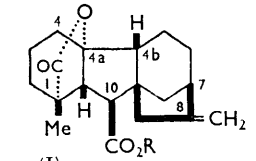
651. *Gibberellic Acid. Part XXIX.* Some Transformation of Gibberellin A_9*

By J. R. Hanson and T. P. C. Mulholland

The preparation of the 8-demethylene-, 2,3-dehydro-, and some other derivatives of gibberellin A_9 is described.

Gibberellin A_9 (I; R = H),[1] isolated from cultures of *Gibberella fujikuroi*, is the simplest known gibberellin. Consequently modification of its structure was of interest in the study of structure–activity relationships. Since only small quantities of gibberellin A_9 were available, other 7-deoxy-gibberellins were used as starting materials for some transformations.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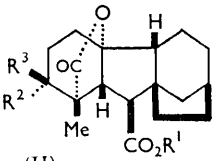
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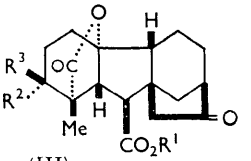
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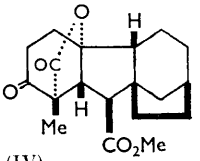
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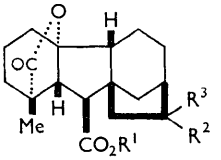
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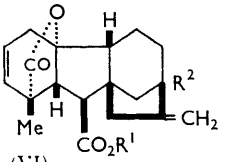
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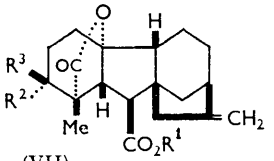
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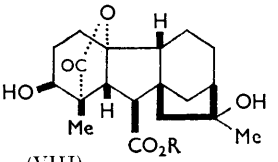
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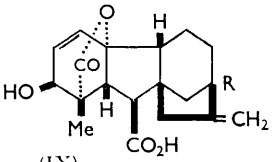

(IX)

In order to assess the importance of the 8-substituent on biological activity, the 8-demethylene derivative (II; $R^1 = R^2 = R^3 = H$) of gibberellin A_9 was prepared. The 8-nor-ketone (III; R^1 = Me, $R^2 = R^3$ = H) [2,3] of gibberellin A_4 methyl ester was first reduced by way of the 8,8-ethylenedithioketal, $C_{21}H_{28}O_5S_2$, to the 2-hydroxy-ester (II; R^1 = Me, $R^2 = R^3$ = H), $C_{19}H_{26}O_5$. Oxidation of this alcohol with chromium trioxide gave the corresponding 2-ketone (IV), $C_{19}H_{24}O_5$, which was reduced through the 2,2-ethylenedithioketal, $C_{21}H_{28}O_4S_2$, yielding 8-demethylenegibberellin A_9 methyl ester (II; R^1 = Me, $R^2 = R^3$ = H), $C_{19}H_{26}O_4$, m. p. 139—141°. Alkaline hydrolysis of this ester gave the required acid (II; $R^1 = R^2 = R^3$ = H), $C_{18}H_{24}O_4$, m. p. 225—227°.

Reduction of the 8-nor-ketone (III; R^1 = Me, $R^2 = R^3$ = H) [1] of gibberellin A_9 methyl ester, with sodium borohydride, gave a single 8-alcohol (V; R^1 = Me, R^2 = OH, R^3 = H), $C_{19}H_{26}O_5,H_2O$. The 8-hydroxyl group was tentatively assigned the β-configuration by analogy with the corresponding reduction [4-6] of the 16-nor-ketones of kaurene and phyllocladene. Alkaline hydrolysis of the hydroxy-ester gave the corresponding acid

* Part XXVIII, preceding Paper.

[1] B. E. Cross, R. H. B. Galt, and J. R. Hanson, *Tetrahedron*, 1962, **18**, 451.
[2] J. F. Grove, J. MacMillan, T. P. C. Mulholland, and W. B. Turner, *J.*, 1960, 3049.
[3] D. C. Aldridge, J. R. Hanson, and T. P. C. Mulholland, Part XXVIII, preceding Paper.
[4] L. H. Briggs, B. F. Cain, R. C. Cambie, and B. R. Davis, *J.*, 1962, 1840.
[5] L. H. Briggs, B. F. Cain, R. C. Cambie, B. R. Davis, P. S. Rutledge, and J. K. Wilmshurst, *J.*, 1963, 1345.
[6] J. R. Hanson, unpublished results.

