Total Synthesis of (±)-12-Methoxyabieta-8,11,13-trien-6-one, a Versatile Intermediate for Diterpene Syntheses†

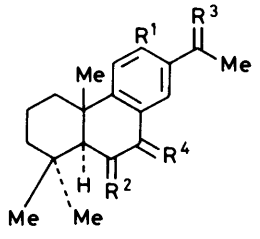
Ajoy K. Banerjee* and María Celia Sulbarán de Carrasco
Centro de Química, Instituto Venezolano de Investigaciones Científicas, I.V.I.C., Apartado 1827, Caracas 1010-A, Venezuela

The title compound (**1**) has been synthesized from perhydro-4α-methoxy-5,5,8a-trimethylnaphthalen-1-one (**12**). The formyl derivative (**14**) was subjected to Robinson annelation with 4-diethylaminobutan-2-one methiodide to obtain the adduct (**15**) and this, on heating with sodium methoxide in methanol, yielded the tricyclic ketone (**16**). The enolate of (**16**), generated by treatment with lithium di-isopropylamide, reacted with acetone in the presence of anhydrous zinc chloride to afford an aldol (**21**) which, on heating with toluene-*p*-sulphonic acid in benzene, provided the dienone (**22**); subsequent treatment with sulphuric acid in methanol produced the dimethoxyabietatriene (**6**) whose conversion into the desired ketone (**1**) was accomplished by treatment with trichloromethylsilane and sodium iodide followed by oxidation of the resulting compound with Jones' reagent and then methylation with dimethylsulphate and alkali. Elimination of C-6 carbonyl group of the ketone (**1**) and subsequent oxidation with chromium trioxide and acetic acid yielded the ketone (**3**) which, on demethoxylation with silicon tetrachloride and sodium iodide, yielded sugiol (**2**).

The value of the title ketone (**1**) as synthetic intermediate has been demonstrated[1] in the synthesis of several diterpenes. In connection with programmes directed towards the synthesis[2] of terpenes, we sought an alternative and convenient route for this ketone (**1**) whose utility in the synthesis of naturally occurring diterpenes stems from the versatality of the differentially functional groups. In this paper we disclose[3] the strategy designed to achieve the synthesis of the ketone (**1**), an important terpene precursor, and its transformation to sugiol (**2**).[1]

The alcohol (**8**)[4] was chosen as reference material since it appeared to be a favourable synthon for the desired ketone (**1**) and permits a wide range of structural variation. Treatment of the alcohol (**8**) with dihydropyran in dry methylene dichloride containing pyridinium toluene-*p*-sulphonate (PPTS)[5] yielded the oily pyranyl derivative (**9**) in 88% yield. Hydroboration, followed by oxidation of the resulting organoborane with alkaline hydrogen peroxide,[6] provided the means of converting the unsaturated pyranyl derivative (**9**) to the alcohol (**10**) whose homogeneity and purity were confirmed by t.l.c. with different solvents. In its ^{1}H n.m.r. spectrum the alcohol (**10**) exhibited a multiplet centred between δ 3.82—4.12 whose integration (four protons) corresponded to hydrogens at C-1, C-4, and C-2'.‡ Treatment of the alcohol (**10**) with methyl iodide and sodium hydride in tetrahydrofuran (THF) yielded the methoxy derivative (**11**) which on oxidation with Jones' reagent[7] yielded the ketone (**12**). In its ^{1}H n.m.r. spectrum the ketone (**12**) exhibited a multiplet centred at δ 3.65 with a half-band width ($W_{\frac{1}{2}}$) value of 15 Hz indicating the axial nature[2,8] of the C-4 proton‡ and the equatorial nature of the C-4 methoxy group of the ketone (**12**). As the hydroboration reaction involves the *cis* addition of the B–H moiety to the double bond, the bridgehead hydrogen of the ketone (**12**) and of the alcohol (**10**) must possess the axial configuration. This logic led us to assume that the bridgehead hydrogen and the C-4 methoxy group of the ketone (**12**) were α-oriented. Therefore it is reasonable to assume that the A/B ring fusion of the ketone (**12**) as well as that of the alcohol (**10**) must possess the *trans* configuration. These arguments led us to conclude that the A/B ring fusion of the ketone (**12**) as well as that of the alcohol (**10**) is in the more stable *trans* configuration. In order to confirm this assumption, the ketone (**12**) was subjected to Clemmensen reduction[9] which was found to be more suitable than other methods tried. The deoxygenated material obtained in satisfactory yield on treatment with trichloromethylsilane and sodium iodide[10] afforded the alcohol (**13**) whose spectroscopic data were in accord with those published.[11]

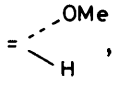
In order to complete the synthesis of the ketone (**1**), the ketone (**12**) was formylated with ethyl formate and base at room temperature to afford the formyl derivative (**14**). In the ^{1}H n.m.r. spectrum of the formyl derivative (**14**) the vinyl proton appeared as a doublet centred at δ 7.05 (*J* 6 Hz) owing to approximately *cis*-planar coupling[12] with the hydrogen of the hydroxy group.

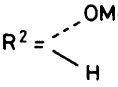


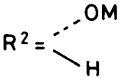
(**1**) R^1 = OMe, R^2 = O, R^3 = Me, H, R^4 = H, H

