266. *The Chemistry of Gum Labdanum. Part IV.* The Structure of a New Diterpene Acid.*

By T. G. Halsall and M. Moyle.

A new diterpene acid isolated [1] from gum labdanum is 6-oxocativic acid (6-oxolabd-7-en-15-oic acid).

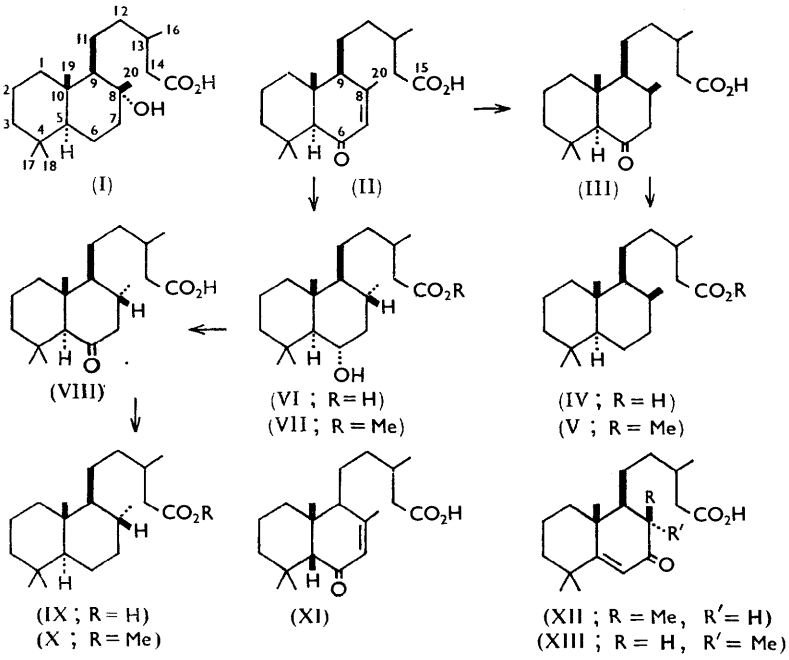
The acidic fraction [1] of gum labdanol contains labdanolic acid [2] (I) and a new diterpene acid, $C_{20}H_{32}O_3$, which has an αβ-unsaturated ketone grouping in it. This acid has now been shown to be 6-oxocativic acid (II).

The formula of the new acid, after allowance for one double bond and the two carbonyl groups, indicated that it was bicyclic. Its ultraviolet spectrum ($\lambda_{max.}$ 2390 Å; ε 11,750) suggested that there were two alkyl substituents on the double bond of the αβ-unsaturated ketone system and that the double bond was probably not exocyclic. In view of the occurrence of both labdanolic acid and the new keto-acid in gum labdanum a possible structure for the acid was (II). This is 6-oxocativic acid.[3]

* Part III, *J.*, 1957, 4401.

[1] Cocker, Halsall, and Bowers, *J.*, 1956, 4259.
[2] Cocker and Halsall, *J.*, 1956, 4262.
[3] Cf. Zeiss and Grant, *J. Amer. Chem. Soc.*, 1957, **79**, 1201.

The keto-group of the new acid proved to be exceedingly inert. No carbonyl derivatives of the acid were obtained and an attempt to reduce the keto-group with lithium aluminium hydride led to the reduction of the double bond instead. On catalytic hydrogenation of the acid only one mol. of hydrogen was taken up and a saturated keto-acid (III) was obtained. This confirms the absence of an isolated double bond. The keto-group of the saturated acid was also exceedingly unreactive but by Wolff–Kishner

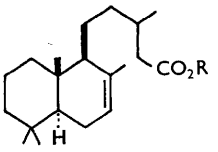


reduction under very vigorous conditions dihydrocativic acid [3] (IV), characterised as its methyl ester, was obtained, the yield being about 60% after allowance for recovered keto-acid. This shows that the carbon skeleton of the new acid is the same as that of labdanolic acid and supports structure (II). The other possible structures for the acid which were considered were (XI), (XII), and (XIII). The last two are not consistent with the position of the peak in the ultraviolet spectrum—the calculated position would be 2420—2440 Å—or, what is more important, with the inertness of the carbonyl group in the acid and its reduction products. Further, structure (XIII) can be excluded as it would require inversion at $C_{(8)}$ during conversion into dihydrocativic acid. Structure (XI) requires inversion at $C_{(5)}$ at some stage in the conversion of the acid into dihydrocativic acid. Arguments given below, concerning optical rotatory dispersion data, lead to the exclusion of structure (XI). In the subsequent discussion the chemistry of the acid, 6-oxocativic acid [cativic acid is (XIV; R = H)],[3] is examined in terms of structure (II).

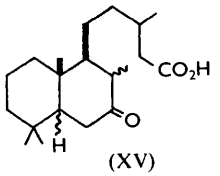
The hydrogenation product from 6-oxocativic acid is (III), with the 20-methyl group axial, in view of conversion of the acid into dihydrocativic acid (IV). Structure (III) has three axial methyl groups situated 1 : 3 with respect to the carbonyl group and these along with the equatorial 18-methyl group will cause intense steric hindrance about the carbonyl group. In the corresponding 7-oxo-compound (XV) the keto-group would be much less hindered.