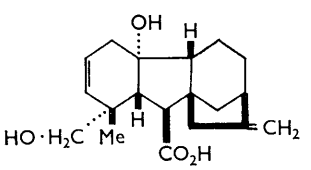
(V; $R^1 = R^3 = H$, $R^2 = OH$), $C_{18}H_{24}O_5$; hydrolysis of the parent nor-ketone gave the keto-acid (III; $R^1 = R^2 = R^3 = H$), $C_{18}H_{22}O_5,H_2O$.

Treatment of gibberellin A_9 with bromine in chloroform yielded a derivative, $C_{19}H_{24}Br_2O_4$, m. p. 198—200°, but the nuclear magnetic resonance spectrum showed that it was a mixture of isomers. The coupling constant (J = 8—9 c./sec.) for the 10,10a quartet suggested that some epimerisation had occurred at position 4b. Hydrogenation of gibberellin A_9 with a palladium catalyst gave a mixture of 8-epimeric dihydro-derivatives (V; $R^1 = R^2 = H$, R^3 = Me), $C_{19}H_{26}O_4$, m. p. 198—200°. The methyl ester was not fully resolved into epimers by crystallisation, but yielded the major component (V; $R^1 = R^3$ = Me, $R^2 = H$), $C_{20}H_{28}O_4$, with m. p. 182—186°, and a smaller uncharacterised fraction, m. p. 163—175°. The infrared spectra of the two fractions were indistinguishable from each other, and from the spectrum of the uncharacterised ester, m. p. 186—188°, prepared [1] by hydrogenating gibberellin A_9 methyl ester.

The 2,3-unsaturated gibberellin A_5 (VI; $R^1 = H$, $R^2 = OH$) occurs in green plants,[7] but its 7-deoxy-analogue (VI; $R^1 = R^2 = H$) has not been isolated from natural sources. The latter compound was prepared from gibberellin A_4 methyl ester (VII; R^1 = Me, $R_2 = H$, $R^3 = OH$). Treatment of the 2-methanesulphonyloxy-derivative (VII; R^1 = Me, $R^2 = H$, $R^3 = O{\cdot}SO_2Me$), $C_{21}H_{28}O_7S$, m. p. 140°, of the ester with collidine yielded the 2,3-dehydro-ester (VI; R^1 = Me, $R^2 = H$), $C_{20}H_{24}O_4$, m. p. 149—152°, $[\alpha]_D$ −150°. Alkaline hydrolysis of the dehydro-ester then gave the corresponding acid (VI; $R^1 = R^2 = H$), $C_{19}H_{22}O_4$, $[\alpha]_D$ −164°.

Kitamura *et al.* reported,[8] without experimental detail, that dehydration of the methyl esters of either gibberellin A_4 (VII; $R^1 = R^2 = H$, $R^3 = OH$) or gibberellin A_2 (VIII; R = H) with phosphorus oxychloride in pyridine gave a dehydro-derivative, $C_{20}H_{24}O_4$, m. p. 145—146°. In our hands dehydration of the two esters with phosphorus oxychloride did not yield pure products, possibly owing to partial epimerisation at position 4b (cf. ref. 9). Although the products were similar to the ester (VI; R^1 = Me, $R^2 = H$), $[\alpha]_D$ −150°, the specific rotations were different ($[\alpha]_D$ −92° and −94°, respectively).

The ultraviolet spectra of the 2,3-dehydro-ester (VI; R^1 = Me, $R^2 = H$) and the corresponding acid, like those of gibberellins A_5 and its methyl ester,[7] showed inflections at about 225 mμ. Attempts to reduce the ester to gibberellin A_9 methyl ester by specific hydrogenation of the 2,3-ethylenic bond failed. With the partially poisoned catalyst [10] previously used to convert gibberellic acid (IX; R = OH) and gibberellin A_7 (IX; R = H) into their 3,4-dihydro-derivatives, reduction was incomplete and not specific; further hydrogenation with a palladium–carbon catalyst yielded a mixture of 8-epimeric dihydro-gibberellin A_9 methyl esters (V; $R^1 = R^2$ = Me, $R^3 = H$), m. p. 170—175°, the infrared spectrum of which was identical with that of material of m. p. 182—186° described above.



