860. *The Chemistry of Extractives from Hardwoods. Part XXVII.* The Structure of Terminolic Acid.*

By F. E. King and T. J. King.

Terminolic acid, $C_{30}H_{48}O_6$, a tetrahydroxy-triterpene of the oleanolic acid series, has been conclusively related to arjunolic acid [2 : 3 : 23(or 24)-trihydroxyolean-12-en-28-oic acid] through the formation of methyl arjunolate on forced Wolff–Kishner reduction of methyl terminonate, a monoketonic oxidation product of methyl terminolate.

The position of the hydroxyl group thus eliminated was inferred from the acid-catalysed dehydration of methyl terminonate to a cyclic enol ether, a reaction attributed to the condensation of the carbonyl and the 23(or 24)-hydroxyl group. From further data which indicate a relationship to sumaresinolic acid it is concluded that the fourth hydroxyl group occupies the 6-position and has the β(axial)-conformation.

Terminolic acid,[1] $C_{30}H_{48}O_6$, is a new triterpene isolated from *Terminalia ivorensis* during an examination of the heartwood of certain *Terminalia* species. It belongs to the oleanolic acid series and resembles arjunolic acid, which was recently obtained from *T. arjuna* and identified as 2 : 3 : 23(or 24)-trihydroxyolean-12-en-28-oic acid [2] (I). Terminolic acid is a tetrahydroxy-compound, and its botanical association with arjunolic acid led us tentatively to regard it as a hydroxyarjunolic acid. Further investigation has confirmed this and it has now been shown that the triterpene from *T. ivorensis* is 6β-hydroxyarjunolic acid (II; R = H).

Immediately after the experiments recorded in Part XXIII,[1] it was observed that methyl terminolate (II; R = Me) yielded a highly crystalline *iso*propylidene compound. This new derivative—actually (III; R = Me)—in contrast to the parent ester, was

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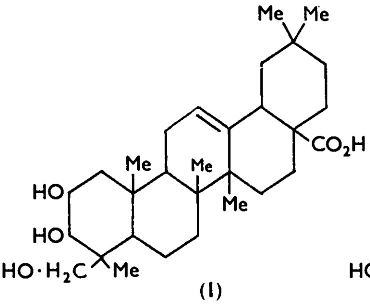
* Part XXVI, *J.*, 1956, 1384.

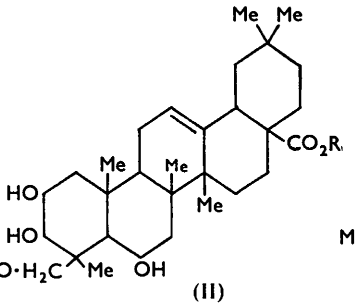
[1] King, King, and Ross, *J.*, 1955, 1333.

[2] *Idem*, *J.*, 1954, 3995.

resistant to periodate oxidation, and its formation therefore involved at least one of the hydroxyl groups in the original 1 : 2-glycol. With acetic anhydride–pyridine the methyl *O*-*iso*propylideneterminolate yielded an acetate, which although at first believed to be a diacetyl compound, was shown on further consideration of the acetylation products of the triterpene to be a monoacetate. Mild hydrolysis of the acetate eliminated the *iso*propylidene residue leaving an acetoxy-triol which, like methyl *O*-*iso*propylideneterminolate, was unaffected by sodium periodate. It was thus apparent that the *iso*propylidene compound



(I)



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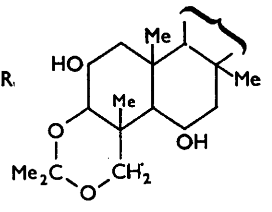

(III)

(III; R = Me) is the derivative of a 1 : 3-glycol, such as, for example, the 3 : 23-diol hederagenin, and the probable occurrence in terminolic acid of a 3 : 23(or 24)-glycol unit was substantiated by the isolation of formaldehyde from the copper-catalysed pyrolysis of methyl terminolate.[3] The evidence of the periodate test implies, moreover, that the acetylisable substituent of the *iso*propylideneterminolate must be located at the 2-position. Consequently, terminolic acid contains the 2 : 3 : 23(or 24)-trihydroxy-system present in arjunolic acid (I).

Oxidation of methyl *O*-*iso*propylideneterminolate revealed a marked difference between the remaining hydroxyl groups. When the chromic oxide–pyridine reagent [4] was used, the product consisted of a mono-oxo-compound [methyl *O*-*iso*propylideneterminonate (IV; R = Me)], and attempts to prepare a diketone led to degradation, presumably in the double-bond region of the molecule. Optimum yields of the keto-ester were obtained with two equivalents of oxidising agent, the second molecule apparently forming a stable chromate. The identity of the acetyl derivative of methyl *O*-*iso*propylideneterminonate with the product obtained by oxidation of methyl *O*-acetyl-*O*-*iso*propylideneterminolate indicated that the oxidised substituent was not the readily acetylated hydroxyl group.