(**2**) R^1 = OH, R^2 = H, H, R^3 = Me, H, R^4 = O

(**3**) R^1 = OMe, R^2 = H, H, R^3 = Me, H, R^4 = O

(**4**) R^1 = OH, R^2 =  , R^3 = R^4 = H, H

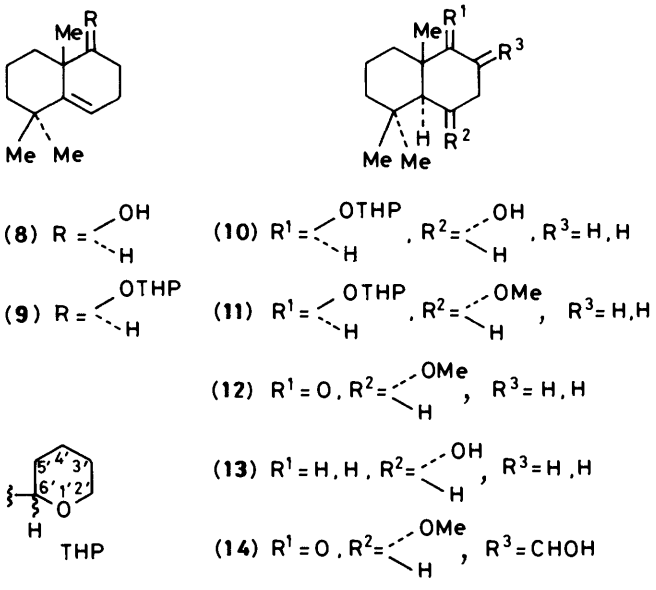
(**5**) R^1 = OMe, R^2 =  , R^3 = R^4 = H, H

(**6**) R^1 = OMe, R^2 =  , R^3 = Me, H, R^4 = H, H

(**7**) R^1 = OH, R^2 = O, R^3 = Me, H, R^4 = H, H

† Part of this work was presented (A. K. B.) at the Fifth International Congress on Organic Synthesis, Freiburg, West Germany, August 27—30, 1984.

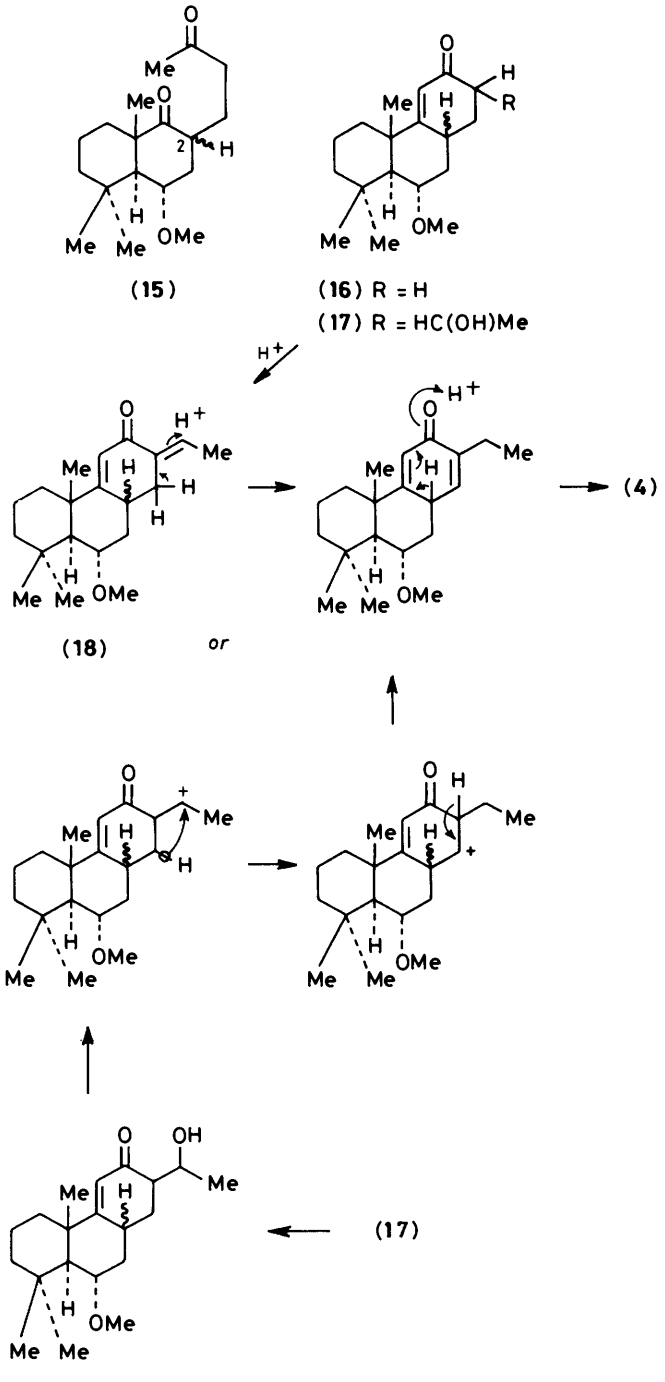
‡ Systematic numbering.



On treatment of the formyl derivative (**14**) with D_2O, the doublet at δ 7.05 changes to a singlet. The proton of the hydroxy group of the formyl derivative (**14**) appeared as doublet centred at δ 16.00 (*J* 6 Hz) arising by its coupling with the vicinal proton. The formyl derivative (**14**) was subjected to Robinson annelation with 4-diethylaminobutan-2-one methiodide following the procedure of Howell and Taylor.[13] The oily adduct (**15**) proved to be a mixture of C-2 epimers as evidenced by the appearance of two singlets for the acetyl groups at δ_H 2.06 and δ 2.08. The adduct (**15**) on heating under reflux with sodium methoxide in methanol afforded the α,β-unsaturated ketone (**16**) whose ^{1}H n.m.r. spectrum showed that it was a mixture of C-10a epimers.* The completion of the synthesis of the ketone (**1**) did not require the separation of the α- and β-epimer of the ketone (**16**) and thus this compound was utilized for the next step.†

Our next objective was to introduce the isopropyl group at C-2 of the ketone (**16**). In our synthetic plan we envisaged the transformation of the ketone (**16**) into the hydroxy ketone (**17**) and its conversion into the olefin (**18**) which, on being subjected to 1,4-addition reaction with dimethylcopper lithium, would give the desired C-2 isopropylated ketone (**20**). To this end, the ketone (**16**) was treated with lithium di-isopropylamide (LDA) and then acetaldehyde in the presence of zinc chloride[14] to afford the hydroxy ketone (**17**) as a mixture of diastereoisomers which, on heating with benzene and toluene-*p*-sulphonic acid (PTSA), did not yield the desired olefin (**18**) but instead produced an oily product which had a molecular ion *m*/*z* 302 in its mass spectrum. In its i.r. spectrum the product exhibited absorption bands of the hydroxy group (3 350 cm^{-1}) while the ^{1}H n.m.r. spectrum showed a triplet at δ 1.18 (*J* 7 Hz), a quadruplet at δ 2.54 (*J* 7.5 Hz), and two aromatic protons at δ 6.56 and 6.81. On the basis of the spectroscopic data, the phenol (**4**) appeared to be the logical structure of the oily product, a possible mechanism of whose formation from the hydroxy derivative (**17**) is explained in Scheme 1. As the desired olefin (**18**) was not obtained, an alternative method was tried.

