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DITERPENE CHEMISTRY—I

TRANSFORMATIONS OF 8(17),14-LABDADIEN-13-OL (MANOOL)*

P. K. GRANT, R. T. WEAVERS and in part C. HUNTRAKUL
Department of Chemistry, University of Otago, Dunedin, New Zealand

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Abstract—Reaction of manool with $Pb(OAc)_4$/NBS gave a high yield of bromoorthoacetate, the structures being confirmed by chemical degradation. Mechanisms to account for the formation and reactions of the bromoorthoacetates are proposed. Syntheses of orthoesters are reported.

The allylic acetylation of 8(17)-labden-13-ol (1) using lead tetraacetate/N-bromosuccinimide in refluxing benzene[1] was investigated as a route to the synthesis of 8(17)-labdene-7α,13-diol (2). Although the required acetate (3) was isolated[2] the major product of the reaction proved to be a tribromo compound, $C_{22}H_{35}O_3Br_3$.

Modification of the allylic acetoxylation procedure gave improved yields of the tribromo compound and in addition a dibromo compound, $C_{22}H_{36}O_3Br_2$, was obtained.

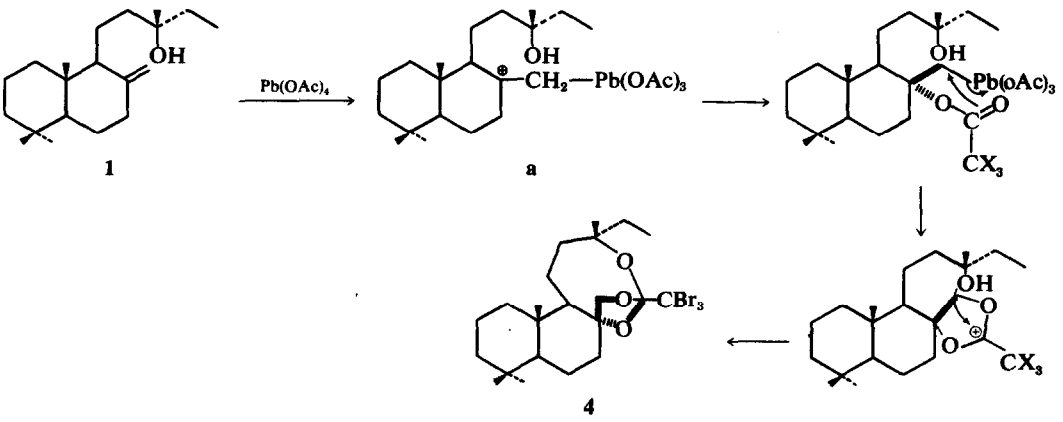
The IR spectrum of the tribromo compound showed no hydroxyl or carbonyl absorptions and possessed CBr stretching bands (732, 723 cm^{-1}) and strong CO stretching bands (1199, 1172, 1130, 1110, 1093 and 1044 cm^{-1}), indicating that all three oxygen atoms were involved in ether linkages. The mass spectrum confirmed the molecular weight (584) and showed the characteristic three bromine quartet. The presence of a substantial M-CBr_3 peak and the absence of M-HBr or M-Br_2, coupled with the fact that attempted dehydrobromination with lithium chloride/lithium carbonate in dimethyl formamide was unsuccessful, pointed to the existence of a CBr_3 moiety attached to a tertiary carbon. PMR showed the usual ring A methyls at δ 0·78, 0·79, 0·88 and the C-14 methyl triplet at δ 0·97. The C-13 methyl signal at δ 1·38 was substantially downfield from its position in 8(17)-labden-13-ol (1) (δ 1·14), a fact consistent with ether formation to C-13. The only low-field pattern was an AB system, H_A δ 4·57, H_B δ 4·20 (J_{AB}8Hz), which could be assigned to the C-17 protons with C-17 involved in an ether linkage. Any remaining ether linkages could only be to tertiary centres; C-8 was the most probable of these in view of the low-field position of the C-17 protons and was also mechanistically feasible. That these were the sole points of attachment was confirmed by subsequent reactions. The incorporation of ether linkages to carbons 8, 13 and 17 in the normal labdane skeleton, combined with the presence of a CBr_3 unit plus an additional carbon atom, led to the postulation of the orthoester structure, labdane-8, 13, 17-tribromoorthoacetate (4). This structure was confirmed by subsequent reaction sequences. An 8β-oxygen linkage was ruled out by the absence of methyl signals in the range δ 0·95–1·15 characteristic of a C-10 methyl in such a system.