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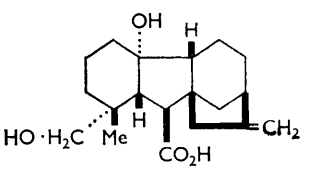

(XI)

Reduction of the 2,3-dehydro-acid (VI; $R^1 = R^2 = H$), $[\alpha]_D$ −164°, with lithium aluminium hydride at room temperature resulted only in fission of the lactone ring, giving the hydroxy-acid (X), $C_{19}H_{26}O_4$, $[\alpha]_D$ −88°. Similar reduction of gibberellin A_9, $[\alpha]_D$ −22°,[1] yielded the analogous hydroxy-acid (XI), $C_{19}H_{28}O_4$, $[\alpha]_D$ −46°. Edwards *et al.*[11]

[7] J. MacMillan, J. C. Seaton, and P. J. Suter, *Tetrahedron*, 1960, **11**, 60.
[8] H. Kitamura, N. Takahashi, Y. Seta, and Y. Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1958, **22**, 434.
[9] D. C. Aldridge, J. F. Grove, R. N. Speake, B. K. Tidd, and W. Klyne, *J.*, 1963, 143.
[10] D. F. Jones and P. McCloskey, *J. Appl. Chem.*, 1963, **13**, 324.
[11] O. E. Edwards, A. Nicolson, J. W. Apsimon, and W. B. Whalley, *Chem. and Ind.*, 1960, 624.

tried unsuccessfully to deduce the orientation of the lactone ring in 2-epitetrahydrogibberellic acid on the basis of the positive value for the molecular rotation difference, lactone — acid. It is interesting to note that though Δ_D for (I; R = H) — (XI) is also positive (+24°), in (VI; $R^1 = R^2 = H$) — (X) Δ_D is — 76°.

Experimental

Melting points are corrected. Light petroleum had b. p. 60—80° and solutions were dried with sodium sulphate. Alumina was Woelm, acid, grade II. Unless otherwise stated, infrared spectra were determined for Nujol mulls, and ultraviolet spectra and specific rotations for ethanol solutions.

Gibberellin A_9.—(*a*) *Bromination.* Gibberellin A_9 (12 mg.) in chloroform (1 ml.) was treated at room temperature with bromine (6·7 mg.) in chloroform (0·67 ml.). After 24 hr. the mixture was evaporated *in vacuo* at room temperature. Crystallisation of the residue from ether gave prisms (8·6 mg.), m. p. 167—169°, of a substance (Found: C, 48·4; H, 5·3; Br, 33·4. Calc. for $C_{19}H_{24}Br_2O_4$: C, 47·9; H, 5·1; Br, 33·6%). The nuclear magnetic resonance spectrum showed that the product was a mixture.

(*b*) *Hydrogenation.* Gibberellin A_9 (27 mg.) was hydrogenated at room temperature with a palladium catalyst in acetic acid (uptake 1·0 mole in 13 min.). The recovered product crystallised from ether–light petroleum (b. p. 40—60°) in prisms (22 mg.) of *dihydrogibberellin A_9* (V; $R^1 = R^2 = H$, R^3 = Me, a mixture of 8-epimers), m. p. 198—200° (Found: C, 71·8; H, 8·0. $C_{19}H_{26}O_4$ requires C, 71·7; H, 8·2%); $\nu_{max.}$ ~3080br and 1745 cm.$^{-1}$.

Methylation of the derivative (9 mg.) with ethereal diazomethane gave a crude ester, m. p. 170—183°, which, after two crystallisations from ethyl acetate–light petroleum, yielded *dihydrogibberellin A_9 methyl ester* as prisms (6 mg.), m. p. 182—186°, consisting essentially of one 8-epimer (Found: C, 72·3; H, 8·5. $C_{20}H_{28}O_4$ requires C, 72·3; H, 8·5%), $\nu_{max.}$ 1779 and 1736 cm.$^{-1}$, identical with the spectrum of the uncharacterised material of m. p. 186—188° obtained [1] by hydrogenating gibberellin A_9 methyl ester.

