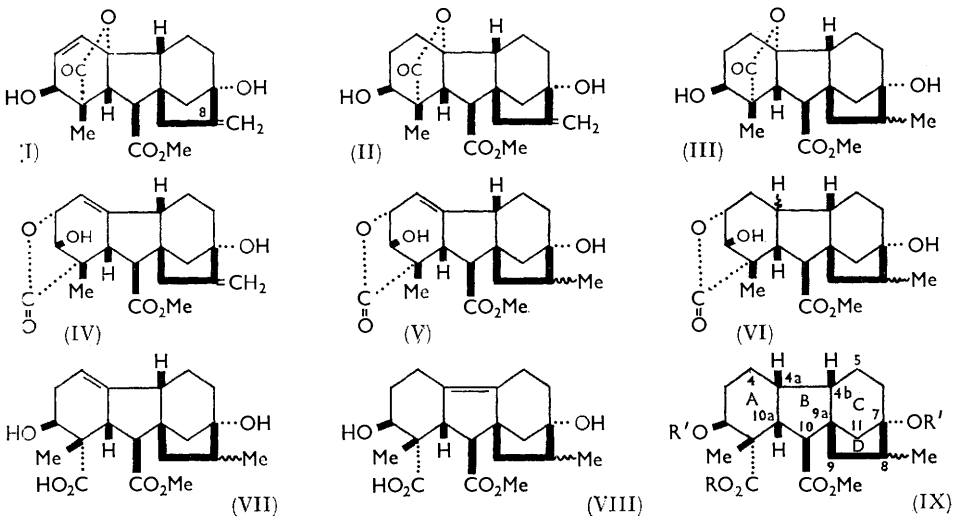
484. *Gibberellic Acid. Part XXII.* Stereochemistry of the Hydrogenolysis Products.*

By D. C. Aldridge, John Frederick Grove, P. McCloskey, and W. Klyne.

The hydrogenolysis products of methyl gibberellate are shown to have rings A/B *cis*-fused, and their absolute configuration and the conformation of ring A are deduced from optical rotatory dispersion studies. Pairs of reduction products, epimeric at position 8, have been inter-related and correlated with the reduction products of allo- and epiallo-gibberic acid.

Catalytic reduction of methyl gibberellate (I) and the isomeric gibb-4-ene 1→3-lactone [1] (IV) involves competing reactions in ring A. Hydrogenation to completion at room temperature leads, by way of the dihydro-compounds, gibberellin A_1 methyl ester [2] (II) and the 8-epimeric esters [1] (V), respectively, to mixtures of neutral 8-epimeric tetrahydro-esters [3] (III) and (VI), which are stable to further reduction; on the other hand hydrogenolysis of the lactone bridge gives rise to unsaturated tetrahydro-acids (VII) and (VIII) which, depending on the accessibility of the ethylenic bond, may undergo further hydrogenation to the completely saturated 8-epimeric hexahydro-acids (IX; R = R′ = H).



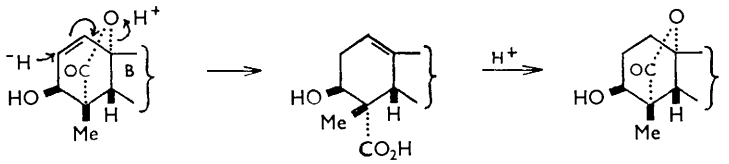
Although methyl gibberellate and the ester (IV) yielded the same acidic products (cf. ref. 1) they responded differently to a change of reaction medium from neutral to acidic. Reproducibility of results was high but the yields recorded in the present work differ somewhat from those reported earlier [1,3] with different catalyst preparations. In a neutral polar solvent with palladium–charcoal or platinum as catalyst, methyl gibberellate absorbed *ca.* 2 mol. of hydrogen, yielding acidic products (63—75%) which were mainly unsaturated. In acetic acid, although the uptake of hydrogen and the proportion of fully reduced (hexahydro) acids were increased, the yield of total acidic product actually fell (31—41%).

Addition of a proton donor to the reaction medium should facilitate hydrogenolysis,

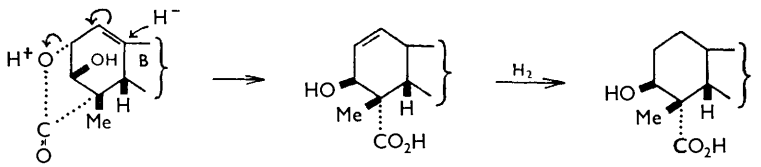
* Part XXI, *J.*, 1963, 154.

[1] Cross, Grove, and Morrison, *J.*, 1961, 2498.
[2] Grove, Jeffs, and Mulholland, *J.*, 1958, 1236.
[3] Cross, *J.*, 1960, 3022.

proceeding by way of an allylic shift following attack by hydrogen ion (Scheme 1), but will also promote the regeneration of the 1→4a-lactone bridge by addition of the liberated carboxyl group across the 4,4a-ethylenic bond of the unsaturated acid, a reaction which proceeds in parallel with the hydrogenation of the trisubstituted double bond. The latter is difficult to reduce,[1] and with methyl gibberellate in acetic acid, lactone formation takes precedence, lowering the yield of acidic products.



SCHEME 1. Hydrogenolysis of methyl gibberellate.



SCHEME 2. Hydrogenolysis of the ester (IV).

With the ester (IV), although a change from neutral to acidic medium resulted both in an increased uptake of hydrogen, from *ca.* 2·5 to 2·8 mol., and in an increased yield of hexahydro-acids, the total acidic product usually exceeded 90% in each case. Here the allylic shift accompanying hydrogenolysis (Scheme 2) leads initially to the formation of a gibb-3-ene in which the disubstituted double bond is easily accessible for further hydrogenation. However, the tendency of the double bond to migrate to the more hindered tri- and tetra-substituted positions was reflected in the isolation in significant amounts of the Δ^{4}- and $\Delta^{4a(4b)}$-acids (VII) and (VIII).

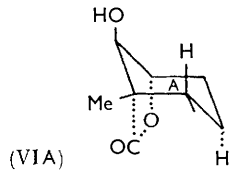
The complex mixture of acidic products resulting from the catalytic reduction of methyl gibberellate in neutral solution was separated by chromatography on buffered Celite into the 8-epimeric hexahydro-acids (IX; R = R′ = H), m. p. 269—271°,[1] and (double) m. p. 240—241° and 253—254°; the corresponding gibb-4-enes (VII), m. p. 223—224° and 240—242°, respectively; and the gibb-4a(4b)-ene (VIII), m. p. 218—222°; together with two minor products which are probably artefacts (see Experimental section). Reduction of the ester (IV) under the same conditions gave the same major acidic products with the exception of the gibb-4-ene (VII), m. p. 223—224°, a difference which is without significance in view of the isolation of the 8-epimer from both series. The positions of the double bond in the unsaturated acids (VII) and (VIII) was assigned on the basis of the ultraviolet end-absorption of these compounds, the more intense absorption at 205 mμ being associated with the tetrasubstituted double bond in (VIII). The shape of the absorption curves for the gibb-4-enes (VII) differed markedly from that of the gibb-4-ene 1→3-lactone (V).[1] The 8-epimeric gibb-4-enes (VII), which formed methyl 8-epi-tetrahydrogibberellate (III) and methyl tetrahydrogibberellate, respectively, when heated in an acid medium, furnished the hexahydro-acids (IX; R = R′ = H), together with the lactones (III), on further catalytic reduction, a reaction which served to interrelate the configuration at position 8 in these products. The gibb-4a(4b)-ene (VIII) resisted further catalytic hydrogenation and consequently appeared [with the hexahydro-acids (IX; R = R′ = H)] as one of the three major products of reduction of methyl gibberellate and the ester (IV) under acidic conditions; it also resisted relactonisation and the configuration at position 8 is unknown.

Although the published physical properties are significantly different, the infrared

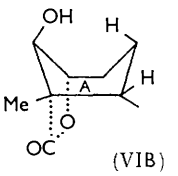
spectra of the methyl gibberellate hydrogenolysis products " Hydrogeno II " and " Hydrogeno III," obtained by Japanese workers,[4] are identical with those of the 8-methyl compounds, (VII), m. p. 240—242° and (IX; R = R′ = H), m. p. 240—241°, respectively. No products in the 8-epi-methyl series were evidently isolated by them.

Catalytic hydrogenolysis of the dihydro-esters (V), m. p. 232—235° and 171—172°, isolated[1] from the neutral fraction after the uptake of 1 mol. of hydrogen by the ester (IV) in neutral solution in the presence of palladium–charcoal, gave the hexahydro-acids (IX; R = R′ = H), m. p. 269—271° and 240—241°, respectively, reactions which are indicative of the relative configuration at position 8 in the dihydro-esters. The 8-epi-methyl ester (V), m. p. 232—235°, with boiling dilute mineral acid underwent aromatisation of ring A, and the methyl esters of dihydroallogibberic acid (X; R = H, 4bα)[5] and the dihydroepiallogibberic acid, m. p. 234—235°[6] (X; R = H, 4bβ), were obtained by chromatographic separation. Both these reduction products therefore have the 8-epi-configuration; the dihydroepiallogibberic acid of m. p. 178—180°[6] must then belong to the 8-methyl series. The isolation of both esters (X; R = Me), epimeric at position 4b, on acid-catalysed degradation of the dihydro-ester (V), shows that a gibb-4a(4b)-ene intermediate of type (XI), known to be involved in the aromatisation of ring A of gibberellic acid,[6] must also be involved in the aromatisation of gibb-4-ene 1→3-lactones.

The major neutral products from the catalytic hydrogenation of the 8-epimeric dihydro-esters (V) were the corresponding 4aξ-tetrahydro-esters (VI). The 8-epi-methyl ester (VI) was the main component of the neutral fraction from the reduction in neutral medium of the ester (IV). The configuration at position 4a in these tetrahydro-compounds is unknown. The structure (VIA) with the gibbane (4aα) stereochemistry is presumably more stable than the ring A boat structure (VIB), molecular models of which show a strong interaction between the 4β-hydrogen and 2β-hydroxyl group; but (VIB) would be obtained by reduction at the less hindered β-face.

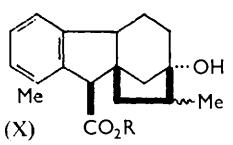


(VIA)

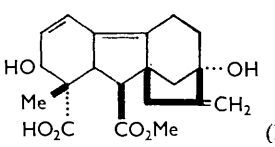


(VIB)

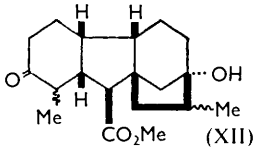
The stereochemical relationship in rings A/B between methyl gibberellate and the hexahydro-acids (IX; R = R′ = H) depends on whether the overall process of hydrogenolysis of the lactone bridge occurs with retention or inversion of configuration at position 4a. Initially[7] we argued that hydrogenation of a gibb-4-ene would take place *trans* to the liberated 1-carboxylic acid group with inversion of configuration in the product (IX; R = R′ = H); and on the basis of the sign and amplitude of the Cotton effect in



(X)



(XI)



(XII)

the rotatory dispersion curve A (see Figure) of the ketone (XII), m. p. 156—158°,* obtained by oxidation of the 8-epi-methyl acid (IX; R = R′ = H) and decarboxylation of the

* M. p. subsequently raised to 159—161°.

[4] Hsu, Takahashi, Miyao, Kawarada, Kitamura, Tamura, and Sumiki, *Agric. Biol. Chem.*, 1961, **25**, 865; Takahashi, Seta, Kitamura, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1959, **23**, 509.

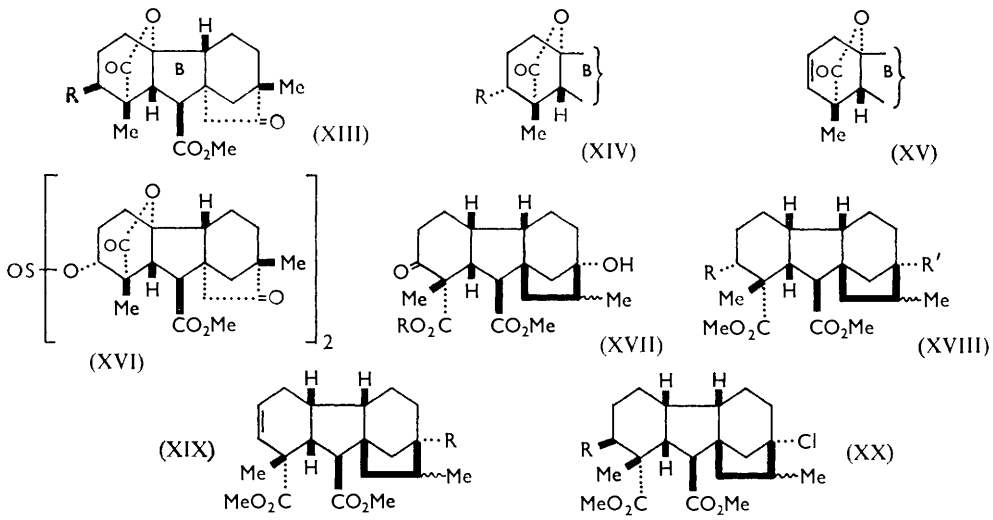
[5] Mulholland, *J.*, 1958, 2693.

[6] Grove and Mulholland, *J.*, 1960, 3007.

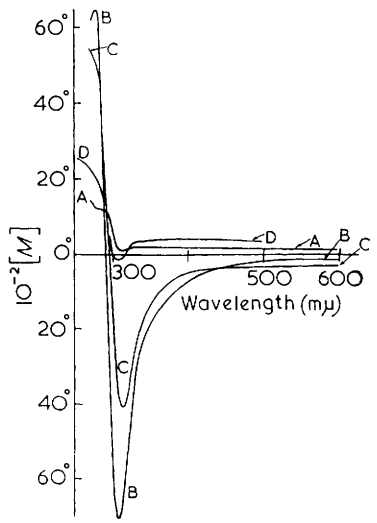
[7] Cross, Grove, McCloskey, Mulholland, and Klyne, *Chem. and Ind.*, 1959, 1345.

product, the absolute configurations (XII) and (I) were (correctly) deduced for ring A of the ketone and gibberellic acid, respectively.