The dibromo compound, $C_{22}H_{36}O_3Br_2$, also showed no hydroxyl or carbonyl absorption in the IR and possessed a CBr stretching band at 703 and strong CO stretching bands (1198, 1141, 1110, 1088, 1050, 1024 cm^{-1}). The mass spectrum, which confirmed the molecular weight (506), showed the characteristic two bromine triplet, and possessed a substantial M-$CHBr_2$ peak. A very sharp singlet at δ 5·62 confirmed the presence of a $CHBr_2$ grouping attached to a tertiary carbon. Ring A methyls appeared at δ 0·75, 0·78, 0·89, the C-14 methyl triplet at δ 0·93, and the C-17 protons as an AB system, H_A δ 4·39, H_B δ 3·84 (J_{AB} 8Hz). The C-13 methyl appeared at δ 1·24. The compound showed similar spectral characteristics to the tribromoorthoester (4), the major differences being those expected for replacement of one bromine from the α-carbon of the orthoester functionality by a hydrogen, and was assigned as labdane-8,13, 17-dibromoorthoacetate (5).

No evidence for the existence of an unbrominated or a monobrominated orthoester, or their hydrolysis products, could be found.

A combination of the mechanism of lead tetraacetate on double bonds[3] with the reaction of alcohols with acetoxonium ions[4] leads to a likely mechanism for the formation of the orthoesters (Scheme 1). The carbonium ion generated by initial attack on the double bond would be preferentially attacked from the less hindered α-face

*Nomenclature use is according to J. W. Rowe's third revised rules for diterpene nomenclature. The term 'labdane' implies the configurations of Carbons 5, 8, 9, 10 and 13, specification only being necessary when a deviation from the normal labdane stereochemistry occurs.



1 a 4

SCHEME 1. Formation of tribromoorthoester (X = H or Br)

with resultant formation of an α-acetoxonium ion. Intramolecular nucleophilic attack by the C-13 hydroxyl then gives an orthoester in which there has been no racemization at C-13 as observed.

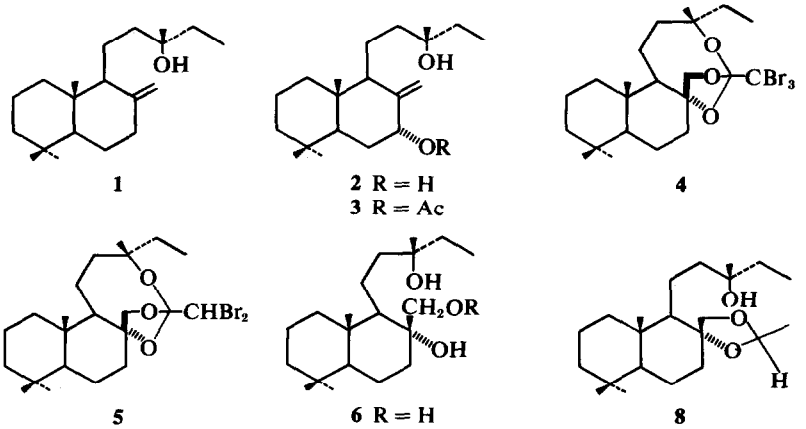
In order to determine the stage at which bromination occurred, the dibromoorthoester was treated with NBS in refluxing benzene, but no bromination was observed. Thus, the bromination step probably occurs at an early stage in the mechanism, possibly involving bromination of the acetate group as has been observed in acylic esters.[5] Treatment of the dibromoester with bromine in refluxing pyridine gave the tribromorthoester.

Lithium aluminium hydride reduction of the tribromoorthoester (4). Simple orthoesters have been reduced in good yield to the corresponding acetals,[6] the tribromoorthoester on LAH reduction, both at room temperature and in refluxing ether gave three major products: a triol (6), $C_{20}H_{38}O_3$, a diol acetate (7), $C_{22}H_{40}O_4$ and an hydroxy acetal (8), $C_{22}H_{40}O_3$. Spectral data for these reduction products are contained in Table 1.

All the reduction products showed the usual labdane ring A methyl signals and the C-13 and C-14 methyl signals of the normal hydroxylated side chain. The absence of methyl signals in the δ 0·95–1·15 range eliminated the possibility of an 8β hydroxyl group. Consequently all the products possessed the normal labdane C-8 configuration.

