A New Atisane Diterpene: *ent*-16α-Hydroxyatis-13-en-3-one from *Androstachys johnsonii* Prain

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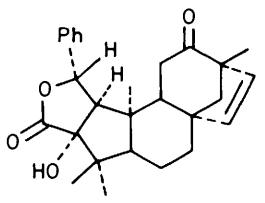
The title diterpene, a rare example of the naturally occurring *ent*-atis-13-ene type, has been isolated as the 2-benzylidene derivative from the heartwood hexane extract of *Androstachys johnsonii* Prain. Its structure was determined by n.m.r. and *X*-ray crystallography. It is suggested that the title compound is biogenetically produced from an *ent*-12-oxybeyer-15-ene precursor. An interesting reaction reported here was found to convert a vicinal diol into a monoketone using the diethyl azodicarboxylate–triphenylphosphine–benzoic acid system.

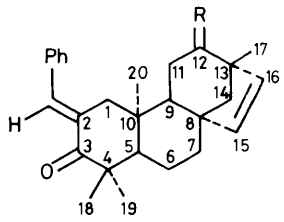
The family of atisane diterpenoids is usually associated with the family of kaurane diterpenoids and in this respect the members commonly have endocyclic unsaturation in the C/D rings, usually between carbons 15 and 16, the latter bearing a pendant methyl group or a functionalized derivative thereof. However, in principle all the tetracyclic and pentacyclic diterpenes, including the beyerane and trachylobane families, can be derived from one common precursor.[1] It is surprising, therefore, that only one report [2] has appeared of the occurrence of atisanes and beyeranes in the same plant. Furthermore, this was the first report of a *naturally* occuring *ent*-atis-13-ene in which the double bond was situated between carbons 13 and 14, these carbons being the equivalent of the beyerane carbons 15 and 16, using the accepted numbering convention for these systems. We had previously prepared the first *ent*-atis-13-ene from an *ent*-beyer-15-ene by the reductive rearrangement of the derived 12-*p*-tosylhydrazone [3] and we now wish to report the isolation of a further example of a naturally occurring *ent*-atis-13-ene from the heartwood of *Androstachys johnsonii* Prain, a Euphorbiaceae which had hitherto yielded only *ent*-beyer-15-ene diterpenes.[4]

Our customary procedure for preparing the ring-contracted hydroxy lactone (**1**)[5] in large quantities utilized the mother-liquors from the heartwood hexane extract (see Experimental section). When mother-liquors rich in the minor components were used, dense, yellow crystal clusters were obtained, as well as large amounts of compound (**1**). Chromatography of this yellow product gave *ent*-benzylidenebeyer-15-en-3-one (**2**), *ent*-2-benzylidenebeyer-15-ene-3,12-dione (**3**), the new compound *ent*-2-benzylidene-16α-hydroxyatis-13-en-3-one (**4**), and occasionally small quantities of the primary aldol product (**5**). All four compounds were formed from the natural 2-unsubstituted 3-keto diterpenes present in the wood extract. Spectral and chemical evidence showed that compounds (**2**)—(**4**) had identical ring A structures, and that (**4**) possessed a tertiary hydroxy group, as no n.m.r. signal for a geminal methylene or methine hydrogen system appeared in its spectrum.

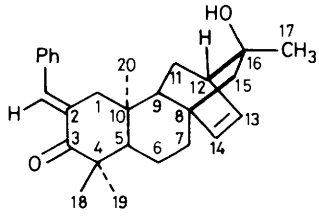
That compound (**4**) did not have a beyerane skeleton became apparent on comparing its ^{1}H n.m.r. spectrum with those of related beyeranes such as (**2**) and (**3**). In place of the typical beyer-15-ene proton AB quartet, the spectrum of compound (**4**) showed a five-line pattern, integrating for two hydrogens,



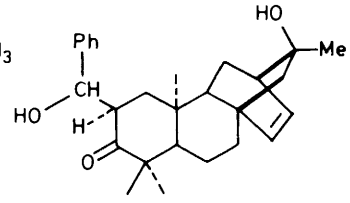
(**1**)



(**2**) R = H_2
(**3**) R = O

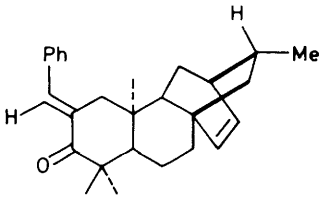


(**4**)

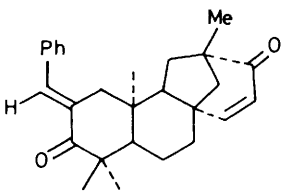


(**5**)

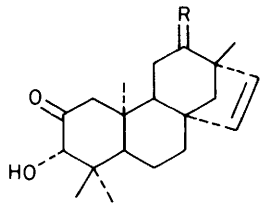
formed by a triplet at δ 6.08 (*J* 8.0 and 6.5 Hz) with a broad centre line which had a shoulder, and a doublet at δ 5.8 (*J* 8.0 Hz). Decoupling an allylic proton signal at δ 2.3 resulted in the collapse of the single proton triplet to a broad doublet (*J* 8.0 Hz), and this indicated the partial structure $(C_2)\rangle CH–CH{=}CH\langle(C_2)$. Addition of the shift reagent Eu(fod)$_3$ to the n.m.r. sample of compound (**4**) caused all the methyl group singlet signals to move downfield, but had little effect on the isolated olefinic protons of ring D. This suggested that the strongly complexed tertiary hydroxy group in compound (**4**) was not orientated towards the latter olefinic protons, but at the same time it had to be sufficiently close to the 17-methyl group in order to influence it. Therefore this tertiary alcohol group could be placed confidently on the *ent*-α-side of the C/D ring system. Placing the alcohol function on C-16 satisfied all the necessary structural requirements of compound (**4**) to give an n.m.r. spectrum as obtained.