Inversion at position 4a necessarily implies a change in the conformation of ring A which should be reflected in the chemical reactions of the 2-hydroxyl group; a comparison



was therefore made between the 8-epi-methyl ester (IX; R = Me, R′ = H) and the 2(*ax*)-hydroxy-keto-ester (XIII; R = OH), m. p. 226—228° [3] [keto-ester *A*,[8] derived from gibberellin A_1 methyl ester (II) by rearrangement of rings C/D], in which the 2-hydroxyl substituent has the same β-configuration.



Optical rotatory dispersion curves of the ketones: (A) (XII), m. p. 159—161°; (B) (XII), m. p. 124°; (C) (XXII); and (D) 5β-cholestan-3-one.

Toluene-*p*-sulphonylation of the corresponding 2(*eq*)-hydroxy-keto-ester (XIV; R = OH) [1] took place readily and a 78% yield of product was obtained in 40 hr. at room temperature with 2·5—3 mol. of reagent. Under the same conditions the 2(*ax*)-hydroxy-epimer (XIII; R = OH) was largely unchanged. Although on one occasion previously [9]

[8] Aldridge, Grove, Speake, Tidd, and Klyne, Part XX, *J.*, 1963, 143.
[9] MacMillan, Seaton, and Suter, *Tetrahedron*, 1960, **11**, 60.

a 48% yield of the derivative (XIII; R = *p*-Me·C_6H_4·SO_3) had been obtained with 1·5 mol. of reagent in 80 hr., this result could not be repeated in the present study and a comparable yield was only obtained after 2 weeks.

MacMillan *et al.*[9] found that the anhydro-keto-ester (XV) was obtained when the derivative (XIII; R = *p*-Me·C_6H_4·SO_3) of the 2(*ax*)-hydroxy-ester was boiled with collidine for 6 hr. Surprisingly, we found that the derivative (XIV; R = *p*-Me·C_6H_4·SO_3) of the 2(*eq*)-hydroxy-epimer also gave a good yield of the anhydro-compound (XV) under the same conditions. However, when the reaction time was reduced to 1 hr., the derivative (XIV; R = *p*-Me·C_6H_4·SO_3) was largely unchanged whereas a 37% yield of the anhydro-compound (XV) was obtained from the derivative (XIII; R = *p*-Me·C_6H_4·SO_3).

Like many of its relatives the 8-epi-methyl ester (IX; R = Me, R′ = H) showed dimorphism; it was the major constituent of the epimeric mixture of 2-hydroxy-esters obtained by sodium borohydride reduction of the 2-ketone (XVII; R = Me), which could be obtained by chromic oxide oxidation of both epimers. The 2-hydroxy-epimer (XVIII; R = R′ = OH) of the 8-epi-methyl ester (IX; R = Me, R′ = H) was obtained in about 10% yield by chromatography of the mixture from the borohydride reduction. Both epimers were stable to 0·01N-sodium hydroxide which brings about epimerisation at position 2 in 2-hydroxygibbane 1→4a-lactones.[1]

Toluene-*p*-sulphonylation of the 8-epi-methyl ester (IX; R = Me, R′ = H) occurred readily, and the 2,7-ditoluene-*p*-sulphonate and both the 2- and the 7-monotoluene-*p*-sulphonate were obtained. The monotoluene-*p*-sulphonates were oriented by the oxidation with chromic oxide of the 7-toluene-*p*-sulphonate, to a 2-ketone. The 2-toluene-*p*-sulphonate, which was formed in larger amount and was not oxidised under the same conditions, was recovered after 1 hour's boiling with collidine. In the same conditions of toluene-*p*-sulphonylation, 54% of the 2-hydroxy-epimer (XVIII; R = R′ = OH) was recovered and only 31% of an oily monotoluene-*p*-sulphonate was obtained. This was recovered from boiling collidine and shown to be the 7-toluene-*p*-sulphonate by oxidation by chromic oxide to the toluene-*p*-sulphonate of the ketone (XVII; R = Me).

The anhydro-compound (XV), together with the 2(*eq*)-chloro-ester (XIV; R = Cl), was obtained by the action of phosphorus pentachloride in ether at room temperature on the 2(*ax*)-hydroxy-keto-ester (XIII; R = OH). Under the same conditions 63% of the 2(*eq*)-hydroxy-epimer (XIV; R = OH) was recovered and the anhydro-compound (XV) was not among the products. Under more vigorous conditions the 2(*ax*)-chloro-ester (XIII; R = Cl) was the only product obtained from the 2(*eq*)-hydroxy-ester (XIV; R = OH). The configurations at position 2 of the chloro-esters (XIII and XIV; R = Cl) were allocated on the basis of the infrared stretching frequencies of the carbon–halogen linkages.[10]

Replacement of hydroxyl by chlorine, by means of phosphorus pentachloride, is known to take place with inversion of configuration.[11] Thionyl chloride, on the other hand, usually reacts by a cyclic mechanism, with predominant retention of configuration; but an attempt to prepare the 2(*eq*)-chloro-ester (XIV; R = Cl) from the 2(*eq*)-hydroxy-ester (XIV; R = OH) by using this reagent was unsuccessful and the only product was the sulphite (XVI).

A preliminary study of the elimination of water from the 8-epi-methyl ester (IX; R = Me, R′ = H) by means of phosphorus pentachloride in light petroleum underlined the desirability of converting the 1-methoxycarbonyl residue into a methyl group before attempting to draw any analogy with the behaviour of 3-hydroxy-triterpenoids, in which the mode of elimination under these conditions is diagnostic of the equatorial or axial nature of the hydroxyl group. Thus, treatment of the hydroxy-ester under the usual conditions gave ambiguous results; of the three crystalline products isolated in low yield,

[10] Barton, Page, and Shoppee, *J.*, 1956, 331.
[11] Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 392.

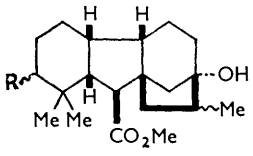
one was the 7-chloro-4aβ-gibb-2-ene (XIX; R = Cl) and the other two were the saturated dichloro-compounds (XVIII; R = R′ = Cl) and (probably) (XX; R = Cl). However, treatment of the 2-epimeric hydroxy-esters with 2 mol. of phosphorus pentachloride in ether for 4 hr. furnished results of greater significance. The ester (XVIII; R = R′ = OH) afforded a mixture of the 4aβ-gibb-2-enes (XIX; R = OH) and (XIX; R = Cl). Under the same conditions 36% of the epimer (IX; R = Me, R′ = H) was recovered: only minor amounts of the gibb-2-enes (XIX; R = OH and Cl) were formed and the major products were the isomeric chloro-esters (XVIII; R = Cl, R′ = OH) and (XX; R = OH) oriented by the oxidation of the alcohol (XX; R = OH) to a 2-ketone under conditions where the 2(*ax*)-chloro-ester (XVIII; R = Cl, R′ = OH) (C–Cl, 696 cm.$^{-1}$) was unaffected. The chloro-ester (XVIII; R = Cl, R′ = OH) was stable to phosphorus pentachloride under the above conditions but more prolonged treatment gave the 2(*ax*)-7-dichloro-compound (XVIII; R = R′ = Cl) without formation of 4aβ-gibb-2-enes. These results indicate that the 4aβ-gibb-2-enes (XIX; R = OH and Cl), produced from the ester (IX; R = Me, R′ = H), are derived directly by elimination of water and not by elimination of hydrogen chloride from the chloro-ester (XVIII; R = Cl, R′ = OH). With thionyl chloride the 8-epi-methyl ester (IX; R = Me, R′ = H) underwent substitution at the 7-position, giving the chloro-ester (XX; R = OH), but the 2-hydroxy-group was unaffected.

Evidence for the axial configuration of the 2-hydroxy-substituent in gibberellin A_1, including the formation of the 2α(*eq*)-alcohol as the major product on borohydride reduction of a 2-ketone, has already been presented [1] and is confirmed by the reactions of the keto-ester (XIII; R = OH) and its 2-hydroxy-epimer. The equatorial alcohol was more readily toluene-*p*-sulphonylated and the derived toluene-*p*-sulphonate was more stable than the axial alcohol to olefin-forming elimination; and with phosphorus pentachloride in ether the latter gave the gibb-2-ene in good yield in conditions where the equatorial alcohol underwent substitution.

The 8-epi-methyl ester (IX; R = Me, R′ = H), by contrast, was largely regenerated on borohydride reduction of the 2-ketone; the 2-hydroxyl group, which has the same (β) absolute configuration as in the keto-ester (XIII; R = OH), was more readily toluene-*p*-sulphonylated than the epimer, and the toluene-*p*-sulphonate resisted elimination. With phosphorus pentachloride the difference between the 2-hydroxy-epimers was not so clear as with the keto-ester (XIII; R = OH) and its 2-hydroxy-epimer; but whereas the ester (XVIII; R = R′ = OH) gave only elimination and no substitution products, the ester (IX; R = Me, R′ = H) gave mainly substitution products and only a low yield of gibb-2-enes.

These results clearly indicate that a change in the conformation of ring A has taken place as a result of hydrogenolysis leading to the ester (IX; R = Me, R′ = H). Decisive evidence for the equatorial nature of the 2-hydroxy-group in compound (IX; R = R′ = H) was obtained from a pinacol reaction undergone by the alcohol (XXI; R = β-OH) prepared from the 8-epi-methyl acid (IX; R = R′ = H) by standard methods. Rosenmund reduction of the acid chloride (XXIII; R = OMe, R′ = Cl) obtained by the action of thionyl chloride on the diacetate (IX; R = H, R′ = Ac) unexpectedly yielded two isomeric aldehydes, one of which (XXIII; R = OMe, R′ = H) was identified as the normal product by the fact that the parent acid was regenerated on oxidation, whilst the second aldehyde was identified as (XXIII; R = H, R′ = OMe) in which the ester and the formyl group have been transposed. This result may be explained by assuming a cyclic oxonium intermediate which could decompose under attack by hydrogen anion to yield either the normal or the abnormal aldehyde. Oxidation of the abnormal product yielded the acid (XXIII; R = OH, R′ = OMe) isomeric with that of the normal series since methylation of both acids gave the same dimethyl ester (IX; R = Me, R′ = H). Reduction of the ethylene thioketal of the aldehyde (XXIII; R = OMe, R′ = H) by Raney nickel, followed by saponification of the protecting acyl groups, yielded the alcohol

(XXI; R = β-OH). Under the influence of phosphorus pentachloride, elimination of water now occurred from the alcohol (XXI; R = β-OH), with concomitant contraction of ring A, yielding the chloro-olefin (XXIV); a saturated chloro-ester, probably the 2α,7-dichloro-derivative of the alcohol (XXI; R = OH) was also formed. Ozonolysis of the



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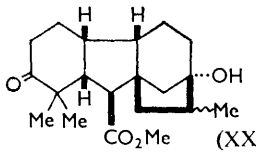

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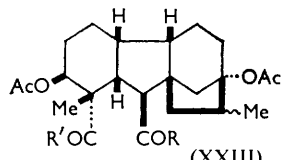

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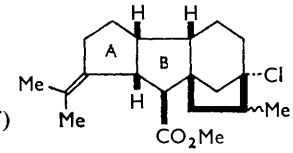

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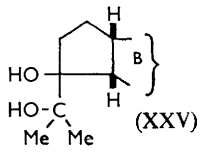

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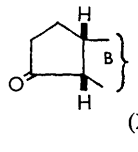

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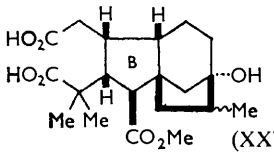

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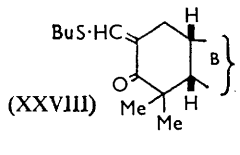

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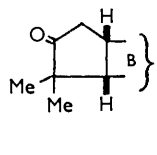
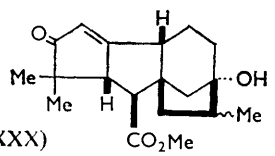


(XXIX)

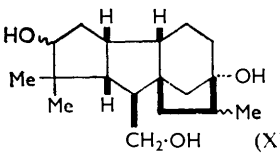
olefin (XXIV) gave acetone, characterised as the dinitrophenylhydrazone; and oxidation with osmium tetroxide gave a mixture of isomeric glycols (XXV), one of which was cleaved by lead tetra-acetate to acetone and the cyclopentanone (XXVI).

Reduction with sodium in ethanol of the ketone (XXII), obtained by oxidation of the alcohol (XXI; R = β-OH) with chromic oxide, yielded the parent alcohol (XXI; R = β-OH) together with the 2α-hydroxy-epimer (XXI; R = α-OH) in the ratio 83 : 17. This result is in good agreement with the ratio of equatorial : axial alcohols usually obtained by this procedure from A/B-*trans*-3-oxo-triterpenoids.

Nevertheless, proof of the A/B-*cis*-fusion in the acids (IX; R = R′ = H), to be expected in the light of current knowledge of the results of hydrogenation of model tetrahydroindanes [12] analogous to the unsaturated acids (VII), was obtained as follows. Pyrolysis of the dicarboxylic acid (XXVII), obtained by ozonolysis of the butylthiomethylene



(XXX)



(XXXI)

derivative (XXVIII) of the ketone (XXII), gave the A-nor-ketone (XXIX). Bromination and dehydrobromination of the A-nor-ketone afforded the conjugated cyclopentenone (XXX), reduction of which under equilibrating conditions, because of the known relative stabilities of *cis*- and *trans*-bicyclo[3,3,0]octanones,[13] can only lead to a *cis*-fused product. The pair of epimeric triols (XXXI) obtained on reduction with lithium in liquid ammonia was identical with the pair of compounds obtained by a similar reduction of the ketone (XXIX), thus establishing the A/B-*cis*-fusion in this compound and in the 8-epi-methyl acid (IX; R = R′ = H).

The optical rotatory dispersion curve for the ketone (XXVI) showed a positive Cotton

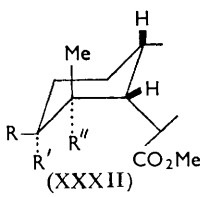
[12] Dauben, *Bull. Soc. chim. France*, 1960, 1338; Dauben, McFarland, and Rogan, *J. Org. Chem.*, 1961, **26**, 297; Boyce and Whitehurst, *J.*, 1960, 4547.

[13] Granger, Nau, and Nau, *Bull. Soc. chim. France*, 1960, 1225.

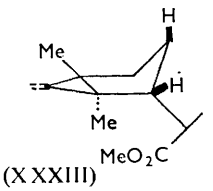
effect, consistent with the octant rule.[14] The ketone (XXIX) also showed the expected small positive Cotton effect.

