355. *Gibberellic Acid. Part XXVI.* A Novel Displacement of Acetoxyl by Acetyl on Use of Zinc and Acetic Anhydride.*

By D. F. Jones, John Frederick Grove, and J. MacMillan.

On treatment with zinc and boiling acetic anhydride, methyl gibberellate (IV) and the 2,7-di-*O*-acetyl derivative (V) undergo a novel displacement reaction, yielding methyl 7-acetoxy-2-acetyl-1-carboxy-4a-hydroxy-1-methyl-8-methylenegibb-3-ene-10-carboxylate 1→4a-lactone (VIII). Chemical and spectroscopic evidence for structure (VIII) is presented, and the reaction mechanism is discussed.

Gibberellic acid and the nor-ketone (VI) of methyl gibberellate undergo analogous reactions.

Kitamura *et al.*[1] reported that the derivative (I) of gibberellin A_1 was hydrogenolysed to the corresponding derivative (II) of gibberellin A_4 by zinc and acetic anhydride. We have been unable to confirm this result; no reaction took place under a variety of conditions. With the same reagents we have found that methyl gibberellate (IV) and the 2,7-di-*O*-acetyl derivative (V) give the same product, assigned structure (VIII) on the evidence presented below. The nor-ketone (VI) yielded the analogous compound (IX), while gibberellic acid (VII) gave the mixed anhydride (X) as a glass which was converted by methanolysis into the acid (XI) and thence into the ester (VIII) by methylation.

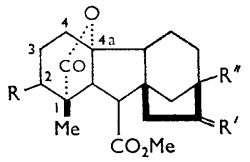
The monoacetate (XII) of the known[2] 1→3-lactone (XV) was obtained as a minor product from both methyl gibberellate (IV) and the diacetate (V). The monoacetate was distinct from the known[3] monoacetate (XIII), and yielded the diacetate (XIV), also obtained from the 1→3-lactone (XV). The monoacetate (XII) is almost certainly derived from the diacetate (XIV) during work-up, since the latter compound gave the former on alumina.

The reaction product (VIII), $C_{24}H_{28}O_7$, from methyl diacetyl gibberellate (V), $C_{24}H_{28}O_8$, contained one acetoxyl group, and its infrared spectrum showed bands attributable to γ-lactone (1783 cm.$^{-1}$) and ester carbonyl and/or ketone (1747 and 1735 cm.$^{-1}$). Microhydrogenation indicated the presence of two double bonds, one of which was shown to be

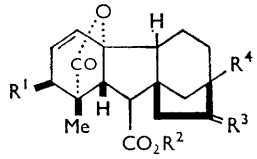
* Part XXV, *J.*, 1963, 2606.

[1] Kitamura, Takahashi, Seta, Karawada, and Sumiki, *Bull. Agric. Chem. Soc. Japan*, 1959, **23**, 344.
[2] Cross, *J.*, 1960, 3022.
[3] Cross, Grove, and Morrison, *J.*, 1961, 2498.

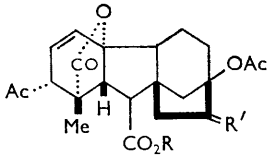
in an exocyclic methylene group since ozonolysis of (VIII) gave the nor-ketone (IX), obtained directly from the nor-ketone (VI) with zinc and boiling acetic anhydride.