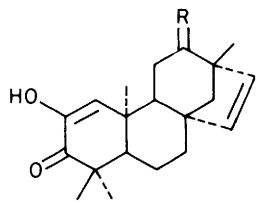
(6)



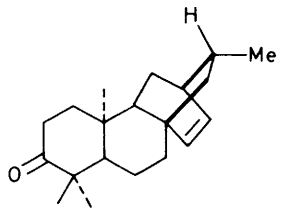
(7)



(13) R = O
(14) R = NNHTs



(15) R = NNHTs
(16) R = O



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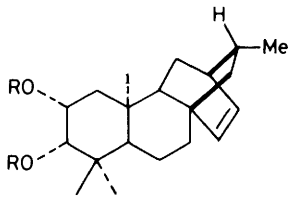
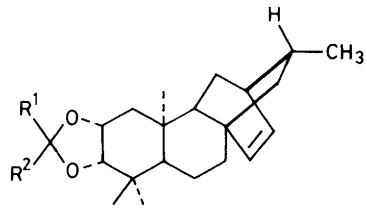
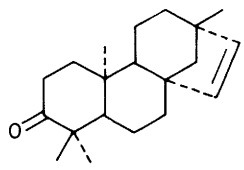


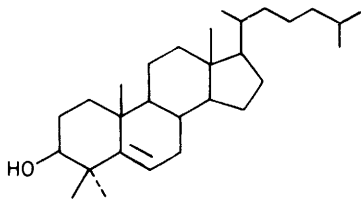
(9) R = Ac
(11) R = H



(17) $R^1 = R^2 = Me$
(18) $R^1 = Ph$ $R^2 = H$



(10)



(12)

This conclusion was further confirmed by the mass spectrum of compound (**4**), as the most intense ion occurred at *m/z* 332, corresponding to the retro-Diels–Alder loss of the fragment C_3H_6O, which was assigned to the two-carbon bridge bearing both the 17-methyl group and the hydroxy group. This retro-Diels–Alder rearrangement is typical[2,3] of these bicyclo-[2.2.2.]octene systems and provided strong evidence that compound (**4**) was in fact an atisane diterpene.

The Eu(fod)$_3$ shift experiment with compound (**4**) also defined the stereochemistry of the styrene system attached to ring A. A downfield shift of the vinyl hydrogen signal in the n.m.r. spectrum, with no effect on the aromatic ring hydrogen signals, indicated a *cis* relationship of this vinyl hydrogen with the carbonyl group at C-3 in compound (**4**) and, by analogy, also in the other benzylidene ketones (**2**), (**3**), (**6**), and (**7**).

Evidence for the assigned structure of compound (**4**) was also obtained from the ^{13}C n.m.r. spectra, by correlation with model compounds such as (**6**), (**8**), (**9**), and (**11**), in which C-16 lacks an oxygen function. The correlation has been reported elsewhere,[6] but the preparation of these compounds will be reported here [see Experimental section and structures (**13**)—(**18**)].

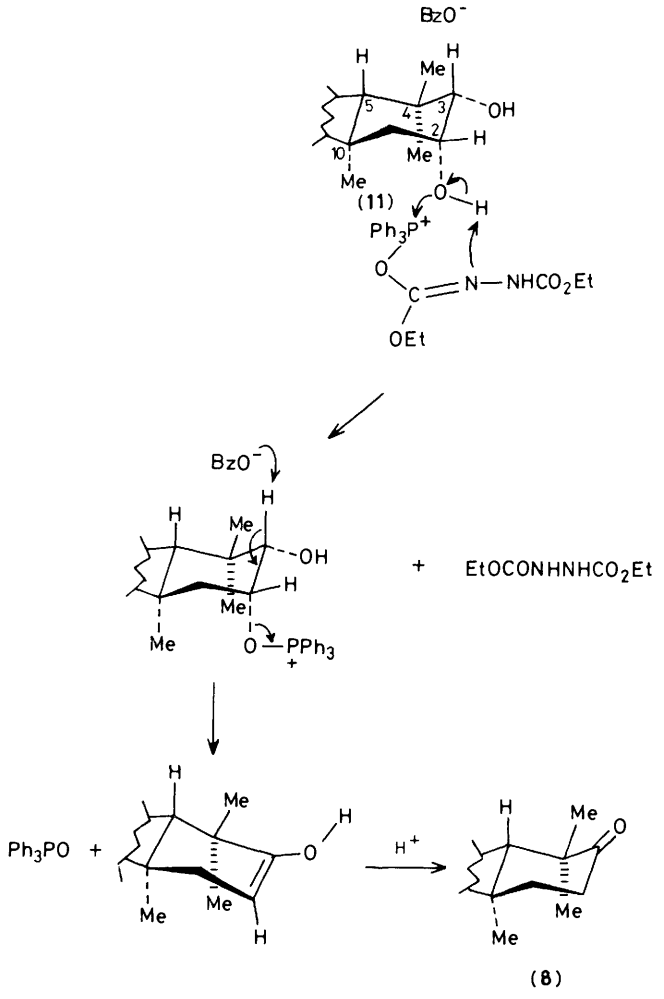
The ^1H n.m.r. signals for the C-17 and C-20 methyl groups, as well as the signals of the olefinic protons at C-13 and C-14 for these atis-13-enes, showed interesting features. In the beyer-15-enes the C-20 methyl group is effectively shielded by the double bond at C-15, and occurs as the highest-field signal.[3,4] Conversely, the C-17 methyl group is usually one of the lowest-field signals, especially when a 12-oxygen function is present[3,4] [*c.f.* (**2**) and (**3**)]. In the case of the (16*S*)-atis-13-ene series of compounds, the shielding effect of the bridge double bond on the C-20 methyl group is even more pronounced, and this reflects the shorter non-bonding distance between the two functions, as well as the change to a more favourable angle for through-space interaction.