Molecular models show that, like methyl gibberellate (I), the more stable configuration for the 10-methoxycarbonyl substituent in the 8-epi-methyl ester (IX; R = Me, R′ = H) is β, and, as expected, this ester was stable, apart from hydrolysis of the 1-methoxycarbonyl substituent, to boiling 2N-sodium hydroxide.

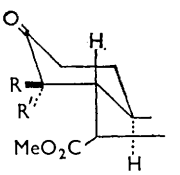
The chemistry of the 2-epimeric reduction products (IX; R = Me, R′ = H) and (XVIII; R = R′ = OH) of the ketone (XVII; R = Me) is consistent only with their being in the " non-steroid-like " conformation (XXXII; R, R′ = H, OH, R″ = CO_2Me), a conformation not previously reported for a *cis*-fused hexahydroindane.[6,15] Like gibberellin A_1,[8] both epimers showed positive plain rotatory dispersion curves and it is of interest that such a major change in the conformation of ring A should leave the sign of the plain curves unaltered. The octant rule predicts a positive Cotton effect for conformation (XXXII; RR′ = O, R″ = Me) of the ketone (XXII); the observed negative Cotton effect ($10^{-2}a$, −95°) indicates that the non-bonded interaction between the 10-methoxycarbonyl group and the substituents at position 1 forces ring A into a conformation close to the " distorted chair " (XXXIII).[16] This situation is analogous to that in the A/B-*trans*-series (XXXIV; R = Me, R′ = H), discussed in the following paper,[17] where replacement of hydrogen by methoxycarbonyl at position 1 inverts the sign of the Cotton effect owing to the adoption of the conformation (XXXV).



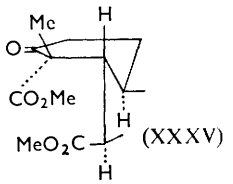
(XXXII)



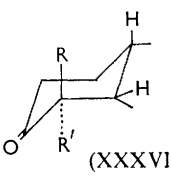
(XXXIII)



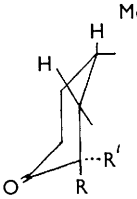
(XXXIV)



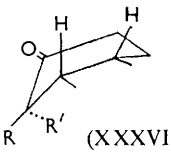
(XXXV)



(XXXVI)



(XXXVII)

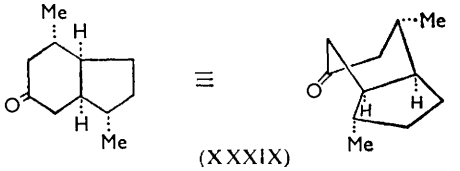


(XXXVIII)

The 8-epi-methyl-keto-acid (XVII; R = H) was decarboxylated in boiling water to a mixture of the two isomeric ketones (XII), m. p. 159—161°[7] (curve A of Figure) and m. p. 124° (curve B), the (less stable) former being converted into the latter with base. The only explanation of this result, since the corresponding ester (IX; R = Me, R′ = H) is stable to alkali, is that it involves inversion of configuration of the 1-methyl substituent, the unlikely possibility that the isomeric ketones represent stable rotational isomers having been excluded (see Experimental section). The large amplitude ($10^{-2}a$, −136°) of curve B, which is comparable with that found for the guaiol[18] degradation product (+)-*cis*-hexahydro-3,7-dimethylindan-5-one ($10^{-2}a$, +143°)[19] (XXXIX), suggests that the ketone of m. p. 124° has the " twist " conformation[20,21] (XXXVIII; R = Me, R′ = H), the isomer, m. p. 159—161° ($10^{-2}a$, −11°), adopting the " steroid-like " conformation (XXXVII; R = H, R′ = Me) present in 5β-cholestan-3-one[22] (curve D); however,

[14] Moffitt, Woodward, Moscowitz, Klyne, and Djerassi, *J. Amer. Chem. Soc.*, 1961, **83**, 4013.
[15] Acklin and Prelog, *Helv. Chim. Acta*, 1959, **42**, 1239.
[16] Allinger and Da Rooge, *Tetrahedron Letters*, 1961, 676.
[17] Aldridge and Grove, Part XXIII, following paper.
[18] Minato, *Tetrahedron*, 1962, **18**, 365, and earlier references.
[19] Eisenbraun, George, Riniker, and Djerassi, *J. Amer. Chem. Soc.*, 1960, **82**, 3648.
[20] Johnson, Bauer, Margrave, Frisch, Drieger, and Hubbard, *J. Amer. Chem. Soc.*, 1961, **83**, 606.
[21] Djerassi and Klyne, *Proc. Nat. Acad. Sci. Washington*, 1962, **48**, 1093.
[22] Djerassi and Closson, *J. Amer. Chem. Soc.*, 1956, **78**, 3761.

the alternative pair of conformations (XXXVIII; R = H, R′ = Me) and (XXXVII; R = Me, R′ = H) cannot be excluded by the rotatory dispersion evidence, and the configuration at position 1 in the isomeric ketones (XII) is therefore not proved. The (negative) signs of the Cotton effects exclude the " non-steroid-like " conformation (XXXVI) for these ketones, and the tentative proposal [23] that they had the A/B-*trans*-configurations (XXXIV; R = Me, R′ = H) and (XXXIV; R = H, R′ = Me), respectively, is invalidated by the present work.



(XXXIX)

The " twist " conformation of the ketone (XXXIX) makes all the substituents on the cyclohexanone ring equatorial. The ketone (XVII; R = Me), which gives a similar curve ($10^{-2}a$, −132°), presumably also exists in the " twist " conformation which is readily derived by further distortion of the " distorted chair " conformation favoured for the ketone (XXII). This difference in the ring A conformations of the ketones (XXII) and (XVII; R = Me), revealed by the amplitudes of the rotatory dispersion curves, is reflected in the different results obtained on reduction by borohydride. Whereas reduction of the ketone (XXII) gave mainly the 2α(*ax*)-hydroxy-epimer, reduction of the ketone (XVII; R = Me) took place predominantly from the hindered α-face, to give the thermodynamically more stable 2β(*eq*)-hydroxy-ester (IX; R = Me, R′ = H).

The 3-butylthiomethylene derivative (XXVIII) was most conveniently prepared by methylation of the 3-butylthiomethylene derivative of the ketone (XII), m. p. 124°, prepared in turn from the 3-hydroxymethylene analogue.

A strong band near 870 cm.$^{-1}$, absent in the spectrum of the ester (IX; R = Me, R′ = H) and first noticed for the chloro-ester (XX; R = OH), is present with all the 7-chlorogibbane derivatives examined; 870 cm.$^{-1}$ is considerably higher than any value previously reported for a C–Cl stretching frequency, but it is clearly associated with the presence of a chlorine substituent at this position.

Experimental

M. p.s are corrected. Alumina of grade II and pH 4 was used in chromatography. Unless otherwise stated, infrared spectra were obtained for Nujol mulls, and ultraviolet spectra and optical rotations for ethanol solutions. Light petroleum had b. p. 60—80°. Identifications were confirmed by mixed m. p. determinations and comparison of infrared spectra.

Methyl Dihydroallogibberate.—The *methyl ester* prepared from the acid [5] with ethereal diazomethane crystallised from light petroleum in needles, m. p. 131° (Found: C, 76·1; H, 8·1. $C_{19}H_{24}O_3$ requires C, 76·0; H, 8·05%).

Methyl Dihydroepiallogibberate.—The oil, obtained by methylation of the dihydroepiallogibberic acid,[6] m. p. 234—236°, with diazomethane in ether, was twice distilled at 100° (bath)/5 × 10^{-4} mm. and the distillate was crystallised from light petroleum, giving the *methyl ester* in needles, m. p. 96° (Found: C, 76·2; H, 7·9. $C_{19}H_{24}O_3$ requires C, 76·0; H, 8·05%).

Catalytic Reduction of the Ester (IV).—(*a*) *In neutral medium.* The ester (1 g.) in ethyl acetate (100 ml.) was hydrogenated in the presence of 25% palladium–charcoal (0·5 g.). Absorption (2·46 mol.) was virtually complete after 4 hr., then the solution was filtered and extracted with aqueous sodium hydrogen carbonate (3 × 50 ml.). Evaporation of the organic layer yielded neutral material (*A*) (0·22 g.), prisms, m. p. 203—226° (from ethyl acetate–light

[23] Cross, Grove, McCloskey, MacMillan, Moffatt, and Mulholland, " Advances in Chemistry Series," Amer. Chemical Society, Washington, D.C., 1961, Vol. XXVIII, p. 3.

petroleum), the infrared spectrum of which was identical with that of the crude neutral product from the catalytic reduction of the 8-epi-methyl ester (V) (see below). The aqueous layer was acidified with concentrated hydrochloric acid and extracted with ethyl acetate (6 × 50 ml.); the extract was washed with water (10 ml.), and on evaporation yielded an amorphous acidic product (*B*) (0·81 g.). The acidic product (*B*), together with similar material (0·15 g.) from another experiment, was chromatographed in ether on a column (8 × 54 cm.) of Celite (Hyflo supercel) (700 g.) previously buffered to pH 7·0 by stirring it with a solution (300 ml.) of sodium dihydrogen phosphate dihydrate (37·44 g.) and disodium hydrogen phosphate dodecahydrate (128·80 g.) in water (to 400 ml.) and adjusting the pH by the addition of sodium hydroxide. Fractional elution with ether (volumes in parentheses) afforded (i) (1 l.), solid (100 mg.); (ii) (200 ml.), gum (10 mg.); (iii) (400 ml.), solid (300 mg.); (iv) (1·6 l.), gum (255 mg.); (v) (2·6 l.), solid (46 mg.); (vi) (1·2 l.), solid (100 mg.); (vii) (1·6 l.), gum (55 mg.).

Fractions (ii), (iv), and (vii) were intractable. Fraction (i) gave prisms (30 mg.), m. p. 252—253°, from ethyl acetate–ether, of a *substance* (Found: C, 63·7, 63·9; H, 7·7, 7·1; OMe, 7·8. $C_{20}H_{26}O_7$ requires C, 63·5; H, 6·9; 1OMe, 8·25%), $\nu_{max.}$ 3470, 3415 (OH), 1777, 1716 cm.$^{-1}$ (C=O) (low end-absorption only in the ultraviolet region). This did not dissolve in sodium hydrogen carbonate. On microhydrogenation it absorbed hydrogen (0·45 mol.).

Fraction (iii) gave: (a) nodules (15 mg.), m. p. 240—241·5° from ethyl acetate–ether, of *methyl* 1α-*carboxy*-2β,7-*dihydroxy*-1β,8-*dimethylgibb*-4-*ene*-10β-*carboxylate* (VII) (Found: C, 66·3; H, 7·7. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·7%), $\nu_{max.}$ 3470, 3325 (OH), ~2700, and 1710 cm.$^{-1}$ (C=O), ε 5360, 4750, 2430, 850, and 290 at 203, 205, 210, 215, and 220 mμ, respectively; and (b) prisms (10 mg.), m. p. 218—221·5°, from ethyl acetate–ether, of *methyl* 1α-*carboxy*-2β,7-*dihydroxy*-1β,8ξ-*dimethylgibb*-4a(4b)-*ene*-10β-*carboxylate* (VIII) (Found: C, 65·9; H, 7·7%), $\nu_{max.}$ 3460, 3380, 3235 (OH), 1730 (sh), 1716 (sh), and 1703 cm.$^{-1}$ (C=O), ε 10,800, 10,600, 6560, 4200, and 2540, at 202, 205, 210, 215,and 220 mμ, respectively.

Fraction (v) formed platelets (15 mg.), m. p. 269—271°, from ethyl acetate–ether, of the 8-epi-methyl acid (IX; R = R′ = H) [1] (Found: C, 65·7; H, 8·4; OMe, 9·1. Calc. for $C_{20}H_{30}O_6$: C, 65·55; H, 8·25; 1OMe, 8·5%), $\nu_{max.}$ (in $CHCl_3$), 1724 and 1703 (sh) cm.$^{-1}$ (C=O), $[\alpha]_D^{26}$ +50·0° (*c* 0·92). The *diacetate* (IX; R = H, R′ = Ac), prepared in acetic anhydride–pyridine during 7 hr. at 100°, crystallised from ether–light petroleum (b. p. 40—60°) in needles, m. p. 251—252° (Found: C, 64·05; H, 7·6. $C_{24}H_{34}O_8$ requires C, 64·0; H, 7·6%), $\nu_{max.}$ 3255 (monomeric carboxylic acid OH), 1735, and 1702 cm.$^{-1}$ (C=O), $\nu_{max.}$ (in CCl_4) OH absent, 1736, 1702, and 1685 cm.$^{-1}$. The diacetate was not readily extracted from ether by sodium hydrogen carbonate. In the absence of pyridine the acetylation product was the mixed *anhydride* (IX; R = R′ = Ac), needles, m. p. 128—129° (Found: C, 63·6; H, 7·4. $C_{26}H_{36}O_4$ requires C, 63·4; H, 7·4%), $\nu_{max.}$ 1814 and 1735 cm.$^{-1}$ (C=O), which gave the acetate (IX; R = H, R′ = Ac) when heated for 1 hr. at 100° with saturated sodium hydrogen carbonate solution.

Fraction (vi) gave prisms (25 mg.), m. p. 240—241° or 253—254°, from ethyl acetate–ether, of *methyl* 1α-*carboxy*-2β,7-*dihydroxy*-1β,8-*dimethylgibbane*-10β-*carboxylate* (IX; R = R′ = H) (Found: C, 64·4; H, 8·2. $C_{20}H_{30}O_6$,0·5H_2O requires C, 64·0; H, 8·3%), $\nu_{max.}$ 3475, 3370 (OH), 1730, 1716 (sh), 1699 (sh) (C=O), and 1656 (sh) (H_2O) cm.$^{-1}$, or (in $CHCl_3$) 1717 (sh) and 1709 cm.$^{-1}$, $[\alpha]_D^{19}$ +54° (*c* 0·815). The *methyl ester* formed leaflets, m. p. 213—214°, from ethyl acetate–light petroleum (1 : 2) (Found: C, 66·1; H, 8·7. $C_{21}H_{32}O_6$ requires C, 66·3; H, 8·5%).