Cautious hydrolysis of the *iso*propylideneterminonate with very dilute sulphuric acid afforded a trihydroxyketo-ester, methyl terminonate. The keto-triol was also obtained in small yield by the action of chromic oxide–pyridine on methyl terminolate, oxidation of the 3- and the 23(or 24)-hydroxyl group presumably being inhibited by the formation of a cyclic chromate. The product underwent periodate oxidation indicative of the α-glycol unit and yielded formaldehyde under the appropriate conditions of pyrolysis. No ketonic derivatives were obtainable from methyl terminonate, but this is attributable to steric hindrance of the oxo-group, the presence of which was established, however, by light absorption. Moreover, the normal Wolff–Kishner reaction was without effect on the keto-ester, but reduction of the keto-group took place under forcing conditions,[5] and the formation thereby of methyl arjunolate confirmed the intimate relationship existing between the two triterpenes.

Of the various positions available for the fourth hydroxyl group, several can be rejected forthwith—position 1, for example, being excluded by the periodate titration data which indicate the presence in terminolic acid of only one α-glycol unit. The situation of the remaining hydroxylic substituent was unexpectedly disclosed through the use of somewhat more concentrated acid (actually hydrochloric acid) for the hydrolysis of methyl *O*-*iso*propylideneterminonate. In place of the methyl terminonate previously formed, a product

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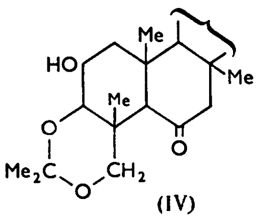
[3] Tsuda and Kitagawa, *Ber.*, 1938, **71**, 1604.

[4] Poos, Arth, Beyler, and Sarett, *J. Amer. Chem. Soc.*, 1953, **75**, 422.

[5] Barton, Ives, and Thomas, *J.*, 1955, 2056.

was obtained which, though tending to solvate and therefore being difficult to analyse, clearly contained less than the six oxygen atoms of the original triterpene molecule. Analysis of the crystalline diacetate and dibenzoate demonstrated conclusively the loss of a molecule of water, and this was accompanied by the disappearance of carbonyl absorption from the ultraviolet spectrum. The α-glycol system, however, remained intact and it was therefore inferred that the carbonyl group formed by oxidising the unorientated substituent had undergone condensation with the 23(or 24)-hydroxyl. In agreement with this conclusion methyl terminonate reacted easily and irreversibly with the more concentrated mineral acid, to form the identical anhydro-derivative. The facility with which this intramolecular condensation occurs thus restricts, for stereochemical reasons, the remaining oxygenated substituent to the neighbouring 6- or 7-position.



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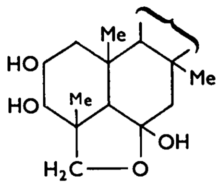

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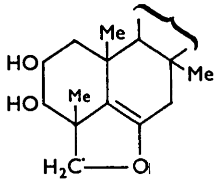

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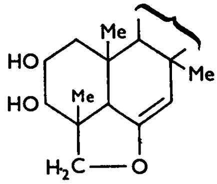

(VII)

The acid-induced interaction of the carbonyl and the hydroxyl group and the accompanying loss of water were consequently attributed to hemiacetal formation followed by dehydration to an enol ether. On the assumption, later confirmed, that the carbonyl group is attached to the 6-position, the resulting products contain an additional 5-membered ring, as shown in (V; R = Me) and in (VI or VII; R = Me). Support for the enol ether formulation was found in the ultraviolet spectrum of the end product, which not only lacked the ketonic-carbonyl absorption, but also exhibited intensified absorption at 200—220 mμ due to the introduction of a new ethylenic link. This was still more evident in the case of the enol ether from methyl dihydro-12-oxoterminonate (VIII), which was prepared from methyl tri-*O*-acetyldihydro-12-oxoterminolate (described in Part XXIII as the tetra-acetate) by oxidation and hydrolysis. Acid-treatment of the product (VIII), which is devoid of ethylenic unsaturation, gave a derivative analogous to the oxide (VI or VII), having typical double-bond absorption at 200—220 mμ.

On the other hand, the absorption band at *ca.* 1660 cm.$^{-1}$ characteristic of the simple enol ethers [6] is missing from the infrared spectrum of methyl anhydroterminonate, but no comparative data are available for enol ethers which are part of a rigid, highly substituted, cyclic structure. It is possible, therefore, that in these circumstances the normal vinyl ether band is displaced towards longer wavelengths where it is obscured by the intense absorption of the methoxycarbonyl group. In view of the mild conditions required to effect the change (N/50-acid at room temperature) it is highly improbable that a skeletal change has occurred which has resulted in the migration of the double bond away from the 5 : 6-position. That drastic rearrangement has not taken place is indicated, for example, by the formation, from methyl di-*O*-acetylanhydroterminonate with one equivalent of *N*-bromosuccinimide, of a compound which has the characteristic absorption of a homoannular diene and is thus almost certainly the corresponding 9(11)-dehydro-compound.

The choice of position 6 for the fourth and readily oxidisable hydroxyl group of terminolic acid rests on analogies between its derivatives and those of sumaresinolic acid [7] (IX). Methyl sumaresinonate, for example, does not give ketonic derivatives and cannot be reduced by the Wolff–Kishner method except under forcing conditions. However, the 6-hydroxyl group in sumaresinolic acid is unaffected by acetic anhydride–pyridine, and this supposed divergence in the behaviour of the respective triterpene esters led to a re-examination of the acetylation of methyl terminolate. It was then found that the product formed

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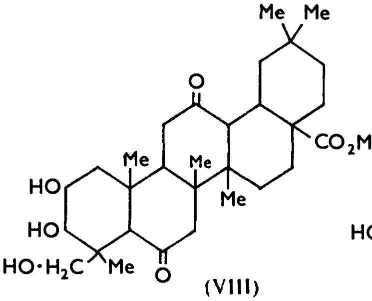
[6] Meakins, personal communication; cf. *J.*, 1953, 4170.