Reduction of the double bond of 6-oxocativic acid with lithium in ammonia gave the saturated hydroxy-acid (VI) characterised as its methyl ester (VII). Oxidation of this followed by hydrolysis gave the acid (VIII) which differed, as would be expected, from

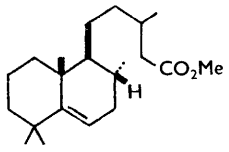
that obtained on hydrogenation of 6-oxocativic acid, the 20-methyl group being in the more stable equatorial position. Wolff–Kishner reduction of the acid (VIII) gave 8β(H)-labdan-15-oic acid (IX), m. p. 86—88°, $[\alpha]_D$ −6°. This acid was also obtained by dehydration of methyl 6α-hydroxy-8β(H)-labdan-15-oate (VII) to methyl 8β(H)-labd-5-en-15-oate (XVI) followed by hydrogenation and hydrolysis.



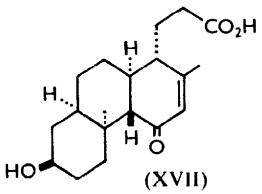
(XIV)



(XV)



(XVI)



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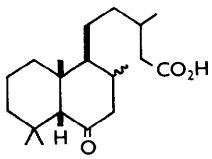
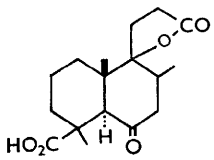


(XVIII)



(XIX)

Hydrogenation of methyl labd-8(20)-en-15-oate has already been shown [2] to give a mixture of methyl labdan-15-oate (V) and the 8β(H)-isomer (X). The former was obtained crystalline from the mixture and the residues were hydrolysed to an acid characterised as its cyclohexylamine salt, $[\alpha]_D$ +14°. Further investigation of this acid and its salt has shown that it was still impure and on further purification an acid, m. p. 82—84°, $[\alpha]_D$ +1°, was obtained. This is obviously mainly 8β(H)-labdan-15-oic acid still contaminated with a little of the 8α(H)-isomer. Persistent efforts to remove the impurity were, however, unsuccessful.

The optical rotatory dispersion curve * of 6-oxocativic acid (II) has a positive multiple Cotton effect {R.D. in dioxan (*c* 0·1): $[M]^{25} \times 10^{-2}$, (7000 Å) + 0·64°, (5890 Å) + 1·15°, (3725 Å) + 27·8°, (3650 Å) + 22·1°, (3600 Å) + 25·1°, (2925 Å) − 60·5°}. Compound (XVII) with an αβ-unsaturated ketone grouping similar to that found in 6-oxocativic acid but with antipodal stereochemistry shows [4] a similar but antipodal multiple Cotton effect with troughs at 3700 and 3590 Å and a peak at 3075 Å.

The optical rotatory dispersion curves of the two saturated keto-acids (III) and (VIII) show single positive Cotton effects † {(III) R.D. in methanol (*c* 0·1): $[M] \times 10^{-2}$, (3100 Å) + 29·0°, (2800 Å) — 32·5°, (VIII) R.D. in methanol (*c* 0·04): $[M]$ (3200 Å) + 21·1°, (2700 Å) — 31·1°}. Application of the " octant rule " [5] to both these ketones predicts positive Cotton effects. For the corresponding keto-acids (*e.g.*, XVIII) with a *cis*-ring fusion the " octant rule " [5] predicts that the Cotton effect would be negative for both conformations of each acid. The rotatory dispersion curve in methanol of the similar ketone [6] (XIX) derived from marrubiin also shows [4] a single positive Cotton effect.

An attempt was made to prepare methyl 6-oxocativate from methyl cativate (XIV; R = Me) by oxidation at position 6 with selenium dioxide. However, infrared- and ultraviolet-spectroscopic examination of the two products indicated that they were the diene (XX) and the αβ-unsaturated aldehyde (XXI). Oxidation of methyl cativate with potassium dichromate, followed by hydrolysis of the product, gave the αβ-unsaturated

* This curve was determined by Professor C. Djerassi.

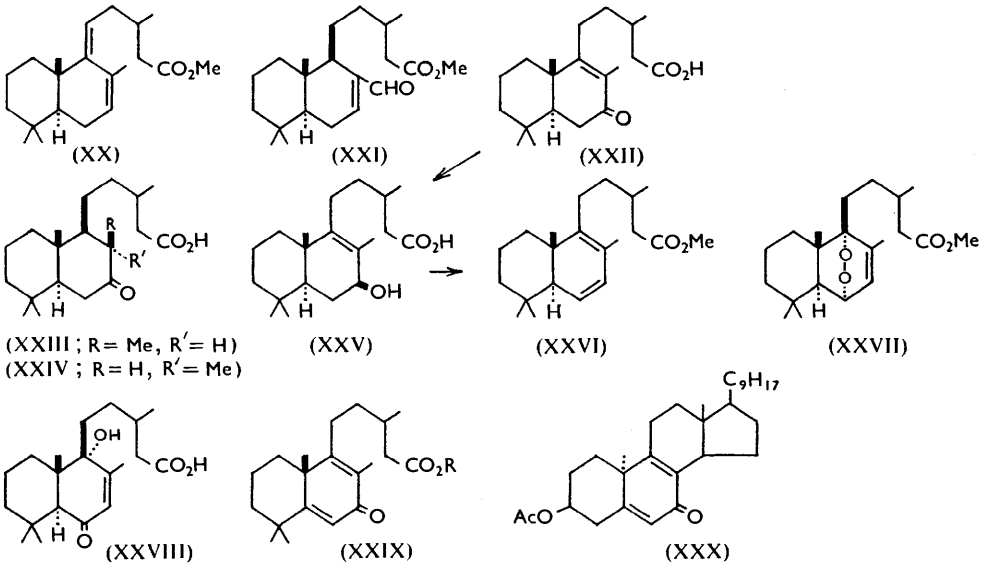
† These curves were determined by Dr. W. Klyne.

