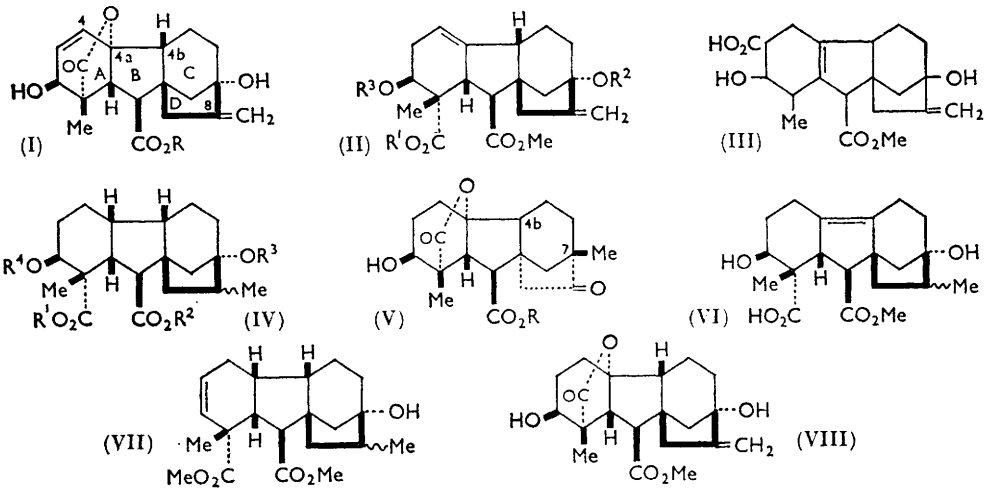
487. *Gibberellic Acid. Part XXV.* Some New Reduction Products of Gibberellic Acid and its Methyl Ester.*

By T. P. C. Mulholland.

A non-lactonic acid, $C_{20}H_{26}O_6$, obtained by catalytic reduction of methyl gibberellate, is shown to have structure (II; $R^1 = R^2 = R^3 = H$). Reduction of gibberellic acid yielded 8-epi-tetrahydrogibberellic acid and the hydrogenolysis product, $C_{19}H_{26}O_6,H_2O$ (XVI; $R^1 = R^2 = R^3 = R^4 = H$), and the 4aβ-dihydro-derivative of the latter.

The course of complete hydrogenolysis of methyl gibberellate (I; R = Me) was outlined in Part XXII.[1] Controlled hydrogenation (1 mol. uptake) in ethyl acetate with a palladium–carbon catalyst gave [2] gibberellin A_1 methyl ester and a new hydrogenolysis product, a non-lactonic monobasic acid, $C_{20}H_{26}O_6$, m. p. 238—241° (decomp.), which is assigned structure (II; $R^1 = R^2 = R^3 = H$). The acid was the major product when hydrogenation was carried out with a palladium–barium carbonate catalyst in ethyl acetate containing pyridine.[3] It appears to be identical with the compound "Hydrogeno I," m. p. 236—237° (decomp.), obtained by Hsü *et al.*[4] by hydrogenolysis of methyl gibberellate with a palladium–carbon catalyst in ethanol, but the results of degradation of the two acids showed some differences. "Hydrogeno I" was assigned the formula $C_{20}H_{28}O_6$ but the structure (III) ($C_{20}H_{26}O_6$).



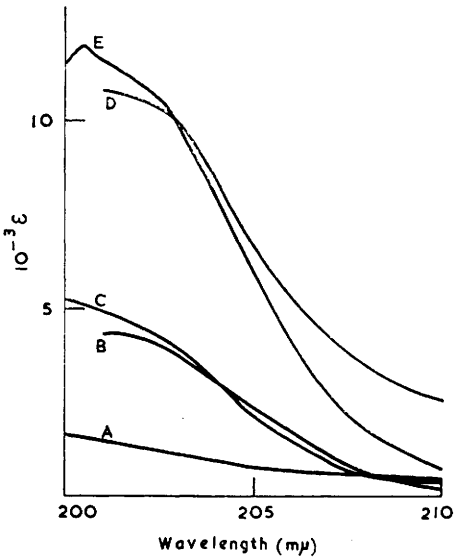
The acid, m. p. 238—241° (decomp.), contains a methoxyl group and two ethylenic bonds, one of which is in the terminal methylene grouping ($\nu_{max.}$ 895 cm.$^{-1}$ and formation of formaldehyde on ozonolysis of the methyl ester). Microhydrogenation with a palladium catalyst in acetic acid resulted in the uptake of only one mol. of hydrogen, but with some batches of Adams catalyst two mol. were absorbed, yielding the 8-tetrahydro- and 8-epi-tetrahydro-derivatives (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$), m. p. 236—238° and 267—269° (decomp.), respectively, whose structures have been established.[1] The latter

* Part XXIV, preceding paper.

[1] Aldridge, Grove, McCloskey, and Klyne, Part XXII, *J.*, 1963, 2569.
[2] Grove, Jeffs, and Mulholland, *J.*, 1958, 1236.
[3] Jones, unpublished results.
[4] Hsü, Takahashi, Miyao, Kawarada, Kitamura, Tamura, and Sumiki, *Agric. Biol. Chem.*, 1961, **25**, 865.

compound was also obtained [5] by hydrogenolysis of methyl gibberellate with Adams catalyst in acetic acid.

The second ethylenic bond in the acid (II) is assigned the trisubstituted 4,4a-position on the following grounds: the infrared spectrum (bands at 912 and 864 cm.$^{-1}$) is consistent with this view; the ultraviolet end-absorption (Figure; cf. refs. 1 and 5), though not distinguishing between di- and tri-substituted groups, is too weak for a tetrasubstituted group; the presence of a 3,4(disubstituted)-bond is unlikely because the acid was not oxidised by active manganese dioxide, and a disubstituted bond should be readily hydrogenated, as in methyl gibberellate. The allylic shift which accompanies hydrogenolysis has been discussed previously.[1]



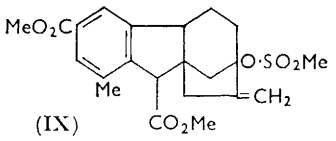
Ultraviolet absorption curves for (A) the ester (VII),[1] (B) subtraction curve (E − gibberellin A_1 methyl ester),[6] (C) the ester (XVI; $R^1 = R^2 = Me$, $R^3 = R^4 = H$), (D) the acid (VI),[1] and (E) the acid (II; $R^1 = R^2 = R^3 = H$).

When the acid was boiled with aqueous hydrochloric acid the lactone ring was reconstituted and rings C and D were rearranged as expected, giving the 7α-gibbane (V; R = H, 4bβ) [6-8] and its 4b-epimer [6] (" Product B " [7]), both of which were obtained similarly [7] from gibberellin A_1 methyl ester (VIII). Attempts were made to lactonise ring A without concomitant rearrangement of rings C and D. In acetic acid no reaction occurred but in acetic acid containing a little hydrochloric acid a neutral mixed fraction was obtained. The main constituents were the 4bβ,7α-gibbane (V; R = Me) and a product consisting essentially of gibberellin A_1 methyl ester which gave a mixture of methyl tetrahydro- and 8-epi-tetrahydro-gibberellate on hydrogenation. " Hydrogeno I " was reported [4] to yield gibberellin A_1 methyl ester on mild treatment with mineral acid.