The hydroxy ketone (**17**), on passage through a column of acidic alumina, yielded only the olefin (**19**) in 53% yield whose

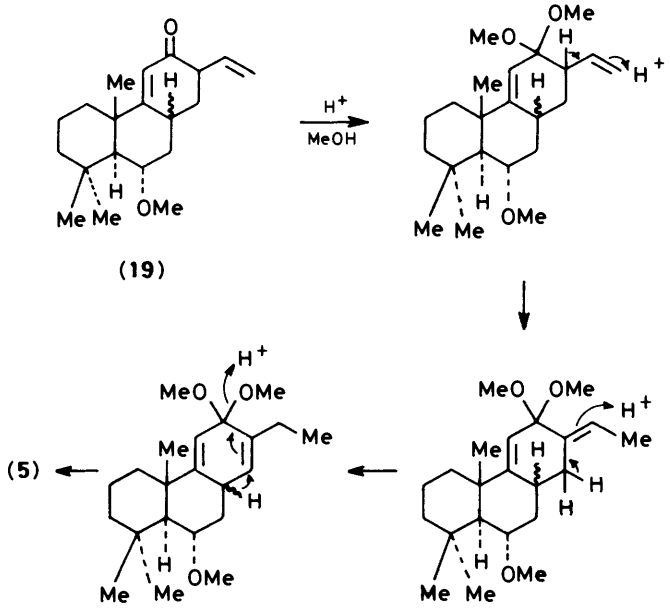


Scheme 1.

* Systematic numbering.

† On one occasion[3] an attempt was made to separate the C-10 epimers of ketone (**16**) by chromatographic purification. The major epimer, m.p. 64—65 °C, obtained in 60% yield and the minor epimer, m.p. 72—74 °C, obtained in 12% yield were speculated to be the β- and α-epimer, respectively, on the basis of three factors: (i) the conformational stability analysed by an inspection of molecular models, (ii) the dihedral angle between 10a-H and the C-4–C-4a double bond and their allylic coupling constants (T. A. Wittstruck, S. K. Malhotra, and H. J. Ringold, *J. Am. Chem. Soc.*, 1963, **85**, 1699; L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' 2nd ed., Pergamon, Oxford, 1969, p. 316), and (iii) literature analogy (T. A. Spencer, R. J. Friary, W. W. Schmiegal, J. F. Sincome, and O. S. Watt, *J. Org. Chem.*, 1968, **33**, 719). No experimental evidence was sought to verify the assignments and thus any attempt to justify the assignments is highly speculative. As no definite conclusion was sought on the stereochemical assignment at C-10a of the ketone (**16**), it was considered worthwhile not to discuss in detail the stereochemical arguments in the text.

structure was confirmed by ^{1}H n.m.r. spectrometry. The absence of the vinyl methyl signals in the ^{1}H n.m.r. spectrum clearly indicated that the expected olefin (**18**) was not formed during the dehydration of the hydroxy ketone (**17**). An attempt was therefore made to convert the olefin (**19**) into the desired olefin (**18**) by warming the former with 1% methanolic sulphuric acid. Instead of obtaining the desired olefin (**18**), the dimethoxy phenolic derivative (**5**) was isolated whose identity was confirmed by comparison of its spectral properties with those of an authentic specimen, prepared by methylation of the phenol (**4**) with dimethlyl sulphate and alkali. The mechanism of the formation of compound (**5**) from the olefin (**19**) is depicted in Scheme 2. Again, as the desired olefin (**18**) could not be prepared

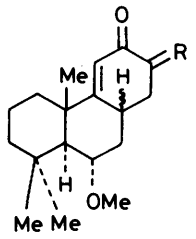


Scheme 2.

our initial plan to obtain the isopropyl derivative (**20**) had to be abandoned and thus an alternative route was explored.

Reaction of the enolate of the ketone (**16**), generated by treatment with LDA, with acetone in the presence of zinc chloride[14] yielded an aldolic product (**21**) as a mixture of C-10a epimers* in satisfactory yield. Absence of freshly fused zinc chloride afforded an inferior yield of the aldolic product (**21**) along with other unidentified products. The configurational assignment of the C-12 hydrogen of the aldol (**21**) was not considered but from a study of the literature[15] one may be tempted to assume that the C-12 hydrogen of the aldol (**21**) has the α-configuration. One singlet at δ 1.26 (6 H) in the ^{1}H n.m.r. spectrum was assigned to the C(OH)*Me*$_2$ methyl groups. Two broad signals at δ 4.55 and 5.25 were assigned to the OH proton of the aldol (**21**), a mixture of C-10a epimers. These signals disappeared when the spectral solvent D_2O was added. The aldol (**21**), on dehydration with PTSA in benzene, yielded the isopropylidene ketone (**22**). None of the expected aromatic derivative was obtained. Probably this is due to the stability of compound (**22**) toward the acid employed. The appearance of singlets at δ 1.80 and 2.20, each of which corresponded to three hydrogens, indicated the presence of two vinylic methyl groups. When the ketone (**22**) was heated with methanolic sulphuric acid it yielded the dimethoxyabietatriene (**6**) as evidenced by its spectral data.

* Systematic numbering.