The inter-relationship of the three reduction products was established. Pyridine/acetic anhydride acetylation of the triol (6) gave the diol acetate (7), thus establishing the presence of one primary and two tertiary hydroxyl groups in the triol. The primary alcohol carbinol protons showed the usual downfield shift on acetylation. Acid catalysed reaction of the triol with acetaldehyde gave the hydroxy acetal (8) and confirmed the presence of a vicinal diol system in the triol. The carbinol type protons (C-17) appeared as an AB system, the coupling constant (J_{AB} 9Hz) falling within the range reported for tetrahydrofuranoid rings.[7]

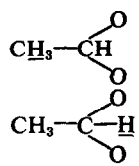
On this evidence the triol was formulated as



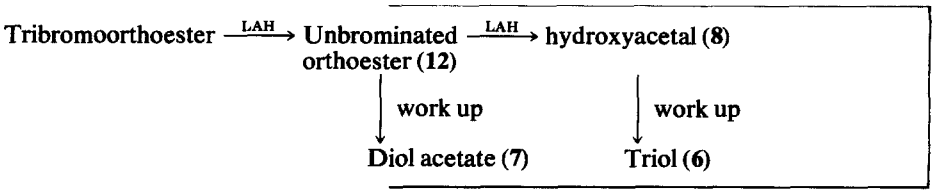
1 2 R = H 3 R = Ac 4

5 6 R = H 7 R = Ac 8

Table 1. Spectral data of some reduction products and hydrolysis products of orthoesters.

	IR (cm^{-1})	PMR (δ)			
Labdane-8,13,17-triol (**6**)	3430 (OH) 1030, 1041, 1094, 1134, (C—O)	ring A Me's 0·73, 0·79, 0·87	C_{13}Me 1·13	$C_{17}H$'s 3·57 (br)	
17-Acetoxylabdane-8,13-diol (**7**)	1732, 1232 (acetate) 1148, 1185 (C—O)	0·79, 0·81, 0·86	1·13	H_A 4·33, H_B 4·05 (J_{AB} 11Hz)	acetate, 2·10
8,17-O-ethylidenelabdan-13-ol (**8**)	3090 (OH) 1190, 1140, 1111, 1092, 1087, 1047, (C—O)	0·69, 0·74, 0·87	1·14	H_A 3·79, H_B 3·69 (J_{AB} 9Hz)	 1·32 (doublet) J 5Hz 5·10 (quartet) J 5Hz
17-Bromoacetoxylabdane-8,13-diol (**10**)	3300, 3200 (OH) 1753, 1293 (bromoacetate) 1142, 1162 (C—O)	0·81, 0·83, 0·89	1·15	H_A 4·43, H_B 4·14 (J_{AB} 11Hz)	—CH_2Br 3·90
17-Dibromoacetoxylabdane-8,13-diol (**11**)	3360 (OH) 1756, 1739, 1278 (bromoacetate) 1020, 1140 (C—O)	0·81, 0·85, 0·89	1·16	H_A 4·50, H_B 4·22 (J_{AB} 11Hz)	—$CHBr_2$ 5·91

labdane-8,13,17-triol (6). This structure was unequivocally proven by the synthesis of the triol by osmium tetroxide hydroxylation of 8(17)-labden-13-ol (1), osmylation proceeding from the less hindered α-face to give the vicinal 8α,17-diol. The diol acetate and hydroxy acetal were thus 17-acetoxylabdane-8,13-diol (7) and 8,17-O-ethylidenelabdan-13-ol (8) respectively. The products of the hydride reduction of the tribromoorthoester can be accounted for by the following reaction scheme:



The structure of the triol confirms that the tribromoorthoester has ether functions attached to C's 8, 13 and 17 as proposed. No loss of configuration has occurred in either formation or reduction of the orthoester as the specific rotations of the synthetic and degradative triols were identical.

Base treatment of the tribromoorthoester. McElvain[8] reported that treatment of a dibromoorthoester with ethanolic KOH gave the mono brominated orthoester and finally the unbrominated orthoester. Treatment of the tribromoorthoester (4) with alcoholic NaOH gave the dibromoorthoester (5). Also obtained was a very unstable compound which possessed no hydroxyl or carbonyl absorptions in the IR and showed strong CO stretching at 1256, 1044, 1008 and 990 cm^{-1}. The PMR spectrum possessed the usual ring A methyls, δ 0·73, 0·80, 0·90, the C-14 methyl triplet, δ 0·90, the C-17 protons as an AB system H_A δ 4·29, H_B, 3·71 (J_{AB} 8Hz), and a low field singlet at δ 3·54, consistent with a CH_2Br system. On the basis of its spectral similarity to the di- and tribromoorthoesters, it was assigned as labdane-8,13,17-monobromoorthoacetate (9).

The bromine atoms are rendered slightly positive by the strong electron withdrawal of the three orthoester oxygens and hence undergo base catalysed electrophilic (H^+) substitution.

Acid hydrolysis of the orthoesters. Acid hydrolysis of orthoesters[9] gives dihydroxy esters and the corresponding derivatives were obtained from the mono and dibromoorthoesters. Table 1 lists the spectral data of the hydrolysis products.

The monobromoorthoester hydrolysed very rapidly even when attempts were made to exclude moisture and consequently was not completely characterised as the orthoester but as the hydrolysis product, 17-bromoacetoxylabdane-8,13-diol (10), $C_{33}H_{39}O_4Br$. The mass spectrum of (10) showed M^+-H_2O (428) as the highest mass peak with the characteristic one bromine doublet and LAH reduction gave labdane-8,13,17-triol (6).