The neutral fraction (*A*), in methanol, was adsorbed on alumina (1 g.) which was added to the top of a column (15 × 1 cm.) of alumina. Elution (10 ml. fractions) with benzene–methanol (200 : 1) gave fractions (i) (100 ml.) gum (22 mg.), (ii) (100 ml.) solid (82 mg.), (iii) (80 ml.) gum (14 mg.), and (iv) (40 ml.) gum (5 mg.). Fractions (i) and (iii) were intractable, as were additional fractions (95 mg.) obtained by further elution with benzene–methanol (100 : 1 and 20 : 1). Fraction (ii) crystallised from ethyl acetate in prisms (58 mg.), m. p. 232—234°, of the 8-epi-methyl ester (VI). Fraction (iv) crystallised from ethyl acetate in needles (3 mg.), m. p. 258—261°, of the 8-methyl epimer (VI).

(*b*) *In acidic medium* (cf. ref. 1). The ester (3·57 g.) in acetic acid (75 ml.) was hydrogenated in the presence of a pre-reduced Adams platinum oxide (0·5 g.). Absorption of hydrogen (2·77 mol.) was complete after 16 hr. The mixture was filtered and, after removal of the solvent *in vacuo*, the residual gum, in ethyl acetate, was separated into neutral and acidic portions. The neutral fraction (0·26 g.) was not examined further. A solution of the acidic fraction (3·4 g.) in hot ethyl acetate (30 ml.) immediately deposited crystals (1·4 g.), m. p. 256—262°, of the crude 8-epi-methyl acid (IX; R = R′ = H). Recrystallisation of this, and

fractional crystallisation of the residue, yielded the 8-methyl acid (IX; R = R′ = H) (0·4 g.), its 8-epimer (1·2 g.), and a solid solution (0·15 g.), m. p. 212—217°, of the 8ξ-methyl acid (VIII) with the 8-epi-methyl acid (VII) (see below) (*ca.* 4 : 1), inseparable by fractional crystallisation but separated as the methyl esters by chromatography on alumina in ether.

Catalytic Reduction of Methyl Gibberellate.—(*a*) *In neutral medium.* A typical reduction of methyl gibberellate (5 g.) in methanol with palladium–charcoal or Adams catalyst, followed by chromatography of the crude acidic product (3·33 g.) on Celite in the manner described above for the ester (IV), gave the same products and, in addition, the following:

(i) [In association with the substance, $C_{20}H_{26}O_7$ (17 mg.)], fine needles (18 mg.), m. p. 197—198° (from ethyl acetate–light petroleum), of a *substance* (Found: C, 63·9, 63·5; H, 8·1, 8·0. $C_{21}H_{32}O_7$ requires C, 63·6; H, 8·1%), $\nu_{max.}$ 3445 (OH), 1749, 1725—1730 (sh) cm.$^{-1}$ (C=O), or (in MeCN) 1777 and 1737 cm.$^{-1}$, ε 600, 560, 400, and 240 at 203, 205, 210, and 220 mμ, respectively.

(ii) [In association with the 8-methyl acid (VII) (10 mg.)], prisms (100 mg.), m. p. 223—224°, from ethyl acetate, of the 8-*epi-methyl acid* (VII) (Found: C, 65·9; H, 7·7; OMe, 8·6. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·7; 1OMe, 8·5%), $\nu_{max.}$ 3470, 3250, ~3200 (OH), and 1700 cm.$^{-1}$ (C=O), ε 6970, 6500, 4770, 2500, 850, 320, and 200 at 197, 200, 205, 210, 215, 220, and 225 mμ, respectively. The *methyl ester* formed leaflets, m. p. 141·5—142°, from ether–light petroleum (Found: C, 66·9; H, 8·0. $C_{21}H_{30}O_6$ requires C, 66·6; H, 8·0%).

(*b*) *In acidic medium.* Methyl gibberellate (6·7 g.) in acetic acid (125 ml.) was hydrogenated in the presence of pre-reduced Adams platinum oxide (1 g.). Absorption of hydrogen (2·04 mol.) was complete after 4·5 hr. The mixture was filtered, the solvent removed *in vacuo*, and the residual gum in ethyl acetate was separated into neutral and acidic fractions. The neutral fraction (3·16 g.) was not examined further. Fractional crystallisation of the acidic portion (2·76 g.) from ethyl acetate gave the 8-methyl acid (IX; R = R′ = H) (100 mg.), its 8-epimer (475 mg.), and the 8ξ-acid (VIII) (100 mg.).

Catalytic Reduction of the 8-Epimeric Esters (V).—(*a*) *In neutral medium.* The ester, m. p. 171—172°[1] (15 mg.), in ethyl acetate (8 ml.) was reduced with hydrogen (uptake, 1·0 mol.) in the presence of 10% palladium–charcoal (10 mg.). The gummy product was separated, as described above, into acidic (12 mg.) and neutral (3 mg.) fractions. The latter crystallised from ethyl acetate–light petroleum in prisms, m. p. 258—261°, of *methyl* 1α-*carboxy*-2β,3α,7-*trihydroxy*-1β,8-*dimethyl*-4aξ-*gibbane*-10β-*carboxylate* 1→3-*lactone* (VI) (Found: C, 66·0; H, 7·8. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·7%), $\nu_{max.}$ 3490, 3395 (broad) (OH), 1756, and 1713 cm.$^{-1}$ (C=O). It gave a straw-yellow colour with concentrated sulphuric acid.

The 8-epi-methyl ester, m. p. 232—235°[1] (36 mg.), when reduced in the same way afforded acidic (32 mg.) and neutral (9 mg., m.p. 218—228°) fractions. The infrared spectrum of the neutral fraction was identical with that of the neutral fraction (see above) from the catalytic reduction of the ester (IV). It was chromatographed in benzene–methanol (200 : 1, 25 ml.) on alumina (10 × 0·6 cm.). Elution with the same solvent (100 ml.) and crystallisation of the product (7·5 mg.) from ethyl acetate–light petroleum gave prisms, m. p. 233—236°, $\nu_{max.}$ 3550 (sh), 3500 (OH), 1760, and 1715 cm.$^{-1}$ (C=O), or m. p. 227—234°, $\nu_{max.}$ 3472, 3378 (OH), 1764, and 1712 cm.$^{-1}$ (C=O), of *methyl* 1α-*carboxy*-2β,3α,7-*trihydroxy*-1β,8-*epi-dimethyl*-4aξ-*gibbane*-10β-*carboxylate* 1→3-*lactone* (VI) (Found: C, 66·0; H, 7·9%). This gave a colourless solution in concentrated sulphuric acid. In chloroform the infrared spectra of the two crystalline forms were identical.

Further elution of the column with benzene–methanol (50 : 1, 25 ml.) gave needles (1 mg.), m. p. 225—242°, $\nu_{max.}$ 3480 (OH), 1741, 1713, and 1704 (sh) cm.$^{-1}$ (C=O).

(*b*) *In acidic medium.* The ester, m. p. 171—172°[1] (20 mg.), in acetic acid (5 ml.) took up 1·9 mol. of hydrogen in the presence of Adams platinum oxide. After the catalyst had been filtered off and the solvent removed *in vacuo*, the gummy product crystallised from ethyl acetate in prisms (11 mg.), m. p. 230—232° (decomp.), of methyl 1α-carboxy-2β,7-dihydroxy-1β,8-dimethyl-4aβ-gibbane-10β-carboxylate (IX; R = R′ = H).

Under the same conditions the 8-epimer (V), m. p. 232—235°, gave the 8-epi-methyl hexahydro-acid (IX; R = R′ = H), m. p. 269—271°.

Action of Hydrochloric Acid on Methyl 1α-*Carboxy*-2β,3α,7-*trihydroxy*-1β,8-*epi-dimethyl-gibb*-4-*ene*-10β-*carboxylate* 1→3-*lactone* (V).—The ester, m. p. 232—235° (30 mg.), was heated under reflux for 30 min. with 3N-hydrochloric acid (2 ml.), and the cooled solution was extracted with ethyl acetate. The organic layer was washed with sodium hydrogen carbonate

solution, and the neutral fraction (24 mg.) obtained on recovery was chromatographed on alumina (6 × 0·5 cm.) in benzene (10 ml.). Elution of the column with benzene (60 ml.) gave a gum (5 mg.) which crystallised from light petroleum in needles of the methyl dihydroepiallogibberate, m. p. 96°. Continued elution of the column with benzene–ether (50 : 1, 20 ml.; and 20 : 1, 20 ml.) gave a gum (7 mg.) which crystallised from light petroleum in rosettes of needles of methyl dihydroallogibberate, m. p. 129—131°.

Reactions of the 8-*Epimeric Acids* (VII).—(*a*) *Lactonisation.* The acid (VII), m. p. 240—241·5° (5 mg.), in methanol (1 ml.) and concentrated hydrochloric acid (1 drop) was refluxed for 3 hr. The solution was then evaporated and the residual gum was treated with a few drops of sodium hydrogen carbonate and filtered. The neutral residue formed prisms (1 mg.), m. p. 266—268°, from ethyl acetate, of methyl tetrahydrogibberellate.[3] The acidic fraction (2·5 mg.), recovered by acidification of the aqueous solution and extraction with ethyl acetate, was unchanged acid (VII) having m. p. 218—222°, raised to 233—238° by washing with ether.

The 8-epimer, m. p. 223—224° (20 mg.), was refluxed in dioxan (1 ml.) containing concentrated hydrochloric acid (1 drop) for 12 hr. The mixture was evaporated and the residue was separated into neutral and acidic products by extraction with sodium hydrogen carbonate and recovery. The neutral product (12·5 mg.), prisms, m. p. 237—240°, was identified as methyl 8-epi-tetrahydrogibberellate.[3] The acidic fraction (6·5 mg.) was rubbed with ethyl acetate, yielding crystals (3·5 mg.), m. p. 217—218°, of the 8-epi-methyl acid (VII).

(*b*) *Hydrogenation.* The acid (VII), m. p. 240—241·5° (5·9 mg.), in acetic acid was hydrogenated in the presence of platinum oxide (absorption, 0·44 mol.) during 1 hr. The mixture was filtered and evaporated and the gummy product was crystallised from ethyl acetate, yielding fine needles (2·5 mg.), m. p. 236—239·5°, of the acid (IX; R = R′ = H) (low-melting form).

The 8-epimer (VII) (7·4 mg.) was reduced in the same way yielding, from ethyl acetate, prisms (2·5 mg.), m. p. 261—266°, of the 8-epi-methyl acid (IX; R = R′ = H). Evaporation of the mother-liquor gave a gum which was treated with aqueous sodium hydrogen carbonate and extracted with ethyl acetate. Recovery of the neutral fraction gave a gum (1 mg.) which readily gave crystals, m. p. 239—241°, of methyl 8-epi-tetrahydrogibberellate.

Toluene-p-*sulphonates of the Keto-ester* (XIII; R = OH) *and its* 2(eq)-*Hydroxy-epimer* (XIV; R = OH).—(*a*) The keto-ester (XIV; R = OH) (100 mg.) and toluene-*p*-sulphonyl chloride (150 mg.) in pyridine (2 ml.) were kept for 40 hr. at room temperature. The solvent was removed *in vacuo*; after the addition of water (2 ml.) and working up in the usual way, the gummy product (140 mg.) crystallised from ethyl acetate in felted needles (95 mg.), m. p. 222°, of the *toluene*-p-*sulphonate* (Found: C, 63·0; H, 6·45. $C_{27}H_{32}O_8S$ requires C, 62·8; H, 6·2%). The residue obtained by evaporation of the mother-liquors was chromatographed on alumina (20 × 1 cm.) in benzene. Elution with benzene–methanol (200 : 1, 300 ml.) afforded the toluene-*p*-sulphonate (17 mg.), followed by [with benzene–methanol (100 : 1, 150 ml.)] starting material (6 mg.).

(*b*) In an identical experiment with the keto-ester (XIII; R = OH), starting material (45 mg.) was recovered on crystallisation of the crude product. Extension of the reaction time to 80 hr., afforded a mixture (82 mg., m. p. 185—195°) of the keto-ester (XIII; R = OH) and its toluene-*p*-sulphonate. After 14 days the product consisted of the toluene-*p*-sulphonate, plates (74 mg.), m. p. 206—207°.[9]

Collidine Treatment of the Above Toluene-p-*sulphonates.*—The toluene-*p*-sulphonate (26·5 mg.) was heated under reflux in collidine (1·5 ml.) for a given period of time, the solvent was rapidly removed *in vacuo*, and, after working up in the usual way, the product was investigated as follows: (*a*) *After* 6 *hours' heating.* The derivative (XIV; R = *p*-Me·C_6H_4·SO_3) afforded a yellow gum (17 mg.) from which starting material (2 mg., 7·5%), m. p. 216—219°, was obtained by crystallisation from ethyl acetate. Chromatography in benzene on an alumina column (7 × 1 cm.) of the residue from the mother-liquors gave, after elution with benzene–methanol (200 : 1, 40 ml.), prisms (10 mg., 57%), m. p. 155—157°, of the anhydro-keto-ester (XV).[9]

Under the same conditions the toluene-*p*-sulphonate of the keto-ester (XIII; R = OH) gave [9] the anhydro-keto-ester (XV) in 90% yield.

(*b*) *After* 1 *hour's heating.* The derivative (XIV; R = *p*-Me·C_6H_4·SO_3) (25·1 mg.), m. p. 220—221°, was recovered.

Under the same conditions the derivative (XIII; R = *p*-Me·C_6H_4·SO_3) gave a gum (22·7 mg.) which yielded starting material (10·6 mg., 40%) on crystallisation from ethyl acetate–light

petroleum. The residue from the mother-liquors was chromatographed in benzene on alumina (10 × 0·5 cm.). After the anhydro-keto-ester (XV) (prisms, 6·5 mg., 37%, m. p. 158—159°) had been eluted with benzene (120 ml.), benzene–methanol (200 : 1, 60 ml.) afforded the keto-ester (XIV; R = OH) (3·1 mg.), m. p. 224°.

Action of Phosphorus Pentachloride on the Keto-ester (XIII; R = OH).—Phosphorus pentachloride (63·5 mg., 1·1 mol.) was added with vigorous shaking to the keto-ester (XIII; R = OH) (100 mg.) in ether (30 ml.). After 2 hr. the solution was washed with water, and the product, on recovery, was chromatographed on alumina (10 × 1 cm.) in benzene. After elution with benzene (375 ml., 25-ml. portions) and crystallisation of the products had given a series of fractions (59 mg.) of m. p. 145° to 190°, elution with benzene–methanol (200 : 1, 100 ml.) afforded starting material (32 mg.). The material of m. p. 145—190° was separated by fractional crystallisation from ethyl acetate–light petroleum (with hand-picking) into plates, m. p. 150—156° (36 mg., 38%) of the anhydro-compound (XV) and needles, m. p. 215—217°, $[\alpha]_D^{25}$ +37° (*c* 0·12) (23·5 mg., 22%), of methyl 1α-carboxy-2α-chloro-4aα-hydroxy-1β,7-dimethyl-8-oxo-7α-gibbane-10β-carboxylate 1→4a-lactone[9] (XIV; R = Cl), $\nu_{max.}$ 775 cm.$^{-1}$ (C–Cl).

