.3%). This was recrystallized from hexane, mp 72.5—73 °C[12] (lit,[5] mp 69 °C), IR 3610 and 3430 cm^{-1}, ^1H NMR δ=0.61 (3H, s, C_{3a}-CH_3), 3.72 (3H, s, -OCH_3), 6.4—6.9 (3H, m, aromatic protons). ^1H NMR (C_5D_5N) δ=0.89 (3H, s, C_{3a}-CH_3), 3.69 (3H, s, -OCH_3), 6.7—7.3 (3H, m, aromatic protons). Found: C, 77.56; H, 8.74%. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68%.

This work was supported by a Grant-in-Aid for Scientific Research No. 60540353 from the Ministry of Education, Science and Culture.

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