[7] Ruzicka, Jeger, Grob, and Hösli, *Helv. Chim. Acta*, 1943, **26**, 2283; Ruzicka, Norymberski, and Jeger, *ibid.*, 1945, **28**, 380; Djerassi, Thomas, and Jeger, *ibid.*, 1955, **38**, 1304.

by pyridine–acetic anhydride was a triacetate and that full esterification to the tetra-acetyl compound required perchloric acid as catalyst. The position of the free hydroxyl group in methyl tri-*O*-acetylterminolate was determined by oxidation with chromic oxide–pyridine, the product being hydrolysed to methyl terminonate. Contrariwise, methyl tetra-*O*-acetylterminolate resists complete hydrolysis, a monoacetate being obtained, and in this respect also there is a resemblance to methyl sumaresinolate diacetate in which the 6-acetoxy-group is stable to alkali.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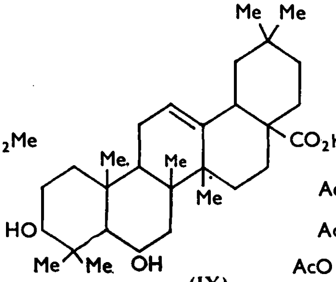
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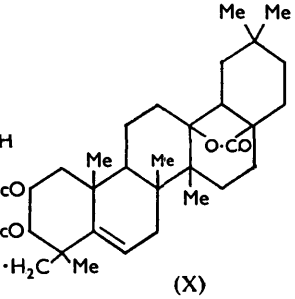
(X)

Reduction of methyl *O*-*iso*propylideneterminonate with sodium borohydride regenerated the original *iso*propylidene-triterpene ester, whereas sodium–ethanol reduction yielded an amorphous product. It is probable, therefore, owing to the hindered nature of the keto-group that the hydroxyl substituent in question has the β(axial)-configuration, thus further resembling the corresponding group in sumaresinolic acid.

Other evidence pointing to the existence of a 6β-hydroxyl group in terminolic acid was obtained from treatment of the acid or its methyl ester with hydrobromic–acetic acid, the product after deacetylation giving a compound which appeared to be an anhydro-lactone $C_{30}H_{46}O_5$. Its composition was confirmed by the formation of a triacetate and tribenzoate, and the periodate reaction showed that the α-glycol unit remained unimpaired. An *iso*propylidene derivative was obtained which readily formed a monoacetate. It followed therefore that the hydroxyl group eliminated was that situated in ring B, and its extrusion accompanying the formation of an unsaturated lactone (X) exactly corresponds to the behaviour of the 6β-substituent in sumaresinolic acid under similar conditions.

The resulting 5 : 6-double bond is characteristically inert, being resistant to catalytic hydrogenation and having no colour reaction with tetranitromethane. However, its presence was demonstrated by ultraviolet absorption indicative of a trisubstituted ethylenic link, and by the formation from the anhydroterminolic lactone triacetate (X) of an epoxide (XI). The nature of this product was determined by analysis, the absence of light absorption at *ca.* 290 mμ excluding the alternative keto-structure. Treatment of the acetyl-epoxide with hydrogen chloride in chloroform gave rise to a chlorohydrin formulated as (XII) by analogy with the corresponding product from the steroid 5 : 6α-epoxides.[8] Pyridine regenerated the epoxide from the chlorohydrin, whereas aqueous alkalis converted it into a trihydroxy-epoxide which was stable to hydrogen chloride in chloroform but with methanolic hydrochloric acid formed a new product believed to be a 5 : 6-diol. The chlorohydrin triacetate is unaffected by chromic oxide in both pyridine and acetic acid, thus showing the hydroxyl group to be attached to the tertiary 5-carbon atom. This supports the conclusion based on light-absorption data that anhydroterminolic lactone contains a trisubstituted double bond. The position of the unsaturated link as α to a CH_2 group was further demonstrated by oxidation of the lactone triacetate with chromic oxide–acetic acid to a derivative shown by analysis and ultraviolet absorption to be an αβ-unsaturated ketone (XIII). Oxidation has, therefore, occurred presumably at the 7-position, thus adding confirmation to the view that the hydroxyl in ring B is attached to $C_{(6)}$.

Because of the strongly acid medium used in the conversion of terminolic acid into the anhydro-lactone, the possibility of a molecular rearrangement cannot be excluded without

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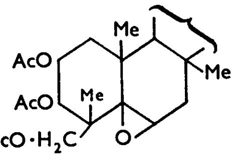
[8] Spring and Swain, *J.*, 1939, 1356.

further investigation. By reaction with hydrogen chloride–acetic acid at room temperature, methyl sumaresinolate forms an anhydro-derivative,[7] and under these milder conditions methyl terminolate also gave the anhydroterminolate (XIV), the light absorption of which was compatible with the presence of two non-conjugated double bonds. The product (XIV) was characterised by a crystalline *iso*propylidene derivative, alternatively prepared from methyl *O*-acetyl-*O*-*iso*propylideneterminolate by dehydration with phosphoryl chloride–pyridine followed by hydrolysis with aqueous alkali. Since the occurrence of carbonium ion rearrangements is highly improbable in basic media, the formation of the identical product by both methods virtually excludes the possibility of nuclear rearrangement in the preparation of the anhydroterminolate.