The C-13 olefinic proton signals in the benzylidene derivative (**4**) were unexceptional in that the 14-H signal appeared as a doublet slightly broadened by allylic coupling to 12-H, while the 13-H signal appeared as a triplet with the middle line quite broad, indicating the two couplings to 14-H and 12-H. Also, the two resonances were sufficiently far apart (δ 5.82 and 6.08) that no overlap occurred. However, in the 16-deoxy series of compounds of synthetic derivation[3] the situation was quite different. In the spectrum of the diacetate (**9**), taken at 60 or 100 MHz, the two olefinic proton signals overlapped extensively and gave rise to what appeared to be a relatively simple pattern of a broad singlet and a quartet. At 220 MHz, more lines were discernible, and sub-spectral analysis revealed the complete pattern. Thus the chemical shift of the 14-H proton was δ 5.87 and consisted of a doublet of doublets, with *J* 8.0 and 1.75 Hz, while 13-H resonated at δ 5.93 as a quartet, with *J* 8.0 and 6.0 Hz.[2]

The ketone precursor of the atisane diterpene derivative (**4**) could have originated in the plant *via* a common intermediate[1] that gave rise to the many beyeranes. Alternatively, and more probably in this particular plant, a 12-oxygenated beyer-15-ene could be a precursor since evidence, both published[3] and unpublished,[7] indicates that the conversion of an oxygenated beyerane bicyclo[3.2.1]octene system into the isomeric atisane bicyclo[2.2.2]octene system takes place readily. The reverse conversion of a 16-hydroxyatisane into a 12-hydroxybeyerane has been reported.[8]

A further possibility, that the alcohol (**4**) was an artefact produced from the beyerane (**3**) by nucleophilic attack of base on the 12-carbonyl group (thus inducing a rearrangement), followed by reduction by benzaldehyde, was tested and discarded for the following reason. Pure compound (**3**), when treated for a prolonged period with benzaldehyde and alcoholic base using conditions identical with those for the preparation of compound (**4**), was found to be stable and failed to yield even a trace of (**4**). Thus there is little doubt that the parent *ent*-16α-hydroxyatis-13-en-3-one is present in the heartwood of *Androstachys johnsonii*.

The structures of the other compounds isolated from the yellow crystals were determined quite readily. *ent*-2-Benzyl-

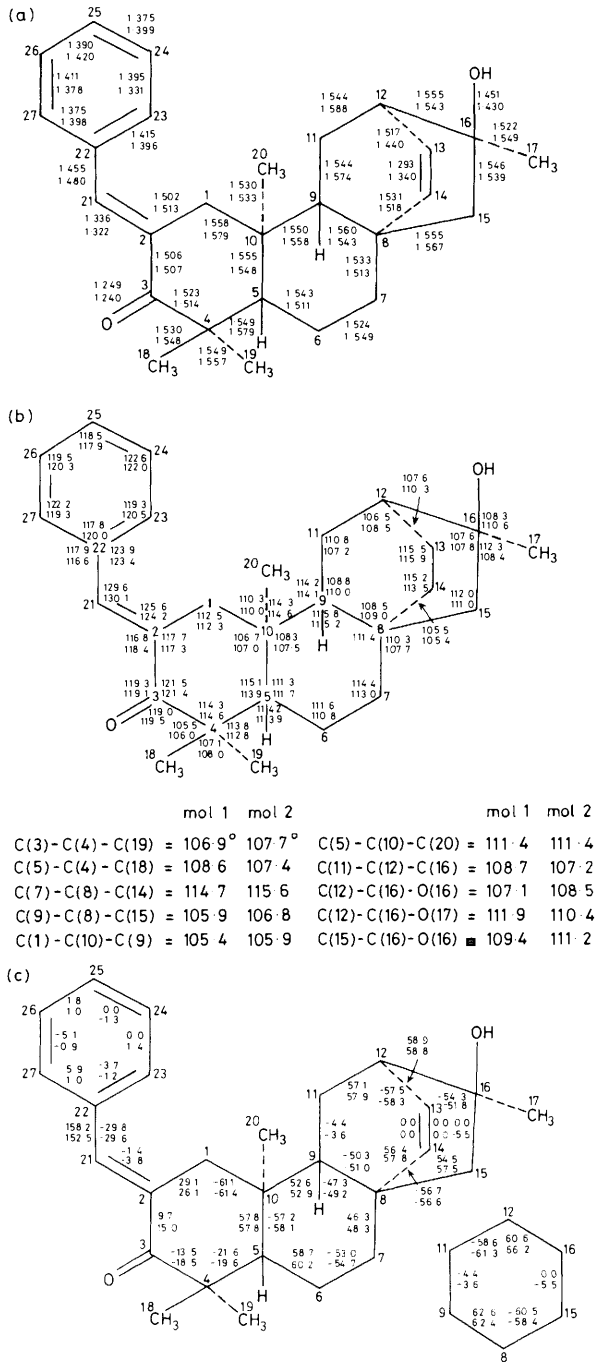


Scheme.

idenebeyer-15-en-3-one (**2**) was prepared from authentic stachenone (**10**) and found to be identical with that isolated. The structure of *ent*-2-benzylidenebeyer-15-ene-3,12-dione (**3**) was evident from its spectral characteristics, and the position of the carbonyl group at C-12 was confirmed by rearranging the C/D system to the α,β-unsaturated enone (**7**) with the sulphuric acid–acetic anhydride reagent.[9]

In order to prepare compound (**6**) for the ^{13}C n.m.r. analysis,[6] *ent*-atis-13-en-3-one (**8**) was required. The available compound having this atis-13-ene skeleton was the 2α,3α-diol (**11**),[3] and conversion of this diol function into the 3-monoketone (**8**) was conveniently carried out by a reaction developed by one of us (L. P. L. P.) utilizing the Bose reagent system[10] (diethyl azodicarboxylate–benzoic acid–triphenylphosphine, sometimes referred to as the DEAD CAT reagent). Reaction of the 2-axial-3-equatorial diol (**11**) with this reagent in tetrahydrofuran (THF) at room temperature led to a rapid, mildly exothermic reaction, and the ketone (**8**) was obtained in good yield, possibly by the route illustrated in the Scheme.