[4] Professor C. Djerassi, personal communication.

[5] Moffitt, Moscovitz, Woodward, Djerassi, and Klyne, unpublished work; cf. Djerassi, Cais, and Mitscher, *J. Amer. Chem. Soc.*, 1959, **81**, 2391.

[6] Cocker, Cross, Duff, Edward, and Holley, *J.*, 1953, 2540; Burn and Rigby, *J.*, 1957, 2964.

keto-acid (XXII). This was also obtained by oxidation of methyl labd-8- and -8(20)-en-15-oate. Hydrogenation of the acid (XXII) gave 7-oxolabdan-15-oic acid (XXIII) with the 20-methyl group axial. On treatment with alkali the acid underwent isomerisation at position 8 to give 7-oxo-8β(H)-labdan-15-oic acid (XXIV) with the more stable equatorial methyl group.



Reduction of the keto-acid (XXII) with sodium borohydride gave the 7β-hydroxy-acid (XXV), dehydration of which with methanolic sulphuric acid gave the diene (XXVI). An attempt was made to form the epidioxide (XXVII) from this diene by photo-oxidation with oxygen in the presence of eosin. The epidioxide should rearrange with alkali to 9-hydroxy-6-oxocativic acid (XXVIII) which might be reduced with zinc and acetic acid to 6-oxocativic acid.[7] The only compound isolated, however, was, not the epidioxide, but the dienone (XXIX; R = Me) characterised as the acid (XXIX; R = H) ($\lambda_{max.}$ 2470 Å; ε 16,400) which was also obtained by oxidation of methyl 7-oxolabd-8-en-15-oate with selenium dioxide followed by hydrolysis. Formation of the dienone is not unexpected. Photo-oxidation of lumisteryl acetate yields [8] the dieneone (XXX) ($\lambda_{max.}$ 2460 Å; ε 11,800) as well as the β-epidioxide.

Experimental

Rotations refer to solutions in $CHCl_3$ at room temperature. M. p.s were determined on a Kofler block and are corrected. The alumina used for chromatography (unless otherwise stated) was alumina of activity I—II which had been deactivated with 5% of 10% aqueous acetic acid. Light petroleum refers to the fraction with b. p. 60—80°. Unless otherwise stated, ultraviolet spectra were determined on ethanol solutions and infrared spectra on natural films.

Isolation of 6-*Oxocativic* (6-*Oxolabd*-7-*en*-15-*oic*) *Acid* (II).—The mixed methyl esters obtained by methylation of the acidic fraction of gum labdanum were separated by the chromatographic procedures described by Cocker, Halsall, and Bowers [1] to give a fraction consisting of a pale yellow oil with $\lambda_{max.}$ 2385 Å (ε ~10,000). This fraction was dissolved in a small volume of methanol and cooled to −60°. The crystals which formed were separated by rapid filtration. This procedure was repeated twice, to give *methyl* 6-*oxocativate* (6-*oxolabd*-7-*en*-15-*oate*) as needles, m. p. 45—46°, $[\alpha]_D$ +13° (*c* 1·95) (Found: C, 75·35; H, 10·1. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·25%), $\lambda_{max.}$ 2390 Å (ε 11,750), $\nu_{max.}$ 1738 and 1668 cm.$^{-1}$.

[7] Cf. Halsall, Rodewald, and Willis, *J.*, 1959, 2798.
[8] Bladon, *J.*, 1955, 2176.

The crystalline ester (5·0 g.), methanol (60 c.c.), and 11% potassium hydroxide solution (45 c.c.) were heated under reflux under nitrogen for 1·5 hr. The product was isolated by ether-extraction after acidification, and crystallised several times from benzene–light petroleum and then aqueous methanol to give 6-oxocativic (6-oxolabd-7-en-15-oic) acid as prisms (3·65 g.), m. p. 114—115°, $[\alpha]_D$ +13° (*c* 1·98) (Found: C, 75·1; H, 9·9. Calc. for $C_{20}H_{32}O_3$: C, 74·95; H, 10·05%), $\lambda_{max.}$ 2390 Å (ε 11,700), $\nu_{max.}$ (in CS_2) 1708 and 1668 cm.$^{-1}$. The *cyclohexylamine salt* was crystallised several times from ethyl acetate to give needles, $[\alpha]_D$ +11° (*c* 1·12) (Found: C, 74·25; H, 10·65. $C_{26}H_{45}O_3N$ requires C, 74·4; H, 10·8%), $\lambda_{max.}$ 2390 Å (ε 11,000).

Action of Lithium Aluminium Hydride on 6-Oxocativic Acid.—Lithium aluminium hydride was added at 0° to a stirred solution of 6-oxocativic acid (100 mg.) in tetrahydrofuran (20 c.c.). After being stirred at 0° for 3½ hr., the mixture was decomposed with ethyl acetate and then with sulphuric acid, and the product was isolated with ether. The infrared spectrum of the product indicated that the double bond, but not the carbonyl group, of 6-oxocativic acid had been reduced, there being a strong band at 1710 cm.$^{-1}$ but no band at 1670 cm.$^{-1}$.