Action of Phosphorus Pentachloride on the Keto-ester (XIV; R = OH).—(*a*) When the keto-ester (XIV; R = OH) had been treated as described above for the keto-ester (XIII; R = OH), crystallisation of the crude product (84 mg.) from ethyl acetate–light petroleum afforded starting material (52·5 mg.). The residue in benzene–light petroleum (1 : 1) was chromatographed on alumina (7 × 1 cm.), and the following gummy fractions were eluted: (i) benzene–light petroleum (1 : 1, 50 ml.) (0·5 mg.), giving needles, m. p. 199—202°; (ii) benzene (100 ml.), giving an intractable gum (0·5 mg.); (iii) benzene–methanol (200 : 1, 50 ml.) (10 mg.), giving prisms (1 mg.), m. p. 156—159°, of the chloro-ester (XIII; R = Cl) (see below); and (iv) benzene–methanol (200 : 1, 70 ml.) (14 mg.), giving starting material (10·5 mg.).

(*b*) The keto-ester (250 mg.) in ether (50 ml.) was shaken with phosphorus pentachloride (475 mg., 3·5 mol.) for 18 hr. and the product, in benzene, was chromatographed on alumina (15 × 1 cm.). Elution with benzene–ether (10 : 1, 200 ml.) gave a gum (109 mg.) which crystallised from ethyl acetate–light petroleum in needles, m. p. 168°, $\nu_{max.}$ 1780, 1750, and 1735 cm.$^{-1}$, or prisms, m. p. 159°, $\nu_{max.}$ 1780, and 1745 cm.$^{-1}$, of *methyl 1α-carboxy-2β-chloro-4aα-hydroxy-1β,7-dimethyl-8-oxo-7α-gibbane-10β-carboxylate* 1→4a-*lactone* (XIII; R = Cl) (78 mg.). $[\alpha]_D^{25}$ +42° (*c* 0·5) (Found: C, 63·5; H, 6·7. $C_{20}H_{25}ClO_5$ requires C, 63·1; H, 6·6%). In CS_2 the infrared spectra of the two crystalline modifications were identical, $\nu_{max.}$ 1780, 1745 (C=O), and 720 cm.$^{-1}$ (C–Cl).

Action of Thionyl Chloride on the Keto-ester (XIV; R = OH).—(*a*) Thionyl chloride (33 mg.) in chloroform (0·5 ml.) was added portionwise during 30 min. to the ester (50 mg.) in chloroform (0·5 ml.) containing dimethylaniline (34 mg.). The deep orange solution was kept at 0° for 10 min. and then heated at 60° for 45 min. The cooled red mixture was poured into N-hydrochloric acid at 0° and the solution was extracted with chloroform. The organic layer, on washing with sodium hydrogen carbonate and recovery, furnished a green gum which crystallised from ethyl acetate–light petroleum (charcoal) in needles (25 mg.), m. p. 300—302°, of the *sulphite* (XVI) (Found: C, 62·6; H, 6·4; S, 3·7. $C_{40}H_{50}O_{13}S$ requires C, 62·3; H, 6·5; S, 4·2%), $\nu_{max.}$ OH absent. Chromatography on alumina (7 × 0·8 cm.) of the residue from the mother-liquors and elution with benzene–methanol (400 : 1) gave the sulphite (XVI) (8 mg.), followed by starting material (9 mg.).

(*b*) The ester (40 mg.) was heated under reflux with thionyl chloride (0·3 ml.) for 4 hr. After removal of the thionyl chloride by distillation under reduced pressure the residue, in chloroform, was washed with sodium hydrogen carbonate and recovered. Chromatography of the brown solid on alumina in the usual way yielded the ester (XIV; R = OH) (38 mg.).

Methyl 2β,7-Dihydroxy-1β,8-epi-dimethyl-4aβ-gibbane-1α,10β-dicarboxylate (IX; R = Me, R′ = H).—Methylation of the acid (IX; R = R′ = H), m. p. 269—271° (decomp.),[1] with diazomethane gave the *methyl ester* (IX; R = Me, R′ = H), prisms (from ether), m. p. 165—166°, $\nu_{max.}$ 3350 (broad) (OH), 1739, and 1706 cm.$^{-1}$ (ester C=O), or m. p. 177—178°, $\nu_{max.}$ 3450 (OH), 1734, and 1721 (sh) cm.$^{-1}$ (ester C=O), $[\alpha]_D^{22}$ +43° (*c* 1·0) (Found: C, 66·5; H, 8·6. $C_{21}H_{32}O_6$ requires C, 66·3; H, 8·5%). The infrared spectra of the two forms were identical in $CHCl_3$ solution.

The ester (50 mg.) was recovered after 2 hours' shaking with 0·01N-sodium hydroxide (22·5 ml.), in which it was readily soluble, followed by extraction with ethyl acetate.

The *diacetate* (IX; R = Me, R′ = Ac), prepared by methylation of the acid (IX; R = H, R′ = Ac), crystallised from 1 : 1 ether–light petroleum (b. p. 40—60°) in needles, m. p. 169—170° (Found: C, 64·7; H, 8·0. $C_{25}H_{36}O_8$ requires C, 64·6; H, 7·8%).

The ester (IX; R = Me, R′ = H) (40 mg.) and toluene-*p*-sulphonyl chloride (42 mg., 2 mol.) in pyridine (1 ml.) were kept for 8 days at room temperature. After working up in the usual way the gummy product (53 mg.) was chromatographed on alumina (8 × 1 cm.) in benzene. The following gummy fractions were eluted: (i) benzene–ether (10 : 1, 75 ml.), 8·5 mg.; (ii) benzene–ether (1 : 1, 500 ml.), 19 mg.; (iii) ether (150 ml.), followed by benzene–methanol (400 : 1, 100 ml.), 8 mg.; and (iv) benzene–methanol (100 : 1, 75 ml.), 10 mg., prisms, m. p. 166—167°, of the ester (IX; R = Me, R′ = H).

Fraction (i) crystallised from ethyl acetate–light petroleum in needles (6 mg.), m. p. 212—215°, of the *ditoluene*-p-*sulphonate* (Found: C, 61·6; H, 6·6. $C_{35}H_{44}O_{10}S_2$ requires C, 61·0; H, 6·4%).

Crystallisation of fraction (ii) from ethyl acetate–light petroleum gave the 2-*toluene*-p-*sulphonate* (14 mg.), plates, m. p. 141—143°, or micro-crystalline powder, m. p. 120—121° and 136—138° (Found: C, 61·7, 61·7; H, 7·2, 7·3. $C_{28}H_{38}O_8S,CH_3{\cdot}CO_2Et$ requires C, 61·7; H, 7·4%). The two forms had characteristic infrared spectra in the 7—15 μ region; the spectra in $CHCl_3$ were identical, $\nu_{max.}$ 3564 (OH), 1737 (sh), 1727 (ester C=O), and 1600 cm.$^{-1}$ (aromatic ring).

Similar treatment of fraction (iii) gave the 7-*toluene*-p-*sulphonate*, plates (5 mg.), m. p. 209—211° (Found: C, 62·8; H, 7·4. $C_{28}H_{38}O_8S$ requires C, 62·9; H, 7·2%).

The 2-toluene-*p*-sulphonyl derivative was recovered after 1 hour's heating under reflux with collidine and after attempted oxidation in acetone with the chromic oxide–sulphuric acid reagent (see below).

Oxidation of the 7-toluene-*p*-sulphonate (1 mg.) with the chromic oxide–sulphuric acid reagent gave a ketone (0·6 mg.), plates, m. p. 165—167°, identical with the toluene-*p*-sulphonate of the keto-ester (XVII; R = Me) (see below).

Oxidation of the 8-*Epi-methyl ester* (IX; R = Me, R′ = H).—The ester (150 mg.) in acetone (5 ml.) at 0° was treated with the chromic oxide–sulphuric acid reagent [3] (0·2 ml.). After 1 hr. at room temperature, water (20 ml.) was added and the solution was extracted with ethyl acetate (3 × 10 ml.). The recovered solid (144 mg., 96%; m. p. 205—208°) crystallised from ethyl acetate–light petroleum in felted needles (109 mg.), m. p. 212—213° (decomp.), $[\alpha]_D^{23}$ −36° (*c* 0·25), of *methyl* 7-*hydroxy*-1β,8-*epi-dimethyl*-2-*oxo*-4aβ-*gibbane*-1α,10β-*dicarboxylate* (XVII; R = Me) (Found: C, 66·9; H, 8·2. $C_{21}H_{30}O_6$ requires C, 66·6; H, 8·0%), $\nu_{max.}$ 3200 (broad) (OH), 1744, and 1702 cm.$^{-1}$ (C=O).

The keto-ester (XVII; R = Me) (10 mg.) and toluene-*p*-sulphonyl chloride (10 mg.) in pyridine were kept for 2 weeks at room temperature. The gummy product in benzene was chromatographed on alumina (5 × 0·5 cm.). Benzene–ether (20 : 1, 15 ml.) eluted the *toluene*-p-*sulphonate* (1·5 mg.), plates, m. p. 167° (from ethyl acetate–light petroleum) (Found: C, 63·1; H, 6·8. $C_{28}H_{36}O_8S$ requires C, 63·2; H, 6·8%), $\nu_{max.}$ OH absent, 1750, 1738, 1700, (C=O), and 1596 cm.$^{-1}$ (aromatic ring). Further elution of the column with benzene–methanol (50 : 1) gave starting material (5 mg.).

Reduction of the Keto-ester (XVII; R = Me).—Sodium borohydride (50 mg.) in methanol (1 ml.) at 0° was added with stirring to the keto-ester (50 mg.) in methanol (2 ml.). After 1 hr. at room temperature the excess of hydride was decomposed with acetic acid, and the solvent was removed *in vacuo*. After water (5 ml.) had been added to the residue, ether-extraction furnished a gum (44 mg.) which crystallised from ether in prisms (20 mg.), m. p. 170—171°, of the ester (IX; R = Me, R′ = H). The gummy residue (23 mg.) from the mother-liquors was chromatographed in benzene on alumina (5 × 0·5 cm.). Fractional elution (10 ml. portions) with benzene–methanol (200 : 1) gave (volume of eluant in parentheses): (i) (30 ml.) gum (10 mg.); (ii) (30 ml.) inter-band (1 mg.); and (iii) (100 ml.) gum (13 mg.) which crystallised from ether in prisms, m. p. 174°, of the ester (IX; R = Me, R′ = H).

Fraction (i) crystallised from ether in prisms (5 mg.), m. p. 128°, $[\alpha]_D^{23}$ +5° (*c* 0·5), of *methyl* 2α,7-*dihydroxy*-1β,8-*epi-dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylate* (XVIII; R = R′ = OH) (Found: C, 66·3; H, 8·7. $C_{21}H_{32}O_6$ requires C, 66·3; H, 8·5%), $\nu_{max.}$ 3530 and 1717 cm.$^{-1}$.

On a larger scale (500 mg.) the yields of the 8-epi-methyl ester (IX; R = Me, R′ = H) and its 2-hydroxy-epimer (XVIII; R = R′ = OH) averaged 70% and 10%, respectively.

Oxidation of the ester (XVIII; R = R′ = OH) (5 mg.) with chromic oxide, as described

above for the ester (IX; R = Me, R′ = H), gave the keto-ester (XVII; R = Me) (4 mg.), m. p. 212—213° (decomp.).

The ester (XVIII; R = R′ = OH) was recovered after 2 hours' shaking with 0·01N-sodium hydroxide as described for the ester (IX; R = Me, R′ = H).

Attempted reduction of the keto-ester (XVII; R = Me) with hydrogen and Adams platinum oxide in acetic acid in the presence of perchloric acid was unsuccessful and only starting material was recovered.

Toluene-p-*sulphonation of the Ester* (XVIII; R = R′ = OH).—The ester (46 mg.) and toluene-*p*-sulphonyl chloride (46 mg.) in pyridine (1 ml.) were set aside for 8 days at room temperature. After working up in the usual way, the gummy product (56 mg.) was chromatographed on alumina (7 × 1 cm.) in benzene. Elution with benzene–ether (10 : 1, 100 ml.) gave a gum (20 mg.) which on distillation at 160° (bath)/6 × 10^{-3} mm. afforded the oily 7-*toluene*-p-*sulphonate*, $\nu_{max.}$ (in CS_2) 1740, 1705, 1600 (aromatic ring), 1290, and 1280 $cm.^{-1}$ ($Ar{\cdot}SO_2$), characterised as the 2-ketone (see above).

Further elution of the column with benzene–methanol (200 : 1, 50 ml.) gave starting material (25 mg.), m. p. 124—126°.

The 7-toluene-*p*-sulphonate was recovered after 1 hour's heating under reflux with collidine. Oxidation of the derivative (8 mg.) with chromic oxide in acetone gave the toluene-*p*-sulphonate (6 mg.), m. p. 165—166°, of the keto-ester (XVII; R = Me).

Action of Phosphorus Pentachloride on the 8-*Epi-methyl Ester* (IX; R = Me, R′ = H), *and its* 2-*Hydroxy-epimer* (XVIII; R = R′ = OH).—(*A*) *In light petroleum.* The finely powdered 8-epi-ester (IX; R = Me, R′ = H) (0·25 g.) was suspended in light petroleum (b. p. 40—60°; 75 ml.) and shaken with phosphorus pentachloride (0·29 g., 2·1 mol.). After 3 hr., with much of the solid undissolved, more light petroleum (25 ml.) was added and, after a further 1 hr., more phosphorus pentachloride (0·25 g.). Shaking was then continued for a further 18 hr. Thereafter the reaction mixture was washed with water (which removed a little undissolved solid), followed by sodium hydrogen carbonate. Recovery yielded a pale yellow gum (0·27 g.) which was redissolved in light petroleum (b. p. 40—60°) and chromatographed on alumina (7 g.), giving the following fractions (eluant in parentheses): (i) (light petroleum, 400 ml.), gum (59 mg.); (ii) (light petroleum–ether, 99 : 1, rising to 49 : 1; 700 ml.), gummy crystals (89 mg.); (iii) (light petroleum–ether, 95 : 5, rising to 9 : 1; 725 ml.), gummy crystals (56 mg.), and (iv) (ether, 200 ml., followed by acetone, 100 ml.), gum (16 mg.).