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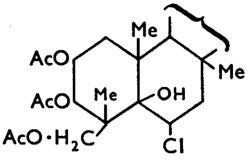

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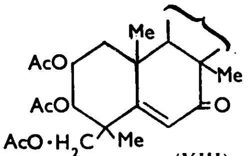

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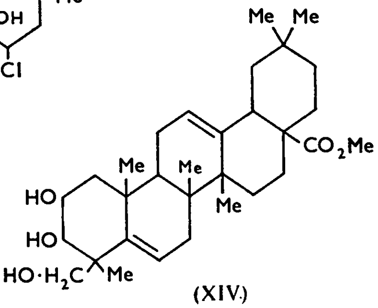

(XIV)

Finally, when oxidised with hydrogen peroxide in acetic acid, methyl tri-*O*-acetylanhydroterminolate gave an amorphous product, presumably methyl 2 : 3 : 23(or 24)-tri-*O*-acetyl-5 : 6-epoxyanhydrodihydro-12-oxoterminolate, from which was prepared a crystalline chlorohydrin. The hydroxyl group in this derivative being resistant to oxidation, the preceding epoxide must have originated in an isolated tri- or tetra-substituted double bond, *i.e.*, at the 5 : 6-position, a conclusion which provides additional support for the structure attributed to terminolic acid.

EXPERIMENTAL

Except where otherwise stated, acylations were in pyridine and were carried out for 12—15 hr. at room temperature or for 1 hr. at 100°, and hydrolyses with alkali were under reflux with 2N-methanolic potassium hydroxide for 1 hr. Optical rotations are recorded for chloroform solutions and sodium light at room temperature. Analytical samples were normally dried to constant weight at 150° in a vacuum or at 10° below the m. p. whichever was the lower. Light absorption data are for ethanol solutions.

Methyl O-iso*Propylideneterminolate.*—Methyl terminolate (5 g.) was treated in acetone (50 c.c.) with 3 drops of concentrated hydrochloric acid. After a few minutes the iso*propylidene derivative* began to separate in nearly cubic prisms, and after several hours at 0° the virtually pure product (5·5 g.) was collected. The crystals contained acetone of crystallisation and would not crystallise except from that solvent; they had m. p. 144—148° (effervescence), [α] +27° (*c* 1·22) (Found, in an air-dried specimen : C, 71·6; H, 9·5. $C_{34}H_{54}O_6,C_3H_6O$ requires C, 72·0; H, 9·8. Found, in a specimen dried at 120° : C, 73·4; H, 9·7. $C_{34}H_{54}O_6$ requires C, 73·1; H, 9·7%). The *monoacetate hydrate* crystallised from methanol in thick transparent plates which at 100° changed to a white anhydrous powder, m. p. 219—220°, [α] −5·5° (*c* 1·26) (Found : C, 71·6; H, 9·5. $C_{36}H_{56}O_7$ requires C, 72·0; H, 9·4%). The benzoate was amorphous.

Methyl 2-O-*Acetylterminolate.*—The above acetate (1 g.) was warmed for a few minutes in methanol containing 2 drops of concentrated hydrochloric acid. After 1 hr. the crystalline product (0·8 g.) was collected and crystallised from methanol as the hydrate as shining rectangular plates which at 100° became opaque (but retained their shape), giving the anhydrous *ester*, m. p. 220—221°, [α] +12° (*c* 1·24) (Found : C, 70·5; H, 9·3. $C_{33}H_{52}O_7$ requires C, 70·7; H, 9·35%). This compound was unaffected by treatment for 24 hr. at room temperature with aqueous-ethanolic sodium metaperiodate.

Methyl O-iso*Propylideneterminonate.*—Methyl *O-iso*propylideneterminolate (4 g.) in pyridine (30 c.c.) was added to pyridine–chromic oxide (30 c.c. containing 1·4 g., *ca.* 2 mol., of chromic oxide) at room temperature; the orange chromic complex immediately dissolved and was rapidly replaced by a dark brown precipitate; oxidation was complete in 1 hr. The solution was filtered, the brown solid washed with pyridine, and the combined solutions were poured into water (300 c.c.). The product was collected into ether which was washed several times with water to remove pyridine, and the solvent evaporated. A hot methanolic solution of the residue was diluted until crystallisation began, giving *methyl* O-iso*propylideneterminonate* (3·1 g.) in stout needles. Crystallised from methanol it had m. p. 232—234°, [α] +32° (*c* 0·59) (Found: C, 73·0; H, 9·2. $C_{34}H_{52}O_6$ requires C, 73·3; H, 9·4%); light absorption max. at 292 mμ (ε 30). Using the calculated amount of oxidising agent gave a 32% yield of pure product. The *acetate*, prepared by acetylation of the above alcohol or by similar oxidation (only 1 mol. of oxidising agent required) of methyl *O*-acetyl-*O-iso*propylideneterminolate, crystallised from methanol in stout needles, m. p. 239—240°, [α] +4·5° (*c* 1·05) (Found: C, 72·1; H, 8·9. $C_{36}H_{54}O_7$ requires C, 72·2; H, 9·1%). The *benzoate*, prisms from ethanol, had m. p. 274—275°, [α] −7° (*c* 0·55) (Found: C, 74·5; H, 8·3. $C_{41}H_{56}O_7$ requires C, 74·5; H, 8·5%). None of the above compounds gave the usual ketonic derivatives.