Methyl 6-oxocativate (100 mg.) in ether (25 c.c.) was treated at 0° with lithium aluminium hydride (150 mg.). The mixture was heated under reflux for 1½ hr., then kept overnight at 20°. It was decomposed with ethyl acetate, and then with dilute sulphuric acid, and the product was isolated with ether. Its infrared spectrum indicated complete reduction of the ester group (no band at 1740 cm.$^{-1}$) and that the double bond of the αβ-unsaturated ketone group had been reduced rather than the carbonyl group (strong band at 1710 cm.$^{-1}$; very weak band at 1670 cm.$^{-1}$).

Hydrogenation of 6-Oxocativic Acid.—The acid (1·8 g.) in ethyl acetate (75 c.c.) was hydrogenated at atmospheric pressure in the presence of Adams catalyst (250 mg.). One mole of hydrogen was taken up during 15 min. After removal of the catalyst, evaporation under reduced pressure gave a solid which crystallised from aqueous methanol to give *6-oxolabdan-15-oic acid* (III) as needles, m. p. 66—68°, $[\alpha]_D$ +30° (*c* 1·73) (Found: C, 74·55; H, 10·55. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·65%). The *cyclohexylamine salt* (needles from ethyl acetate) had $[\alpha]_D$ +29° (*c* 1·23) (Found: C, 74·15; H, 10·95; N, 3·4. $C_{26}H_{47}O_3N$ requires C, 74·05; H, 11·25; N, 3·3%).

The acid with ethereal diazomethane gave a product which was adsorbed from light petroleum on alumina. Elution with benzene–light petroleum (1 : 2) gave *methyl 6-oxolabdan-15-oate*, b. p. 160° (bath)/0·5 mm., n_D^{16} 1·4940, $[\alpha]_D$ +28° (*c* 1·46) (Found: C, 74·8; H, 10·8. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%), $\nu_{max.}$ 1738 and 1712 cm.$^{-1}$ (no band at 3400 or 1668 cm.$^{-1}$).

Wolff–Kishner Reduction of 6-Oxolabdan-15-oic Acid.—The acid (750 mg.), diethylene glycol (25 c.c.), hydrazine (3·0 c.c.), and potassium hydroxide (2·0 g.) were heated under reflux (internal temperature 155—160°) for 5 hr. [The hydrazine was prepared as follows: 100% hydrazine hydrate (20 c.c.) and potassium hydroxide were heated under reflux for 3 hr. and then distilled: repetition of this process with the distillate gave a product, b. p. 113°/760 mm., which was used for the reduction.] Excess of hydrazine was distilled off and the mixture heated at 225° for 5 hr. The crude product was isolated with ether; with ethereal diazomethane it gave a product which was adsorbed from light petroleum on alumina (60 g.; 3% deactivated). Elution with light petroleum (250 c.c.) gave an oil (270 mg.) [fraction (i)]. Further elution with light petroleum gave nothing. Elution with light petroleum–benzene (2 : 1; 350 c.c.) gave an oil (305 mg.) [fraction (ii)].

The infrared spectrum of fraction (i) indicated that it was non-ketonic; that of fraction (ii) ($\nu_{max.}$ 1738 and 1715 cm.$^{-1}$) indicated that it was methyl 6-oxolabdan-15-oate. Fraction (i) became semi-solid {$[\alpha]_D$ +16° (*c* 2·25)}. It was crystallised several times from methanol (cooling to −60°) to give methyl labdan-15-oate (dihydrocativate), m. p. and mixed m. p. 43—44°, $[\alpha]_D$ +24° (*c* 1·91) (Found: C, 78·15; H, 11·9. Calc. for $C_{21}H_{38}O_2$: C, 78·2; H, 11·9%). The yield was 60% after allowance for recovered starting material. The infrared spectrum of the methyl ester was identical with that of methyl dihydrocativate.

Lithium–Ammonia Reduction of 6-Oxocativic Acid.—The acid (1·30 g.) and ether (75 c.c.) were added separately during 20 min. to a stirred solution of lithium (250 mg.) in ammonia (200 c.c.). After a further 20 minutes' stirring, ethanol was added dropwise to discharge the blue colour. After evaporation of the ammonia, the product was isolated with ether and treated with diazomethane. The methylated product was adsorbed from light petroleum on alumina (60 g.; 3% deactivated). Elution with light petroleum–benzene (1 : 1) gave *methyl 6α-hydroxy-8β(H)-labdan-15-oate* (VII) as an oil (1·20 g.), n_D^{18} 1·4985, $[\alpha]_D$ +20° (*c* 2·14) (Found:

C, 74·4; H, 11·4. $C_{21}H_{38}O_3$ requires C, 74·5; H, 11·3%), $\nu_{max.}$ 3500 (br.) cm.$^{-1}$ (OH) (no band due to αβ-unsaturated or saturated ketone).

Hydrolysis of the ester gave the acid as a gum, $[\alpha]_D$ +20° (*c* 2·12). The *2-amino-2-methylpropan-1-ol salt* was crystallised from ethyl acetate to constant rotation, giving needles, $[\alpha]_D$ +18° (*c* 1·20 in EtOH) (Found: C, 69·5; H, 11·25. $C_{24}H_{47}O_4N$ requires C, 69·7; H, 11·45%).