Fractions (i) and (iv) were intractable. Fraction (ii) crystallised from ether–light petroleum (1 : 1), giving a mixture of (*a*) leaflets (15 mg.) and (*b*) prisms (12 mg.) which were separated manually. Recrystallisation of (*a*) from ether–light petroleum (1 : 1) gave leaflets (5·5 mg.), m. p. 168—171°, of *methyl* 7-*chloro*-1β,8-*epi-dimethyl*-4aβ-*gibb*-2-*ene*-1α,10β-*dicarboxylate* (XIX; R = Cl) (Found: C, 66·3; H, 7·65. $C_{21}H_{29}ClO_4$ requires C, 66·2; H, 7·6%), $\nu_{max.}$ 1748, 1700 (sh) (C=O), 1655, 735 (C=C), and 878 $cm.^{-1}$ (C–Cl), ε 2320, 710, and 390 at 200, 210 and 220 mμ, respectively. Recrystallisation from ether of material (*b*) gave prisms (8 mg.), m. p. 154—155°. of a product, $\nu_{max.}$ (OH absent) 1740, 1727, 875, 782, 743, 718, and 698 $cm.^{-1}$ (negligible absorption above 200 mμ), probably methyl 2β,7-dichloro-1β,8-epi-dimethyl-4aβ-gibbane-1α,10β-dicarboxylate (XX; R = Cl) but giving an unsatisfactory analysis.

Fraction (iii) recrystallised from light petroleum (b. p. 40—60°) as needles (26 mg.), m. p. 165—168°, which on recrystallisation gave a mixture (17 mg.) of (*a*) needles, m. p. 170—171°, and (*b*) prisms, m. p. 164·5—165·5°, $\nu_{max.}$ 1727 (C=O), 870, and 696 $cm.^{-1}$ (C–Cl), resolidifying when seeded with the needles (*a*) and then remelting at 170—171°, of *methyl* 2α,7-*dichloro*-1β,8-*epi-dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylate* (XVIII; R = R′ = Cl) (Found: C, 60·4; H, 7·4; Cl, 17·0. $C_{21}H_{30}Cl_2O_4$ requires C, 60·4; H, 7·2; Cl, 17·0%). The infrared spectra of the two forms were identical in carbon tetrachloride, $\nu_{max.}$ 1745 (sh) and 1738 $cm.^{-1}$.

(*B*) *In ether.* (*a*) The ester (IX; R = Me, R′ = H) (576 mg.) in ether (300 ml.) was shaken with phosphorus pentachloride (632 mg.) for 4 hr. The solution was washed with aqueous sodium hydrogen carbonate, and the neutral solute (579 mg.) was recovered and chromatographed on alumina (17 × 2 cm.) in benzene. The following gummy fractions were obtained: (i) benzene (150 ml.), 4 mg.; (ii) benzene (250 ml.), 10 mg.; (iii) benzene–ether (20 : 1, 350 ml.), 8 mg.; (iv) benzene–ether (20 : 1, 250 ml.), 44 mg.; (v) benzene–ether (20 : 1, 300 ml.; and 10 : 1, 100 ml.) 48 mg.; (vi) benzene–ether (3 : 1, 300 ml.; and 1 : 1, 150 ml.), 21 mg.; (vii) benzene–ether (1 : 1, 1 l.) 34 mg.; (viii) benzene–methanol (200 : 1, 200 ml.), 25 mg.; and (ix) benzene–methanol (100 : 1, 250 ml.; and 50 : 1, 150 ml.) 207 mg., which crystallised from ethyl

acetate–light petroleum in prisms (175 mg.), m. p. 165°, of the ester (IX; R = Me, R′ = H). Fractions (iii) and (v) were intractable. Fraction (i) crystallised from light petroleum in plates (1 mg.), m. p. 100—101°, $\nu_{max.}$ OH absent, 1745 cm.$^{-1}$ (C=O). Fractions (ii) and (vi) gave the 4aβ-gibb-2-enes (XIX; R = Cl), plates (2 mg.), m. p. 165°, and (XIX; R = OH), needles (9 mg.), m. p. 163°, respectively (see below). Fraction (iv) crystallised from ethyl acetate–light petroleum in needles (20 mg.), m. p. 180—181°, $[\alpha]_D^{17}$ −21° (*c* 0·36), of *methyl* 2α-*chloro*-7-*hydroxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylate* (XVIII; R = Cl, R′ = OH) (Found: C, 63·8; H, 8·0. $C_{21}H_{31}ClO_5$ requires C, 63·2; H, 7·8%), $\nu_{max.}$ 3480, 3405 (OH), 1732 (C=O), and 696 cm.$^{-1}$ (C–Cl).

Fraction (vii) was repeatedly recrystallised from ethyl acetate–light petroleum, giving plates (7 mg.), m. p. 166—167°, $[\alpha]_D^{22}$ +50° (*c* 0·16), of *methyl* 7-*chloro*-2β-*hydroxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylate* (XX; R = OH) (Found: C, 63·5; H, 7·9. $C_{21}H_{31}ClO_5$ requires C, 63·2; H, 7·8%), $\nu_{max.}$ 3225 (OH), 1734, 1717 cm.$^{-1}$ (C=O), and 870 cm.$^{-1}$ (C–Cl).

Similar results were obtained when the reaction time was reduced to 2 hr.

(*b*) The ester (XVIII; R = R′ = OH) (50 mg.) in ether (25 ml.) was shaken with phosphorus pentachloride (58 mg.) for 2 hr. After being worked up as described in (*a*) above, the gummy product (52 mg.) was chromatographed on alumina (7 × 1 cm.) in light petroleum (25 ml.), giving the following gummy fractions which were crystallised from ether: (i) benzene (125 ml.), plates (16 mg.), m. p. 160—163°; recrystallisation from ether gave the chloro-ester (XIX; R = Cl), m. p. 165°; (ii) benzene–ether (20 : 1, 75 ml.; and 5 : 1, 100 ml.), needles (24 mg.), m. p. 160—163°; (iii) benzene–methanol (200 : 1, 100 ml.), needles (3 mg.), m. p. 124—126°, of the ester (XVIII; R = R′ = OH).

Recrystallisation of fraction (ii) from ethyl acetate–light petroleum furnished *methyl* 7-*hydroxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibb*-2-*ene*-1α,10β-*dicarboxylate* (XIX; R = OH), needles, m. p. 163°, $[\alpha]_D^{23}$ +54° (*c* 0·2) (Found: C, 69·2; H, 8·3. $C_{21}H_{30}O_5$ requires C, 69·6; H, 8·3%), $\nu_{max.}$ 3485 (OH), 1745 (C=O), 1656, and 735 cm.$^{-1}$ (C=C), ε [λ (mμ) in parentheses] 1650 (200), 1220 (205), 750 (210), 560 (215), 435 (220), and 250 (230).

Action of Thionyl Chloride on the 8-*Epi*-*methyl Ester* (IX; R = Me, R′ = H).—The ester (50 mg.) and thionyl chloride (0·3 ml.) were heated under reflux for 30 min. in the presence of calcium carbonate. The excess of thionyl chloride was removed by distillation under reduced pressure and the gummy product (50 mg.), in ethyl acetate, was washed with sodium hydrogen carbonate and recovered. Chromatography on alumina (9 × 1 cm.) in benzene furnished the following fractions which were crystallised from ethyl acetate–light petroleum: (i) benzene–ether (20 : 1, 75 ml.), 3 mg.; (ii) benzene–ether (1 : 1, 75 ml.), 8 mg.; (iii) benzene–methanol (400 : 1, 75 ml.), 12 mg., interband; and (iv) benzene–methanol (200 : 1, 75 ml.; and 100 : 1, 25 ml.), 25 mg. of the ester (IX; R = Me, R′ = H).

Fraction (i) crystallised in plates (1·2 mg.), m. p. 293—294°, $\nu_{max.}$ OH absent. Fraction (ii) gave the chloro-ester (XX; R = OH), 6 mg.

80% of the ester (IX; R = Me, R′ = H) was recovered when the reaction was allowed to proceed at room temperature for 4 hr. and only traces of gums were obtained by chromatography of the residual mother-liquor.

Oxidation of the Chloro-esters (XVIII; R = Cl, R′ = OH *and* (XX; R = OH).—(*a*) The chloro-ester (XVIII; R = Cl, R′ = OH) (10 mg.) in acetone (0·5 ml.) was recovered after 1 hr. at room temperature with the chromic oxide–sulphuric acid reagent (0·02 ml.).

(*b*) Oxidation of the chloro-ester (XX; R = OH) (3 mg.), in the same way, gave a ketone, needles (1·8 mg.), m. p. 170—172°, $\nu_{max.}$ OH absent, 1733, 1719, and 1693 (C=O), which gave a dinitrophenylhydrazone, m. p. 200—205°, $\nu_{max.}$ 3325 (NH), 1738, 1710 (C=O), 1624, 1595, and 1503 cm.$^{-1}$, with Brady's reagent.

Action of Phosphorus Pentachloride on the Chloro-ester (XVIII; R = Cl, R′ = OH).—(*a*) The chloro-ester (12 mg.) in ether (10 ml.) was shaken with phosphorus pentachloride (12 mg.) for 4 hr. After working up as before the product crystallised from ethyl acetate–light petroleum in needles (11 mg.), m. p. 179—180°, of the chloro-ester (XVIII; R = Cl, R′ = OH).

(*b*) When the reaction time was extended to 64 hr. and the gummy product in benzene was chromatographed on alumina (6·5 × 0·6 cm.), elution with benzene afforded a solid (10 mg.), m. p. 120—145°, which was rechromatographed in light petroleum on alumina (10 × 1 cm.). Elution with benzene–light petroleum (1 : 1) gave needles (3·1 mg.), m. p. 166—167°, from light petroleum, of the dichloro-compound (XVIII; R = R′ = Cl). Further elution with benzene gave needles (4·8 mg.), m. p. 135—136°, $\nu_{max.}$ OH absent. The chloro-ester (XVIII;

R = Cl, R′ = OH) (1·0 mg.) was recovered on elution of the first column with benzene–ether (3 : 1).

Stability of the 8-Epi-methyl Ester (IX; R = Me, R′ = H) *to Alkali*.—The ester (850 mg.) was refluxed with 2N-sodium hydroxide (20 ml.) for 3 hr. The homogeneous solution was cooled, washed with ethyl acetate, acidified with concentrated hydrochloric acid, and extracted with ethyl acetate (10 × 25 ml.). The extract, on recovery and recrystallisation of the product from ethyl acetate, gave (i) the acid (IX; R = R′ = H) (497 mg.), m. p. 260—266°, and (ii) prisms (38 mg.), m. p. 271—273° (decomp.). An equivalent-weight determination (180) indicated this to be mainly the dicarboxylic acid (calc., 176). Remethylation of this and the residue of uncrystallised acidic material with diazomethane and crystallisation gave starting material (232 mg.).

The Acid Chloride (XXIII; R = OMe, R′ = Cl).—The diacetate (IX; R = H, R′ = Ac) (515 mg.) in benzene (3·5 ml.) was treated with thionyl chloride (3·5 ml.) during 18 hr. at room temperature. Evaporation of the solvent and crystallisation of the gummy residue from light petroleum then gave the *acid chloride* (XXIII; R = OMe, R′ = Cl) as prisms (519 mg.), m. p. 133·5—134·5° (Found: C, 61·9; H, 7·3; Cl, 7·4. $C_{24}H_{33}ClO_7$ requires C, 61·5; H, 7·0; Cl, 7·6%).

Rosenmund Reduction of the Acid Chloride (XXIII; R = OMe, R′ = Cl).—The acid chloride (192 mg.) in boiling xylene (1 ml.) was reduced in the presence of 5% palladium–barium sulphate catalyst (30 mg.). Evolution of hydrogen chloride, which was at first rapid, reached 73% of the theoretical yield after 3·5 hr. and then became very slow. The mixture was cooled and filtered and the filtrate was evaporated at 100° under reduced pressure. The solid product was redissolved in benzene and chromatographed on alumina (5 g.). Fractional elution with benzene yielded gummy crystals (81 mg.) which, on recrystallisation from ether, afforded needles (30 mg.), m. p. 159—161° (gas evolution), of *methyl* 2β,7-*diacetoxy*-1α-*formyl*-1β,8-*epi*-*methyl*-4aβ-*gibbane*-10β-*carboxylate* (XXIII; R = OMe, R′ = H) (Found: C, 66·7; H, 8·0. $C_{24}H_{34}O_7$ requires C, 66·3; H, 7·9%), $\nu_{max.}$ (in CCl_4) 2733 (C–H) and 1737 cm.$^{-1}$ (C=O). The *oxime*, prepared by refluxing the aldehyde (13 mg.) with hydroxylamine hydrochloride (3 mg.) and anhydrous sodium acetate (3·5 mg.) in methanol (0·3 ml.) for 3 hr., formed prisms (10 mg.), m. p. 215—216°, from benzene–light petroleum (1 : 2) (Found: C, 64·3; H, 7·8; N, 3·1. $C_{24}H_{35}NO_7$ requires C, 64·1; H, 7·85; N, 3·1%), $\nu_{max.}$ (in $CHCl_3$) 3590, 3345 (broad), 1727, and 1613 cm.$^{-1}$ (broad).

Fractional crystallisation of the residue gave nodules (9 mg.), m. p. 135—145°, also obtained by continued elution of the column with benzene followed by ether. Repeated recrystallisation of the combined solids (35 mg.) from ether afforded minute prisms, m. p. 155—158°, clear at 162° (gas evolution), of *methyl* 2β,7-*diacetoxy*-10β-*formyl*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α-*carboxylate* (XXIII; R = H, R′ = OMe) (Found: C, 66·35; H, 7·9. $C_{24}H_{34}O_7$ requires C, 66·3; H, 7·9%), $\nu_{max.}$ (in CCl_4) 2730 (C–H) and 1740 (broad) cm.$^{-1}$ (C=O).