The DEAD CAT reagent had been well tested hitherto for the conversion of monoalcohols into the epimeric esters, but no report had appeared on its effect and usefulness on vicinal diols. (Since the present work was completed, the reagent has been reported to yield epoxides with *trans*-diaxial carbohydrate diols.) The reaction with alcohols appeared to be very sensitive to steric hindrance,[10] as 4,4-dimethylcholesterol (**12**), when treated under the same conditions as the diol (**11**), gave no ester



	mol 1	mol 2		mol 1	mol 2
C(3)-C(4)-C(19)	106·9°	107·7°	C(5)-C(10)-C(20)	111·4	111·4
C(5)-C(4)-C(18)	108·6	107·4	C(11)-C(12)-C(16)	108·7	107·2
C(7)-C(8)-C(14)	114·7	115·6	C(12)-C(16)-O(16)	107·1	108·5
C(9)-C(8)-C(15)	105·9	106·8	C(12)-C(16)-O(17)	111·9	110·4
C(1)-C(10)-C(9)	105·4	105·9	C(15)-C(16)-O(16)	109·4	111·2

Figure 1. Molecular geometry of compound (**4**) showing the crystallographic numbering scheme used. (a) Bond lengths (Å); (b) bond angles (°); and (c) torsion angles

and was recovered unchanged even after refluxing the reaction mixture overnight and then keeping it at room temperature for 40 days. This suggested that the formation of the intermediate alkoxytriphenylphosphonium benzoate[11] was sterically prohibited by the geminal 4,4-dimethyl group, thus explaining the preferential reaction of the reagent with the 2-hydroxy group of the 2,3-diol (**11**). Further work is in progress to test the utility and stereochemical requirements of this reaction.

Discussion of the X-Ray Structure Analysis of Compound (**4**).—Single crystal *X*-ray analysis was performed to establish

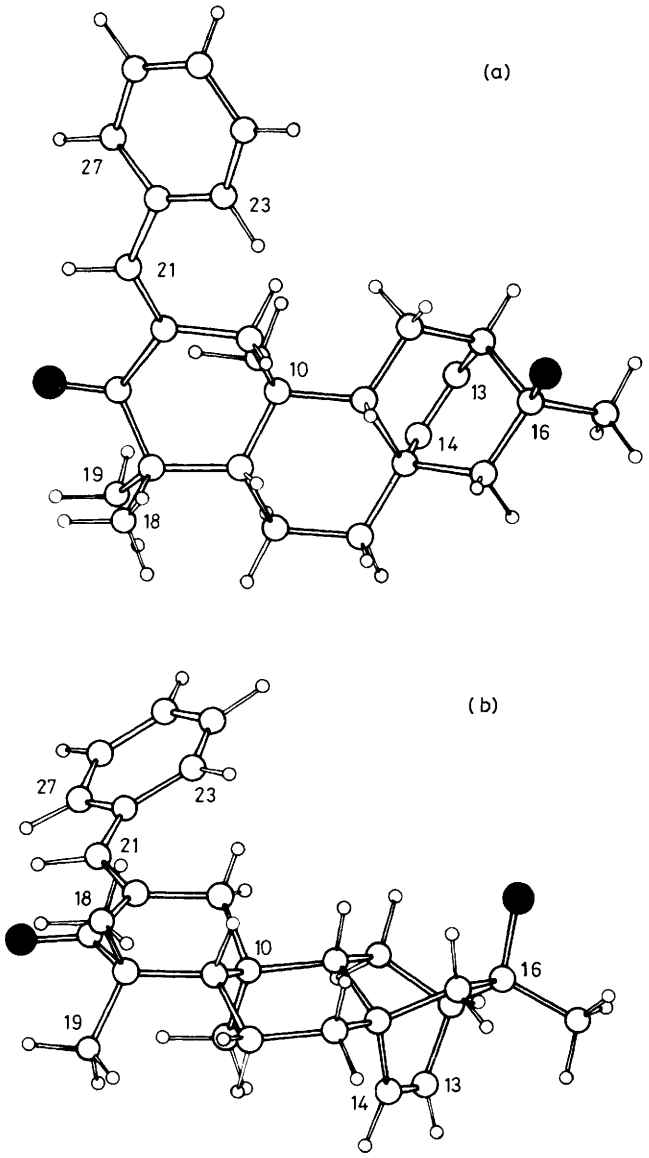


Figure 2. ORTEP Drawings of one molecule of compound (**4**) showing the overall conformation and the configurations at all asymmetric centres.

the configuration at C(16), and the structure was determined to be *ent*-2-benzylidene-16α-hydroxyatis-13-en-3-one (**4**). The crystal studied contained two crystallographically independent molecules of the diterpene, as well as a water molecule. The fractional atomic co-ordinates of the non-hydrogen atoms are listed in the Table, and the atomic numbering and molecular geometry are given in Figure 1. Two ORTEP [12] drawings which illustrate the overall conformation of one molecule, in addition to the configurations at all asymmetric centres, are presented as Figure 2. The conformations of the two crystallographically independent diterpene molecules are virtually identical.

The C(1)–C(2) bond is *cis* to the C(21)–C(22) bond, and the aromatic ring is inclined at approximately 30° to the plane comprised of atoms C(1)–C(2)–C(3)–C(21)–C(22). The crystal structure contains three independent intermolecular hydrogen bonds [*i.e.* O(3)–O(16), 2.95 Å; O(3′)–O(16′), 2.89 Å; and O(16′)–O(w), 2.91 Å].

There are no other intermolecular contacts less than 3.4 Å.

Experimental

General.—Unless otherwise stated, the following generalizations apply. M.p.s were determined on a Kofler hot-stage and are uncorrected. Optical rotations were measured on a Perkin-Elmer 141M automatic polarimeter at 589 nm, using chloroform solutions at room temperature (20—24 °C). I.r. spectra of KBr dispersions were recorded on a Perkin-Elmer 521 spectrophotometer. U.v. spectra were recorded for 95% ethanol solutions: $\lambda_{max.}$ values are followed by ε values in parentheses. Mass spectra were obtained on an AEI MS9 double-focussing mass spectrometer. N.m.r. spectra were obtained in $CDCl_3$ solutions (usually 40 mg per 0.3 ml) using $SiMe_4$ as an internal standard, on a Varian T-60, HA-100, or XL-100 spectrometer system. δ Values are accurate to 0.03 p.p.m. Silica gel for column chromatography was Merck Kieselgel 7734.