The dibromoorthoester was stable to atmospheric conditions but acid hydrolysis in a two phase system at room temperature gave 17-dibromoacetoxylabdane-8,13-diol (11), $C_{22}H_{38}O_4Br_2$. The mass spectrum of 11 showed M^+-H_2O (506) as the highest mass peak with the characteristic two bromine triplet. LAH reduction gave triol 6.

The tribromoorthoester resisted hydrolysis at room temperature and more forcing conditions produced a very complex mixture. Thus bromine substitution confers stability to hydrolysis, in agreement with De Wolfe's observation[10] that reactivities parallel the inductive electron donating power of substituents. Increased bromination would give increased electron withdrawal destabilising the carbonium ion transition state. In view of this trend it is probable that the unhalogenated orthoester, labdane-8,13,17-orthoacetate, (12), would be too unstable to be isolated and would be hydrolysed to the dihydroxy ester (7) in the reduction of the tribromoorthoester (see reaction scheme).

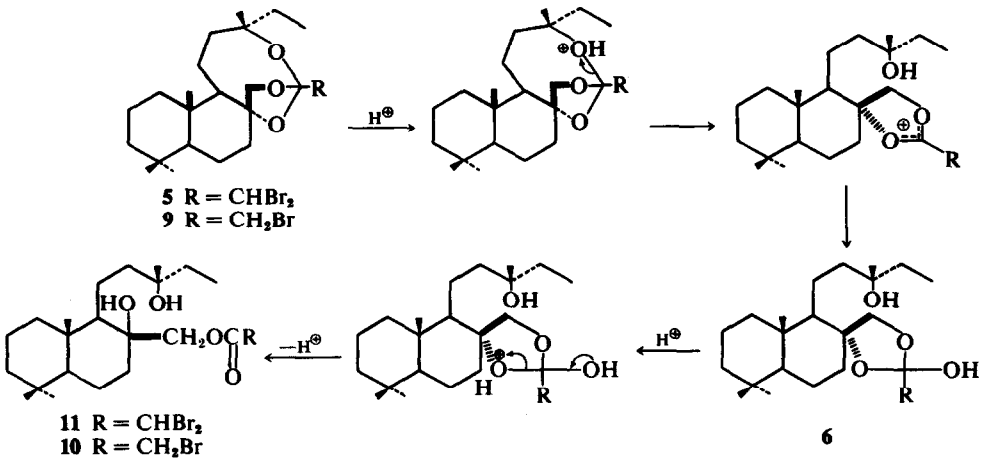
The occurrence of the primary ester grouping can be accounted for in terms of Scheme 2. Because of the greater inductive effects the C-13 oxygen is favoured to undergo the initial protonation which leads, *via* the acetoxonium ion, to the hydroxyorthoester (b). Final protonation at the C-8 oxygen, again because of the greater inductive effect, gives an 8α,13-dihydroxy-17-ester.

Attempted synthesis of orthoesters. (i) Barnes[11] reported the synthesis of tribromoorthoesters by reaction of triols with tribromoacetic acid. This reagent with labdane-8,13,17-triol (6) failed to yield any orthoester product.

(ii) Winstein[4] reported that trityl tetrafluoroborate abstracts a hydride ion from acetals to form dialkoxycarbonium ions. This reaction was attempted on 8,17-O-ethylidenelabdan-13-ol (8); any acetoxonium ion produced could then cyclise with the side chain hydroxyl to give an orthoester. The reaction produced only dehydration products.

(iii) In an attempt to synthesise labdane-8,13,17-orthoacetate (12), 8(17)-labden-13-ol (1) was refluxed with lead tetraacetate in benzene. The two products isolated were established as labdane-8,13,17-diacetoxyorthoacetate (13) and 17-acetoxy-8-labden-13-ol (14).

The diacetoxyorthoester (13), $C_{26}H_{42}O_7$, showed strong acetate (1770, 1219, 1197 cm^{-1}) and CO



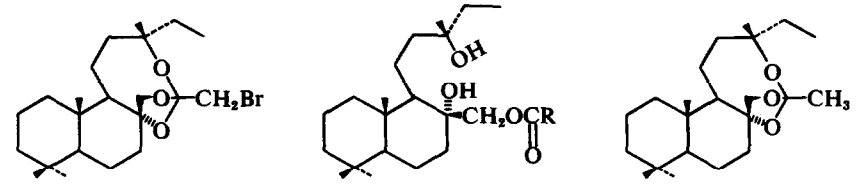
SCHEME 2. Acid hydrolysis of orthoesters

bands (1055, 1019 cm^{-1}) in the IR. Mass spectrum confirmed the molecular weight (466) and showed loss of $CH(OCOCH_3)_2$. PMR spectral data correlated well with that for the bromoorthoesters. Ring A methyls appeared at δ 0·75, 0·78, 0·87, the C-13 methyl at 1·22 and the C-14 methyl triplet at 0·84. An AB system (H_A δ 4·37, H_B 3·72; J_{AB} 8Hz) and a sharp low-field singlet at δ 6·86 were also present. The acetate methyls appeared at δ 2·07 and 2·12. Acid hydrolysis of the diacetoxyorthoacetate gave labdane-8,13,17-triol (**6**).