Methyl Terminonate.—(*a*) Methyl *O-iso*propylideneterminonate (1 g.) was suspended in methanol (25 c.c.), and 1 drop of 6N-sulphuric acid was added. Next day the solution was diluted until crystallisation was complete. *Methyl terminonate* (0·65 g.) separated as plates, crystallising from aqueous methanol, and having double m. p. 221—224° and 260° (double m. p. not always observed), [α] +49° (*c* 2·59) (Found: C, 72·4; H, 9·3. $C_{31}H_{48}O_6$ requires C, 72·1; H, 9·4%); light absorption max. at 293 mμ (ε 24); ε_{210} 4000; ε_{220} 1250; $\varepsilon_{210}/\varepsilon_{220}$ 3·2.

(*b*) Methyl terminolate was oxidised at room temperature with the chromic oxide–pyridine reagent (4·5 mols.) during 24 hr. Working up in the usual way gave methyl terminonate (29%).

(*c*) Methyl tri-*O*-acetylterminolate, oxidised as above, afforded an acetate which gave methyl terminonate (76%) on hydrolysis.

Methyl terminonate acetate was amorphous and no ketone derivatives could be obtained. In aqueous-ethanolic solution the ester reacted with 1·02 mols. of sodium metaperiodate, giving an amorphous neutral product.

Pyrolyses with Copper.—(*a*) A mixture of methyl terminolate (0·5 g.) and precipitated copper (3 g.) was heated at 270—290° for 1 hr., and the evolved gases were passed into saturated aqueous dimedone. After 1 hr. the precipitate (25 mg.) was collected. After it had been purified from methanol it had m. p. 188—189° alone or mixed with formaldehyde dimedone derivative.

(*b*) A similar experiment with methyl terminonate gave 30 mg. of formaldehyde dimedone derivative.

(*c*) A control experiment with methyl oleanolate gave no formaldehyde.

Reduction of Methyl Terminonate.—(*a*) Normal Wolff–Kishner reduction of methyl terminonate with anhydrous hydrazine and sodium ethoxide in ethanol at 180° gave a mixture of acids which after esterification (diazomethane) afforded a small yield of unchanged methyl terminonate together with much amorphous material, possibly methyl 6α-terminolate (see below).

(*b*) Vigorous Wolff–Kishner reduction of methyl terminonate (0·5 g.) by the process described by Barton[5] afforded, after re-esterification, methyl arjunolate (0·3 g.), m. p. and mixed m. p. 214—216°, further characterised as the triacetyl 18α-lactone, m. p. and mixed m. p. 265—266°, [α] +11° (*c* 1·4) (Found: C, 70·1; H, 8·8. Calc. for $C_{36}H_{54}O_8$: C, 70·3; H, 8·9%).

Reduction of Methyl O-iso*Propylideneterminonate.*—(*a*) Methyl *O-iso*propylideneterminonate (0·5 g.) in methanol (10 c.c.) was treated overnight with a slight excess of sodium borohydride. The excess of reagent was decomposed by acid, the solution was poured into water, and the product collected with ether. The residue, after evaporation of the solvent, was dissolved in acetone (5 c.c.) containing 1 drop of concentrated hydrochloric acid. Methyl *O-iso*propylideneterminolate (340 mg.) soon separated and was further characterised as the acetate.

(*b*) Methyl *O-iso*propylideneterminonate was reduced in the usual way with excess of sodium in boiling ethanol. The product resisted attempts to crystallise it, nor could crystalline products be obtained after removal of the *iso*propylidene group by acid hydrolysis.

Acid-rearrangement of Methyl Terminonate.—Methyl *O-iso*propylideneterminonate (2 g.), suspended in methanol (25 c.c.), was treated with 1 drop of concentrated hydrochloric acid. The solid rapidly passed into solution and after about 15 min. *methyl anhydroterminonate* began to separate. After a further 1 hr. at room temperature the product (1·4 g.) was collected; it separated from methanol or aqueous methanol in needles, m. p. 145—147° (slow heating), [α] +85° (*c* 1·0) [Found (average of 6 analyses), after drying at 110°: C, 74·4; H, 9·3. $C_{31}H_{46}O_5$

requires C, 74·7; H, 9·3%]; light absorption: ε_{210} 6000; ε_{220} 3200; $\varepsilon_{210}/\varepsilon_{220}$ 1·86; no selective absorption at *ca.* 290 mμ. The same product was obtained in almost quantitative yield on similar treatment of methyl terminonate. This ester or its *iso*propylidene derivative also afforded the anhydro-derivative after 24 hr. when dissolved in methanol containing 5 times the concentration of sulphuric acid used in the preparation of methyl terminonate from its *iso*propylidene derivative (see above). Methyl anhydroterminonate was stable to alkali, being recovered unchanged after 6 hr. in boiling 2N-methanolic potassium hydroxide. It reacted rapidly at room temperature in aqueous ethanol with 0·97 mol. of sodium metaperiodate. The *diacetate* crystallised from methanol in thick hexagonal plates, m. p. 166—167°, [α] +29° (*c* 1·67) (Found: C, 72·0; H, 8·6; OMe, 5·4; OAc, 14·7. $C_{33}H_{50}O_7$ requires C, 72·1; H, 8·65; 1 OMe, 5·3; 2 OAc, 14·4%). Hydrolysis regenerated the diol. The *dibenzoate* crystallised from methanol in needles, m. p. 235—236° [α] −5·5° (*c* 2·5) (Found: C, 76·4; H, 8·0. $C_{45}H_{54}O_7$ requires C, 76·5; H, 7·7%).