The crystallisation mother-liquors yielded a product (1 mg.), m. p. 163—175°. The infrared spectrum was indistinguishable from that of the fraction of m. p. 182—186°.

(*c*) *Reduction with lithium aluminium hydride* (with Dr. R. H. B. Galt). Gibberellin A_9 (47 mg.) in tetrahydrofuran (8 ml.) was treated with lithium aluminium hydride (47 mg.) at room temperature and the mixture was stored for 16 hr. Ethyl acetate and then water were added dropwise to the mixture at 0°. Recovery from the organic layer and separation of the recovered material into neutral (9 mg.) and acidic (5 mg.) fractions gave intractable products.

The aqueous reaction mixture was acidified to pH 2 with hydrochloric acid and re-extracted with ethyl acetate. Recovery from the extract gave a solid (44 mg.) which crystallised from acetone–light petroleum in needles (36 mg.), m. p. 216—220°, raised to 224° by further crystallisation from ethyl acetate, of *4aα-hydroxy-1α-hydroxymethyl-1β-methyl-8-methylenegibbane-10β-carboxylic acid* (XI), $[\alpha]_D^{18}$ −46° (*c* 0·25) (Found: C, 70·9; H, 8·7. $C_{19}H_{28}O_4$ requires C, 71·2; H, 8·8%); $\nu_{max.}$ 3430, 3300sh, and 1690 cm.$^{-1}$.

The *methyl ester* crystallised from acetone–light petroleum in needles, m. p. 145—146° (Found: C, 72·1; H, 9·1. $C_{20}H_{30}O_4$ requires C, 71·8; H, 9·0%); $\nu_{max.}$ 3150, 1735, 1655, and 890 cm.$^{-1}$.

4aα-Hydroxy-1β-methylgibbane-1α,10β-dicarboxylic Acid 1 ⟶ 4a-Lactone (II; $R^1 = R^2 = R^3 = H$).—A solution of methyl 1α-carboxy-2β,4aα-dihydroxy-1β-methyl-8-oxogibbane-10β-carboxylate 1 ⟶ 4a-lactone (III; R^1 = Me, $R^2 = H$, R^3 = OH) [3] (240 mg.) in chloroform (5 ml.) was treated with ethanedithiol (0·27 ml.) and boron trifluoride–ether complex (0·27 ml.) at room temperature. After storage for 40 hr. the mixture was diluted with chloroform and washed with water and with saturated aqueous sodium chloride solution. Recovery from the organic layer gave a semi-solid product which was chromatographed in benzene on alumina (20 × 1·5 cm.). When thiols had been eluted with benzene, further elution with benzene–methanol (100 : 1) gave a solid which crystallised from ethyl acetate in prisms (200 mg., m. p. 206—207°; 73 mg., m. p. 202—206°) of the *8,8-ethylenedithioketal* derivative (Found: C, 59·7; H, 6·7. $C_{21}H_{28}O_5S_2$ requires C, 59·4; H, 6·65%); $\nu_{max.}$ 3510, 1755, and 1730 cm.$^{-1}$.

The above derivative (266 mg.) was heated at 100° with dioxan (50 ml.) and Raney nickel (8 g.) for 8 hr. The recovered product was chromatographed in benzene on alumina (30 × 2·0

cm.). Elution of the column with benzene–methanol (100 : 1) gave *methyl* 1α-*carboxy*-2β,4aα-*dihydroxy*-1β-*methylgibbane*-10β-*carboxylate* 1 ⟶ 4*a*-*lactone* (II; R^1 = Me, R^2 = H, R^3 = OH) (189 mg.) which formed prisms, m. p. 117—118°, from ethyl acetate–light petroleum (b. p. 40—60°) (Found: C, 68·3; H, 7·9. $C_{19}H_{26}O_5$ requires C, 68·2; H, 7·8%); $\nu_{max.}$ in dioxan 3460, 1777, and 1738 cm.$^{-1}$.