(**20**) R = Pr^i, H
(**21**) R = $Me_2C(OH)$, H
(**22**) R = CMe_2

Thought was next given to the problem of replacing the C-6 methoxy group of compound (**6**) with a carbonyl group. In order to realize this objective the dimethoxyabietatriene (**6**) was treated with $MeSiCl_3$ and sodium iodide in acetonitrile[10] at 25—35 °C. The resulting material, which exhibited strong hydroxy group absorption in the i.r. spectrum and a weak signal for a methoxy group in the ^{1}H n.m.r. spectrum, was carefully oxidized with Jones' reagent at 0 °C. The crude oxidized product (exhibiting strong carbonyl and hydroxy group absorptions in its i.r. spectrum) was methylated with dimethyl sulphate and alkali under which only the aromatic phenol would undergo methylation. On chromatographic purification the resulting product yielded the target ketone (**1**), a colourless oily material whose spectroscopic data lent support for its structure. Attempted oxidation of the abietatriene (**6**) with nitronium tetrafluoroborate[16] to replace the C-6 methoxy group by a carbonyl group to obtain compound (**1**) in a single step proceeded in only poor yield.†

The ketone (**1**) on treatment with silicon tetrachloride and sodium iodide[17] underwent demethoxylation to yield the phenol (**7**) in excellent yield; the identity of the product was confirmed by a mixed m.p. comparison with an authentic specimen.[1] Its i.r. spectrum was indistinguishable from that of an authentic specimen. Taking into account the yield and purity of the product the reagent 'cocktail' silicon tetrachloride–sodium iodide proved to be superior to the other demethylating reagents such as trimethylsilyl chloride and sodium iodide.[18]

In order to confirm further the identity of the ketone (**1**), its carbonyl group was eliminated by Clemmensen reduction.[9] The crude deoxygenated material which showed complete absence of the carbonyl absorption in its i.r. spectrum was oxidized with chromic acid in acetic acid at room temperature to afford the ketone (**3**) in good yield. Some other attempts to shift the C-6 carbonyl group of the ketone (**1**) in the C-7 position to obtain the ketone (**3**) did not proceed in satisfactory yield. The identity of the ketone (**3**) was confirmed by a mixed m.p. comparison with an authentic specimen.[1] Its i.r. spectrum was identical with that of an authentic specimen.

Treatment of ketone (**3**) with silicon tetrachloride and sodium iodide[16] brought about cleavage of 12-methoxy group to afford the diterpenic alcohol sugiol (*2*) whose identity was confirmed by mixed m.p. comparison with an authentic specimen.[1] Our synthetic sugiol was indistinguishable in spectroscopic (i.r.) and chromatographic behaviour from an authentic specimen.

The conversion of ketone (**1**) into the phenol (**7**), ketone (**3**), and sugiol (**2**) confirmed the identity of the former. As the ketone (**1**) has already been utilized for the synthesis[1] of some

† The identity of the ketone (**1**) could not be confirmed by direct comparison owing to non-availability of an authentic specimen of the ketone (**1**) and thus an attempt was made to convert the ketone (**1**) into a known ketone (**3**) and a diterpene alcohol sugiol (**2**).

natural products related to diterpenes, the acquisition of the ketone (**1**) formally completed the total synthesis of some tricyclic diterpenes. The present synthesis proceeds *via* intermediates which can be utilized for the synthesis of other diterpenes either directly or by chemical modification of intermediates at varying levels of functional and structural complexity.

Experimental

M.p.s were determined on a Kofler hot-stage and are corrected. Unless otherwise stated, i.r. spectra were taken on a Perkin-Elmer 337 spectrophotometer for KBr discs or liquid films, and ^{1}H n.m.r. spectra, recorded on a Varian A-90 spectrometer, were measured in CCl_4 with $SiMe_4$ as internal standard. Mass spectra were recorded on Dupont 21-492 B and Hitachi Perkin-Elmer RMU-6H spectrometers at 70 eV using a direct-inlet system. Column chromatography was carried out with Neutral Brockmann alumina or silica gel (BDH). T.l.c. plates were coated with silica gel having a thickness of *ca.* 2 mm and the spots were located by exposing the dried plates to iodine vapour. Unless otherwise stated, all organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Microanalyses were carried out in the Franz Pascher Microanalytiches Laboratorium at Bonn, Germany. All compounds described herein are racemic although the prefix (±) is omitted and only one enantiomer is depicted in the structural formula.

Dry solvents were distilled immediately before use. THF was distilled from lithium aluminium hydride. Ether was distilled from sodium metal.

1,2,3,4,4a,5,6,7-*Octahydro*-1,1,4a-*trimethyl*-5β-(*tetrahydropyran*-2-*yloxy*)*naphthalene* (**9**).—To stirred, dry pyridine (5 ml) was added PTSA monohydrate (900 mg) at room temperature. After the mixture had been stirred for 30 min, the excess of pyridine was removed on a water-bath at *ca.* 55—60 °C to obtain pyridinium toluene-*p*-sulphonate (PPTS) (1.32 g), m.p. 118—119 °C (from acetone).

A solution of the alcohol (**8**) (7.68 g) and dihydropyran (12 ml) in dry methylene dichloride (4 ml) containing PPTS (1 g) was stirred for 5 h at room temperature. The resulting solution was diluted with ether, washed with semi-saturated brine, dried, and evaporated. A yellowish liquid was obtained which, on chromatographic purification over alumina (eluant hexane), yielded the pyranyl derivative (**9**) (9.68 g, 88%). The product could not be distilled owing to its tendency to decompose; *m/z* 194 ($M^+ - C_5H_8O$) and 176 ($M^+ - C_5H_8O - H_2O$); $\nu_{max.}$ 1 650 cm^{-1} (C=C); δ 1.02 (3 H, s), 1.08 (3 H, s), 1.10 (3 H, s) (together 3 × Me), 4.85 (1 H, t, *J* 6 Hz, 6′-H), and 5.35 (1 H, t, *J* 4.5 Hz, 8-H).