*Methyl Tri-*O*-acetyldihydro-*12*-oxoterminonate.*—*Methyl tri-*O*-acetyldihydro-*12*-oxoterminolate* (1 g.) (Found: C, 67·5; H, 8·6. $C_{37}H_{56}O_{10}$ requires C, 67·25; H, 8·5%), previously described as the tetra-acetate, was oxidised with excess of chromic oxide–pyridine overnight at 0°. Working up in the usual way gave *methyl triacetyldihydro-*12*-oxoterminonate* (0·8 g.) in rhombic tablets (from methanol), m. p. 205°, [α] −45° (*c* 1·08) (Found: C, 67·3; H, 8·3. $C_{37}H_{54}O_{10}$ requires C, 67·45; H, 8·3%).

*Methyl Dihydro-*12*-oxoterminonate.*—Saponification of the corresponding triacetate gave *methyl dihydro-*12*-oxoterminonate*, flattened needles (from aqueous methanol), m. p. 208—210°, [α] −45° (*c* 1·06) (Found: C, 70·3; H, 9·0. $C_{31}H_{48}O_7$ requires C, 69·9; H, 9·1%); the compound showed no ethylenic absorption at 210—230 mμ.

*Methyl Anhydrodihydro-*12*-oxoterminonate.*—The above diketone (0·85 g.) in methanol (10 c.c.) was treated with 1 drop of concentrated hydrochloric acid. After 3 hr. water was added to the solution and *methyl anhydrodihydro-*12*-oxoterminonate* (0·64 g.) was precipitated; it crystallised from aqueous methanol in leaflets or prisms, m. p. 266—267°, [α] −19° (*c* 0·95) (Found: C, 72·3; H, 8·8. $C_{31}H_{46}O_6$ requires C, 72·3; H, 9·0%); light absorption: ε_{210} 2000; ε_{220} 1200. The compound was unchanged after 8 hours' boiling with 2N-methanolic potassium hydroxide. The *diacetate* crystallised in needles, m. p. 170—172°, [α] −59° (*c* 1·03), from aqueous methanol (Found: C, 69·8; H, 8·3. $C_{35}H_{50}O_8$ requires C, 70·2; H, 8·4%).

*Methyl Di-*O*-acetylanhydrodehydroterminonate.*—Methyl di-*O*-acetylanhydroterminonate (0·6 g.) with *N*-bromosuccinimide (0·18 g., 1 mol.) in carbon tetrachloride (50 c.c.) was boiled for 5 hr. The precipitated succinimide was removed and the filtrate evaporated. The residue of crude *methyl di-*O*-acetylanhydrodehydroterminonate* crystallised from methanol or aqueous methanol in hydrated needles (0·23 g.), m. p. 240—242°, [α] −44° (*c* 0·24) (Found, in an air-dried sample: C, 69·9; H, 8·2. $C_{35}H_{48}O_7,H_2O$ requires C, 70·2; H, 8·4. Found, in a vacuum-dried sample: C, 72·4; H, 8·3. $C_{35}H_{48}O_7$ requires C, 72·4; H, 8·3%); light absorption max. at 283 mμ (ε 7300).

Acetylation of Methyl Terminolate.—(*a*) Acetylation of methyl terminolate with acetic anhydride–pyridine gave *methyl tri-*O*-acetylterminolate*, crystallising from aqueous methanol or methanol in leaflets, m. p. 160—162°, [α] +19° (*c* 1·53) (Found, after drying at the m. p.: C, 69·2; H, 8·8. $C_{37}H_{56}O_9$ requires C, 68·9; H, 8·75%). Oxidation of the triacetate with chromic oxide–pyridine followed by alkaline hydrolysis gave the known methyl terminonate in excellent yield.

(*b*) Acetylation of methyl terminolate or its triacetate with acetic anhydride containing 1 drop of perchloric acid for ½ hr. at room temperature gave the tetra-acetate previously described;[1] it crystallised from methanol in tablets, m. p. 168—170°, and from aqueous methanol in rods, m. p. 187—189°, [α] −13° (*c* 1·8) (Found: C, 68·2; H, 8·6. Calc. for $C_{39}H_{58}O_{10}$: C, 68·2; H, 8·5%).

Methyl 6-O-*Acetylterminolate.*—Methyl tetra-*O*-acetylterminolate was hydrolysed with boiling aqueous-methanolic potassium hydroxide during 1 hr. Dilution of the solution with water precipitated the *monoacetate* which separated from aqueous methanol in flattened needles, m. p. 216—218°, [α] +21° (*c* 1·06) (Found: C, 70·5; H, 9·3. $C_{33}H_{52}O_7$ requires C, 70·7; H, 9·35%).