Preparation of the Mixture of Compounds (**1**)—(**4**).—The hexane extract of the milled heartwood of *Androstachys johnsonii* Prain [4b] was concentrated until the major compound, *ent*-3β-hydroxybeyer-15-ene-2,12-dione (**13**), crystallized out. After separation of the crystals, the remaining viscous yellow oil eventually set to a honey-like crystalline mass as the hexane evaporated. This same solid material (100 g) was dissolved in ethanol (200 ml) and treated at 0 °C with benzaldehyde (20 ml) and 30% aqueous NaOH solution (30 ml). After 12—15 h of vigorous stirring with free access to air, the resulting dark solution had turned into a stiff paste owing to precipitation of the lactone (**1**). This paste was diluted with water (200 ml) and stirred for a further 6 h, to complete the separation of compound (**1**), before it was filtered to yield a yellow crystalline mass which was washed with water (1 l) and 50% ice-cold, aqueous methanol (200 ml). The product was crystallized from acetone–methanol giving 35 g of the lactone (**1**). The concentrated mother-liquor from the latter crystallization gave a further crop of compound (**1**) admixed with dense, yellow crystalline clusters consisting mainly of a mixture of compounds (**2**)—(**4**). Hand separation of the white needles of the lactone (**1**) (15 g) left 10 g of the yellow material.

Separation of Compounds (**2**)—(**4**).—A solution of the yellow material, from above, in benzene was applied to a silica gel column and chromatographed using hexane–ethyl acetate mixtures (range 98:2 to 90:10) as the eluting solvent. The components eluted as follows: ent-2-*benzylidenebeyer*-15-*en*-3-*one* (**2**) (0.34 g) as pale yellow laths from methanol, m.p. 114—116 °C; $[\alpha]_D$ +126° (*c* 2.2); $\lambda_{max.}$ 210 (ε 73 260), 226sh (9 860), and 296 nm (22 100); $\nu_{max.}$ 1 673 and 1 590 cm^{-1}; δ 0.67 (3 H, s, 20-Me), 1.01 (3 H, s, 17-Me), 1.13 and 1.17 (2 × 3 H, 2 × s, 18-and 19-Me), 2.22 (1 H, d of d, J_{gem} 16.0 Hz, $J_{allylic}$ 2.0 Hz, plus broadening due to W coupling to 20-Me by 2 Hz, 1β-H), 3.03 (1 H, d of d, J_{gem} 16.0 Hz, $J_{allylic}$ 2.0 Hz, 1α-H), 5.45 and 5.70 (2 H, ABq, *J* 5.5 Hz, 16- and 15-H respectively), 7.33 (5 H, s, aromatic), and 7.47 (1 H, q, $J_{allylic}$ 2.0 and 2.0 Hz, styryl-H) (Found: C, 86.2; H, 9.3%; M^+, 374.2602. $C_{27}H_{34}O$ requires C, 86.58; H, 9.15%; M^+, 374.2609).

ent-2-*Benzylidenebeyer*-15-*ene*-3,12-*dione* (**3**) (0.87 g), as pale yellow needles from methanol, m.p. 168—171.5 °C; $[\alpha]_D$ −161° (*c* 2.3); $\lambda_{max.}$ 210 (ε 8 700), 221 (9 042), and 295 nm (17 262); $\nu_{max.}$ 1 705, 1 667, and 1 593 cm^{-1}; δ 0.73 and 1.10 (2 × 3 H, 2 × s, 20- and 17-Me respectively), 1.18 (6 H, s, 19- and 18-Me), 2.86 (1 H, d of d, J_{gem} 16.0 Hz, $J_{allylic}$ 2.0 Hz, 1α-H), 5.63 and 6.07 (2 H, ABq, *J* 5.5 Hz, 16- and 15-H respectively), 7.33 (5 H, s, aromatic), and 7.50 (1 H, q, $J_{allylic}$ 2.0 and 3.0 Hz, styryl-H) (Found: C, 83.3; H, 8.3. $C_{27}H_{22}O_2$ requires C, 83.46; H, 8.30%).

ent-2-*Benzylidene*-16α-*hydroxyatis*-13-*en*-3-*one* (**4**) (0.74 g), pale yellow, hexagonal plates from methanol, m.p. 193—198 °C (decomp.); $[\alpha]_D$ +104° (*c* 2.0); $\lambda_{max.}$ 210 (ε 10 813), 217 (11 274),

Table. Atomic co-ordinates for the non-hydrogen atoms of compound (**4**) with e.s.d.s in parentheses