6-*Oxo*-8β(H)-*labdan*-15-*oic Acid* (VIII).—(*a*) The above hydroxy-ester (1·00 g.) was oxidised in acetone with 8N-chromic acid according to the method of Bowers *et al.*[9] and the product was adsorbed from light petroleum on alumina (60 g.; 3% deactivated). Elution with light petroleum–benzene (2 : 1) gave several identical fractions (940 mg.). The product crystallised readily in the absence of solvent but proved very soluble. The total product in methanol (5 c.c.) was cooled to −60° and the resulting crystals were rapidly filtered off. This process was repeated twice, to give *methyl* 6-*oxo*-8β(H)-*labdan*-15-*oate* as needles, m. p. 64—65°, $[\alpha]_D$ +29° (*c* 2·26) (Found: C, 74·75; H, 11·05. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%), $\nu_{max.}$ (melt) 1738 and 1712 cm.$^{-1}$.

Hydrolysis of the ester with 12% methanolic potassium hydroxide gave 6-*oxo*-8β(H)-*labdan*-15-*oic acid* as needles (from aqueous methanol), m. p. 116—118°, $[\alpha]_D$ +31° (*c* 2·02) (Found: C, 74·5; H, 10·75. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·65%). The *cyclohexylamine salt* was crystallised to constant rotation from ethyl acetate to give needles, $[\alpha]_D$ +28° (*c* 2·12) (Found: C, 74·2; H, 11·05. $C_{26}H_{47}O_3N$ requires C, 74·05; H, 11·25%).

(*b*) In a subsequent experiment the hydroxy-ester was hydrolysed and then oxidised with 8N-chromic acid–acetone to give 6-oxo-8β(H)-labdan-15-oic acid as needles (from aqueous methanol), m. p. 116—118°.

(*c*) The lithium–ammonia reduction of 6-oxocativic acid was repeated, but the excess of lithium was decomposed with ammonium chloride. The resulting acid was methylated, methyl 6-oxo-8β(H)-labdan-15-oate, m. p. 64—65°, being obtained.

Wolff–Kishner Reduction of 6-*Oxo*-8β(H)-*labdan*-15-*oic Acid*.—The acid (500 mg.), 100% hydrazine hydrate (2·0 c.c.), redistilled diethylene glycol (20 c.c.), and potassium hydroxide (1·5 g.) were heated under reflux for 3 hr. Excess of hydrazine was then distilled off until the internal temperature reached 220°. The mixture was then heated under reflux for 5 hr. at 225°. The product was isolated with ether and methylated with diazomethane, to give a product which was adsorbed from light petroleum on alumina (35 g.; 3% deactivated). Elution with light petroleum (150 c.c.) gave *methyl* 8β(H)-*labdan*-15-*oate* (X) (400 mg.) as a mobile oil, n_D^{14} 1·4890, $[\alpha]_D$ −6° (*c* 1·08) (Found: C, 78·5; H, 11·7. $C_{21}H_{38}O_2$ requires C, 78·2; H, 11·9%). It had no infrared band indicative of a ketone group.

The ester was hydrolysed and converted into its *cyclohexylamine salt*, needles (from ethyl acetate), $[\alpha]_D$ −4° (*c* 2·02) (Found: C, 76·5; H, 11·8. $C_{26}H_{49}O_2N$ requires C, 76·6; H, 12·1%), and *2-amino-2-methylpropan-1-ol salt*, needles (from ethyl acetate), $[\alpha]_D$ −4° (*c* 1·93) (Found: C, 72·55; H, 11·8. $C_{24}H_{47}O_3N$ requires C, 72·5; H, 11·9%).

Regeneration of the acid from the salts, followed by crystallisation from aqueous methanol, gave 8β(H)-*labdan*-15-*oic acid* (IX) as needles, m. p. 86—88°, $[\alpha]_D$ −6° (*c* 2·10) (Found: C, 77·65; H, 11·85. $C_{20}H_{36}O_2$ requires C, 77·85; H, 11·75%).

In a second experiment with 400 mg. of keto-acid the reduction was carried out by adding the potassium hydroxide after formation of the hydrazone. Working up as described above gave methyl 8β(H)-labdan-15-oate as an oil (320 mg.), n_D^{14} 1·4890, $[\alpha]_D$ −6° (*c* 2·05). Hydrolysis gave the acid characterised as its cyclohexylamine salt {needles, $[\alpha]_D$ −4° (*c* 2·04), from ethyl acetate}.

Dehydration of Methyl 6α-*Hydroxy*-8β(H)-*labdan*-15-*oate* (VII) *with Thionyl Chloride*.—The hydroxy-ester (250 mg.), thionyl chloride (2·0 c.c.), and benzene (30 c.c.) were heated under reflux for 3 hr. Excess of thionyl chloride was removed under reduced pressure. An ethereal solution of the residue was then washed thoroughly with sodium hydrogen carbonate solution. The product was adsorbed from light petroleum on alumina (40 g.; 3% deactivated). Elution with light petroleum gave three identical oily fractions (total 210 mg.). These were *methyl* 8β(H)-*labd*-5-*en*-15-*oate*, n_D^{19} 1·4930, $[\alpha]_D$ −59° (*c* 1·89) (Found: C, 79·25; H, 11·25. $C_{21}H_{36}O_2$ requires C, 78·7; H, 11·3%), $\nu_{max.}$ 795 cm.$^{-1}$ (–CH=C). It gave a positive tetranitromethane test. Hydrolysis gave the acid as a gum, characterised as its *2-amino-2-methylpropan-1-ol salt* (needles from ethyl acetate), $[\alpha]_D$ −54° (*c* 1·08) (Found: C, 72·6; H, 11·35. $C_{24}H_{45}O_3N$ requires C, 72·85; H, 11·45%).