Perhydro-4a,8,8-*trimethyl*-4β-(*tetrahydropyran*-2-*yloxy*)*naphthalen*-1-*ol* (**10**).—To a solution of diborane in THF at 0 °C, prepared by the addition of boron trifluoride–ether (13 ml) to a suspension of sodium borohydride (3.85 g) in THF (60 ml) under nitrogen, was added a solution of the tetrahydropyranyl derivative (**9**) (7.71 g) in THF (85 ml). The mixture was stirred for 12 h at 0 °C, and for 1 h at room temperature, and was then cooled to 0 °C and an aqueous solution of sodium hydroxide (45 ml; 10%) was cautiously added followed immediately by aqueous hydrogen peroxide (30 ml; 30%). The reaction mixture was heated under reflux for 1 h, cooled, and diluted with ether. The organic layer was separated, washed, dried, and evaporated to afford a gummy material which was passed over a column of alumina. Elution with benzene afforded the *alcohol* (**10**) (6.40 g, 78%), m.p. 82—84 °C (from hexane); *m/z* 194 ($M^+ - C_5H_8O - H_2O$); ν_{max} (KBr) 3 460 cm^{-1} (OH); δ 0.98 (3 H, s), 1.01 (3 H, s), and 1.18 (3 H, s) (together 3 × Me) (Found: C, 73.0; H, 10.8. $C_{18}H_{32}O_3$ requires C, 72.92; H, 10.88%).

Perhydro-8α-*methoxy*-1,1,4a-*trimethyl*-5β-(*tetrahydropyran*-2-*yloxy*)*naphthalene* (**11**).—A solution of the alcohol (**10**) (2.55 g) in THF (50 ml) was added dropwise to a suspension of sodium hydride (2.55 g) in THF (20 ml) under nitrogen. The mixture was warmed for 10 min, followed by the addition of methyl iodide (15 ml) and the mixture was then heated under reflux for 6 h, cooled, diluted with water, and extracted with ether. The dried extract, on trituration with methanol and a drop of water, yielded the *title product* (**11**) (2.33 g, 87%), m.p. 76—78 °C (from methanol–water); *m/z* 208 ($C_{14}H_{24}O$) and 85 (C_5H_9O); δ 0.92 (6 H, s), 1.08 (3 H, s) (together 1-Me_2 and 4a-Me), and 3.31 (3 H, s, OMe) (Found: C, 73.45; H, 11.0. $C_{19}H_{34}O_3$ requires C, 73.50; H, 11.04%).

Perhydro-4α-*methoxy*-5,5,8a-*trimethylnaphthalen*-1-*one* (**12**).—A solution of the bisether (**11**) (2.20 g) in acetone (30 ml) was cooled to 0 °C and treated with Jones' chromic acid reagent (5 ml). The resulting solution was stirred for 40 min at 0 °C, then was treated with propan-2-ol to destroy the excess of the oxidant, diluted with water, and extracted with ether. The extract was washed, dried, and evaporated. The resulting dense liquid was chromatographed on alumina (hexane as eluant) to afford the *title ketone* (**12**) (1.05 g, 67%), m.p. 44—45 °C (from hexane); *m/z* 224 (M^+) and 177 ($M^+ - Me - MeOH$); $\nu_{max.}$(KBr) 1 710 cm^{-1} (C=C); δ 1.08 (6 H, s), 1.18 (3 H, s) (together 5-Me_2 and 8a-Me), 3.35 (3 H, s, OMe), and 3.65 (1 H, m, $w_{\frac{1}{2}}$ 15 Hz, 4-H) (Found: C, 75.0; H, 10.8. $C_{14}H_{24}O_2$ requires C, 74.95; H, 10.78%).

Perhydro-4a,8,8-*trimethylnaphthalen*-1α-*ol* (**13**).—The ketone (**13**) (500 mg) was suspended in 20% hydrochloric acid (25 ml) and the mixture was heated under reflux for 8 h in the presence of amalgamated mossy zinc (8 g). The organic product was extracted with ether and the extract was washed, dried, and evaporated to give the deoxygenated product (432 mg); *m/z* 210 (M^+).

To a solution of the crude product (429 mg) and sodium iodide (250 mg) in acetonitrile (3 ml) under nitrogen was slowly added trichloromethylsilane (190 mg). The reaction mixture was stirred for 12 h at room temperature, diluted with water, and extracted with ether. The extract was washed successively with aqueous sodium thiosulphate and brine, and was dried. Evaporation of the solvent yielded an oily material which, on purification over a column of alumina [eluant hexane–benzene (98:2)] yielded the alcohol (**13**) (210 mg) which, mixed with an authentic specimen,[11] did not exhibit any depression in m.p. Its i.r. spectrum was indistinguishable from that of an authentic specimen.

Perhydro-2-*hydroxymethylene*-4α-*methoxy*-5,5,8a-*trimethylnaphthalen*-1-*one* (**14**).—To a stirred solution of the ketone (**12**) (4.61 g) in freshly distilled ethyl formate (50 ml) cooled to 0 °C under nitrogen were added sodium hydride (60% dispersion in mineral oil) and dry methanol (1 ml). The mixture was stirred at 0 °C for 25 min, dry ether (55 ml) was added, and the resulting mixture was stirred for 7 h at room temperature. Ice was added and the basic aqueous mixture was extracted with ether (3 × 30 ml). The combined extracts were washed with 5% aqueous sodium hydroxide. The alkaline washings were combined, cooled to 0 °C, and acidified with dil. hydrochloric acid. Into the acidic material was bubbled nitrogen for 50 min during which time yellowish crystals appeared. The solid was filtered off and washed with water until the filtrate was not acidic to litmus paper. The material was dried *in vacuo* at 25 °C to yield the formyl derivative (**14**) (4.67 g, 90%), m.p. 69—70 °C; *m/z* 252

(M^+) and 220 (M^+ − MeOH); $\nu_{max.}$(KBr) 1 660 (C=O) and 1 590 cm^{-1} (C=C); δ 0.96 (3 H, s), 0.99 (3 H, s), and 1.01 (3 H, s) (together 3 × Me), 3.29 (3 H, s, OMe), 3.63 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 4-H), 7.05 (1 H, d, *J* 6 Hz, C*H*OH ⇌ CH=O), and 16.00 (1 H, d, *J* 6 Hz, OH, exchangeable by D_2O). The sample was found to be unstable and thus no analytical sample was prepared.