A solution of the above ester (167 mg.) in acetone (10 ml.) was treated with a chromium trioxide–sulphuric acid reagent [12] (0·20 ml.; 8N with respect to O) at 0°. After 2·5 hr. the mixture was concentrated *in vacuo* at room temperature and diluted with water. The product (138 mg.; m. p. 151—154°) was precipitated. It crystallised from ethyl acetate–light petroleum (b. p. 40—60°) in prisms, m. p. 154—155°, of *methyl* 1α-*carboxy*-4aα-*hydroxy*-1β-*methyl*-2-*oxogibbane*-10β-*carboxylate* 1 ⟶ 4*a*-*lactone* (IV) (Found: C, 69·2; H, 7·2. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3%); $\nu_{max.}$ (OH absent), 1777, 1730, and 1720 cm.$^{-1}$.

The above keto-ester (132 mg.) in chloroform (3 ml.) was treated with ethanedithiol (0·15 ml.) and boron trifluoride–ether complex (0·15 ml.). After 43 hr. the product was recovered and chromatographed as described above giving the 2,2-*ethylenedithioketal* derivative (155 mg.), which crystallised from ethyl acetate in prisms, m. p. 221—222° (Found: C, 61·9; H, 6·9. $C_{21}H_{28}O_4S_2$ requires C, 61·75; H, 6·9%); $\nu_{max.}$ 1766 and 1736 cm.$^{-1}$.

The above derivative (147 mg.) was heated at 100° with Raney nickel (4 g.) in dioxan for 7 hr., but desulphurisation was incomplete and was completed by repeated treatment with fresh Raney nickel (3 g.) in dioxan for 15 hr. at 100°. The product (105 mg.) crystallised from light petroleum (b. p. 80—100°) giving prisms (72 mg.), m. p. 139—141°, of *methyl* 1α-*carboxy*-4aα-*hydroxy*-1β-*methylgibbane*-10β-*carboxylate* 1 ⟶ 4*a*-*lactone* (II; R^1 = Me, R^2 = R^3 = H) (Found: C, 72·2; H, 7·8. $C_{19}H_{26}O_4$ requires C, 71·7; H, 8·2%); $\nu_{max.}$ 1777 and 1739 cm.$^{-1}$. More product (22 mg.; m. p. 134—139°) was recovered from the mother-liquor.

Hydrolysis of the Ester.—The above ester (79 mg.) was boiled with 2N-sodium hydroxide (16 ml.) and methanol (4 ml.) for 7 hr. The cooled, ethyl acetate-washed solution was acidified with hydrochloric acid. Recovery of the product by ethyl acetate extraction gave a gum (65 mg.). This was heated at 100° for 15 min., then crystallised from ether yielding prisms (32 mg.), m. p. 220—224°, raised to 225—227° by recrystallisation, of the required *acid* (II; R^1 = R^2 = R^3 = H) (Found: C, 71·1; H, 7·6. $C_{18}H_{24}O_4$ requires C, 71·0; H, 7·95%); $\nu_{max.}$ ~3280, 1757, and 1730 cm.$^{-1}$.

Methyl 1α-*Carboxy*-4aα-*hydroxy*-1β-*methyl*-8-*oxogibbane*-10β-*carboxylate* 1 ⟶ 4*a*-*Lactone* (III; R^1 = Me, R^2 = R^3 = H).[1]—(*a*) *Hydrolysis.* The ester (100 mg.) was boiled with methanol (5 ml.) and 2N-sodium hydroxide (10 ml.) for 6 hr. The solution was acidified, diluted with water, and extracted with ethyl acetate. The extract was washed with sodium hydrogen carbonate solution, and evaporated giving an intractable gum (2 mg.). The aqueous alkaline solution was acidified and extracted with ethyl acetate. Recovery from the extract gave 4aα-*hydroxy*-8-*oxogibbane*-1α,10β-*dicarboxylic acid* 1 ⟶ 4*a*-*lactone* (III; R^1 = R^2 = R^3 = H) (95 mg.) which crystallised from ethyl acetate–light petroleum in prisms, m. p. 125—128° (Found: C, 64·2; H, 7·1. $C_{18}H_{22}O_5$,H_2O requires C, 64·3; H, 7·2%); $\nu_{max.}$ 3469, 1753, 1725, and 1700 cm.$^{-1}$.