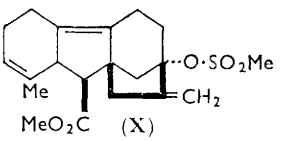
Hsü *et al.*[4] boiled the bismethanesulphonyloxy-derivative of the methyl ester, m. p. 139—140°, of " Hydrogeno I " with collidine and obtained a neutral gum, and a crystalline monobasic acid, m. p. 188—189°, which yielded the same neutral product with diazomethane. These products were considered, on slender evidence, to have an aromatic ring A, the neutral product being ascribed structure (IX). Repetition of this work with the acid (II; $R^1 = R^2 = R^3 = H$) gave no aromatic products. The bismethanesulphonate, $C_{23}H_{32}O_{10}S_2$, m. p. 138—139°, gave, with collidine, a small intractable acid fraction and two major neutral products.

[5] Cross, Grove, and Morrison, *J.*, 1961, 2498.
[6] Aldridge, Grove, Speake, Tidd, and Klyne, Part XX, *J.*, 1963, 143.
[7] Cross, *J.*, 1960, 3022.
[8] Takahashi, Kitamura, Kawarada, Seta, Takai, Tamura, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1955, **19**, 267.

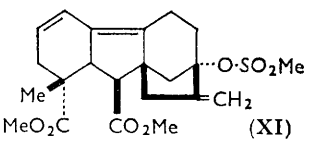
The first, $C_{20}H_{26}O_5S$, m. p. 88—90°, contained one methoxyl group and seemed to be unstable, much loss occurring during crystallisation. The ultraviolet spectrum showed no peaks between 200 and 300 mμ but intense end-absorption consistent with the presence of three unconjugated ethylenic bonds. The nuclear magnetic resonance spectrum revealed only three protons attached to ethylenic bonds. One of these protons appeared



(IX)



(X)



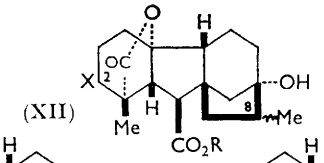
(XI)

at $\tau = 4{\cdot}8$, overlapping a doublet centred at $\tau = 4{\cdot}67$, the latter being ascribed to the exocyclic methylene protons. Hence all the possible structures except (X) are excluded. In addition, the methyl group at position 1 caused a broad singlet at $\tau = 8{\cdot}3$ and is therefore attached to an ethylenic bond, as in (X). But the peak due to the methoxycarbonyl group was a doublet at $\tau = 6{\cdot}27$ and the product may be a mixture of epimers.

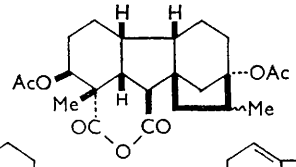
The second, gummy, product, $C_{22}H_{28}O_7S$, contained two methoxyl groups, showed a maximum at 254 mμ (ε 6610), and is considered to consist essentially of the heteroannular diene [XI; cf. the 3,4a(4b)-diene gibberellenic acid [9]]. But in another experiment the corresponding product had a broader maximum at 262 mμ (ε 5570) and the nuclear magnetic resonance spectrum showed it to be a complex mixture. The change in ultraviolet absorption may be due to the presence, in the second product, of the corresponding homoannular 3,4a(10a)diene, which might be expected to absorb at *ca.* 275 mμ, the value found for the analogous product obtained by Hsü *et al.*

Takahashi *et al.*[10] reported that hydrogenation of gibberellic acid with Adams catalyst in methanol (uptake 2·3 mol.) gave as the main products, dihydrogibberellin A_1 and two saturated non-lactonic dibasic acids, m. p. 290—295° (decomp.) ($C_{19}H_{28}O_6$) and 184—186° (decomp.) ($C_{19}H_{28}O_6,1{\cdot}5H_2O$). The correct formula for the latter compound is probably $C_{19}H_{26}O_6$ (see below).

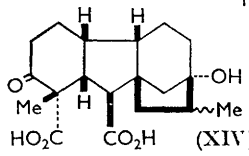
In the present work, under similar conditions, three products were isolated: 8-epi-tetrahydrogibberellic acid, a saturated non-lactonic, dibasic acid, $C_{19}H_{28}O_6,H_2O$, m. p. 300—302° (decomp.), and an unsaturated non-lactonic acid, $C_{19}H_{26}O_6,H_2O$, with an indefinite m. p. *ca.* 170° and 220° (decomp.).



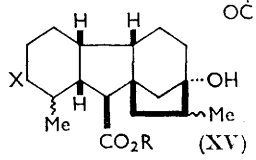
(XII)



(XIII)



(XIV)



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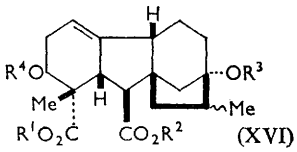

(XVI)

8-Epi-tetrahydrogibberellic acid (XII; R = H, X = H, β-OH), decomp. 288—290°, was identical with authentic material.[11] The infrared spectrum was indistinguishable from that of "dihydrogibberellin A_1," m. p. 270—272° (decomp.), obtained by the Japanese workers. Esterification gave the known methyl ester, m. p. 237—242°,[7] and

[9] Moffatt, *J.*, 1960, 3045.
[10] Takahashi, Seta, Kitamura, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1959, **23**, 509.
[11] (*a*) McCloskey, unpublished work; (*b*) Brian, Grove, and MacMillan, *Fortschr. Chem. org. Naturstoffe*, 1960, **18**, 350.

oxidation of the acid gave the corresponding keto-acid (XII; R = H, X = O) whose methyl ester, m. p. 136°, was also identical with authentic material.[7] Hydrogenation of the 8-epiketo-ester (XII; R = Me, X = O) gave the 2α-epimer (XII; R = Me, X = H, α-OH) of methyl 8-epi-tetrahydrogibberellate, previously obtained with sodium borohydride.[5] Alkaline hydrolysis of the product yielded the corresponding acid, decomp. *ca.* 290°, and a little 8-epi-tetrahydrogibberellic acid. Similarly the 8-epimeric keto-ester (XII; R = Me, X = O), m. p. 160°,[7] was converted, through the 2α-alcohol, m. p. 217—219°, into the 2α-epimer, m. p. 249—250° (decomp.), of tetrahydrogibberellic acid, together with a smaller amount of tetrahydrogibberellic acid.

The dibasic acid, $C_{19}H_{28}O_6,H_2O$, was shown to have the 8-epi-structure (IV; $R^1 = R^2 = R^3 = R^4 = H$) by the identity of its dimethyl ester, m. p. 173—175°, and diacetyl dimethyl ester, m. p. 168—170°, with specimens prepared [1] from the 8-epi-monobasic acid (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$), m. p. 269—271° (decomp.). The acid was different (infrared spectrum and m. p.s of its derivatives) from the acid, m. p. 290—295° (decomp.), obtained by the Japanese workers.

Heating the dibasic acid with acetic anhydride gave the diacetyl intramolecular 6-ring [ν(CO) 1802, 1754 cm.$^{-1}$] anhydride (XIII) which with water yielded a dibasic acid diacetate, $C_{23}H_{32}O_8$ (IV; $R^1 = R^2 = H$, $R^3 = R^4 = Ac$), whose dimethyl ester was identical with the above diacetyl dimethyl ester, m. p. 168—170°. Thus, anhydride formation did not involve inversion of configuration at the 10-position (cf. refs. 12 and 13); and, since the 1-carboxyl group is α- [6] and the 10-carboxyl group β-oriented [13] in the dibasic acid, the anhydride must be a *trans*-anhydride. Models show that this should be possible, in contrast to ring-D seco-acids [12,13] in which only *cis*-anhydride formation can occur.

Oxidation of the dibasic acid gave the dibasic keto-acid (XIV) which was readily decarboxylated to the monobasic keto-acid (XV; R = H, X = O). The methyl ester, m. p. 124°, of this acid was identical with the alkali-stable ester obtained similarly [1] from the 8-epi-monobasic acid (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$). The acid corresponding to the less stable isomeric ester, m. p. 159—161°, was not encountered.