Relationship Between the Isomeric Aldehydes (XXIII; R = OMe, R′ = H) *and* (XXIII; R = H, R′ = OMe) *and the Acid* (IX; R = R′ = H).—(*a*) *Oxidation of the aldehyde* (XXIII; R = OMe, R′ = H). The aldehyde (10 mg.) in acetic acid (0·2 ml.) was treated with a solution of chromic oxide [0·175 ml. of a solution containing the oxide (100 mg.) in water (0·5 ml.) and acetic acid (to 10 ml.)]. The mixture was set aside for 2 hr., treated with a few drops of methanol, diluted with water, and extracted with ether. Recovery and crystallisation of the product (13 mg.) afforded the diacetate (IX; R = H, R′ = Ac), needles (7 mg.), m. p. 244—246°.

(*b*) *Oxidation of the aldehyde* (XXIII; R = H, R′ = OMe). Similar oxidation of this aldehyde (10 mg.) gave *methyl* 2β,7-*diacetoxy*-10β-*carboxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α-*carboxylate* (XXIII; R = OH, R′ = OMe) as needles (6 mg.), m. p. 260—262°, from 1 : 1 ether–light petroleum (b. p. 40—60°) (Found: C, 64·1; H, 7·7. $C_{24}H_{34}O_8$ requires C, 64·0; H, 7·6%). Methylation (diazomethane) gave the methyl ester (IX; R = Me, R′ = Ac) as needles, m. p. 168·5—169·5° (from 1 : 1 ether–light petroleum).

Methyl 2β,7-*Dihydroxy*-1,1,8-*epi*-*trimethyl*-4aβ-*gibbane*-10β-*carboxylate* (XXI; R = OH).—Dry hydrogen chloride was passed for 90 min. through chloroform (1 ml.) containing the aldehyde (XXIII; R = OMe, R′ = H) (120 mg.) and ethane-1,2-dithiol (0·2 ml.) at 0—5°, and the mixture was then evaporated under reduced pressure. The residual crystals (143 mg.) were chromatographed on a short column of alumina in ether and, after elution, the product was crystallised from 1 : 2 ether–light petroleum (b. p. 40—60°), yielding blades, m. p. 138—139°, of the *ethylene dithioketal* (Found: C, 61·2; H, 7·65. $C_{26}H_{38}O_6S_2$ requires C, 61·2; H, 7·45%).

The dithioketal (125 mg.) in dioxan (5 ml.) was heated at 100° with Raney nickel (3 ml. of settled suspension in dioxan) for 8 hr. The mixture was cooled and filtered, the residue was washed with methanol, and the filtrate and washings were evaporated, yielding a crystalline residue (100 mg.) which formed needles, m. p. 149·5—150° [from light petroleum (b. p. 40—60°)], of the *diacetate* of the alcohol (XXI; R = β-OH) (Found: C, 68·7; H, 8·7. $C_{24}H_{36}O_6$ requires C, 68·5; H, 8·6%), $\nu_{max.}$ 1735 cm.$^{-1}$.

The diacetate (571 mg.) was refluxed with 10% ethanolic potassium hydroxide (25 ml.) under nitrogen for 6 hr. Dilution of the cooled solution with water (150 ml.), extraction with ether, and recovery gave crystals (438 mg., m. p. 140—145°) which on recrystallisation from 1 : 1 ether–light petroleum (b. p. 40—60°) yielded prisms, m. p. 144—145°, of *methyl* 2β,7-*dihydroxy*-1,1,8-*epi*-*trimethyl*-4aβ-*gibbane*-10β-*carboxylate* (XXI; R = OH) (Found: C, 71·7; H, 9·7. $C_{20}H_{32}O_4$ requires C, 71·4; H, 9·6%), $\nu_{max.}$ 3470 (OH) and 1716 cm.$^{-1}$ (C=O).

The diacetate (XXI; R = OAc) was regenerated in high yield when the alcohol was heated with acetic anhydride in pyridine for 6 hr. at 100°.

Action of Phosphorus Pentachloride on the Alcohol (XXI; R = β-OH).—The finely powdered alcohol (200 mg.) was suspended in light petroleum (10 ml.) and shaken with phosphorus pentachloride (275 mg., 2·2 mol.) at room temperature for 1 hr. The small excess of reagent was decomposed by addition of water, the layers were separated, and the light petroleum solution was washed with sodium hydrogen carbonate and evaporated, yielding a colourless oil (212 mg.), $\nu_{max.}$ (in CS_2) OH absent, 1628, 1637, and 867 cm.$^{-1}$, $E^{1\%}_{1\,cm.}$ 198 at 201 mμ. Chromatography of the oil on alumina (5 g.) in light petroleum (b. p. 40—60°) (followed by infrared spectroscopy) yielded an oily olefinic fraction (141 mg.), then fractions containing progressively smaller proportions of olefin (as judged by the intensity of the band at 1637 cm.$^{-1}$), and finally a crystalline fraction (14 mg.) which formed prisms, m. p. (i) 88—89° or (ii) 95—96°, from light petroleum (b. p. 40—60°), of *methyl* 2α,7-*dichloro*-1,1,8-*epi*-*trimethyl*-4aβ-*gibbane*-10β-*carboxylate* (Found: C, 64·5; H, 8·2; Cl, 18·8. $C_{20}H_{30}Cl_2O_2$ requires C, 64·3; H, 8·1; Cl, 19·0%), $\nu_{max.}$ 1720 (C=O) and 875 cm.$^{-1}$ (C–Cl); no OH absorption (negligible ultraviolet absorption).

Absorption of ozone by the crude olefin (9 mg.) in acetic acid (1 ml.) appeared to be complete after 13 min. at room temperature. After 30 min., the mixture was set aside for 1 hr., then diluted with water, and the solution was distilled from a small retort, during passage of a current of air, until the volume had been reduced to half. The distillate was passed into 2,4-dinitrophenylhydrazine hydrochloride in methanol. After dilution with water the crude dinitrophenylhydrazone was extracted with benzene and chromatographed on alumina in ether. Two components (i), leaflets, m. p. 100—120°, and (ii) needles, m. p. 140—150°, were separated. Repeated chromatography of the leaflets (i) on alumina (1 × 15 cm.) in ether gave yellow leaflets of acetone 2,4-dinitrophenylhydrazone (<1 mg.), m. p. 122·5—124°. Recrystallisation of the needles (ii) from ethanol yielded yellow needles (*ca.* 1 mg.), m. p. 137—157°, which were again chromatographed on alumina (1 × 15 cm.) in ether and then afforded yellow needles, m. p. 160—162°, of formaldehyde 2,4-dinitrophenylhydrazone.

Oxidation of the Olefin with Osmium Tetroxide.—The above crude olefin fraction (155 mg.) in dioxan (5 ml.) was treated with osmium tetroxide (160 mg.) at room temperature for 4 days. The mixture was diluted with dioxan and hydrogen sulphide was passed through the whole until precipitation was complete.[24] Filtration and evaporation gave a colourless gum (166 mg.) which readily crystallised. Chromatography on alumina (5 g.) yielded fractions: (i) (eluted with benzene), crystals (48 mg.) of the dichloro-compound (see above); (ii) (benzene–ether, 99 : 1; followed by ether), prisms (65 mg.), m. p. 170—180°; and (iii) (chloroform), needles (45 mg.), m. p. 110—120°. Recrystallisation of fraction (ii) from ether afforded prisms, m. p. 177—180°, with previous softening, of a *glycol* (XXV) (Found: C, 64·7; H, 8·8. $C_{20}H_{31}ClO_4$ requires C, 64·8; H, 8·4%), $\nu_{max.}$ 3495, 3485 (OH), 1705 (C=O), and 873 cm.$^{-1}$ (C–Cl). Chromatography of fraction (iii) on alumina (1·5 g.) in ether followed by chloroform, and recrystallisation from ether–light petroleum (b. p. 40—60°), gave needles, m. p. 132—133°, of an isomeric *glycol* (Found: C, 64·7; H, 8·5%), $\nu_{max.}$ 3350, 3320, 3250 (OH), 1727, 1720 (C=O), and 866 cm.$^{-1}$ (C–Cl).

Oxidation of the Glycol (XXV) *with Lead Tetra-acetate.*—The glycol, m. p. 177—180° (27 mg.), in acetic acid (1 ml.) and chloroform (0·25 ml.) was treated with lead tetra-acetate (65 mg.) at room temperature in a retort, which was at once sealed for 45 hr. The vessel was opened and

[24] Barton and Elad, *J.*, 1956, 2085.

immediately connected to two traps, in series, containing 2,4-dinitrophenylhydrazine hydrochloride (saturated solution in 2N-hydrochloric acid). Water (1 ml.) was added to the reaction mixture and a stream of nitrogen was passed through the system. The yellow crystals of acetone 2,4-dinitrophenylhydrazone, m. p. 123—124°, deposited in the traps during 24 hr. at room temperature, followed by 5 hr. at 0°, were recovered and weighed (4·2 mg., 45% on glycol oxidised; see below).

The main reaction mixture was diluted with water and extracted with ether. The extract was washed with sodium hydrogen carbonate and evaporated, yielding a gum (25 mg.) which was separated into (i) ketonic (10 mg.) and (ii) non-ketonic (12·5 mg.) components by the Girard procedure. Component (ii) was unchanged glycol (XXV) (12·5 mg.), m. p. 178—180°. Chromatography of component (i) on alumina in ether, recovery, and crystallisation from light petroleum (b. p. 40—60°) afforded the *cyclopentanone* (XXVI) as needles (7 mg.), m. p. 109—109·5° (Found: C, 65·9; H, 7·6. $C_{17}H_{23}ClO_3$ requires C, 65·7; H, 7·4%), $\nu_{max.}$ (in CS_2) 1735 and ~1742 (sh) cm.$^{-1}$.

Oxidation of the Alcohol (XXI; R = OH).—The alcohol (100 mg.) in acetone (2 ml.) at 0·5° was treated, dropwise during 5 min., with the 8N-chromic oxide–sulphuric acid reagent [3] (0·085 ml.) and then set aside for 2·5 hr. Methanol (1 drop) was next added and the mixture was diluted with water and extracted with ether. Recovery gave the *ketone* (XXII) as a colourless gel (100 mg.) which formed a glass on distillation at 125° (bath)/0·1 mm. (Found: C, 71·65; H, 9·1. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%), $\nu_{max.}$ (in $CHBr_3$) 3587 (OH), 1725, and 1700 cm.$^{-1}$ (C=O). For characterisation the product was converted into the *7-acetate 2,4-dinitrophenylhydrazone* which formed golden-yellow leaflets, m. p. 212—214°, from ethanol (Found: C, 60·4; H, 6·9; N, 10·45. $C_{28}H_{36}N_4O_8$ requires C, 60·4; H, 6·5; N, 10·1%).

Reduction of the Ketone (XXII).—(*a*) *With sodium in ethanol.* The ketone (62 mg.) in boiling ethanol (7·5 ml.) was treated with sodium (0·5 g.) during 30 min. The solution was cooled, diluted with water, and extracted with ether. Recovery gave a gum (61 mg.) which was chromatographed on alumina (3 g.), yielding, on elution with ether, a sticky gel (12 mg.) from which were separated, by the Girard procedure, unreduced ketone (8 mg.) and crude non-ketonic material (4 mg., brown gum). Continued elution with ether, and then chloroform, gave gummy crystals, (i) (33 mg.) m. p. *ca.* 140° and (ii) (10 mg.) m. p. 175—185°. Fractional crystallisation afforded prisms (30 mg.), m. p. 144—145°, of the alcohol (XXI; R = OH) and leaflets (6 mg.), m. p. 188—191°, of the *2α-hydroxy-epimer* (Found: C, 71·6; H, 9·7. $C_{20}H_{32}O_4$ requires C, 71·4; H, 9·6%).

(*b*) *With sodium borohydride.* The ketone (67 mg.) in methanol (0·5 ml.) was treated at 0—5° with sodium borohydride (5 mg.) in water (0·1 ml.). After 5·5 hr. the mixture was diluted with water and extracted with ether. Recovery gave a gum (65 mg.) which was chromatographed on alumina (2 g.), yielding the following fractions: (i) (ether, 10 ml.), gum (17 mg.); (ii) (ether, 5 ml.), gum (1 mg.); (iii) (ether, 40 ml.), gum (6 mg.); (iv) (ether–chloroform, 99 : 1, 30 ml.), gum (1 mg.); (v) (ether–chloroform, 49 : 1, 30 ml.), gum (5 mg.); (vi) (ether–chloroform, 19 : 1, 30 ml.), gummy crystals (5 mg.), m. p. 130—155°; (vii) (ether–chloroform 9 : 1, 30 ml.), gummy crystals (4 mg.) m. p. 147—160°; (viii) (chloroform, 17 ml.), slightly gummy crystals (20 mg.), m. p. 175—188°; and (ix) (chloroform, 40 ml.), gum (3 mg.).

A portion of fraction (viii), after being rinsed with ether, had m. p. 183—187°, undepressed on admixture with the 2α-hydroxy-epimer of the alcohol (XXI; R = OH), and the infrared spectra were identical. Fractions (vi) and (vii), which were mixtures, contained the 2β-hydroxy-epimer, m. p. 144—145°; treatment of fraction (i) by the Girard procedure gave a fraction (12 mg.) which, although apparently non-ketonic, was nevertheless shown to be unreduced starting material by comparison of infrared spectra.

Oxidation of the 8-Epi-methyl Acid (IX; R = R′ = H).—(*a*) *To a mixture of the isomeric ketones* (XII). The acid (50 mg.) in acetone (5 ml.) was treated at 0—5° with the 8N-chromic oxide–sulphuric acid reagent [3] (0·04 ml.) and set aside at 0—5° for 5 hr. After dilution with water, the precipitate was collected and recrystallised from acetone, giving leaflets (39 mg.), m. p. 155—157° (decomp.), of *methyl 1α-carboxy-7-hydroxy-1β,8-epi-dimethyl-2-oxo-4aβ-gibbane-10β-carboxylate* (XVII; R = H) (Found: C, 66·2; H, 7·8; OMe, 8·7. $C_{20}H_{28}O_6$ requires C, 65·9; H, 7·7; OMe, 8·5%), $\nu_{max.}$ 3400 (OH), ~2600, 1740, 1715, and 1704 cm.$^{-1}$ (C=O), or (in dioxan) 1735 cm.$^{-1}$ (broad).