Anhydroterminolic Lactone.—Methyl terminolate or sodium terminolate (5 g.) was dissolved in 50% hydrogen bromide–acetic acid (50 c.c.) and after 48 hr. at room temperature the purplish-red solution was poured into water. The precipitated solid would not crystallise, so it was immediately hydrolysed for 2 hr. by boiling 2N-methanolic potassium hydroxide (150 c.c.). Cautious addition of water then precipitated a dark oil from which the solution was decanted; excess of water then precipitated the product as a yellow powder which was collected and dried. This crude product, crystallised first from slightly aqueous acetone and then from acetone, gave the *lactone* in needles (1·4 g.), m. p. 320° (vac.), [α] +17·5° (*c* 0·8) (Found: C, 73·6; H, 9·3. $C_{30}H_{46}O_5$ requires C, 74·0; H, 9·5%); light absorption: ε_{210} 1300; ε_{220} 350; $\varepsilon_{210}/\varepsilon_{220}$ 3·7 (cf. for cholesterol:[9] ε_{210} 1600; ε_{220} 400; $\varepsilon_{210}/\varepsilon_{220}$ 4·0). The double bond present in anhydroterminolic lactone was inert towards catalytic reduction and failed to give a colour with tetranitromethane. In aqueous ethanol at room temperature it reacted in 2 hr. with 1·01 mol. of sodium metaperiodate. The *triacetate* crystallised from methanol in leaflets, m. p. 211—212°, [α] +8° (*c* 2·77) (Found: C, 70·2; H, 8·4. $C_{36}H_{52}O_8$ requires C, 70·55; H, 8·55%). The *tribenzoate* crystallised from ethanol in small prisms, double m. p. 262—263° and 278°, [α] +71° (*c* 1·02) (Found: C, 77·0; H, 7·25. $C_{51}H_{58}O_8$ requires C, 76·7; H, 7·3%).

Anhydro-O-iso*propylideneterminolic Lactone*.—Anhydroterminolic lactone (1 g.), suspended in acetone (50 c.c.), was treated with 1 drop of concentrated hydrochloric acid. The solid dissolved almost immediately and within a few minutes the iso*propylidene lactone* (1·0 g.) crystallised. It separated from ethanol in plates, m. p. 326—328° (vac.), [α] +23° (*c* 1·18) (Found: C, 74·8; H, 9·4. $C_{33}H_{50}O_5$ requires C, 75·2; H, 9·6%). The free hydroxy-group in this compound was not oxidised by chromic oxide–pyridine. The *acetate* crystallised in large prisms (from methanol), m. p. 271—272°, [α] −4° (*c* 1·8) (Found: C, 73·8; H, 9·3. $C_{35}H_{52}O_6$ requires C, 73·9; H, 9·2%). The *benzoate* crystallised from ethanol in prisms, m. p. 326—328° (vac.), [α] +10° (*c* 1·05) (Found: C, 76·5; H, 8·6. $C_{40}H_{54}O_6$ requires C, 76·15; H, 8·6%).

2-O-*Acetylanhydroterminolic Lactone*.—*O*-Acetyl*iso*propylideneterminolic lactone (0·5 g.), suspended in methanol (20 c.c.), was warmed with 5 drops of concentrated hydrochloric acid during ½ hr. Water precipitated the acetyl-lactone (0·34 g.) which crystallised from methanol in flattened needles, m. p. 294°, [α] −13° (*c* 1·4) (Found: C, 73·0; H, 8·8. $C_{32}H_{48}O_6$ requires C, 72·7; H, 9·15%). The acetate did not react with periodate.

Anhydroepoxyterminolic Lactone.—Tri-*O*-acetylanhydroterminolic lactone (1·5 g.) in glacial acetic acid (15 c.c.) was treated for 3 hr. at 100° with excess (1 c.c.) of 30% hydrogen peroxide. The product was isolated by dilution with water, followed by crystallisation from aqueous methanol, giving the *acetyl-epoxide* (1·3 g.) as plates or leaflets, m. p. 244—245° after sintering at 231°, [α] −13° (*c* 1·22) (Found: C, 68·5; H, 8·4. $C_{30}H_{52}O_9$ requires C, 68·8; H, 8·3%); a solution in ethanol was virtually transparent to light of wavelength >210 mμ. Alkaline hydrolysis afforded *anhydroepoxyterminolic lactone*, crystallising from methanol in needles, m. p. 327—329° (vac.), [α] −12° (*c* 1·02) (Found: C, 71·4; H, 9·4. $C_{30}H_{46}O_6$ requires C, 71·7; H, 9·2%).

Tri-O-*acetyl*-6-*chloro*-5-*hydroxyarjunolic Lactone*.—Tri-*O*-acetylanhydroepoxyterminolic lactone (0·5 g.) in dry chloroform (25 c.c.) was treated at room temperature with hydrogen chloride for 1 hr. The solvent was removed in a vacuum and the residue crystallised from ethanol, giving the *chlorohydrin* (0·42 g.) as rhombic tablets, m. p. 236° (effervescence), [α] −39° (*c* 0·62) (Found: C, 64·9; H, 7·9; Cl, 5·3. $C_{36}H_{53}O_9Cl$ requires C, 65·0; H, 8·0; Cl, 5·3%). The chlorohydrin reverted to the epoxide on melting, with evolution of hydrogen chloride, or in warm pyridine. Methanolic alkali converted it into the trihydroxy-epoxide, characterised as the acetate. The chlorohydrin was recovered unchanged after treatment at room temperature with an excess of chromic oxide in acetic acid containing a little sulphuric acid, or with chromic oxide–pyridine, for 10 days.