Reduction of the keto-acid (XV; R = H, X = O) through the thioketal gave the deoxo-derivative (XV; R = H, $X = H_2$), an octahydroepiallogibberic acid, whose methyl ester was also obtained by reduction of the above keto-ester of m. p. 124°. Catalytic hydrogenation of the keto-acid (XV; R = H, X = O) yielded a mixture from which, after methylation, two ring-A alcohols and an unidentified alkoxyl-containing gum were isolated. No lactones were obtained.

The unsaturated dibasic acid, $C_{19}H_{26}O_6,H_2O$ (XVI; $R^1 = R^2 = R^3 = R^4 = H$), yielded the known [1] 8-epi-dimethyl ester (XVI; $R^1 = R^2 = Me$, $R^3 = R^4 = H$), m. p. 141—142°. The ultraviolet end absorption of this ester (Figure) was similar to that of the corresponding 4,4a-unsaturated monobasic acid (XVI; $R^1 = R^3 = R^4 = H$, $R^2 = Me$).[1]

With boiling dilute hydrochloric acid the unsaturated dibasic acid gave a lactonic fraction which on methylation yielded *ca.* 50% of methyl 8-epi-tetrahydrogibberellate but the rest of the esterified material was intractable. As with the 4,4a-unsaturated acid (II; $R^1 = R^2 = R^3 = H$), the trisubstituted ethylenic bond in the unsaturated dibasic acid was resistant to hydrogenation except that with Adams catalyst in methanol it gave a mixture of starting material and the saturated 8-epi-dibasic acid (IV; $R^1 = R^2 = R^3 = R^4 = H$).

The unsaturated dibasic acid is probably identical with the acid of m. p. 184—186° (decomp.) obtained by Takahashi *et al.*[10] since the infrared spectra were indistinguishable and the methyl esters had similar m. p.s. But the acid, m. p. 184—186°, yielded a crystalline anhydride diacetate, m. p. 185—186°, with acetic anhydride, while the acid (XVI; $R^1 = R^2 = R^3 = R^4 = H$) gave only a gummy diacetyl 6-ring anhydride

[12] Grove and Mulholland, *J.*, 1960, 3007.
[13] Bourn, Grove, Mulholland, Tidd, and Klyne, Part XXI, *J.*, 1963, 154.

[ν(anhydride CO), 1802, 1760 cm.$^{-1}$] which did not crystallise when seeded with the above anhydride of m. p. 185—186° kindly provided by Professor Sumiki. Attempted hydrolysis of the gummy unsaturated anhydride with water and methylation of the product, as described above for the saturated anhydride (XIII), gave a gummy acetyl ester different (in $[\alpha]_D$ and infrared spectrum) from the non-crystalline dimethyl ester diacetate of the unsaturated dibasic acid (XVI; $R^1 = R^2 = R^3 = R^4 = H$). The non-identity of the acetylated esters suggests that the gummy anhydride was a *cis*-anhydride formed by inversion of the 10-carboxyl group, but the failure to isolate solid products makes the interpretation ambiguous.

The dibasic acid, m. p. 290—295° (decomp.), obtained by Takahashi *et al.* is considered to be the 8-epimer of the dibasic 8-epi-acid (IV; $R^1 = R^2 = R^3 = R^4 = H$). This follows from the identity [4,10] of its dimethyl ester with the monomethyl ester of " Hydrogeno III." The latter, a hydrogenolysis product of methyl gibberellate, has been shown [1] to have an infrared spectrum identical with that of the 8-methyl compound (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$). It is interesting that, although in the present work both hydrogenolysis products had the 8-epi-configuration, in the Japanese work the analogous products had differing 8-configurations.

Experimental

M. p.s are corrected. Unless otherwise stated, specific rotations and ultraviolet spectra were determined for ethanol solutions and infrared spectra for Nujol mulls. Compounds were identified by mixed m. p.s and infrared spectra. Light petroleum had b. p. 40—60°. " Hyflo Super Cel " Celite and Woelm grade II acid alumina were used. Nuclear magnetic resonance spectra were obtained for deuterochloroform solutions (tetramethylsilane as internal standard at $\tau = 10{\cdot}000$) with an A.60 Varian Associates spectrometer (60 mc.).

Methyl 1α-*Carboxy*-2β,7-*dihydroxy*-1β-*methyl*-8-*methylenegibb*-4-*ene*-10β-*carboxylate* (II; $R^1 = R^2 = R^3 = H$).—The acidic fraction (1·80 g.) from controlled hydrogenation of methyl gibberellate with a palladium–carbon catalyst in ethyl acetate [2] crystallised from ethyl acetate, giving the *acid* as prisms (1·15 g.), m. p. 237—238° (decomp.), raised to 238—241° (decomp.) (needles) {$[\alpha]_D^{21}$ +79° (*c* 1·10)} by recrystallisation from water (Found: C, 66·5, 66·0; H, 7·3, 7·3; OMe, 8·9; active H, 0·74%; equiv., 348, 357. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·2; OMe, 8·6; 3H, 0·83%; *M*, 362), $\nu_{max.}$ 3493, 3278, 1728sh, 1708, 1657, 912, 895, and 864 cm.$^{-1}$ (no strong bands below 800 cm.$^{-1}$). Hsü *et al.*[4] give m. p. 236—237° (decomp.) for " Hydrogeno I."

The acid gave no colour with concentrated sulphuric acid. Microhydrogenation in acetic acid gave an uptake of 1·0 mol. with a palladium catalyst and 1·4, 1·6 mol. with Adams catalyst (see below).

The *methyl ester*, prepared with diazomethane, was a gum (Found: OMe, 19·1, 14·65. $C_{21}H_{28}O_6$ requires 2OMe, 16·5%), $\nu_{max.}$ 3450, 1727br cm.$^{-1}$.

The bismethanesulphonate of the methyl ester formed prisms, m. p. 138—139°, from ethyl acetate–light petroleum (Found: C, 51·8; H, 6·2. Calc. for $C_{23}H_{32}O_{10}S_2$: C, 51·9; H, 6·1%), $\nu_{max.}$ (OH absent), 1729, 1720, 1660, 1180, 1165, and 900 cm.$^{-1}$. The bismethanesulphonate of the methyl ester of " Hydrogeno I " has m. p. 139—140°.[4]

Heating the acid with boiling acetic anhydride for 2 hr. followed by distillation of the recovered product (3×10^{-3} mm., bath 150°) gave the acetic acid mixed *anhydride* with the 2,7-*diacetyl-acid* as a gum (Found: C, 64·2; H, 6·9; OMe, 7·7. $C_{26}H_{32}O_9$ requires C, 63·9; H, 6·6; OMe, 6·3%), $\nu_{max.}$ (OH absent), 1816 and 1737 cm.$^{-1}$.

Ozonolysis of the Methyl Ester (II; $R^1 = Me$, $R^2 = R^3 = H$).—The ester (207 mg.) in acetic acid (10 ml.) was ozonised at 15—20° until uptake ceased (19 min.). The solution was diluted with water (10 ml.), then steam-distilled for 20 min. Addition of a saturated solution of dimedone to the distillate gave the dimedone derivative of formaldehyde (53·5 mg., 0·33 mol.), m. p. 180—182°. The fraction involatile in steam was intractable.

Reactions of the Acid (II; $R^1 = R^2 = R^3 = H$).—(1) *Attempted oxidation.* (*a*) No solid products were obtained when the acid was oxidised with the chromium trioxide–sulphuric acid reagent.[14]

[14] Curtis, Heilbron, Jones, and Woods, *J.*, 1953, 457.