Atom	*x/a*	*y/b*	*z/c*	Atom	*x/a*	*y/b*	*z/c*
C(1)	0.422 7(6)	0.755 9(5)	0.993 60(8)	C(2′)	0.357 8(6)	0.488 8(6)	0.836 72(9)
C(2)	0.545 6(6)	0.905 4(5)	0.995 42(9)	C(3′)	0.424 6(7)	0.592 2(6)	0.853 83(10)
C(3)	0.580 8(7)	1.001 6(6)	0.977 48(9)	C(4′)	0.493 4(6)	0.560 3(6)	0.871 32(10)
C(4)	0.482 3(6)	0.958 7(6)	0.959 36(9)	C(5′)	0.447 8(5)	0.398 1(6)	0.873 69(8)
C(5)	0.366 1(6)	0.799 3(5)	0.958 90(8)	C(6′)	0.448 0(7)	0.353 1(7)	0.895 13(10)
C(6)	0.315 7(7)	0.738 9(6)	0.937 62(9)	C(7′)	0.431 1(7)	0.202 6(7)	0.895 96(11)
C(7)	0.182 8(7)	0.591 9(7)	0.938 26(9)	C(8′)	0.300 9(6)	0.091 9(5)	0.884 85(9)
C(8)	0.196 4(6)	0.484 1(6)	0.951 58(8)	C(9′)	0.289 9(5)	0.143 3(5)	0.863 69(9)
C(9)	0.263 7(5)	0.550 1(5)	0.972 33(8)	C(10′)	0.307 2(5)	0.294 8(5)	0.862 80(8)
C(10)	0.399 4(5)	0.699 3(5)	0.971 65(8)	C(11′)	0.153 1(6)	0.025 1(6)	0.852 70(10)
C(11)	0.280 7(6)	0.438 9(6)	0.984 62(9)	C(12′)	0.081 1(7)	−0.109 3(7)	0.867 13(12)
C(12)	0.215 9(6)	0.295 5(6)	0.973 34(11)	C(13′)	0.049 1(7)	−0.066 3(8)	0.885 94(13)
C(13)	0.290 4(7)	0.326 7(6)	0.953 17(13)	C(14′)	0.160 0(7)	0.038 9(7)	0.895 66(11)
C(14)	0.281 3(7)	0.420 5(7)	0.942 26(10)	C(15′)	0.317 1(7)	−0.042 7(6)	0.881 96(11)
C(15)	0.046 7(7)	0.355 0(6)	0.956 25(10)	C(16′)	0.190 0(7)	−0.159 7(6)	0.870 27(12)
C(16)	0.055 7(7)	0.242 0(7)	0.969 33(11)	C(17′)	0.123 3(11)	−0.298 2(8)	0.882 89(17)
C(17)	−0.018 9(9)	0.095 2(8)	0.959 67(16)	C(18′)	0.655 6(8)	0.643 5(8)	0.867 18(13)
C(18)	0.409 4(8)	1.048 2(8)	0.960 65(13)	C(19′)	0.464 7(9)	0.623 6(7)	0.890 56(11)
C(19)	0.578 3(8)	1.008 8(8)	0.940 47(10)	C(20′)	0.181 2(6)	0.304 6(6)	0.871 39(11)
C(20)	0.523 3(6)	0.699 2(6)	0.963 98(10)	C(21′)	0.326 7(7)	0.533 9(6)	0.820 08(12)
C(21)	0.628 2(6)	0.960 3(6)	1.011 59(10)	C(22′)	0.266 9(6)	0.458 9(7)	0.800 89(10)
C(22)	0.620 6(6)	0.895 4(6)	1.030 99(9)	C(23′)	0.289 2(7)	0.351 0(7)	0.793 57(10)
C(23)	0.492 6(7)	0.787 9(7)	1.039 68(10)	C(24′)	0.234 2(9)	0.289 1(9)	0.776 04(11)
C(24)	0.495 6(10)	0.739 6(9)	1.058 98(11)	C(25′)	0.155 0(8)	0.330 5(11)	0.764 11(13)
C(25)	0.618 5(9)	0.793 3(11)	1.070 12(13)	C(26′)	0.131 9(8)	0.440 3(11)	0.771 43(12)
C(26)	0.744 3(9)	0.900 3(10)	1.061 80(13)	C(27′)	0.188 4(8)	0.504 4(8)	0.789 61(13)
C(27)	0.741 8(7)	0.953 3(8)	1.042 57(11)	O(3′)	0.427 0(6)	0.707 7(5)	0.853 21(9)
O(3)	0.688 5(6)	1.122 9(5)	0.977 93(8)	O(16′)	0.233 4(6)	−0.182 7(5)	0.851 03(9)
O(16)	−0.010 4(6)	0.232 4(5)	0.988 62(8)	O(W)	0.5624	0.0	0.1667
C(1′)	0.328 6(6)	0.338 4(5)	0.839 93(9)				

225sh, and 294 nm (18 259); $\nu_{max.}$ 3 490, 1 665, and 1 590 cm^{-1}; δ 0.53 (3 H, s, 20-Me), 1.16 (9 H, s, 17-, 18-, and 19-Me), 1.87 (1 H, s, exchanges with D_2O, 17-OH), 2.23 (1 H, br d of d, J_{gem} 16.0 Hz, $J_{allylic}$ 3.0 Hz, 1β-H), 2.83 (1 H, d of d, J_{gem} 16.0 Hz, $J_{allylic}$ 2.0 Hz, 1α-H), 5.83 (1 H, d, *J* 8.0 Hz, 14-H), 6.08 (1 H, t, $J_{13,12} = J_{13,14}$ 8.0 Hz, collapses to d, $J_{13,14}$ 8.0 Hz on irradiation at 2.30, 13-H), 7.30 (5 H, s, aromatic), and 7.50 (1 H, q, $J_{allylic}$ 2.0 and 3.0 Hz, styryl-H) (Found: C, 82.9; H, 8.9%; M^+, 390.2562. $C_{27}H_{34}O_2$ requires C, 83.03; H, 8.77%; M^+, 390.2559).

ent-16α-*Hydroxy*-2α-*hydroxybenzyl*)*atis*-13-*en*-3-*one* (**5**).—Preparative t.l.c. (benzene–ethyl acetate, 9:1; silica gel) of a fraction containing both compounds (**4**) and (**5**) yielded pure *compound* (**5**) as crystals from hexane (0.12 g), m.p. 185—189.5 °C; $[\alpha]_D$ +106° (*c* 0.75); $\lambda_{max.}$ 210 (ε 16 450), 220 (16 625), and 277 nm (11 200); $\nu_{max.}$ 3 536, 1 755, 1 676, 1 623, and 1 492 cm^{-1}; δ 0.76 and 1.02 (2 × 3 H, 2 × s, 20- and 17-Me respectively), 1.13 (6 H, s, 19- and 18-Me), 1.60 (1 H, exchanges with D_2O, *ent*-16α-OH), 2.40 (1 H, br, sharpens on irradiation at 6.33, *ent*-2β-H), 5.82 (1 H, d, *J* 8.0 Hz, 13-H), 6.13 (1 H, m, perturbed on irradiation at 2.30, 14-H), 6.33 (1 H, br s, collapses to a sharp singlet on irradiation at 2.30, benzyl H), and 7.23 (5 H, br s, aromatic). The benzylic alcohol proton signal was not evident in the spectrum, possibly because of rapid proton exchange.