1,4b,5,6,7,8,8a,9,10,10a-*Decahydro*-9α-*methoxy*-4b,8,8-*trimethylphenanthren*-3(2H)-*one* (**16**).—To a solution of hydroxymethylene ketone (**14**) (1.21 g) in dry methanol (36 ml) cooled in an ice-bath under nitrogen was added a solution of sodium methoxide [prepared from sodium (440 mg) in methanol (12 ml)]. To the stirred mixture was added dropwise a cold solution of 4-diethylaminobutan-2-onemethiodide (13 g) in dry methanol (15 ml). The resulting mixture was stirred for 20 h at room temperature, cooled, acidified with dil. hydrochloric acid (10%), and extracted several times with ether. The combined extracts were washed, dried, and evaporated to obtain a dark oily material which, on chromatographic purification over alumina (eluant benzene), produced the adduct (**15**) (1.02 g, 71%); *m/z* 294 (M^+) and 262 (M^+ − MeOH); $\nu_{max.}$ 1 710 cm^{-1} (CO); δ 2.06 (3 H, s) and 2.08 (3 H, s) (MeCO for α- and β-epimer). The experiment was repeated thrice to collect more adduct.

A solution of sodium methoxide [prepared from sodium (560 mg) and dry methanol (92 ml)] was slowly added under nitrogen to a solution of the adduct (**15**) (2.51 g) in methanol (110 ml) cooled to 0 °C. The deep orange coloured mixture was stirred at room temperature for 12 h, heated under reflux for 7 h, diluted with water and extracted with ether. The extracts were washed, dried, and evaporated to afford a yellow oil (2.45 g) which, on trituration with ether–hexane, afforded the ketone (**16**) (1.72 g), m.p. 62—72 °C; *m/z* 276 (M^+). The ketone (**16**) (1.70 g) was rechromatographed over silica gel. On elution with benzene, 50 fractions were collected (each fraction 15 ml). Fractions (10—25) were combined to obtain the *ketone* (**16**) as a solid (1.41 g, 60%), m.p. 64—65 °C (from ether–hexane); *m/z* 276 (M^+); $\nu_{max.}$(KBr) 1 648 cm^{-1} (CO); δ 0.98 (3 H, s), 1.04 (3 H, s), 1.08 (3 H, s) (together 3 × Me), 3.30 (3 H, s, OMe), 3.64 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 9-H), and 5.78 (1 H, d, *J* 1.5 Hz, 4-H) (Found: C, 78.2; H, 10.25. $C_{18}H_{28}O_2$ requires C, 78.21; H, 10.21%).

Fractions (26—35) yielded an oily material (18 mg) which was not homogeneous in t.l.c. and thus was not examined.

Fractions (36—50) were combined and evaporated to afford a solid (280 mg, 12%), m.p. 72—74 °C (from ether–hexane); *m/z* 276 (M^+); $\nu_{max.}$(KBr) 1 650 cm^{-1} (CO); δ 0.96 (3 H, s), 0.98 (3 H, s), and 1.12 (3 H, s) (together 3 × Me), 3.26 (3 H, s, OMe), 3.68 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 9-H), and 5.90 (1 H, d, *J* 2.4 Hz, 4-H) (Found: C, 78.2; H, 10.25. $C_{18}H_{28}O_2$ requires C, 78.21; H, 10.21%).

4b,8a-trans-2-*Ethyl*-4b,5,6,7,8,8a,9,10-*octahydro*-9α-*methoxy*-4b,8,8-*trimethylphenanthren*-3-*ol* (**4**).—To a solution of LDA (800 mg) in ether (20 ml) at 0 °C under nitrogen was added a solution of the ketone (**16**) (1 g) in anhydrous benzene (20 ml). To this lithium enolate solution were added fused zinc chloride (10 ml; 0.5M) in diethyl ether and freshly distilled acetaldehyde (4 ml). The reaction mixture was stirred at 0 °C for 30 min, then for 2 h at room temperature, and was then diluted with ether. The ether layer was washed successively with saturated aqueous ammonium chloride and brine, dried, and evaporated. The crude β-hydroxy ketone (**17**) (1.42 g), completely free from the ketone (**16**) as evidenced by t.l.c., was directly used for the next step; *m/z* 302 ($M^+ - H_2O$) and 273 (M^+ − Me − MeOH); $\nu_{max.}$(film) 3 425 (OH) and 1 670 cm^{-1} (CO).

The crude β-hydroxy ketone (**17**) (1.38 g) and PTSA (100 mg) was heated under reflux in benzene (60 ml) for 10 h under a Dean–Stark trap. The reaction mixture was diluted with ether, washed successively with 5% aqueous sodium hydrogen carbonate and brine, and then dried. Evaporation of the solvent followed by chromatographic purification over silica gel [eluant benzene–ether (8:2)] yielded the *phenol* (**4**) [580 mg, 54% from ketone (**16**)], m.p. 72—74 °C (from ether); *m/z* 302 (M^+) and 270 (M^+ − MeOH); δ 0.94 (3 H, s), 1.01 (3 H, s), 1.10 (3 H, s) (together 8-, 8-, and 4b-Me), 1.18 (3 H, t, *J* 7 Hz, CH_2*Me*), 2.54 (2 H, q, *J* 7.5 Hz, CH_2Me), 3.29 (3 H, s, OMe), 3.63 (1 H, m, $w_{\frac{1}{2}}$ 12 Hz, 9-H), 5.01 (1 H, s, OH, exchangeable with D_2O), and 6.56 (1 H, s) and 6.81 (1 H, s) (together 1-H and 4-H) (Found: C, 79.45; H, 10.0. $C_{20}H_{30}O_2$ requires C, 79.42; H, 10.00%).