(*b*) With manganese dioxide. The acid (300 mg.) was shaken with active manganese dioxide [15] (3·0 g.) in dioxan (50 ml.) for 116 hr. The gummy product (263 mg.) showed only weak end-absorption [$E^{1\%}_{1\,cm.}$ (mμ) 210 (210), 131 (215), 94 (220), 8 (225), 6 (230)]. The gum in acetone was deposited on Celite (2 g.), and the dried Celite placed on a column of Celite (50 g.) treated with a 2M-phosphate buffer of pH 6·2 (50 ml.) [16] and made up in chloroform–light petroleum (1 : 1). Elution with the same solvent yielded gums showing no inflections in the region 210—230 mμ, and further elution with chloroform gave starting material (212 mg.).

(2) *Hydrogenation.* The acid (500 mg.) in acetic acid (75 ml.) was shaken in hydrogen at room temperature with a reduced Adams catalyst (112 mg.) (uptake, 2·0 mol. in 18 hr.). The recovered product crystallised from ethyl acetate, giving (i) methyl 1α-carboxy-2β,7-dihydroxy-1,8-epi-dimethyl-4aβ-gibbane-10β-carboxylate (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$) as prisms (108 mg.), m. p. 258—267° (decomp.) raised to 267—269° (decomp.) by recrystallisation, $[\alpha]_D^{19}$ +45° (*c* 0·44). The acid and its methyl ester (prisms, m. p. 173—175°, from ether) were identical with authentic specimens,[1] (ii) nodules (48 mg.; m. p. 225—236°) which on recrystallisation gave the 8-epimeric acid [1] as needles, m. p. 236—238°, $[\alpha]_D^{19}$ +56° (*c* 0·78).

(3) *Action of acid.* (*a*) Treating the acid with acetic acid for 14 days at room temperature, or at 100° for 2 hr. or for 5 hr. under reflux, gave starting material.

(*b*) The acid (90 mg.), in acetic acid (3·0 ml.) containing 3N-hydrochloric acid (0·10 ml.), was kept at room temperature for 24 hr. Recovery gave semicrystalline neutral (22 mg.) and acidic (66 mg.) fractions. Crystallisation of the neutral product from ethyl acetate–light petroleum gave prisms and needles (18 mg.), m. p. 229—235°, $[\alpha]_D^{22}$ +61° (*c* 0·92), of a mixture (see below). The acidic fraction yielded starting material [11 mg.; m. p. 222—223° (decomp.)].

Keeping the mixture for 3 days before working up increased the yield of neutral gums but not that of crystalline neutral product, m. p. 220—238°, $[\alpha]_D^{22}$ +59° (*c* 0·46).

The crystalline neutral product (108 mg.) was chromatographed in benzene on alumina (24 × 2·5 cm.). Elution with 25-ml. portions gave the following main fractions: (i) benzene (100 ml.), and benzene–methanol (200 : 1; 625 ml.), giving 2 mg. on recovery; (ii) (200 : 1; 175 ml.), giving 20 mg., m. p. 193—227°; (iii) (200 : 1; 175 ml.), 12 mg. m. p. 155—170°; (iv) (150 : 1, 200 ml.; 100 : 1, 75 ml.), 5 mg.; (v) (100 : 1; 250 ml.), 55 mg. m. p. 227—240°.

Fraction (ii), $[\alpha]_D^{19}$ +58° (*c* 0·50), crystallised from ethyl acetate–light petroleum in needles (8 mg.), m. p. 221—227°, of methyl 1α-carboxy-2β,4aα-dihydroxy-1β,7-dimethyl-8-oxo-4bβ,7α-gibbane-10β-carboxylate 1 ⟶ 4a-lactone (V; R = Me).

Fraction (iii), $[\alpha]_D^{18}$ +54° (*c* 0·42), crystallised in the same way, gave needles (5 mg.), m. p. 165—170°, of an unidentified product ($\nu_{max.}$ 3400, 1747, 1724, and 883 cm.$^{-1}$) showing only weak end-absorption (no C=C) [$E^{1\%}_{1\,cm.}$ (mμ) 16 (201), 12 (205, 210, 215), and 10 (220)] and giving no colour with concentrated sulphuric acid.

Fraction (v), $[\alpha]_D^{21}$ +68° (*c* 0·60), crystallised as needles (40 mg.), m. p. 234—238° (decomp.), $[\alpha]_D^{18}$ +66° (*c* 0·87) (Found: C, 66·0; H, 7·5. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·2%), $\nu_{max.}$ ~3610, 3520, 1758, 1711, 1653, 923, 899, and 875 cm.$^{-1}$ or (in MeCN) 1768 and 1732 cm.$^{-1}$. The spectra were almost identical with those of gibberellin A_1 methyl ester, m. p. 233—235° (decomp.), $[\alpha]_D$ +46°.[2] Hydrogenation of the new *ester* (26 mg.) with a palladium catalyst (0·8 mol. uptake) in acetic acid gave a mixture of methyl tetrahydro- and 8-epi-tetrahydro-gibberellate which crystallised from ethyl acetate–light petroleum in prisms (12 mg.), m. p. 243—246°, $[\alpha]_D^{22}$ +45° (*c* 0·49) (Found: C, 65·05; H, 7·9. Calc. for $C_{20}H_{28}O_6$: C, 65·9; H, 7·7%).

(*c*) The acid (330 mg.) was boiled with hydrochloric acid (20 ml.; 1 vol. of concentrated acid in 5 vol. of water) for 1·75 hr. The crystals (164 mg.), m. p. 240—245°, which separated at 0° were filtered off and crystallised from ethyl methyl ketone–ether, giving 2β,4aα-dihydroxy-1β,7-dimethyl-8-oxo-4bβ,7α-gibbane-1α,10β-dicarboxylic acid 1⟶4a-lactone (V; R = H) as prisms (106 mg.), m. p. 260—262° (decomp.), $[\alpha]_D^{19}$ + 50° (*c* 1·03) (Found: C, 62·5; H, 7·25. Calc. for $C_{19}H_{24}O_6,H_2O$: C, 62·3; H, 7·15%). Further purification on a column of Celite buffered at pH 6·2 (elution with chloroform) raised the m. p. to 270—271° (decomp.).

The aqueous acidic mother-liquor was extracted with ethyl acetate. Recovery from the extract and washing of the product (0·13 g.) with ether gave a solid which crystallised from ethyl methyl ketone in prisms (8 mg.), m. p. 268—270° (decomp.), of the epimeric 4α-acid (V; R = H,4bHα).

[15] Attenburrow, Cameron, Chapman, Evans, Hems, Jansen, and Walker, *J.*, 1952, 1094.
[16] Stodola, Nelson, and Spence, *Arch. Biochem. Biophys.*, 1957, **66**, 438.

Action of Collidine on Methyl 2β,7-*Bismethanesulphonyloxy*-1β-*methyl*-8-*methylenegibb*-4-*ene*-1α,10β-*dicarboxylate* (II; R^1 = Me, R^2 = R^3 = SO_2Me).—The compound (2·13 g.) was boiled with collidine (20 ml.) for 6 hr. and the solution was kept at 0° for 2·5 days. The liquid was decanted from crystalline material and concentrated to small volume *in vacuo*. The residue and crystals were mixed with ethyl acetate and dilute hydrochloric acid, and the organic layer was washed with dilute hydrochloric acid and extracted with sodium hydrogen carbonate solution. Recovery from the ethyl acetate gave a neutral gum (1·42 g.). Acidification of the alkaline extract and recovery of the acidic product in ethyl acetate gave an intractable acidic gum (83 mg.).