ent-3β-*Hydroxybeyer*-15-*ene*-2,12-*dione* 12-p-*Tosylhydrazone* (**14**).—To a cooled solution of the α-ketol (**13**)[2] (1.05 g, 0.03 mol) in glacial acetic acid (15 ml), was added solid *p*-tosylhydrazine (0.52 g, 0.03 mol) which quickly dissolved. Within 20 min the reaction mixture had thickened to a white paste, consisting of crystalline compound (**14**), to which ethanol (20 ml) was added to facilitate occasional stirring for a further 2 h before it was filtered. The crude product, when washed with ethanol until free of acetic acid, left the pure *ketol hydrazone* (**14**) (1.46 g, 95% yield) as fine, white crystals. Recrystallization from acetone was effective if carried out quickly, but prolonged contact with this solvent resulted in hydrazone exchange, regenerating the parent 12-ketone. Recrystallization from dioxane–methanol or THF–methanol gave long needles, m.p. 210—216 °C (decomp.); $\nu_{max.}$ 3 415br, 3 240br, 1 707, 1 640, and 1 597 cm^{-1}; δ 0.67, 0.69, 1.13, and 1.16 (4 × 3 H, 4 × s, 4 × Me), 2.40 (3 H, s, ArMe), 3.92 (1 H, b, *ent*-3α-H), 5.47 and 5.77 (2 H, ABq, *J* 6.0 Hz, 16- and 15-H respectively), 7.17—7.90 (4 H, 1,4-disubstituted benzene), and 8.21 (1 H, br s, NH). [**Note:** this compound (**14**) was not stable on storage and no analysis was carried out; however see the related compound (**15**) below.]

ent-2α-*Hydroxybeyera*-1,15-*diene*-3,12-*dione* 12-p-*Tosylhydrazone* (**15**).—*Method* (*a*). To a solution of the hydrazone (**14**) (0.60 g), in dioxane (8 ml) and ethanol (5 ml), was added a solution of KOH (400 mg) in water (3 ml), and the mixture warmed to 70 °C for 2 min before it was left to stand at room temp. After 12 h the reaction mixture was acidified with acetic acid and poured onto ice. The resulting solid was crystallized from acetone–methanol–water, yielding *stable*, colourless needles of *diosphenol hydrazone* (**15**) (0.55 g), m.p. 255—256 °C (decomp.); $[\alpha]_D$ −159° (*c* 1.68, THF); $\nu_{max.}$ 3 438br, 3 180, 3 065, 1 665, 1 645, 1 605, and 1 575 cm^{-1}; δ 1.00, 1.07, 1.14, and 1.16 (4 × 3 H, s, 4 × Me), 2.40 (3 H, s, ArMe), 5.50 and 5.85 (2 H, ABq, *J* 6.0 Hz, 16- and 15-H respectively), 6.20 (1 H, s, 1-H), and 7.28 and 7.86 (4 H, AA′, MM′, pseudo *J* 8.0 Hz, 1,4-disubstituted benzene) (Found: C, 67.3; H, 7.3; N, 5.85. $C_{27}H_{34}N_2O_4S$ requires C, 67.19; H, 7.10; N, 5.80%).

Method (*b*). Compound (**15**) was prepared in the same manner as for the preparation of compound (**14**) above, but using the diosphenol (**16**)[2] instead of the ketol (**13**). The yield was practically quantitative and the purification was the same as for method (*a*).

ent-(16S)-2β,3β-*Dihydroxyatis*-13-*ene* (**11**).—The tosylhydrazone (**14**) (1.86 g) in dioxane (20 ml) and ethanol (20 ml), was reduced at 5—10 °C with $NaBH_4$ (1.2 g) overnight. The reaction mixture was poured onto ice, acidified with dilute HCl, and the resulting solid *diol* (**11**) was crystallized from aqueous methanol as needles, m.p. 190—192 °C (0.56 g); $[\alpha]_D$ −10.3° (*c* 1.34, THF); $\nu_{max.}$ 3 552, 3 490, 3 425br, 725, 715, and 700 cm^{-1}; δ 0.72 (3 H, d, *J* 6.5 Hz, 17-Me), 0.86 (3 H, s, 20-Me), 1.00 (6 H, s, 19- and 18-Me), 2.25 (1 H, br m, allylic 12-H), 3.16 (1 H, br, $w_{\frac{1}{2}}$ 9.0 Hz, *ent*-3α-H), 4.04 (1 H, q, *J* 3.5 and 7.0 Hz, *ent*-2α-H), 5.87 (1 H, apparent s, 14-H), and 5.94 (1 H, apparent doublet, *J* 3.0 Hz, collapses to a singlet on irradiation at δ 2.25, 13-H) [Found: C, 78.7; H, 10.5%; M^+, 304.2401; base peak *m/z* 262.1934. $C_{20}H_{32}O_2$ requires C, 78.9; H, 10.59%; M^+, 304.2402: $C_{17}H_{26}O_2$ (M^+ − propene) requires 262.1933].

Similarly the tosylhydrazone (**15**) was reduced, and the product worked up as described above, to yield pure compound (**11**). When the sequence from the ketol (**13**) (20.0 g) was carried through without crystallizing any intermediates, the yield of pure diol (**11**) was 14.0 g (73%).

The *diacetate* (**9**) was prepared, from the diol (**11**) (0.606 g) in pyridine and acetic anhydride, and obtained as needles (0.770 g) from aqueous methanol, m.p. 173—174.5 °C; $[\alpha]_D$ −35° (*c* 0.85); $\nu_{max.}$ 1 740 and 1 240 cm^{-1}; δ 0.72 (3 H, d, *J* 7.0 Hz, 17-Me), 0.84, 0.89, and 1.00 (3 × 3 H, 3 × s, 18-, 19-, and 20-Me respectively), 2.00 (6 H, s, 2 × COMe), 2.23 (1 H, m, 12-H), 4.58 (1 H, d, *J* 3.5 Hz, *ent*-3α-H), 5.27 (1 H, q, *J* 3.5 and 7.0 Hz, *ent*-2α-H), 5.87 (1 H, d of d, *J* 8.0 and 1.75 Hz, 14-H), and 5.93 (1 H, q, *J* 8.0 and 6.0 Hz, 13-H) (Found: C, 74.0; H, 9.3%; M^+, 388.2626. $C_{24}H_{36}O_4$ requires C, 74.19; H, 9.34%; M^+, 388.2613).