The allylic acetate (**14**), $C_{22}H_{38}O_3$, showed hydroxyl (3460 cm^{-1}) and acetate absorption (1720, 1222 cm^{-1}) in the IR. The C-13 methyl signal at δ 1·14 indicated a free hydroxyl group on the side chain. The Δ^8 allylic acetate was confirmed by the lowfield position of the C-17 protons signal (δ 4·57), the deshielding[12] of the C-10 methyl (δ 0·99) together with the absence of an olefinic proton signal.

Formation of the diacetoxyorthoester can be accommodated by Scheme 1, with acetoxylation occurring in place of bromination. The allylic acetate (**14**) can also be derived from the same scheme; elimination from the carbonium ion (a) to the Δ^8 olefin followed by acetate displacement at C-17.

(iv) Since silver acetate–iodine oxidation of olefins is regarded as proceeding through an acetoxonium ion, silver acetate-iodine oxidation of 8(17)-labden-13-ol (**1**) could generate the required 8,17 acetoxonium ion. Because orthoesters are very sensitive to acid conditions[9] (hydrolysing to alcohols and esters) benzene was used as the solvent instead of AcOH. The reaction products showed no orthoester, the two major



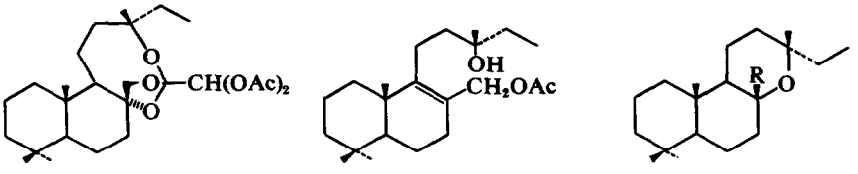


Table 2. PMR of 8,13-epoxylabdanes

	Methyls (δ)					
	4α	4β	10β	13	8β	14 (triplet)
17-Iodo-8,13-epoxylabdane (15)	0·85	0·79	0·79	1·39	—	0·85
8,13-Epoxylabdane (16)	0·85	0·80	0·77	1·18	1·27	0·84

products being 17-acetoxy-8-labden-13-ol (14) and 17-iodo-8,13-epoxylabdane (15).

The iodo compound (15), $C_{20}H_{35}OI$, showed only CO stretching in the IR (1173, 1142, 1083, 1013 cm^{-1}). The PMR spectrum showed ring A methyl signals almost identical to those of 8,13-epoxylabdane (16)[13] (Table 2) while the C-13 methyl signal at δ 1·39 was also consistent with an 8,13 ether linkage. A low-field AB system (H_A δ 3·76; H_B 3·61; J_{AB} 11Hz) could be assigned to the C-17 protons attached to an iodine or involved in an oxide linkage. The presence of an 8,13-epoxy linkage was confirmed by hydrogenolysis over Pd on charcoal to the known 8,13-epoxylabdane (16), reaction proceeding very slowly. The iodo compound proved resistant to alkaline hydrolysis and was unaffected by LAH in refluxing ether.

The PMR spectrum showed long range coupling of the upfield spin-pair of the AB system, indicating that the CH_2I group is held in a fixed conformation, most likely that with the C-I bond bisecting the C_7—C_8—O bond angle. Backside attack by a nucleophile is thus greatly hindered, accounting for the inertness of the iodo compound.

EXPERIMENTAL

M.ps were determined on a Kofler hotstage and are uncorrected. IR spectra, measured on a Perkin Elmer 421 spectrophotometer, are for nujol mulls unless otherwise stated and UV spectra were obtained on a Shimadzu RS 27 spectrophotometer. PMR were recorded in 5–10% $CDCl_3$ solution on a Varian HA-100 spectrometer using TMS as internal standard. Optical rotations were measured in $CHCl_3$ solution on a Perkin Elmer model 141 Digital readout polarimeter. Mass spectra were recorded on an AEI MS 9 mass spectrometer. TLC was used routinely for monitoring reactions and chromatographic separations.