The neutral product was chromatographed on alumina (38 × 2·5 cm.) and eluted first with benzene, giving the following main fractions: (i) (500 ml.), giving a gum (3 mg.) on recovery; (ii) (450 ml.), giving a product (200 mg.) which solidified; (iii) (250 ml.), giving gums (32 mg.); and (iv) (1250 ml.), a violet band, giving an intractable violet-coloured gum (158 mg.). Further elution with benzene–methanol (400 : 1) eluted (v) (750 ml.), a brown band yielding a yellow gum (113 mg.), and (vi) (350 ml.), a yellow gum (677 mg.).

One part of fraction (ii) had m. p. 97—98° but crystallisation of the combined fraction (ii) from ethyl acetate–light petroleum led to the formation of large amounts of intractable gum, together with prisms, m. p. 88—90°, a mixture of methyl 7-methanesulphonyloxy-1-methyl-8-methylenegibba-1,4a(4b)-diene-10-carboxylates (X) (Found: C, 63·6; H, 6·9; S, 7·8; OMe, 8·3. Calc. for $C_{20}H_{26}O_5S$: C, 63·5; H, 6·9; S, 8·5; OMe, 8·2%), $\nu_{max.}$ 1718, 1658, 1597, 1192, 1165, and 870 $cm.^{-1}$, ε (mμ) 26,200 (198, max.), 25,800 (200), 16,000 (205), 8390 (210), 4870 (215), 2840 (220), 1210 (225).

The product from fraction (vi) did not crystallise. A specimen was distilled on to a cold finger (10^{-2} mm., bath 140°), giving a mixture of methyl 7-methanesulphonyloxy-1β-methyl-8-methylenegibba-*xy*-diene-1α,10β-dicarboxylates as a pale yellow glass (A) (Found: C, 60·35; H, 6·5; S, 6·0; OMe, 13·7. Calc. for $C_{22}H_{28}O_7S$: C, 60·5; H, 6·4; S, 7·3. 2OMe, 14·2%), $\nu_{max.}$ (in $CHCl_3$) 1720, ~1665, ~1600, 1175, and 872 $cm.^{-1}$, $\lambda_{max.}$ 254 mμ (ε 6610). After 2 months the crude material could no longer be distilled *in vacuo*. In another experiment the corresponding isomeric gum (Found: C, 60·65; H, 6·5%) was a mixture, giving an identical infrared spectrum but a broad ultraviolet max. at 262 mμ (ε 5570). The corresponding product from "Hydrogeno I" had $\lambda_{max.}$ 275 mμ (ε 6000).[4]

Action of Sodium Hydroxide on the Triene ($\lambda_{max.}$ 254 mμ).—The above gummy triene (A) (127 mg.) was boiled with 2N-sodium hydroxide (10 ml.) for 2·25 hr. The solution was cooled, washed with ether, and acidified and the gummy product (88 mg.) recovered in ethyl acetate, then boiled with water (18 ml.) under nitrogen. Carbon dioxide (0·4 mol.) was evolved during 40 min. Recovery from the solution gave a gum.

Hydrogenation of Gibberellic Acid.—Gibberellic acid (1·00 g.) in methanol (60 ml.) was shaken in hydrogen with a reduced Adams catalyst (200 mg.) (uptake: 2·5 mol. in 80 min.). A solution of the crude product (3·50 g.) in butanol (40 ml.) was diluted with benzene (460 ml.) and then was run on to a column of anhydrous silica (250 g.) buffered with a phosphate buffer (90 ml.; pH 5·4) and made up in benzene–butan-1-ol (92 : 8; saturated with water). Elution with portions of the solvents (saturated with water) gave the following main fractions: (i) (92 : 8; 500 ml.), giving a gum (39 mg.); (ii) (750 ml.), giving a non-lactonic ($\nu_{max.}$ *ca.* 1700 $cm.^{-1}$) product (377 mg.); (iii) (250 ml.), giving mixed fractions (418 mg., lactone content increasing); (iv) (1·5 l.), giving a solid (1·00 g.) with strong lactonic ($\nu_{max.}$ *ca.* 1765 $cm.^{-1}$) absorption; (v) (2 l.), mixed fractions (232 mg., lactone decreasing); (vi) (5 l.), giving a non-lactonic solid (492 mg.; m. p. >200°); (vii) (68 : 32; 5 l.), giving a non-lactonic solid (615 mg.), mainly melting *ca.* 170—200° (decomp.).

Fraction (iv) crystallised from methanol–ethyl acetate, giving, first, impure globular aggregates (41 mg.), m. p. 155—190° and 260—270° (decomp.), then prisms (461 mg.) of 8-epi-tetrahydrogibberellic acid (XII; R = H, X = H, β-OH), m. p. 288—290° (decomp.) (variable) (Found: C, 64·9; H, 7·6. Calc. for $C_{19}H_{26}O_6$: C, 65·1; H, 7·5%). The methyl ester [7] crystallised from ethyl acetate–light petroleum in prisms, m. p. 237—242°.

Fractions (vi) and (vii) crystallised from water and dilute methanol, giving crops of (*a*) needles or stout prisms, m. p. >295° (decomp.) [the main constituent of fraction (vi)] and (*b*) plates or prisms but not needles, less soluble in water, with an indefinite m. p. *ca.* 175—200° (decomp.). Recrystallisation of fraction (*a*) gave 2β,7-*dihydroxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylic acid* (IV; R^1 = R^2 = R^3 = R^4 = H) as needles (487 mg.), m. p. 300—

302° (decomp.), $[\alpha]_D^{29}$ +43° (*c* 1·06) (Found, after drying at 100° for 8 hr.: C, 61·6; H, 8·2. $C_{19}H_{28}O_6,H_2O$ requires C, 61·6; H, 8·2%), $\nu_{max.}$ ~3350br, 1703, 1652sh, (?H_2O) cm.$^{-1}$ [distinct from the spectrum of the 8-epimeric acid, m. p. 290—295° (decomp.), obtained by Takahashi *et al.*[10]], $\nu_{max.}$ (in dioxan) 1730 and 1713 cm.$^{-1}$.

The dimethyl ester formed prisms, m. p. 173—175°, from ether, identical with material prepared [1] from the monobasic acid (IV; $R^1 = R^3 = R^4 = H$, $R^2 = Me$), m. p. 269—271° (decomp.) (Found: C, 66·3; H, 6·7; OMe, 16·6. Calc. for $C_{21}H_{32}O_6$: C, 66·3; H, 8·5; 2OMe, 16·3%).

The dimethyl ester diacetate (IV; $R^1 = R^2 = Me$, $R^3 = R^4 = Ac$), obtained by boiling the ester with acetic anhydride for 2 hr., formed needles [from light petroleum (b. p. 80—100°)], m. p. 168—170°, $[\alpha]_D^{21}$ +25° (*c* 0·87) (Found: C, 65·0; H, 7·95; OMe, 13·1. Calc. for $C_{25}H_{36}O_8$: C, 64·6; H, 7·8; 2OMe, 13·3%), $\nu_{max.}$ 1737 cm.$^{-1}$ (OH absent) or (in CCl_4) 1737 cm.$^{-1}$. The acetate was identical with material prepared [1] by a different method.