(*b*) *Reduction.* The ester (210 mg.) in methanol (5 ml.) was treated with sodium borohydride (104 mg.) for 1 hr. The mixture was concentrated, acidified with dilute hydrochloric acid, diluted with water, and extracted with ethyl acetate. The product recovered from the extract was chromatographed on alumina and eluted with ethyl acetate–light petroleum (b. p. 60—80°; 3 : 7), giving *methyl* 1α-*carboxy*-4aα,8β-*dihydroxy*-1β-*methylgibbane*-10β-*carboxylate* 1 ⟶ 4*a*-*lactone* (V; R^1 = Me, R^2 = OH, R^3 = H) (156 mg.), which formed needles, m. p. 112—114°, from acetone–light petroleum (Found: C, 65·3; H, 8·5. $C_{19}H_{26}O_5$,H_2O requires C, 64·75; H, 8·0%); $\nu_{max.}$ 3534, 3316, 1760, and 1737 cm.$^{-1}$.

Hydrolysis of the 8-*Hydroxy-ester.*—The above product (130 mg.) was hydrolysed as described above giving starting material (37 mg.) and 4aα,8β-*dihydroxy*-1β-*methylgibbane*-1α,10β-*dicarboxylic acid* 1 ⟶ 4*a*-*lactone* (V; R^1 = R^3 = H, R^2 = OH) (60 mg., (which crystallised from ethyl acetate–light petroleum in prisms, m. p. 203—205° (Found: C, 67·4; H, 7·6. $C_{18}H_{24}O_5$ requires C, 67·5; H, 7·55%); $\nu_{max.}$ 3488, 1766, and 1723 cm.$^{-1}$.

Dehydration of Gibberellin A_4 *Methyl Ester* (VII; R^1 = Me, R^2 = H, R^3 = OH).—A solution of the ester [2] (403 mg.) and methanesulphonyl chloride (200 mg.) in pyridine (10 ml.) was

[12] R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J.*, 1953, 457.

kept at room temperature for 40 hr., then evaporated *in vacuo*. The residue was dissolved in ethyl acetate; the solution was washed with dilute hydrochloric acid and with water, dried, and evaporated. The product was chromatographed in benzene on alumina (12 × 1·2 cm.). Elution with benzene–methanol (100 : 1) yielded the *methanesulphonyloxy-derivative* (VII; R^1 = Me, R^2 = H, R^3 = O·SO_2Me) (473 mg.), m. p. 136—139°, which crystallised from ether–light petroleum (b. p. 40—60°) in prisms, m. p. 140° (Found: C, 59·45; H, 6·8. $C_{21}H_{28}O_7S$ requires C, 59·4; H, 6·65%).

The derivative (440 mg.) was boiled with collidine (45 ml.) for 6 hr. Recovery of the product in the usual way gave a solid (328 mg.) which was chromatographed on alumina (24 × 1·3 cm.). Elution of the column with benzene–methanol (300 : 1) yielded (i) solid fractions, m. p. 147—150° (203 mg.), and (ii) intractable gums (92 mg.).

The solid products crystallised from ethyl acetate–light petroleum (b. p. 40—60°) or light petroleum (b. p. 80—100°) in plates (163 mg.) of *methyl* 1α-*carboxy*-4a*α*-*hydroxy*-1β-*methyl*-8-*methylenegibb*-2-*ene*-10β-*carboxylate* 1 ⟶ 4*a*-*lactone* (VI; R^1 = Me, R^2 = H), m. p. 149—152°, $[\alpha]_D^{22}$ −150° (*c* 0·70), $[\alpha]_D^{23}$ −122° (*c* 0·58) in dioxan (Found: C, 73·4; H, 7·5. $C_{20}H_{24}O_4$ requires C, 73·1; H, 7·4%); $\nu_{max.}$ 1773, 1762sh, 1737, 1658, 1621w, 932, 908, and 877 cm.$^{-1}$; $\lambda_{infl.}$ ~223 mμ (log ε 3·22).

Attempted Dehydration with Phosphorus Oxychloride.—(*a*) *Gibberellin* A_4 *methyl ester*. The ester (23 mg.) was heated at 100° for 30 min. with pyridine (1 ml.) and phosphorus oxychloride (0·1 ml.). The mixture was evaporated *in vacuo*. The residue was mixed with ethyl acetate and dilute hydrochloric acid, the organic layer was separated, and on recovery gave a gummy solid (17 mg.). The product was treated with a little ethereal diazomethane, then recovered, and chromatographed on alumina (10 × 0·7 cm.). Elution of the column with benzene gave fractions of prisms (17 mg.) all showing a range of m. p. *ca.* 140—155°. Crystallisation from light petroleum yielded a solid (5 mg.), m. p. 122—155°, $[\alpha]_D^{22}$ −92° (*c* 0·52).