[9] Bowers, Halsall, Jones, and Lemin, *J.*, 1953, 2555.

Hydrogenation of Methyl 8β(H)-*Labd-5-en*-15-*oate*.—The ester was hydrogenated in acetic acid with Adams platinum catalyst, to give methyl 8β(H)-labdan-15-oate as an oil, n_D^{19} 1·4865, $[\alpha]_D$ −6° (*c* 1·94). Hydrolysis gave the free acid whose cyclohexylamine salt (needles from ethyl acetate) had $[\alpha]_D$ −4° (*c* 2·02).

Attempted Preparation of Methyl 8β(H)-*Labdan*-15-*oate from Labdanolic Acid*.—The cyclohexylamine salt ($[\alpha]_D$ +14°) obtained by Cocker and Halsall [2] from the hydrolysis product of the methyl esters remaining after removal of methyl labdan-15-oate from the product of the hydrogenation of methyl labd-8(20)-en-15-oate was decomposed with ethereal hydrogen chloride. The free acid was methylated with diazomethane, and the product crystallised from methanol, further methyl labdan-15-oate, m. p. and mixed m. p. 43—44°, $[\alpha]_D$ +25° (*c* 2·12), being obtained. The residue from the mother-liquors had $[\alpha]_D$ +8° (*c* 2·30). A methanolic solution of the residue was cooled to −60° to give a further crop of methyl labdan-15-oate and a residue with $[\alpha]_D$ +5° (*c* 2·12).

The mixed esters (1700 mg.) with $[\alpha]_D$ +8° to +5° were hydrolysed and the resulting acid was converted into its cyclohexylamine salt. Fractional crystallisation of this from chloroform gave three fractions: (i) 1200 mg., $[\alpha]_D$ +13° (*c* 1·30); (ii) 550 mg., $[\alpha]_D$ +8° (*c* 2·13); and (iii) 330 mg., $[\alpha]_D$ +4° (*c* 2·10). Similar results were obtained on crystallisation from ethyl acetate and of the 2-amino-2-methylpropan-1-ol salt from chloroform or ethyl acetate.

The cyclohexylamine salt, $[\alpha]_D$ +4°, was crystallised several times from light petroleum (b. p. 60—80°) to give needles, $[\alpha]_D$ +10°. The combined mother-liquors were evaporated to dryness, and the acid was liberated and recrystallised from aqueous methanol to give needles, m. p. 82—84°, $[\alpha]_D$ +1° (*c* 2·10) (Found: C, 77·6; H, 11·8. Calc. for $C_{20}H_{36}O_2$: C, 77·85; H, 11·75%)

Reduction of Methyl Labdan-15-*oate with Lithium Aluminium Hydride*.—The ester (500 mg.) and lithium aluminium hydride (100 mg.) in ether (25 c.c.) were kept at 20° for 12 hr. Working up in the usual manner gave *labdan*-15-*ol* (needles from light petroleum), m. p. 47—48°, $[\alpha]_D$ +32° (*c* 1·98) (Found: C, 81·9; H, 13·05. $C_{20}H_{38}O$ requires C, 81·55; H, 13·0%).

Oxidation of Methyl Cativate with Selenium Dioxide.—Methyl labd-7-en-15-oate (cativate) (300 mg.), selenium dioxide (400 mg.), and acetic acid (15 c.c.) were heated at 100° for 2 hr. After addition of water, ether-extraction afforded a product which was adsorbed from light petroleum on alumina (25 g.; 3% deactivated). Elution with light petroleum gave first mainly selenium and then an oil, $\lambda_{max.}$ 2370 Å (ε 8000), $\nu_{max.}$ 1738 and 1600 cm.$^{-1}$, indicative of methyl labd-7,9(11)-dien-15-oate. Elution with benzene afforded an oil, $\nu_{max.}$ 2710, 1738, and 1696 cm.$^{-1}$, indicative of the unsaturated aldehyde, methyl 20-oxolabd-7-en-15-oate.

Methyl 7-*Oxolabd*-8-*en*-15-*oate*.—Methyl labd-8-en-15-oate (10·7 g.), potassium dichromate (12·5 g.), and acetic acid (130 c.c.) were heated under reflux for 6 hr. After most of the acetic acid had been removed under reduced pressure, the mixture was diluted with water. The crude product was isolated by ether-extraction and was heated under reflux for 1½ hr. with methanol (100 c.c.) and 2N-potassium hydroxide (100 c.c.) under nitrogen. The resulting acid was isolated with ether and crystallised several times from benzene–light petroleum to give 7-*oxolabd*-8-*en*-15-*oic acid* (XXII) as needles (6·80 g.), m. p. 154—156° (softening ~151°), unchanged on further crystallisation from aqueous methanol, $[\alpha]_D$ +46° (*c* 1·98) (Found: C, 74·95; H, 10·1. $C_{20}H_{32}O_3$ requires C, 74·95; H, 10·05%), $\lambda_{max.}$ 2495 Å (ε 13,700), $\nu_{max.}$ 1720—1710 (br.) (CO_2H), 1668 (αβ-unsaturated C=O), and 1603 cm.$^{-1}$.