Crystallisation of fraction (*b*) above, m. p. *ca.* 175° (decomp.), and fraction (i) from the chromatogram, from dilute methanol gave plates (463 mg.) of 2β,7-*dihydroxy*-1β,8-*epi*-*dimethylgibb*-4-*ene*-1α,10β-*dicarboxylic acid* (XVI; $R^1 = R^2 = R^3 = R^4 = H$), m. p. 170—200° (decomp.). Some specimens partly resolidified at *ca.* 200° and remelted 225—230° (decomp.), and had $[\alpha]_D^{18}$ +23° (*c* 0·99) (Found, in a sample dried at 100° for 2·5 hr. *in vacuo*: C, 62·2, 61·9; H, 7·7, 7·7. $C_{19}H_{26}O_6,H_2O$ requires C, 61·9; H, 7·7%), $\nu_{max.}$ 3485, ~3277br, ~3180br, 1697, 1658 (?H_2O) cm.$^{-1}$. The spectrum was indistinguishable from that of the acid, m. p. 184—186° (decomp.), obtained similarly by Takahashi *et al.*[10] but assigned the incorrect formula $C_{19}H_{28}O_6,1{\cdot}5H_2O$. The dimethyl ester (XVI; $R^1 = R^2 = Me$, $R^3 = R^4 = H$) crystallised from ether in prisms, m. p. 141—142°, $[\alpha]_D^{17}$ +29° (*c* 1·04) (Found: C, 67·0, 66·7; H, 8·2, 8·2; OMe, 16·1. Calc. for $C_{21}H_{30}O_6$: C, 66·6; H, 8·0; 2OMe, 16·4%), $\nu_{max.}$ 3472, 3363, and 1728 cm.$^{-1}$ or (in $CHCl_3$) 3584, 3460, 1725, and 1704sh cm.$^{-1}$. The ester was identical with the methyl ester of the 8-epi-acid (XVI; $R^1 = R^3 = R^4 = H$, $R^2 = Me$).[1] The ester obtained by Takahashi *et al.*[10] from the acid of m. p. 184—186° (decomp.) had m. p. 140°.

The *diacetyl derivative* (XVI; $R^1 = R^2 = Me$, $R^3 = R^4 = Ac$) of the dimethyl ester, obtained by boiling it with acetic anhydride for 2 hr., was a gum, $[\alpha]_D^{20}$ +71° (*c* 1·47 in MeOH) (Found: C, 64·4; H, 7·6. $C_{25}H_{34}O_8$ requires C, 64·9; H, 7·4%), $\nu_{max.}$ (in $CHBr_3$) 1726 cm.$^{-1}$.

Oxidation of 8-*Epi-tetrahydrogibberellic Acid.*—A suspension of the powdered acid (1·09 g.) in acetone (140 ml.) was shaken with the chromium trioxide reagent [14] (1·0 ml.; 7·5N with respect to O) at room temperature. More oxidant (0·4 ml., 0·2 ml.) was added (after 10 min. and after 1·5 hr., respectively). After 4 hours' shaking, the mixture was concentrated *in vacuo* at 20°, diluted with water, and extracted with ethyl acetate. Recovery from the extract gave a solid which crystallised from methanol–ethyl acetate–light petroleum in prisms (812 mg.) of 4aα,7-*dihydroxy*-1β,8-*epi*-*dimethyl*-2-*oxogibbane*-1α,10β-*dicarboxylic acid* 1→4a-*lactone* (XII; R = H, X = O), m. p. 265—269° (decomp.) raised to 268—270° (decomp.) by recrystallisation or chromatography on Celite (pH 6·2; elution with chloroform), $[\alpha]_D^{24}$ +132° (*c* 0·87) (Found: C, 65·1; H, 7·2. $C_{19}H_{24}O_6$ requires C, 65·5; H, 6·9%), $\nu_{max.}$ 3585, 3310, 1779, 1720, and 1707 cm.$^{-1}$ or (in dioxan) 3600, 3550, 1790, and 1730 cm.$^{-1}$.

The methyl ester formed needles, m. p. 136°, from ethyl acetate–light petroleum, identical with an authentic specimen (m. p. 131—133° [7]).

The *oxime*, prepared in pyridine, crystallised from dilute ethanol in prisms, m. p. 284—286° (decomp.) (Found: C, 62·6; H, 7·05; N, 3·7. $C_{19}H_{25}NO_6$ requires C, 62·8; H, 6·9; N, 3·85%).

Hydrogenation of Methyl 1α-*Carboxy*-4aα,7-*dihydroxy*-1β,8-*dimethyl*-2-*oxogibbane*-10β-*carboxylate* 1→4a-*Lactone* (XII; R = Me, X = O, m. p. 160°).—The ester [7] (104 mg.) in acetic acid (14 ml.) was shaken in hydrogen with a reduced Adams catalyst (101 mg.) (uptake, 1·0 mol. in 7·5 hr.). The recovered product was chromatographed in benzene on alumina (23 × 1·2 cm.), and the column was eluted with 100-ml. portions of benzene and benzene–methanol (ratio in parentheses), giving: (1—4) (benzene); (5—6) (200 : 1), nil; (7—8) (200 : 1), 2 mg.; (9—13) (200 : 1); (13—16) (100 : 1), 1 mg.; (17—18) (100 : 1), 87 mg. m. p. 203—217°. Fractions 17—18 crystallised from ethyl acetate–light petroleum in prisms (71 mg.), m. p. 217—219°, of the 2α-hydroxy-epimer [5] (XII; R = Me, X = H, α-OH) of methyl tetrahydrogibberellate.

Hydrolysis of the Ester.—The above ester (275 mg.) was boiled with N-sodium hydroxide (27 ml.) for 2 hr. The solution was acidified with concentrated hydrochloric acid, extracted with ethyl acetate, and re-extracted after storage for 24 hr. at room temperature. Recovery

from the extracts gave a foam (232 mg.) which was boiled with ethyl acetate for 8 hr. Crystallisation gave material with a wide range of m. p., mainly *ca.* 250°.

The product (206 mg.) was chromatographed on a column of Celite (60 g.) buffered with the phosphate buffer (pH 6·2; 60 ml.) and made up in chloroform. Elution with portions of solvents gave the following fractions: (i) chloroform (750 ml.), yielding 37 mg.; (ii) chloroform–ethyl acetate (20 : 1, 10 : 1, 5 : 1; total 750 ml.); trace; (iii) (3 : 1; 750 ml.), 4 mg.; (iv) (1 : 1; 1 l.), 15 mg.; (v) (1 : 1; 500 ml.), trace; (vi) (1 : 3; 250 ml.), 3 mg.; (vii) (1 : 3; 2·25 l.), 126 mg.

Starting material (20 mg.) was recovered from fraction (i). Fractions (iii) and (iv) crystallised from methanol–ethyl acetate, yielding prisms (13 mg.) of tetrahydrogibberellic acid (methyl ester,[7] m. p. 270—272°).

Fraction (vii) crystallised from methanol–ethyl acetate in prisms (108 mg.) of 2α,4aα,7-*trihydroxy*-1β,8-*dimethylgibbane*-1α,10β-*dicarboxylic acid* 1→4a-*lactone* (XII; R = H, X = H, α-OH), m. p. 249—250° (decomp.), $[\alpha]_D^{24}$ +56° (*c* 0·64) (Found: C, 65·0; H, 7·5. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·5%), $\nu_{max.}$ 3530, ~3375, ~2600, 1757, 1737, and 1716sh cm.$^{-1}$. Esterification gave starting material, m. p. 216—218°

Hydrogenation of Methyl 1α-*Carboxy*-4aα,7-*dihydroxy*-1β,8-*epi-dimethyl*-2-*oxogibbane*-10β-*carboxylate* 1→4a-*Lactone* (XII; R = Me, X = O).—The ester (451 mg.; m. p. 130—132°, prepared[7] from the mixed 8-epimeric methyl tetrahydrogibberellates) was hydrogenated as described above for the 8-epimer, and the product was chromatographed on alumina (26 × 1·7 cm.). After the elution of a substance, m. p. 175—200° (4 mg.), with benzene–methanol (100 : 1), further elution removed fractions (269 mg.), m. p. range 165—169°, followed by mixed fractions (169 mg.), m. p. >170°.

Crystallisation of the fractions of m. p. 165—169° from acetone–light petroleum gave prisms (219 mg.), m. p. 167—169°, of the 2α-hydroxy-epimer [5] (IX; R = Me, X = H, α-OH) of methyl 8-epi-tetrahydrogibberellate.