Lead tetraacetate/N-bromosuccinimide on 8(17)-*labden*-13-*ol* (1). To a stirred solution of (1) (5 g) in dry benzene (400 ml) were added NBS (3·9 g, recrystallised from hot water and dried under vacuum over P_2O_5 for 12 h) and $Pb(OAc)_4$ (7·8 g, with AcOH stabiliser removed by filtration). After refluxing for 1 h, further NBS (3·9 g) and $Pb(OAc)_4$ (7·8 g) were added. The reaction was completed by a further hour's refluxing, another addition of NBS (3·9 g) and $Pb(OAc)_4$ (3·9 g), and a final hour's refluxing. Excess $Pb(OAc)_4$ was removed by the addition of ethane diol (2 ml). The mixture was diluted to twice its initial volume with hexane and filtered through alumina. Removal of solvent followed by chromatography (300 g alumina) gave: (i) 2% ether/hexane—*The tribromoorthoester* (4) (2·1 g), m.p. 138–139° (from hexane). $[\alpha]_D^{25}$ 0° (*c*, 7·67). ν_{max} 1218, 1199, 1172, 1130, 1110, 1093, 1068, 1052, 1044, 1023, 999 (CO); 732, 723 (CBr_3) cm^{-1}. λ_{max} 216 nm. (ε 3,130). PMR Me's at δ 0·78, 0·79, 0·88, 0·97 (t, *J* 7Hz), 1·38; C-17 protons as an AB system H_A 4·57, H_B 4·20 (J_{AB} 8Hz). *M/e* 584 (M^+). (Found: C, 45·0; H, 6·0; Br, 40·9. $C_{22}H_{35}O_3Br_3$ requires C, 45·0; H, 6·0; Br 40·8%). (ii) 7% ether/hexane—*The dibromoorthoester* (5) (1·4 g), m.p. 80–81° (EtOH aq). ν_{max} 1260, 1210, 1198, 1160, 1141, 1110, 1088, 1050, 1024, 994, 963 (CO); 703 (CBr_2) cm^{-1}. λ_{max} 223 nm (ε 1,010). PMR, Me's at δ 0·75, 0·78, 0·89, 0·93 (t, *J* 7Hz), 1·24; C-17 protons as an AB system H_A 4·39, H_B 3·84 (J_{AB} 8Hz); $CHBr_2$ 5·62. *M/e* 506 (M^+) (Found: C, 51·7; H, 7·1; Br, 31·8. $C_{22}H_{36}O_3Br_2$ requires C, 52·0; H, 7·1; Br, 31·4%).

Bromination of the dibromoorthoester (5). 5 (50 mg) in pyridine (5 ml) was refluxed with bromine (0·3 ml) for 1¾ h. Work up by dilution with water, ether extraction, washing with dil. HCl (twice) followed by water, drying and removal of solvent, gave the *tribromoorthoester* (4) (52 mg), identical (m.m.p., IR, PMR) with an authentic sample.

Lithium aluminium hydride reduction of the tribromoorthoester (4). 4 (225 mg) was reduced with excess LAH in dry ether (13 ml) at room temp. for 10 h. Work up by stirring over Na_2SO_4 aq followed by ether extraction and PLC (3 × 80% ether/hexane) gave: (i) The upper band, *an hydroxy acetal* (8) (65 mg), distilled 95°/0·025 mm ν_{max} 3090 (OH); 1190, 1140, 1111, 1092, 1087, 1047, 1004 (CO) cm^{-1}. PMR, Me's at δ 0·69, 0·74, 0·87, 0·88 (t, *J* 7Hz), 1·14; CH_3—CH 1·32 (d, *J* 5Hz); —CH 5·10 (q, *J* 5Hz); C-17 protons as an AB system H_A 3·79, H_B 3·69 (J_{AB} 9Hz). (Found: C, 74·9; H, 11·7. $C_{22}H_{40}O_3$ requires C, 75·0; H, 11·4%). (ii) The middle band, 17-*acetoxylabdane*-8,13-*diol* (7) (60 mg), sublimed 90°/0·025 mm, m.p. 105–106°. ν_{max} 3390 (OH); 1737, 1232 (acetate); 1185, 1148, 1121, 1099, 1081, 1040 (CO) cm^{-1}. PMR, Me's at δ 0·79, 0·81, 0·87, 0·88 (t, *J* 7Hz), 1·13; acetate methyl 2·10; C-17 protons as an AB system H_A 4·33, H_B 4·05 (J_{AB} 11Hz). (Found: C, 71·8; H, 11·0. $C_{22}H_{40}O_4$ requires C, 71·7; H, 10·9%). (iii) The lower band, *labdane*-8,13,17-*triol* (6) (55 mg), sublimed 115°/0·05 mm, m.p. 128–130°, $[\alpha]_D^{25}$ −29° (*c*, 0·0017). ν_{max}^{KBr} 3430 (OH); 1197, 1134, 1059, 1041, 1030, 986 (CO) cm^{-1}. PMR, Me's at δ 0·73, 0·79, 0·87, 0·89 (t, *J* 7Hz), 1·13; C-17 protons as a singlet 3·56. (Found: C, 73·9; H, 11·9. $C_{20}H_{38}O_3$ requires C, 73·6; H, 11·7%).