In a subsequent experiment the crude oxo-ester was adsorbed from light petroleum on alumina (5% deactivated). Elution with light petroleum–benzene (1 : 2) afforded *methyl* 7-*oxolabd*-8-*en*-15-*oate* as an oil, n_D^{20} 1·5100, $[\alpha]_D$ +43° (*c* 2·30) (Found: C, 75·6; H, 10·0. $C_{21}H_{34}O_3$ requires C, 75·4; H, 10·25%), $\nu_{max.}$ 1738, 1668, and 1603 cm.$^{-1}$. The methyl ester gave an oxime which crystallised from aqueous methanol as needles, m. p. 123—124°, $\lambda_{max.}$ 2460 Å (ε 12,000), $\nu_{max.}$ (in $CHCl_3$) 1738 and 1620 cm.$^{-1}$ [lit.,[3] m. p. 121·5—122°; $\lambda_{max.}$ 2460 Å (ε 12,500), $\nu_{max.}$ 1735 and 1620 cm.$^{-1}$].

Oxidation of Methyl Cativate (XIV; R = Me) *with Potassium Dichromate*.—Methyl labd-7-en-15-oate (1·90 g.), potassium dichromate (2·50 g.), and acetic acid (25 c.c.) were heated under reflux for 3 hr. Ethanol was added to destroy excess of oxidant, the mixture was diluted with water, and the product isolated with ether. The product was adsorbed from light petroleum on alumina (80 g.; 3% deactivated). Elution with light petroleum (250 c.c.) gave methyl cativate (250 mg.). Further elution with light petroleum–benzene (2 : 1; 500 c.c.) gave methyl 7-oxolabd-8-en-15-oate as a viscous oil (550 mg.), $\lambda_{max.}$ 2490 Å (ε 13,000), identical with the

methyl oxo-ester from methyl labd-8-en-15-oate. Hydrolysis with 2N-methanolic potassium hydroxide gave the corresponding acid, m. p. 154—156° (softening ~151°).

Oxidation of Methyl Labd-8(20)-en-15-oate with Potassium Dichromate.—Methyl labd-8(20)-en-15-oate (500 mg.), potassium dichromate (750 mg.) and acetic acid (12 c.c.) were heated at 100° for 5 hr. Ethanol (2 c.c.) was added to decompose excess of oxidant. The product was isolated with ether and adsorbed from light petroleum on alumina (40 g.; 3% deactivated). Elution with light petroleum (200 c.c.) gave starting material (290 mg.). Further elution with light petroleum–benzene (2 : 1; 250 c.c.) gave methyl 7-oxolabd-8-en-15-oate, $\lambda_{max.}$ 2490 Å (ε 13,000), as described above, hydrolysis of which gave the acid (needles from light petroleum–benzene), m. p. 154—156° (softening ~151°).

Hydrogenation of 7-Oxolabd-8-en-15-oic Acid (XXII).—7-Oxolabd-8-en-15-oic acid (1·280 g.) in ethanol (50 c.c.) was added to pre-reduced 5% palladium–charcoal (250 mg.) in ethanol (25 c.c.). The uptake of hydrogen (1·0 mol.) was complete after approx. 5 min. The product was isolated in the usual manner and crystallised from aqueous methanol to give *7-oxolabd-15-oic acid* (XXIII) as prisms, m. p. 71—73°, $[\alpha]_D$ −25° (*c* 2·08) (Found: C, 74·9; H, 10·6. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·65%).

The acid with ethereal diazomethane gave a product which was adsorbed from light petroleum on alumina. Elution with light petroleum–benzene (3 : 1) and crystallisation from aqueous methanol gave *methyl 7-oxolabdan-15-oate* as needles, m. p. 54—55°, $[\alpha]_D$ −23° (*c* 2·16) (Found: C, 74·9; H, 10·75. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%), $\nu_{max.}$ in Nujol 1738 and 1708 cm.$^{-1}$ (no band indicative of hydroxyl group or αβ-unsaturated ketone).

Methyl 7-oxolabdan-15-oate (750 mg.) was heated under reflux for 3 hr. in methanol (12 c.c.) with 2N-potassium hydroxide (12 c.c.). The product was isolated with ether and crystallised several times from light petroleum to give *7-oxo-8β(H)-labdan-15-oic acid* (XXIV) as needles, m. p. 105—107°, $[\alpha]_D$ −26° (*c* 2·02) (Found: C, 74·3; H, 10·45. $C_{20}H_{34}O_3$ requires C, 74·5; H, 10·65%).

7-Hydroxylabd-8-en-15-oic Acid.—7-Oxolabd-8-en-15-oic acid (3·5 g.), sodium borohydride (recrystallised from isopropylamine) (750 mg.) and ethanol (75 c.c.) were heated under reflux for 8 hr. Sodium borohydride (500 mg.) was then added and refluxing continued for a further 12 hr. The resulting 7-hydroxylabd-8-en-15-oic acid was isolated with ether but did not crystallise or form a crystalline salt with cyclohexylamine or 2-amino-2-methylpropan-1-ol. With ethereal diazomethane it gave, after distillation, *methyl 7β-hydroxylabd-8-en-15-oate*, b. p. 225° (bath)/0·5 mm., $\nu_{max.}$ 3400 and 1738 cm.$^{-1}$ (no band at 1670 cm.$^{-1}$), no ultraviolet absorption above 2300 Å (end absorption characteristic of a tetrasubstituted double bond: ε_{2100} 5600; ε_{2150} 3750; ε_{2200} 1800) (Found: C, 75·3; H, 10·6. $C_{21}H_{36}O_3$ requires C, 74·95; H, 10·8%).