The last-mentioned ester (1·67 g.) was boiled with N-sodium hydroxide (170 ml.) for 4 hr. Acidification of the cooled solution gave a precipitate (1·31 g.), m. p. 292—298° (decomp.). Part of this (200 mg.) was chromatographed in the usual way on Celite (50 g.) buffered at pH 6·2. A gum (6 mg.) was eluted with chloroform, then a solid (8 mg.) with chloroform–ethyl acetate (1 : 1). Methylation of the latter fraction gave methyl 8-epi-tetrahydrogibberellate, m. p. 234—238°.

Continued elution yielded mixed fractions (17 mg.), then 2α,4aα,7-*trihydroxy*-1β,8-*epi-dimethylgibbane*-1α,10β-*dicarboxylic acid* 1→4a-*lactone* (XII; R = H, X = H, α-OH) (164 mg.) which crystallised from dilute methanol in prisms, m. p. 287—297° (decomp.; variable), $[\alpha]_D^{17}$ +23° (*c* 0·22 in MeOH) (Found: C, 65·0; H, 7·7. $C_{19}H_{26}O_6$ requires C, 65·1; H, 7·5%), $\nu_{max.}$ 3350, 3290, 1774, 1720, and 1690sh cm.$^{-1}$. Esterification gave starting material, m. p. 167—169°.

Oxidation of 2β,7-*Dihydroxy*-1β,8-*epi-dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylic acid* (IV; R^1 = R^2 = R^3 = R^4 = H).—A suspension of the acid (305 mg.) in acetone (25 ml.) was treated with the chromium trioxide reagent (0·30 ml.) at 10°, shaken in ice–water for 1·5 hr., kept for 15 min. at 0°, concentrated *in vacuo* at room temperature, and diluted with water (5 ml.). The precipitate [206 mg.; m p. 120° (decomp.)] was filtered off and washed with water. A gum (71 mg.) (A) was recovered by extraction of the filtrate with ethyl acetate.

The precipitate crystallised from ethyl methyl ketone–light petroleum (charcoal) in needles, m. p. 120° (decomp.), of 7-*hydroxy*-1β,8-*epi-dimethyl*-2-*oxo*-4aβ-*gibbane*-1α,10β-*dicarboxylic acid* (XIV) (Found, in a sample dried at 20° *in vacuo*: C, 61·9; H, 7·8. $C_{19}H_{26}O_6,H_2O$ requires C, 61·9; H, 7·7%), $\nu_{max.}$ 3555, 3440, ~3200br, 1729, 1704, and 1684sh (?H_2O) cm.$^{-1}$.

Decarboxylation of the Acid (XIV).—The acid (464 mg.) was boiled with water (20 ml.) until evolution of carbon dioxide ceased (50 min.). Evaporation gave a solid (443 mg.; m. p. *ca.* 200°). This crude acid (590 mg.) was chromatographed in the usual way on Celite (250 g.) buffered at pH 6·2 and made up in chloroform–light petroleum (1 : 1). Elution with the same solvent removed a solid (559 mg.; m. p. 196—204°) which crystallised from ethyl methyl ketone–light petroleum in plates and prisms (499 mg.) of 7-*hydroxy*-1ξ,8-*epi-dimethyl*-2-*oxo*-4aβ-*gibbane*-10β-*carboxylic acid* (XV; R = H, X = O), m. p. 205—207° (decomp.) (Found: C, 70·7; H, 8·7. $C_{18}H_{26}O_4$ requires C, 70·6; H, 8·55%), $\nu_{max.}$ ~3435br, 1723, and 1705 cm.$^{-1}$.

Decarboxylation of the gum A (200 mg.) from the preceding and similar experiments yielded the same acid (157 mg.).

The methyl ester crystallised from ether–light petroleum in needles, m. p. 124—125°

(Found: C, 71·2; H, 8·8. Calc. for $C_{19}H_{28}O_4$: C, 71·2; H, 8·8%), $\nu_{max.}$ 3345, 3275, 1737, and 1710 cm.$^{-1}$, identical with the alkali-stable ester obtained [1] by a different route.

Reduction of the Ester (XV; R = Me, X = O).—The ester (140 mg.) was treated in chloroform (3 ml.) with boron trifluoride–ether complex (0·20 ml.) and ethanedithiol (0·20 ml.). After 48 hr. at room temperature the mixture was diluted with chloroform and washed with water and saturated sodium chloride solution. Recovery from the organic layer gave a gum which was chromatographed on alumina (10 × 1·7 cm.) in benzene. Thiols were eluted with benzene–light petroleum (1 : 1); further elution with benzene–methanol (100 : 1) gave the gummy thioketal (0·16 g.). This was heated in dioxan (25 ml.) with Raney nickel (5 g.) for 7 hr., and the cooled mixture was filtered. Recovery from the filtrate gave a semicrystalline product (134 mg.) which was chromatographed in benzene on alumina (24 × 1·7 cm.), and the product (116 mg.; m. p. 147—151°) was eluted with benzene–methanol (200 : 1). Crystallisation from light petroleum (b. p. 80—100°) gave *methyl 7-hydroxy-1ξ,8-epi-dimethyl-4aβ-gibbane-10β-carboxylate* (XV; R = Me, X = H_2) as needles (74 mg.), m. p. 153—155° (Found: C, 74·8; H, 9·7. $C_{19}H_{30}O_3$ requires C, 74·5; H, 9·9%), $\nu_{max.}$ 3320, 3255sh, and 1738 cm.$^{-1}$.

Reduction of the Acid (XV; R = H, X = O).—(*a*) *Thioketal method.* The acid (200 mg.) in chloroform (25 ml.) was treated with boron trifluoride–ether complex (0·18 ml.) and ethanedithiol (0·18 ml.). After 2 days at room temperature recovery gave a gum (0·26 g.) which crystallised from ether–light petroleum, giving the *thioketal* as prisms (211 mg.), m. p. 100—130°, setting and remelting at 216—218°. Recrystallisation from ethyl acetate gave prisms, m. p. 218—219° (Found: C, 63·1; H, 7·9. $C_{20}H_{30}O_3S_2$ requires C, 62·8; H, 7·9%). The derivative (670 mg.) and Raney nickel (*ca.* 22 g.) were heated in dioxan (120 ml.) for 10 hr. at 100°. The mixture was filtered (solids A). Evaporation of the filtrate gave a gum (0·10 g.). Solids A were washed with sodium hydrogen carbonate solution and with water; the aqueous filtrates were acidified with hydrochloric acid and extracted with ethyl acetate; recovery from the extract gave another gum (0·43 g.). The combined gums crystallised from acetone–light petroleum (charcoal) in needles (410 mg.; m. p. 135—155°, softening at 125°) which on recrystallisation gave *7-hydroxy-1ξ,8-epi-dimethyl-4aβ-gibbane-10β-carboxylic acid* (XV; R = H, X = H_2) as needles, m. p. 154—155° (air-dried) and 145—147° (dried at 100° *in vacuo*), $[\alpha]_D^{25}$ +15° (*c* 0·95) (Found: C, 74·2; H, 9·7. $C_{18}H_{28}O_3$ requires C, 73·9; H, 9·65%), $\nu_{max.}$ 3240, ~2695br, and 1699 cm.$^{-1}$.

The methyl ester formed needles, m. p. 154—155°, identical with material described above.