(*b*) *Gibberellin* A_2 *Methyl Ester* (VIII; R = Me).—The ester (24 mg.) was dehydrated as described above except that the product was not treated with diazomethane. Chromatography and crystallisation of the product yielded prisms (12 mg.), m. p. 153—165°, $[\alpha]_D^{22}$ −94° (*c* 0·51).

The infrared spectra of the two products were similar to the spectrum of the above ester (VI; R^1 = Me, R^2 = H), $[\alpha]_D$ −150°.

Hydrogenation of the Ester (VI; R^1 = Me, R^2 = H).—(*a*) Microhydrogenation with a palladium catalyst in acetic acid resulted in an uptake of 1·9 mole. (*b*) The ester (50 mg.) was hydrogenated with a 2% palladium–barium carbonate catalyst (50 mg.) in ethyl acetate (8 ml.) containing pyridine (0·3 ml.). After the uptake of 1·1 mole of hydrogen in 6 hr. the product was recovered and chromatographed in benzene on alumina (30 × 0·7 cm.). Elution with benzene–methanol (200 : 1) yielded (i) 19 mg., m. p. 139—165°, $[\alpha]_D^{17}$ +3° (*c* 0·70), (ii) 28 mg., m. p. 157—161°. Both fractions were mixtures and attempts to isolate gibberellin A_9 methyl ester failed.

Further hydrogenation of the combined products in ethyl acetate (8 ml.) with a 10% palladium–carbon catalyst (50 mg.) gave a product, m. p. 159—177°, the infrared spectrum of which was indistinguishable from that of dihydrogibberellin A_9 methyl ester (see above). Chromatography on alumina followed by crystallisation from light petroleum gave dihydrogibberellin A_9 methyl ester, m. p. 170—175° (mixed 8-epimers) (Found: C, 72·3; H, 8·5. Calc. for $C_{20}H_{28}O_4$: C, 72·3; H, 8·5%).

Hydrolysis of the Ester (VI; R^1 = Me, R^2 = H).—The ester (207 mg.) was boiled with 2N-sodium hydroxide (28 ml.) and methanol (7 ml.) for 7 hr. Recovery in the usual way gave a gum (206 mg.) which solidified on heating for 15 min. at 100°. Subsequent crystallisation from ethyl acetate–light petroleum (b. p. 40—60°) and from ethyl acetate gave 4a*α*-*hydroxy*-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1 ⟶ 4*a*-*lactone* (VI; R^1 = R^2 = H) as prisms (129 mg.), m. p. 231—233°, $[\alpha]_D^{20}$ −164° (*c* 0·80) (Found: C, 72·5; H, 6·95. $C_{19}H_{22}O_4$ requires C, 72·6; H, 7·05%); $\nu_{max.}$ 3100, 1743, 1727, 1662, and 1622w, cm.$^{-1}$. Thin-layer chromatography on silica gel G [13] in di-isopropyl ether–acetic acid (95 : 5) revealed a single spot with $R_{\text{gibberellin A}_1}$, 2·5.

Reduction of the Acid (VI; R^1 = R^2 = H).—The acid (96 mg.) in tetrahydrofuran (16 ml.) was reduced with lithium aluminium hydride (96 mg.) as described above for gibberellin A_9. The product crystallised from ethyl acetate in prisms (36 mg.), m. p. 207—209°, $[\alpha]_D^{20}$ −88°

[13] J. MacMillan and P. J. Suter, *Nature*, 1963, **197**, 790.

(*c* 0·60), of 4*aα-hydroxy*-1α-*hydroxymethyl*-1β-*methyl*-8-*methylenegibb*-2-*ene*-10β-*carboxylic acid* (X) (Found: C, 71·4; H, 8·3. $C_{19}H_{26}O_4$ requires C, 71·7; H, 8·2%); $\nu_{max.}$ 3288, 3148, 1705sh, 1677, 1658, and 886 cm.$^{-1}$; ε (mμ) 4200 (210), 1534 (215), 632 (220), 506 (225), and 474 (230).

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