The β-keto-acid (39 mg.) was boiled with water (2 ml.) under reflux for 20 min. The cooled solution was extracted with ether, yielding a colourless gum (33 mg.) which readily crystallised

from warm ether. Fractional crystallisation from ether (assisted by manual separation of crystal types) gave (i) prisms (13 mg.), m. p. 150—155°, raised to 159—161° on recrystallisation from ether, of *methyl 7-hydroxy-1ξ,8-epi-dimethyl-2-oxo-4aβ-gibbane-10β-carboxylate* (XII) (Found: C, 71·5; H, 9·1; OMe, 10·0. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8; OMe, 9·7%), $\nu_{max.}$ 3475 (OH), 1733, and 1699 (C=O) cm.$^{-1}$ or (in $CHCl_3$) 1731 and 1713 cm.$^{-1}$, and (ii) needles (10 mg.), m. p. 124° [from 1 : 1 ether–light petroleum (b. p. 40—60°)], of the *1-methyl epimer* (Found: C, 71·3; H, 8·7%), $\nu_{max.}$ 3300, 3245 (OH), 1737, and 1711 cm.$^{-1}$ (C=O). Admixture with the preceding isomer caused a depression of only 1° in the m. p.

(*b*) *To the ketone* (XII), *m. p.* 124°. The acid (1·505 g.) in acetone (125 ml.) was treated at 0—5° during 13 min. with the 8N-chromic oxide–sulphuric acid reagent [3] (1·3 ml.) and set aside at 0—5° for 18 hr. The precipitated solid was filtered off and washed with water, and the residual β-keto-acid (1·173 g.) was refluxed with water (50 ml.) for 25 min. The cooled solution was extracted for neutral material which was combined with similar material obtained by heating the filtrate and washings (above) with sodium acetate (0·9 g.) at 100° for 40 min. The combined neutral gum (1·24 g.) was heated under reflux with 1% methanolic sodium methoxide (25 ml.) for 1 hr. The cooled solution was diluted with water (50 ml.), and extracted with ether. The recovered neutral material (1·16 g) was redissolved in ether, percolated through a column of alumina (2 g.), and then crystallised from ether, yielding the ketone, m. p. 124° (0·90 g.).

Action of Alkali on the Ketone (XII), m. p. 159—161°.—The ketone (50 mg.) was refluxed with 2N-sodium hydroxide (1 ml.) for 3 hr. and the clear solution was set aside for a further 18 hr. The solution was washed with ether, then acidified and extracted with ether (6 × 10 ml.), yielding a micro-crystalline powder (44 mg.), m. p. 200—205°. Methylation (diazomethane) of this acidic product converted it into a gum (45 mg.) which crystallised in needles, m. p. 122—123° (37 mg.), when seeded with the ketone (XII) of m. p. 124°.

The ketone (XII), m. p. 159—161°, was recovered unchanged after 1·5 hr. in boiling dry benzene.

Derivatives of the Ketone (XII), *m. p.* 124°.—(*a*) The ketone (0·94 g.) in benzene (50 ml.) with ethyl formate (1·5 ml.) was treated with sodium hydride (0·5 g. of a 50% mixture with paraffin), and the mixture was agitated at room temperature during 4 days by passage of a slow current of dry nitrogen. The yellowish mixture was diluted with water and extracted with ether, and the aqueous layer was then acidified with hydrochloric acid and re-extracted with ether. Recovery afforded a gummy solid (0·98 g.) which recrystallised from ether as pale yellowish prisms (0·80 g.) of the *3-hydroxymethylene derivative*, m. p. 134—135° (Found: C, 69·45; H, 8·15. $C_{20}H_{28}O_5$ requires C, 68·9; H, 8·1%), $\nu_{max.}$ (in $CHBr_3$) 3595 (OH), 1721, 1653 (C=O), and 1584 cm.$^{-1}$ (C=C).

(*b*) The hydroxymethylene derivative (250 mg.) in methanol (1·5 ml.) was treated with *N*-methylaniline (0·5 ml.) at room temperature and set aside for 24 hr. with exclusion of moisture. The mixture was next refluxed for 3 hr., then cooled, and the solvent and excess of *N*-methylaniline were removed under reduced pressure. The oily residue crystallised on treatment with light petroleum (b. p. 40—60°), yielding a pale yellow powder (277 mg.). Recrystallisation from ethyl acetate–ether (1 : 2) gave flat needles, m. p. 154·5—155·5°, of the *N-methylanilinomethylene derivative* (Found: C, 73·8; H, 8·2; N, 3·2. $C_{27}H_{35}NO_4$ requires C, 74·1; H, 8·1; N, 3·2%), $\nu_{max.}$ (in $CHCl_3$) 3450 (broad) (OH), 1719 (C=O), 1670 (sh), 1656, and 1602 cm.$^{-1}$.

(*c*) The hydroxymethylene derivative (174 mg.) and butane-1-thiol (0·1 ml.) with toluene-*p*-sulphonic acid (2 mg.) were refluxed in dry benzene (5 ml.), the condensed vapours being continuously freed from the water of reaction by passage through a column of activated alumina (1 g.) before being returned to the reaction vessel. After 9 hr. the mixture was set aside for 18 hr. and then evaporated under reduced pressure. The residue was dissolved in ether, washed with N-sodium hydroxide, recovered, and distilled at 250° (bath)/0·1 mm., yielding the *3-butylthiomethylene derivative* as a pale yellowish glass (204 mg.) (Found: C, 68·4; H, 8·7; S, 6·9. $C_{24}H_{36}O_4S$ requires C, 68·6; H, 8·6; S, 7·6%), $\nu_{max.}$ (in $CHBr_3$) 3460 (OH), 1725, 1670 (C=O), and 1565 cm.$^{-1}$ (C=C).

3-Butylthiomethylene Derivative of Ketone (XXII).—The 3-n-butylthiomethylene derivative of ketone (XII) (275 mg.) in t-butyl alcohol (0·7 ml.) was treated with a solution of potassium (51 mg.) in t-butyl alcohol (2 ml.) with shaking at room temperature for 5 min. Methyl iodide (186 mg.) in the same alcohol (to 0·71 ml.) was added and the mixture, in a stoppered vessel,

was shaken during 10 min. with occasional cooling in ice and then set aside for 16 hr. After dilution with water the mixture was extracted with ether, and the extract was washed with water. Recovery gave a gum (205 mg.). Acidification of the aqueous solution, extraction with ether, and methylation (diazomethane) of the recovered acidic gum (57 mg.) gave more (54 mg.) of the same, but slightly cruder, product. Distillation of the combined fractions at *ca.* 250° (bath)/0·1 mm. gave the 3-*butylthiomethylene derivative* (XXVIII) as a yellowish glass (235 mg.) (Found: C, 69·0; H, 8·9. $C_{25}H_{38}O_4S$ requires C, 69·1; H, 8·8%), $\nu_{max.}$ (in $CHBr_3$) 3580, 3450 (OH), 1725, 1665 (C=O), and 1550 cm.$^{-1}$ (C=C).

Ozonolysis of the 3-*Butylthiomethylene Derivative of Ketone* (XXII).—The butylthiomethylene derivative (XXVIII) (203 mg.) in acetic acid (2 ml.) and ethyl acetate (2 ml.) was treated with a slight excess of ozone at −15°. Water (2 ml.) and 30% w/v hydrogen peroxide (1 ml.) were added and the mixture was set aside at room temperature for 24 hr. and then extracted with ether (10 × 20 ml.). The ether solution was extracted with 2N-sodium carbonate (5 × 5 ml.), and the combined aqueous extracts were washed with ether, acidified, and shaken with ether (10 × 50 ml.). Recovery gave a gum (142 mg.) which partially crystallised on treatment with ether at 0° and yielded 7-*hydroxy*-1,1,8-*epi*-*trimethyl*-10β-*methoxycarbonyl*-2,3-*seco*-4aβ-*gibbane*-2,3-*dioic acid* (XXVII) (59 mg.) as needles, m. p. 199—201°, from ether (Found: C, 62·4; H, 7·9%; equiv., 182. $C_{20}H_{30}O_7$ requires C, 62·8; H, 7·9%; *M*, 382.

Pyrolysis of the Dicarboxylic Acid (XXVII).—The dicarboxylic acid (41 mg.) was heated, under nitrogen, in a narrow tube in series with a trap containing 2N-barium hydroxide, to 300° during 20 min. and the temperature maintained at 300—310° for a further 10 min Evolution of carbon dioxide began at *ca.* 260° and was rapid at *ca.* 280°. After cooling, the residue was extracted into ether and washed with saturated sodium hydrogen carbonate. Recovery gave *methyl* 7-*hydroxy*-1,1,8-*epi*-*trimethyl*-2-*oxo*-A-*nor*-4aβ-*gibbane*-10β-*carboxylate* (XXIX) (32 mg.), prisms, m. p. 165—166° [from ether–light petroleum (b. p. 40—60°)] (Found: C, 71·6; H, 8·9. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%), $\nu_{max.}$ 3511 (OH), ~1725, and 1719 cm.$^{-1}$ (C=O).

Bromination of the Ketone (XXIX).—The ketone (46 mg.) in acetic acid (0·5 ml.) at room temperature was treated portionwise with bromine (25 mg.) in acetic acid (to 1·1 ml.) during 3·5 hr. After 4·5 hr. the mixture, in which a slight excess of bromine persisted, was diluted with water, and the product was extracted in ether and washed with water. Recovery gave slightly gummy crystals (58 mg.) which afforded platelets [from 1 : 1 ether–light petroleum (b. p. 40—60°)], m. p. 178—179°, of *methyl* 3ξ-*bromo*-7-*hydroxy*-1,1,8-*epi*-*trimethyl*-2-*oxo*-A-*nor*-4aβ-*gibbane*-10β-*carboxylate* (Found: C, 57·7; H, 6·95. $C_{19}H_{27}BrO_4$ requires C, 57·1; H, 6·8%), $\nu_{max.}$ ~3550 (broad) (OH), ~1720, and 1700 cm.$^{-1}$ (C=O).

Dehydrobromination of the Bromo-ketone.—The bromo-ketone (53 mg.) was boiled under reflux with collidine (1 ml.) for 7 hr. and then set aside for 18 hr. Collidine hydrobromide (24 mg.) was filtered off and washed with ether, and filtrate and washings were extracted with 2N-hydrochloric acid, water, and saturated aqueous sodium hydrogen carbonate. Recovery from the ether gave a brown neutral gum (47 mg.) which was distilled at 160° (bath)/0·1 mm. and then chromatographed on alumina (1 g.) with ether followed by acetone. Redistillation at 150° (bath)/0·1 mm. of fractions (total 27 mg.) showing $\lambda_{max.}$ 236 mμ gave *methyl* 7-*hydroxy*-1,1,8-*epi*-*trimethyl*-2-*oxo*-A-*norgibb*-3-*ene*-10β-*carboxylate* (XXX) as a pale yellow gum (Found: C, 71·5; H, 8·3. $C_{19}H_{26}O_4$ requires C, 71·7; H, 8·2%), $\lambda_{max.}$ 236 mμ (ε 11,000).

Reduction of the Ketones (XXIX) *and* (XXX).—The ketone (XXX) (31 mg.) in dioxan (0·35 ml.) was added to liquid ammonia (3 ml.) containing methanol (0·3 ml.), cooled in solid carbon dioxide, and the mixture was treated with shaking, with lithium (15 mg.) portionwise during 7 min. After a further 3 min. ammonium chloride (150 mg.) was added and the ammonia evaporated. The residue was dissolved in water and extracted with ether (10 × 20 ml.). Recovery gave a gum (25 mg.) which was chromatographed on alumina (250 mg.), yielding (*a*) gum (3 mg.), (*b*) gummy crystals (13·5 mg.), eluted with ether, and (*c*) gummy crystals (7 mg.), eluted with acetone. Recrystallisation of crystals (*c*) from acetone yielded prisms (1·5 mg.), m. p. 212—214°, of 10β-*hydroxymethyl*-1,1,8-*epi*-*trimethyl*-A-*nor*-4aβ-*gibbane*-2ξ,7-*diol* (XXXI) (Found: C, 73·0; H, 10·55. $C_{18}H_{30}O_3$ requires C, 73·4; H, 10·3%), $\nu_{max.}$ 3260 (OH), no carbonyl absorption.

Recrystallisation of crystals (*b*) from acetone afforded prisms (3·5 mg.), m. p. 204—206°, of the 2ξ-*hydroxy*-*epimer* (Found: C, 73·7; H, 10·3%), $\nu_{max.}$ 3340 (OH), no carbonyl absorption. A mixture of the epimers had m. p. 190—192°.

Reduction of the ketone (XXIX) under the same conditions, and chromatography of the

product, gave the same pair of isomeric triols, identified by mixed m. p. determinations and comparison of infrared spectra.

Rotatory Dispersion Curves.—Values are for [*M*], in methanol, for the ketones. (XII), m. p. 159—161°: negative Cotton effect curve (600 mμ) +100°; (312·5, trough) +50°; (270, peak) +1150°; (260), +1500°. (XII), m. p. 124°: negative Cotton effect curve (600 mμ) −100°; (310, trough) −7100°; (275, peak) +6500°; (270) +6225°. (XXII): negative Cotton effect curve (600 mμ) −300°; (315, trough) −4100°; (272, peak) +5500. (XXVI): positive Cotton effect curve (500 mμ) +550°; (312, peak) +3150°; (272, trough) −1400°. (XXIX): positive Cotton effect curve (500 mμ) +150°; (322, peak) +2300°; (285, trough) −1400°; (280) −1000°. (XVII; R = Me): negative Cotton effect curve (600 mμ) −150°; (310, trough) −5300°; (275, peak) +7900°. The aldehyde (XXIII; R = OMe, R′ = H): positive Cotton effect curve (500 mμ) +250°; (400) +100°; (312, peak) +800°; (280, trough) −350°. The aldehyde (XXIII; R = H, R′ = OMe): positive Cotton effect curve (500 mμ) +600°; (400) +250°; (325, peak) +1250°; (275, trough) −400°. The 8-epi-methyl ester (IX; R = Me, R′ = H); positive plain curve (600 mμ) +100°; (400) +450°; (275) +1500°. (XVIII; R = R′ = OH): positive plain curve (500 mμ) −100°; (400) −15°; (300) +80°.

We are indebted to Miss Jane Jackson and to Messrs. R. E. Blofeld, J. A. Connor, D. Gardner, J. D. Hood, P. M. Jones, and R. G. M. Savidge for technical assistance.

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[*Received, October 1st,* 1962.]