Methyl Labda-6,8-dien-15-oate.—7β-Hydroxylabd-8-en-15-oic acid (3·5 g.), methanol (70 c.c.), and sulphuric acid (5 c.c.) were heated under reflux under nitrogen for 3 hr. The product was isolated with ether and adsorbed from light petroleum on deactivated alumina (150 g.). Elution with light petroleum (350 c.c.) and fractionation gave only *methyl labda-6,8-dien-15-oate*, b. p. 139—141°/0·1 mm., n_D^{17} 1·5050, $[\alpha]_D$ −93° (*c* 2·3), $\lambda_{max.}$ 2710 Å (ε 4600), $\nu_{max.}$ 1738 cm.$^{-1}$ (Found: C, 79·5; H, 10·85. $C_{21}H_{34}O_2$ requires C, 79·2; H, 10·75%).

Oxidation of Methyl Labda-6,8-dien-15-oate.—Sodium (75 mg.) was dissolved in dry ethanol (100 c.c.). Eosin (350 mg.) and the diene ester (3·50 g.) in ethanol (25 c.c.) were added. Oxygen was slowly bubbled through the mixture which was irradiated by a 500 w lamp, the heat from the lamp being sufficient to cause refluxing. After 12 hr. the solvent was removed under reduced pressure and the residue was co-distilled with benzene (2 × 50 c.c.). Extraction of the residue with light petroleum (3 × 50 c.c.) gave a clear oil (3·3 g.), $\lambda_{max.}$ 2460 Å (ε 6100 on *M* 350), $\nu_{max.}$ 3450, 1738, 1658, 1625, and 1603 cm.$^{-1}$. The oil was adsorbed from light petroleum on deactivated alumina (160 g.). Elution with the solvents indicated gave the following fractions: (i) light petroleum (300 c.c.), 910 mg.; (ii) benzene–light petroleum (1 : 4; 300 c.c.), 395 mg.; (iii) benzene–light petroleum (2 : 3, 300 c.c.), 485 mg.; (iv) benzene–light petroleum (3 : 2; 300 c.c.), 470 mg.; (v) benzene (300 c.c.), 315 mg.; (vi) benzene (300 c.c.); 270 mg.; (vii) ether (300 c.c.), 315 mg. Fractions (iv), (v), and (vi) had $\lambda_{max.}$ 2470 Å (ε 10,750, 14,200, and 13,900).

Fractions (v) and (vi) were combined and heated under reflux under nitrogen with methanol (5 c.c.), water (5 c.c.), and potassium hydroxide (1·5 g.). The resulting acid was crystallised several times from light petroleum–benzene, to give needles, m. p. 142—144° (softening at 138°). Three further recrystallisations from aqueous methanol gave *7-oxolabda-5,8-dien-15-oic acid*

(XXIX; R = H) as needles, m. p. 143—145° (softening ~139°) [undepressed on admixture with the acid prepared by selenium dioxide oxidation of methyl 7-oxolabd-8-en-15-oate (see below)], $[\alpha]_D$ −40° (*c* 2·08), $\lambda_{max.}$ 2470 Å (ε 16,400) (Found: C, 75·3; H, 9·4. $C_{20}H_{30}O_3$ requires C, 75·45; H, 9·5%).

The oily *methyl ester* had $[\alpha]_D$ −40° (*c* 2·12), $\nu_{max.}$ 1738, 1658, 1625, and 1605 cm.$^{-1}$ (Found: C, 75·7; H, 9·8. $C_{21}H_{32}O_3$ requires C, 75·85; H, 9·7%).

Irradiation of the diene ester (1·0 g.) in ethanol (50 c.c.) containing eosin (100 mg.) in the presence of oxygen but in the absence of sodium for 12 hr. at room temperature gave the dienone again in 10% yield.

Oxidation of Methyl 7-Oxolabd-8-en-15-oate by Selenium Dioxide.—The methyl ester (920 mg.) in t-butyl alcohol (25 c.c.) and acetic acid (0·4 c.c.) was heated under reflux under nitrogen. Selenium dioxide (600 mg.) was added and refluxing continued for 16 hr. More selenium dioxide (400 mg.) was then added and refluxing continued for a further 12 hr. The solvents were removed under reduced pressure and the residue was extracted with light petroleum. The light petroleum soluble fraction was heated under reflux for 1 hr. with freshly precipitated silver (2·0 g.) and benzene (30 c.c.). The benzene solution was separated from the silver, washed with potassium hydrogen carbonate solution, water, ammonium sulphide solution, ammonia, water, hydrochloric acid, and water, and then dried. The solvent was removed and the residue adsorbed from light petroleum on deactivated alumina (75 g.). Elution with light petroleum–benzene (1 : 1) gave several identical fractions (810 mg. total), with $\lambda_{max.}$ 2470 Å (ε 15,000), $\nu_{max.}$ 1738, 1660, 1625, and 1605 cm.$^{-1}$.

These fractions were hydrolysed under nitrogen with methanolic potassium hydroxide. The resulting acid crystallised from benzene–light petroleum to give 7-oxolabda-5,8-dien-15-oic acid as needles (670 mg.), m. p. and mixed m. p. 143—145° (softening ~140°).

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