(*b*) *Hydrogenation.* The acid (41 mg.) was shaken in hydrogen in acetic acid (7 ml.) with Adams catalyst (72 mg.) (uptake, 1 mol. in 6 hr.). The product was isolated and then boiled with ethyl acetate (3 ml.) and concentrated hydrochloric acid (1 drop) for 1 hr. The material recovered by evaporation partly crystallised from ethyl methyl ketone but had a wide range of m. p. This product was chromatographed on Celite (20 g.) buffered with the phosphate buffer (pH 6·2; 20 ml.) and made up in chloroform–light petroleum (1 : 20). The column was eluted with 25 ml. portions of the same solvents (ratio in parentheses) giving the following fractions: (1—44) (1 : 20 to 1 : 1), fore-run yielding gums (7·5 mg.); (2 : 1) fractions (45—50), a solid (12 mg.), m. p. 160—207°; (2 : 1) (51—62), a solid (13 mg.), m. p. mainly 108—120° (decomp.); (2 : 1) (63—74), gums (11 mg.). The last three products were methylated separately with diazomethane.

Methylated fractions (51—62) crystallised from light petroleum (b. p. 80—100°), giving *methyl 2ξ,7-dihydroxy-1ξ,8-epi-dimethyl-4aβ-gibbane-10β-carboxylate* (XV; R = Me, X = H, OH) as needles (9 mg.), m. p. 137—140° (Found: C, 71·4; H, 9·4; OMe, 10·2). $C_{19}H_{30}O_4$ requires C, 70·8; H, 9·4; OMe, 9·6%), $\nu_{max.}$ 3540, 3365, and 1716 cm.$^{-1}$.

Methylated fractions (45—50) were chromatographed on alumina (18 × 0·5 cm.) in benzene. After a gum (2 mg.) had been eluted with benzene–methanol (200 : 1) further elution with a 20 : 1 mixture removed a solid (8 mg.) which crystallised from light petroleum (b. p. 80—100°) in prisms (6 mg.), melting partly at 70—75° (decomp.) and completely at 110—115°, presumably the 2-epimer of the above alcohol (Found: OMe, 9·3%), $\nu_{max.}$ ~3360br, 1734, and 1716 cm.$^{-1}$.

Methylated fractions (63—74) were chromatographed on alumina (1 × 0·5 cm.) in benzene. Benzene–methanol (100 : 1) eluted an unidentified gum (Found: OMe, 9·2%).

Action of Acetic Anhydride on the Acid (IV; $R^1 = R^2 = R^3 = R^4 = H$).—The acid (175 mg.) was boiled with acetic anhydride (8 ml.) for 2 hr. and the solution was evaporated *in vacuo*. Crystallisation of the residue from benzene–light petroleum gave the *diacetyl* trans-*anhydride*

(XIII) as needles (158 mg.), m. p. 182—183° (softening and re-setting at *ca.* 120—140°), $[\alpha]_D^{21}$ +18° (*c* 0·84) (Found: C, 65·9; H, 7·3. $C_{23}H_{30}O_7$ requires C, 66·0; H, 7·2%), $\nu_{max.}$ 1802, 1754 (6-ring anhydride), and 1728 (ester CO) cm.$^{-1}$ [different from the spectrum of the anhydride (m. p. 165—168°) obtained by Takahashi *et al.*[10] from the acid, decomp. 290—295°] or (in CCl_4) 1805, 1761, and 1734 cm.$^{-1}$.

Hydrolysis of the Anhydride (XIII).—The anhydride (30 mg.) was boiled with water (3 ml.) for 5 hr.; the product obtained by evaporation of the solution *in vacuo* crystallised from dilute ethanol in needles (24 mg.), m. p. 304—306° (decomp.) of 2β,7-*diacetoxy*-1β,8-*epi*-*dimethyl*-4aβ-*gibbane*-1α,10β-*dicarboxylic acid* (IV; $R^1 = R^2 = H$, $R^3 = R^4 = Ac$), $[\alpha]_D^{16}$ +37° (*c* 0·95) Found: C, 63·5; H, 7·55. $C_{23}H_{30}O_7,H_2O$ requires C, 63·3; H, 7·4%), $\nu_{max.}$ 3240, 3170, and 1754 cm.$^{-1}$. The methyl ester (needles, m. p. 167—169°) was identical with a specimen obtained by acetylating methyl 2β,7-dihydroxy-1β,8-epi-dimethyl-4aβ-gibbane-1α,10β-dicarboxylate (IV; $R^1 = R^2 = Me$, $R^3 = R^4 = H$, see above).

Reactions of the Acid (XVI; $R^1 = R^2 = R^3 = R^4 = H$).—(i) *Hydrogenation.* The acid (326 mg.) in methanol (50 ml.) was shaken in hydrogen at room temperature with a reduced Adams catalyst (219 mg.) for 5 hr., then left in hydrogen for 10 days without shaking (uptake 0·5 mol.). Crystallisation of the product from water and dilute methanol gave the above acid, $C_{19}H_{28}O_6,H_2O$ (IV; $R^1 = R^2 = R^3 = R^4 = H$) as needles (184 mg.), m. p. 299—304° (decomp.), and starting material (96 mg.).

(ii) *Action of acetic anhydride.* The acid (40 mg.) was boiled with acetic anhydride (3·0 ml.) for 4 hr. Evaporation *in vacuo* gave a gummy acetyl anhydride, $\nu_{max.}$ (OH absent), 1802, 1760 (6-ring anhydride C=O), and 1738 cm.$^{-1}$.

Takahashi *et al.*[10] converted their dibasic acid, m. p. 184—186° (decomp.), into a crystalline diacetyl anhydride, m. p. 185—186°, but attempted crystallisation of the gummy anhydride with seeds of the crystalline anhydride failed. The anhydride could not be eluted from alumina.

The gummy anhydride (161 mg.) was boiled with water (30 ml.) for 19 hr. and the solution was evaporated. The residue was treated with diazomethane, and the resulting gummy acetyl ester was chromatographed on alumina. Elution with benzene–methanol (200 : 1) yielded an intractable gum (82 mg.), $[\alpha]_D^{22}$ +10° (*c* 1·56 in MeOH), $\nu_{max.}$ (in $CHBr_3$), 1724 cm.$^{-1}$; the spectrum was different from that of the dimethyl ester diacetate of $[\alpha]_D$ +71° (XVI; $R^1 = R^2 =$ Me, $R^3 = R^4 =$ Ac) (above).

(iii) *Action of hydrochloric acid.* (*a*) The acid (15 mg.), dioxan (2 ml.), and concentrated hydrochloric acid (0·88 ml.) were heated under reflux for 14·5 hr. The mixture was evaporated and the residual gum crystallised from ethyl acetate, giving a solid (3 mg.) which formed prisms, m. p. 255—265° (decomp.), on recrystallisation. The infrared spectrum was almost identical with that of 8-epi-tetrahydrogibberellic acid.

(*b*) The acid (491 mg.) was boiled with water (50 ml.) and concentrated hydrochloric acid (10 ml.) for 2 hr. The product (509 mg.), recovered in ethyl acetate, was chromatographed in the usual way on Celite (25 g.) buffered with the phosphate buffer (pH 6·2; 25 ml.) and made up in chloroform. After the column had been washed with chloroform the lactonic fractions (338 mg.) were eluted with chloroform–ethyl acetate (1 : 1) (600 ml.). The product crystallised from methanol–ethyl acetate–light petroleum in prisms (266 mg.), m. p. 287—289° (decomp.) (Found: C, 65·3; H, 7·45. Calc. for $C_{19}H_{26}O_6$: C, 65·1; H, 7·5%). The infrared spectrum in dioxan closely resembled that of 8-epi-tetrahydrogibberellic acid. Esterification of the acid (50 mg.) with diazomethane gave a gum which crystallised from ethyl acetate–light petroleum, giving methyl 8-epi-tetrahydrogibberellate as prisms (24 mg.), m. p. 240—243°, but the rest of the material did not crystallise.

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