Acetylation of labdane-8,13,17-*triol* (6). 6 (70 mg) was treated with dry pyridine (3 ml) and Ac_2O (2 ml) at room temp. for 20 h. Dilution with water, ether extraction, washing with dilute HCl (twice), water, sat. $NaHCO_3$ and finally water, drying and removal of solvent followed by PLC (75% ether/hexane) gave 17-*acetoxylabdane*-8,13-*diol* (7) (65 mg), identical (m.m.p., IR, PMR) with an authentic sample.

Condensation of labdane-8,13,17-triol (**6**) *with acetaldehyde.* **6** (100 mg) in $CHCl_3$ (10 ml) was treated at room temp with acetaldehyde (0·1 ml) and $HClO_4$ (0·02 ml, 20%) for 6½ h. Washing with sat. $NaHCO_3$ and water, drying, and removal of solvent gave a pale yellow oil (70 mg). PLC (50% ether/hexane) gave the *hydroxy acetal* (**8**) (40 mg), identical (IR, PMR) with an authentic sample.

Osmylation of 8(17)-*labden*-13-*ol* (**1**). **1** (1 g) in pyridine (20 ml) was stirred at room temp. with OsO_4 (1 g) in pyridine (180 ml) for 24 h. A solution of sodium metabisulphite (3 g) in water (100 ml) was then added and stirring continued for 16 h. The mixture was diluted with water (500 ml), $CHCl_3$ extracted (250 ml and 3 × 100 ml), washed with 4N HCl, sat. $NaHCO_3$, and water. Drying and evaporation of solvent gave a semi-crystalline solid (0·70 g), which, on PLC (2 × in ether), gave *labdane*-8,13,17-*triol* (**6**) (0·55 g), identical (m.m.p. IR, PMR) with an authentic sample. (Found: C, 73·6; H, 11·9. $C_{20}H_{38}O_3$ requires C, 73·6; H, 11·7%).

Alkaline debromination of the tribromoorthoester (**4**). **4** (400 mg) in EtOH (70 ml) was refluxed with NaOH (35 ml, 30%) for 4 h. Dilution, ether extraction, washing with water, drying, and removal of solvent gave a brown oil (380 mg). Chromatography (20 g alumina) gave: (i) 7% ether/hexane – *The dibromoorthoester* (**5**) (260 mg), identical (m.m.p., IR, PMR) with an authentic sample. (ii) 15% ether/hexane – *The monobromoorthoester* (**9**) (100 mg). ν_{max} 1414 (perturbed methylene); 1044, 1008, 990, 977, 960 (CO) cm^{-1}. PMR, Me's at δ 0·73, 0·80, 0·90, 0·90 (t, *J* 7Hz), 1·15; C-17 protons as an AB system H_A 4·29, H_B 3·71 (J_{AB} 8Hz); CH_2Br 3·54.

This compound, on standing (or when shaken, in ethereal solution, with dil. aq. acid) readily hydrolysed to the *diol-bromoester* (**10**), m.p. 118–119° (from hexane). ν_{max} 3300, 3200, (OH); 1753, 1293 (ester) 1416 (perturbed methylene); 1162, 1142 (CO). PMR, methyls at δ 0·81, 0·83, 0·89, 0·90 (t, *J* 7Hz), 1·15; C-17 protons as an AB system H_A 4·43, H_B 4·14 (J_{AB} 11Hz); CH_2Br 3·90. *M/e* 428 (M^+-H_2O) (Found: C, 59·4; H, 8·9; Br, 18·1. $C_{22}H_{39}O_4Br$ requires C, 59·1; H, 8·9; Br, 17·9%).

Acid hydrolysis of the dibromoorthoester (**5**). **5** (300 mg) in ether (45 ml) was stirred at room temp. with HCl (45 ml, 50%) for 5 h. Washing the ethereal layer with water, drying, followed by removal of solvent gave the *dioldibromoester* (**11**) (295 mg), m.p. 84–86°. ν_{max} 3360 (OH); 1756, 1739, 1278 (ester); 1140, 1020 (CO) cm^{-1}. PMR, Me's at δ 0·81, 0·85, 0·89, 0·90 (t, *J* 7Hz), 1·16; C-17 protons as an AB system H_A 4·50, H_B 4·22 (J_{AB} 11Hz); CHBr$_2$ 5·91. *M/e* 506 (M^+-H_2O).