4a,10a-trans-1,2,3,4,4a,9,10,10a-*Octahydro*-6,10α-*dimethoxy*-1,1,4a-*trimethylphenanthrene* (**5**).—*Method A*. To a solution of the phenol (**4**) (116 mg) in alcohol (20 ml; 95%) was added freshly distilled dimethyl sulphate (2 ml) and aqueous sodium hydroxide (2 ml; 10%). The reaction mixture was stirred at room temperature for 1 h, then heated at 80 °C for 1 h; it was then diluted with water and extracted with ether. The extracts were washed, dried, and evaporated. Purification of the resulting residue over alumina (eluant benzene) yielded the *dimethoxy compound* (**5**) (80 mg, 66%); *m/z* 316 (M^+) and 269 (M^+ − MeOH − Me); δ 0.96 (3 H, s), 1.04 (3 H, s), 1.12 (3 H, s) (together 1-, 1-, and 4a-Me), 1.18 (3 H, t, *J* 7.5 Hz, CH_2*Me*), 2.54 (2 H, q, *J* 7.5 Hz, CH_2Me), 3.64 (1 H, m, 10-H), 3.29 (3 H, s), and 3.74 (3 H, s) (together 2 × OMe), and 6.56 (1 H, s) and 6.82 (1 H, s) (together ArH) (Found: C, 79.7; H, 10.2. $C_{21}H_{32}O_2$ requires C, 79.70; H, 10.19%).

Method B. The hydroxy ketone (**17**) (200 mg) was passed over a column of alumina (8 g). Elution with benzene yielded the olefin (**19**) (102 mg, 53%); *m/z* 302 (M^+); $\nu_{max.}$(film) 1 670 (CO) and 1 625 cm^{-1} (C=C); δ 5.90 (4 H, m, 4-H, m, 4-H, and CH=CH_2).

The olefin (**19**) (100 mg) was dissolved in methanolic sulphuric (5 ml; 2%) and the solution was heated on water-bath for 5 min. The reaction mixture was diluted with water and extracted with ether. The extracts were washed successively with dil. aqueous sodium carbonate and brine, dried, and evaporated. The residue on purification over a column of alumina (eluant benzene) yielded the dimethoxy compound (**5**) [62 mg, 60% from olefin (**19**)] whose spectroscopic data agreed nicely with those of an authentic specimen of (**5**) already mentioned.

1,4b,5,6,7,8,8a,9,10,10a-*Decahydro*-2-*isopropylidene*-9α-*methoxy*-4b,8,8-*trimethylphenanthren*-3(2H)-*one* (**22**).—To a solution of LDA (4 g) in dry THF (24 ml) at −50 °C was added a solution of the ketone (**16**) (2 g) under nitrogen. The resulting solution was stirred at between −50 and −36 °C for 30 min. A mixture of freshly fused zinc chloride (5.62 g) in dry THF (78 ml) was added and after the mixture had been stirred at −30 °C for 5 min, a mixture of dry acetone (16 ml) and dry THF (20 ml) was added and the resulting mixture was stirred at −35 °C for 30 min, at −10 °C for 1 h, and at 0 °C for 3 h. Aqueous ammonium chloride was added and the product was extracted with ether. The combined extracts were washed, dried, and evaporated. The residue, on chromatographic purification over a column of silica gel [eluant hexane–benzene (1:1)], yielded the aldol (**21**) (1.54 g, 64%), *m/z* 334 (M^+), and 316 ($M^+ - H_2O$); $\nu_{max.}$(film) 3 400 (OH), 1 670 (CO), and 1 600 cm^{-1} (C=C); δ 1.20 [6 H, s, C(OH)Me_2], and 4.55 (1 H, br s) and 5.25 (1 H, br s) (OH for α- and β-epimer, exchangeable by D_2O).

A solution of the aldol (**21**) (900 mg) in anhydrous benzene (60 ml) containing a catalytic amount of PTSA was heated under reflux for 3 h with a Dean–Stark water separator. The cooled reaction mixture was diluted with ether, washed successively with aqueous sodium hydrogen carbonate and brine, dried, and evaporated. The residue was chromatographed over silica gel [eluant benzene–ether (8:2)] to afford the *isopropylidene ketone* (**22**) [323 mg, 38% from aldol (**21**)], m.p. 142—

143 °C (from ether); *m/z* 316 (M^+) and 284 (M^+ − MeOH); $\nu_{max.}$(film) 1 670 (CO) and 1 600 cm^{-1} (C=C); δ 1.80 (3 H, s), and 2.20 (3 H, s) (together C=CMe_2) (Found: C, 79.9; H, 10.35. $C_{12}H_{32}O_2$ requires C, 79.70; H, 10.19%).

6α,12-*Dimethoxyabieta*-8,11,13-*triene* (**6**).—The isopropylidene ketone (**22**) (480 mg) was dissolved in methanolic sulphuric acid (25 ml; 5%) and the solution was heated under reflux for 4 h. The progress of the reaction was monitored by t.l.c. The reaction mixture was diluted with water and extracted with ether. The extracts were washed, dried, and evaporated, and the residue was chromatographed over silica gel. Benzene eluted the oily *dimethoxyabietatriene* (**6**) (124 mg, 25%); *m/z* 330 (M^+) and 283 (M^+ − MeOH); δ 0.96 (6 H, s), 1.11 (6 H, d, *J* 7 Hz, CHMe_2), 1.18 (3 H, s, 10-Me), 3.31 (3 H, s, 6-OMe), 3.76 (3 H, s, 12-OMe), and 6.66 (1 H, s) and 6.86 (1 H, s) (together 2 ArH) (Found: C, 80 2; H, 10.7. $C_{22}H_{34}O_2$ requires C, 79.95; H, 10.61%).