The *acetonide* (**17**) was quantitatively prepared by treating an acetone solution of the diol (**11**), with a drop of 70% $HClO_4$; the insoluble compound (**17**) immediately crystallized out. This acetonide was obtained as needles from THF, m.p. 182—184 °C; $[\alpha]_D$ −29° (*c* 2.02) (Found: C, 79.9; H, 10.7. $C_{23}H_{34}O_2$ requires C, 80.18; H, 10.53%).

The 2,3-O-*benzylidene derivative* (**18**) was prepared from the diol (**11**) (0.50 g), with benzaldehyde (1.0 ml) and tosic acid (20 mg), by azeotropic removal of water with refluxing toluene (50 ml) for 1 h. After washing the cooled toluene solution with aqueous sodium hydrogen carbonate, the solvent was removed and the residue crystallized from acetone as needles of the *cyclic acetal* (**18**) (0.35 g), m.p. 165—169 °C; $[\alpha]_D$ −35° (*c* 2.25) (Found: C, 82.3; H, 9.2. $C_{27}H_{36}O_2$ requires C, 82.61; H, 9.24%).

ent-(16S)-*Atis*-13-*en*-3-*one* (**8**) *from the Corresponding* α-*Diol*.—To a solution, under argon, of the diol (**11**) (1.55 g), benzoic acid (1.28 g), and PPh_3 (2.76 g) in dry THF (20 ml), was added diethyl azodicarboxylate (1.84 g) in dry THF (15 ml) at room temp. The reaction mixture immediately became warm, and after 15 h at room temp. the solvent was evaporated off to give a residue; this was chromatographed on silica gel, eluting with 3% ethyl acetate in benzene, to give the *ketone* (**8**) (1.48 g, 100% crude yield). The nearly pure product was recrystallized from methanol as needles (1.04 g, first crop), m.p. 110—113 °C; $[\alpha]_D$ +18° (*c* 3.0); $\lambda_{max.}$ 289 nm (ε 26); δ 0.72 (3 H, d, *J* 6.0 Hz, 17-Me), 0.77 (3 H, s, 20-Me), 1.02 and 1.07 (2 × 3 H, 2 × s, 18- and 19-Me), 5.93 (1 H, apparent s, 14-H), and 5.98 (1 H, apparent d, *J* 2.5 Hz, 13-H) (Found: C, 83.9; H, 10.6. $C_{20}H_{30}O$ requires C, 83.86; H, 10.56%).

ent-2-*Benzylidene*-11(12→16)abeo-*atis*-13-*ene*-3,12-*dione* (**7**).—The benzylidenediketone (**3**) (0.71 g), was dissolved by warming it with acetic anhydride (20 ml), and then cooled in ice. Sulphuric acid (1 ml, conc.) was then added dropwise and after 5 min the mixture was poured onto ice. The separated solid ketone (**7**) was washed well with water and crystallized as pale yellow rods from acetone–methanol (0.52 g), m.p. 208—212 °C; $[\alpha]_D$ +103.5° (*c* 2.11); $\nu_{max.}$ 1 670, 1 592, 1 573, and 700 cm^{-1}; δ 0.61 (3 H, s, 20-Me), 1.19 (6 H, s, 18- and 19-Me), 1.56 (3 H, s, 17-Me), 2.32 (1 H, br d of d, J_{gem} 18.0 Hz, $J_{allylic}$ 3.0 Hz, 1β-H), 2.76 (1 H, d of d, J_{gem} 18.0 Hz, $J_{allylic}$ 2.0 Hz, collapses to a doublet J_{gem} 18.0 Hz on irradiation at δ 7.88, 1α-H), 5.83 (1 H, d, *J* 10.0 Hz, 13-H), 6.93 (1 H, d of d, *J* 2.0 and 10.0 Hz, collapses to a doublet, *J* 10.0 Hz, on irradiation at δ 1.53, 14-H), 7.33 (5 H, s, aromatic), and 7.50 (1 H, q, $J_{allylic}$ 2.0 and 3.0 Hz, styryl proton) (Found: C, 83.4; H, 8.3. $C_{27}H_{22}O_2$ requires C, 83.46; H, 8.30%).

X-*Ray Data of Compound* (**4**).—A crystal, 0.6 × 0.6 × 0.3 mm, was used for the *X*-ray measurements. The space group was $P3_121$ or $P3_221$ on the basis of Laue group and systematic absences (001, $1 \neq 3n$). Space group $P3_221$ was chosen after the complete *X*-ray analysis revealed that the enantiomorph consistent with this space group had the presumed correct absolute configuration. The unit cell constants, determined from least-squares analysis of the θ values for 25 reflections, were: a = 10.844(2), and c = 66.653(8) Å, resulting in a unit cell volume 6 787.2 $Å^3$. The density was calculated to be 1.17 g cm^{-3} for 12 diterpene molecules and six water molecules in the unit cell. Intensities for 5 393 independent reflections having θ < 75° were measured on an Enraf-Nonius CAD-4 diffractometer, Cu-K_α radiation. After the Lorentz and polarization corrections had been applied, normalized structure factor amplitudes were computed.

The structure was solved by direct methods using a modified version of the MULTAN program;[13] using a total of 3 000 Σ_2 relationships to phase 400 reflections. The solution most probable in terms of the various figures of merit was found to be correct.

The positional and anisotropic thermal parameters of all non-hydrogen atoms were refined by full-matrix least-squares using the 3 996 reflections with $I > 2\sigma(I)$. The weights were the quantities $(1/\sigma_F^2)$ where σ_F is defined by equation H.14 of Stout and Jensen.[14]

A difference map revealed the presence of a water molecule on the two-fold axis. This oxygen atom did not refine properly, presumably owing to disorder. Hydrogen atoms, placed at their calculated positions, were included in the final structure factor calculations.

The final $R(\Sigma||F_o| - |F_c||/\Sigma|F_o|)$, was 8.3% for 3 996 observed reflections and 11.7% for all data. Tables of the hydrogen atomic co-ordinates and the anisotropic thermal parameters are available as a Supplementary Publication (SUP. No. 56146, 3 pp.).* Structure factor tables are available on request from the editorial office.

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* For details of the Supplementary Publications Scheme see Instructions for Authors (1985) in *J. Chem. Soc., Perkin Trans. 1*, 1985, Issue 1.

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