5 : 6-*Dihydroxyarjunolic Lactone*.—Anhydroepoxyterminolic lactone was recovered unchanged after treatment with chloroformic hydrogen chloride for 12 hr. The lactone (0·25 g.) was then boiled for 6 hr. in methanol (25 c.c.) containing concentrated hydrochloric acid (0·5 c.c.); working up in the usual way gave the *diol*, crystallising from aqueous acetone in silky needles, m. p. 316—320° (vac.) (Found: C, 69·1; H, 9·5. $C_{30}H_{48}O_7$ requires C, 69·2; H, 9·3%).

Tri-O-*acetylanhydro*-7-*oxoterminolic Lactone*.—Tri-*O*-acetylterminolic lactone (0·9 g.) was treated with excess of chromic oxide (0·3 g.) in acetic acid (50 c.c.) containing sulphuric acid (1·0 c.c.) for 2 days at room temperature. The *product* was isolated, by pouring the solution into water, as a colourless powder which crystallised from aqueous acetone or aqueous methanol in leaflets (0·34 g.), double m. p. 194—196° and 224°, [α] −26° (*c* 0·72) (Found: C, 68·7; H, 8·25. $C_{36}H_{50}O_9$ requires C, 69·0; H, 8·0%); light absorption max. at 233 mμ (ε 11,000).

Methyl Anhydroterminolate.—Methyl terminolate (2 g.) in acetic acid (25 c.c.) was saturated with hydrogen chloride at room temperature, and after 2 days the solution was poured into water. The amorphous product was hydrolysed and the triol isolated with water and crystallised from acetone–hexane as felted needles (0·67 g.), m. p. 140° (slow heating), [α] +18° (*c* 1·5) (Found: C, 74·5; H, 9·9. $C_{31}H_{48}O_5$ requires C, 74·4; H, 9·7%); light absorption: ε_{210} 5000; ε_{220} 1500.

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[9] Bladon, Henbest, and Wood, *J.*, 1952, 2737.

The acetate was amorphous. A solution of the ester in acetone with a drop of concentrated hydrochloric acid did not deposit any solid but the iso*propylidene* derivative was obtained by pouring the solution into dilute ammonia. From methanol it formed prisms and from aqueous methanol plates, m. p. 202°, [α] +47° (*c* 1·2) (Found : C, 75·2; H, 9·9. $C_{34}H_{52}O_5$ requires C, 75·5; H, 9·7%).

Methyl 2-O-*Acetylanhydro*-O-iso*propylideneterminolate*.—A solution of methyl 2-*O*-acetyl-*O*-*iso*propylideneterminolate (4 g.) in pyridine (50 c.c.) containing excess (0·5 c.c.) of phosphorus oxychloride was boiled for 3 hr. and poured into water. The precipitated solid readily crystallised from aqueous methanol as the *hydrate* (3·1 g.), m. p. 139° (slow heating), [α] +15° (*c* 0·46) (Found, in an air-dried sample: C, 71·9; H, 9·1. $C_{36}H_{54}O_6,H_2O$ requires C, 72·0; H, 9·4%), losing the solvent at the m. p. to give the anhydrous *ester* (Found : C, 74·0; H, 9·5. $C_{36}H_{54}O_6$ requires C, 74·2; H, 9·3%). Alkaline hydrolysis afforded methyl anhydro-*O*-*iso*propylideneterminolate.

Methyl 2-O-*Acetylanhydroterminolate*.—To a suspension of methyl 2-*O*-acetylanhydro-*O*-*iso*propylideneterminolate (1 g.) in methanol were added 5 drops of concentrated hydrochloric acid; the solid dissolved during ½ hr. Next day the solution was poured into water, and the dried precipitate crystallised from a small amount of ether or from ether–hexane, giving methyl 2-*O*-acetylanhydroterminolate (0·6 g.) as prisms, m. p. 185—187°, [α] +1° (*c* 1·04) (Found: C, 73·4; H, 9·6. $C_{33}H_{50}O_6$ requires C, 73·0; H, 9·3%).

Methyl Tri-O-*acetyl*-6-*chlorodihydro*-5-*hydroxy*-12-*oxoarjunolate*.—Methyl tri-*O*-acetylanhydroterminolate, isolated as an amorphous solid by acetylation of pure methyl terminolate (1·4 g.), was treated at 100° for 3 hr. with acetic acid (25 c.c.) containing 30% hydrogen peroxide (2 c.c.). The product was isolated by pouring the solution into water and presumably consisted of methyl tri-*O*-acetyldihydroanhydroepoxy-12-oxoterminolate but it was not found possible to crystallise this or its hydrolysis product. The crude acetate was therefore dissolved in dry chloroform, and a stream of hydrogen chloride was passed in during 1 hr. After a further 2 hr. the solvent was removed under reduced pressure and the residue of the *chlorohydrin* (0·93 g.) readily crystallised from methanol or aqueous methanol in prisms, m. p. 184°, [α] −73° (*c* 0·74) (Found : C, 63·5; H, 7·8; Cl, 5·2. $C_{37}H_{55}O_{10}Cl$ requires C, 63·9; H, 8·0; Cl, 5·1%). The compound was recovered unchanged after attempted oxidation with chromic oxide–acetic acid–sulphuric acid for 5 days at room temperature.

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