12-*Methoxyabieta*-8,11,13-*trien*-6-*one* (**1**).—*Method A.* A solution of the dimethoxyabietatrien (**6**) (100 mg) in dry methylene dichloride (2 ml) was added dropwise to a stirred suspension of nitronium tetrafluoroborate (Aldrich) (90 mg) in methylene dichloride (4 ml) cooled to 0 °C. After the addition, the reaction mixture was stirred at 0 °C for 10 min, and at room temperature for 1 h, and was then quenched with water and extracted with methylene dichloride. The extracts were washed, dried, and evaporated. The residue was purified by column chromatography on silica gel [eluant benzene–ether (99:1)] to afford the ketone (**1**) (12 mg); *m/z* 314 (M^+); $\nu_{max.}$(film) 1 710 cm^{-1} (CO).

Method B. To a solution of sodium iodide (302 mg) in dry acetonitrile (10 ml) under nitrogen were slowly added $MeSiCl_3$ (300 mg) and then the dimethoxyabietatriene (**6**) (500 mg). The reaction mixture was stirred for 10 h at room temperature, diluted with water and then extracted with ether. The extract was washed successively with aqueous sodium thiosulphate and brine, dried, and evaporated.

To the residue dissolved in acetone (2 ml), and cooled to 0 °C, was added Jones' reagent (1 ml). The mixture was stirred for 30 min after which time isopropyl alcohol was added to the reaction mixture which was then extracted with ether. The extracts were washed, dried, and evaporated to obtain an oily material (227 mg) which was heated under reflux with dimethyl sulphate (2 ml), acetone (8 ml), and potassium carbonate (300 mg). The reaction product after dilution with water was taken up in ether. The ether phase was washed, dried, and evaporated. The residue was passed through a column of silica gel; elution with benzene–ether (99:1) yielded the ketone (**1**)[1] (105 mg, 30%); *m/z* 314 (M^+); $\nu_{max.}$(film) 1 710 cm^{-1} (CO); δ 1.01 and 1.08 (each 3 H, s, 4-Me), 1.12 (6 H, d, *J* 7 Hz, CHMe_2), 1.18 (3 H, s, 10-Me), 3.76 (3 H, s, OMe), and 6.6 (1 H, s), and 6.86 (1 H, s) (together 2 ArH) (Found: C, 80.3; H, 9.7. Calc. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62%).

12-*Hydroxyabieta*-8,11,13-*trien*-6-*one* (**7**).—The ketone (**1**) (50 mg) and sodium iodide (27 mg) are dissolved in a mixture of methylene dichloride and acetonitrile (5 ml; 1 : 1). Silicon tetrachloride (0.02 ml) was added from a syringe and the stirred mixture was heated under reflux for 12 h. The reaction mixture was poured into water and extracted with ether several times. The combined extracts were washed thrice with aqueous sodium hydroxide (10%). The combined alkaline washings (20 ml) were acidified with hydrochloric acid (6 ml; 12M) and then extracted with ether. The extract was washed, dried, and evaporated to give the phenol (**7**) (21 mg, 70%), m.p. 133—135 °C (from hexane–acetone) (lit.,[1] 134—135 °C) which remained undepressed on admixture with an authentic specimen; *m/z* 300 (M^+); $\nu_{max.}$(KBr) 3 380 (OH) and 1 702 cm^{-1} (CO), and which was found to be indistinguishable from an authentic sample by direct comparison of the i.r. spectra. (Found: C, 80.1; H, 9.4. Calc. For $C_{20}H_{28}O_2$: C, 79.95; H, 9.39%).

Sugiol (**2**).—A mixture of amalgamated zinc [prepared from mossy zinc (500 mg) and mercury(II) chloride (500 mg)], water (1 ml), conc. hydrochloric acid (1 ml), and the ketone (**1**) (100 mg) was heated under reflux for 3 h. After having cooled, the mixture was diluted with water and extracted with ether. The extract was washed, dried, and evaporated to leave an oily material (95 mg) which did not exhibit a carbonyl adsorption in its i.r. spectrum.

To a solution of the crude oily material (95 mg) in acetic acid (4 ml) was added chromium trioxide (102 mg) and the mixture was stirred at room temperature for 15 h. The deep red mixture was diluted with water and extracted with ether. The extract was washed successively with aqueous sodium hydrogen carbonate solution (2%) and brine, and dried. Elimination of the solvent yielded a thick liquid which, on chromatographic purification over silica gel [eluant hexane–ether (9:1)], yielded the ketone (**3**) (63 mg), m.p. 125—126 °C (from methanol) (lit.,[1] 125—126 °C) which remained undepressed on admixture with an authentic specimen; *m/z* 314 (M^+); $\nu_{max.}$(KBr) 1 665 cm^{-1} (CO), and which was found to be indistinguishable, by direct comparison with the i.r. spectra, from an authentic specimen.

The ketone (**3**) (55 mg) and sodium iodide (28 mg) were dissolved in a mixture of methylene dichloride and acetonitrile (5 ml; 1:1). Silicon tetrachloride (0.03 ml) was added from a syringe and the stirred mixture was refluxed for 10 h. After having cooled, the reaction mixture was poured into water and extracted several times with ether. The combined extracts were washed thrice with aqueous sodium hydroxide (10%). The combined alkaline washings (15 ml) were acidified with hydrochloric acid (4 ml; 12M) and then extracted with ether. The extract was washed, dried, and evaporated to give sugiol (**2**) (35 mg), m.p. 245—247 °C (from methanol) which remained undepressed on admixture with an authentic specimen; *m/z* 300 (M^+); $\nu_{max.}$(KBr) 3 125 (OH) and 1 650 cm^{-1} (CO), and which was found to be indistinguishable, by direct comparison of the i.r. spectra, from an authentic specimen; δ (pyridine) 0.84 (3 H, 5) and 0.86 (3 H, s) (together 4-Me_2), 1.14 (3 H, s 10-Me), 1.36 (6 H, d, *J* 6 Hz, OHMe_2), and 7.15 (1 H, s) and 7.76 (1 H, s) (together 2 ArH) (Found: C, 79.95; H, 9.4. Calc. for $C_{20}H_{28}O_2$: C, 79.95; H, 9.39%).

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