Lithium aluminium hydride reduction of the diolmonobromoester (**10**). **10** (110 mg) was refluxed with excess LAH in dry ether for 2 h. Excess LAH was destroyed with wet ether and then water. The complex was hydrolysed with H_2SO_4 (10 ml, 10%) and the mixture ether extracted. Removal of solvent gave *labdane*-8,13,17-*triol* (**6**) (60 mg), identical (m.m.p., IR, PMR) with an authentic sample.

Reaction of 8(17)-*labden*-13-*ol* (**1**) *with lead tetraacetate.* (**1**) (10 g) in dry benzene (300 ml) was stirred under reflux with $Pb(OAc)_4$ (15·3 g) for 1 h. After two more sequences of addition of $Pb(OAc)_4$ (15·3 g) and refluxing for 1 h, the mixture was diluted with hexane (300 ml) and filtered through alumina. Removal of solvent gave a complex mixture which was partially purified on a neutral alumina column to give: (i) 30% ether/hexane – A mixture which on PLC (3x in 30% ether/hexane) gave: (a) 8(17)-*Labden*-13-*ol* (**1**) (1·4 g), identical (IR) with an authentic sample. (b) *The diacetoxyorthoester* (**13**) (1·2 g), m.p. 50–52°. ν_{max} 1770, 1219, 1197 (acetate); 1124, 1114, 1090, 1070, 1055, 1030, 1019 (CO) cm^{-1}. PMR, Me's at δ 0·75, 0·78, 0·84 (t, *J* 7Hz), 0·87, 1·22; acetate Me's 2·07, 2·12; C-17 protons as an AB system H_A 4·37, H_B 3·72 (J_{AB} 8Hz); CH(OAc)$_2$ 6·86. *M/e* 466 (M^+). (Found: C, 67·1; H, 9·3. $C_{26}H_{42}O_7$ requires C, 66·9; H, 9·1%). (ii) 60% ether/hexane – A mixture which on PLC (2x in 50% ether/hexane) gave 17-*acetoxy*-8-*labden*-13-*ol* (**14**) (0·6 g), distilled 125°/0·01 mm ν_{max} 3450 (OH); 1720, 1222 (acetate), 1199, 1166, 1140, 1119, 1040, 1016 (CO) cm^{-1}. PMR, Me's at δ 0·84, 0·89, 0·89 (t, *J* 7Hz), 0·99, 1·14; acetate Me 2·03; C-17 protons 4·57. (Found: C, 75·5; H, 10·9. $C_{22}H_{38}O_3$ requires C, 75·4; H, 10·9%).

Acid hydrolysis of the diacetoxyorthoester (**13**). **13** (100 mg) in MeOH (15 ml) was treated with HCl (5 ml, 10%) at room temp. overnight. Dilution and ether extraction gave *labdane*-8,13,17-*triol* (**6**), identical (m.m.p., IR, PMR) with an authentic sample.

Iodine/silver acetate on 8(17)-*labden*-13-*ol* (**1**). Iodine (6 g) and silver acetate (10 g) were added successively, in small portions, over a period of 2 h to a stirred solution of **1** (3 g) in dry benzene (150 ml). Filtration of the AgI formed, followed by solvent removal and chromatography (250 g alumina) gave: (i) 10% ether/hexane – 8,13-*Epoxy*-17-*iodolabdane* (**15**) (1·8 g), distilled 75°/0·02 mm, m.p. 46–47°. ν_{max} 1173, 1142, 1124, 1083, 1064, 1046, 1013 (CO) cm^{-1}. PMR, Me's at δ 0·79, 0·79, 0·85, 0·85 (t, *J* 7Hz), 1·39; C-17 as an AB system H_A 3·75, H_B 3·61 (long range coupled, J_{LR} 2Hz) (J_{AB} 11Hz). *M/e* 418 (M^+) (Found: C, 57·7; H, 8·6; I, 30·5. $C_{20}H_{35}IO$ requires C, 57·4; H, 8·4; I, 30·3%). (ii) 1% MeOH/ether – 17-*Acetoxy*-8-*labden*-13-*ol* (**14**). (0·5 g), identical (IR, PMR) with an authentic sample.

Hydrogenolysis of 8,13-*epoxy*-17-*iodolabdane* (**15**). **15** (140 mg) in MeOH (50 ml) was hydrogenolysised over 10% Pd/$BaCO_3$ (50 mg) for thirty days. Filtration and evaporation gave an oil (135 mg) which on PLC (½% ether-hexane) gave 8,13-*epoxylabdane* (**16**) (90 mg), identical with an authentic sample. ν_{max} 1145, 1116, 1078, 1043, 1000, 968, 956 (CO) cm^{-1}. PMR, Me's at δ 0·77, 0·80, 0·84 (t, *J* 7Hz), 0·85, 1·18, 1·27.

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