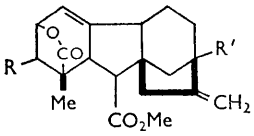
(I) R = R″ = OAc, R′ = O
(II) R = OAc, R′ = O, R″ = H
(III) R = R″ = OAc, R′ = CH_2



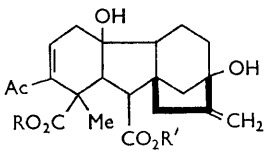
(IV) $R^1 = R^4 = OH$, $R^2 = Me$, $R^3 = CH_2$
(V) $R^1 = R^4 = OAc$, $R^2 = Me$, $R^3 = CH_2$
(VI) $R^1 = R^4 = OH$, $R^2 = Me$, $R^3 = O$
(VII) $R^1 = R^4 = OH$, $R^2 = H$, $R^3 = CH_2$



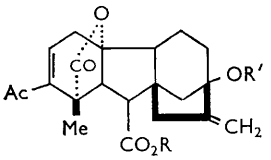
(VIII) R = Me, R′ = CH_2
(IX) R = Me, R′ = O
(X) R = Ac, R′ = CH_2
(XI) R = H, R′ = CH_2



(XII) R = OH, R′ = OAc
(XIII) R = OAc, R′ = OH
(XIV) R = R′ = OAc
(XV) R = R′ = OH

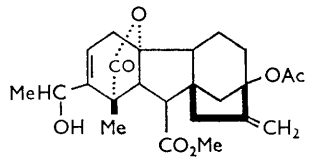


(XVI) R = H, R′ = Me
(XVII) R = R′ = Me
(XVIII) R = R′ = H

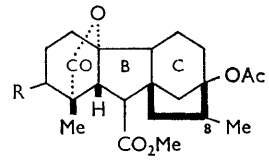


(XIX) R = Me, R′ = H
(XX) R = Me, R′ = Ac
(XXI) R = H, R′ = H

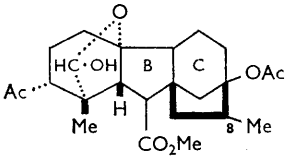
Hydrolysis of (VIII) with aqueous potassium hydroxide afforded the dihydroxy-acid (XVI), lactonised by warming with acetic acid to the lactone (XIX). In contrast to (VIII), the acid (XVI) and its methyl ester (XVII), and the lactone (XIX) and its acetate (XX), showed ultraviolet and infrared absorption typical of conjugated enones. These absorption characteristics were absent in the allyl alcohol (XXII), obtained by borohydride reduction of the acetate (XX); the allylic alcohol (XXII) regenerated the acetate (XX) on oxidation with chromium trioxide. The presence of a *C*-acetyl group was established by the isolation of iodoform from the dibasic acid (XVIII), derived from the monobasic acid (XI) with aqueous alkali.



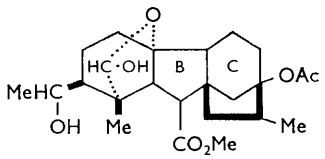
(XXII)



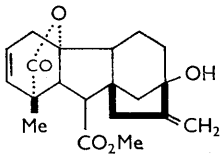
(XXIII: R = α − Ac)
(XXIV: R = β − Ac)



(XXV)



(XXVI)



(XXVII)

Hydrogenation of the esters (VIII) and (XX) gave the respective tetrahydro-derivatives (XXIII) and (XXIV) as mixtures of 8-epimers, which could be separated by chromatography on alumina. The stereochemistry of these tetrahydro-compounds is discussed below, but the conversion of one of the 8-epimers of (XXIV) into an 8-epimer of (XXIII), by treatment with aqueous alkali and then acetic anhydride, showed that the conversion of (VIII) into (XX) involves no skeletal rearrangement.

Borohydride reduction of (XXIII; 8-epimeric mixture) unexpectedly gave (XXV) whose hemiacetal structure was confirmed by the infrared spectrum (hydroxyl band at 3519 cm.$^{-1}$, and no γ-lactone band), by the nuclear magnetic resonance spectrum (single proton peak, τ 5·2), and by re-oxidation to the lactone (XXIII) with manganese dioxide. Similar reduction of (XXIV; 8-epimeric mixture) afforded the diol (XXVI).

The above results showed that (VIII) possessed the system MeCO·CH·C:C, isomerised by aqueous alkali to the conjugated enone system. The allylic alcohol (XXII) shows weak absorption at 222 mμ (ε 1800), characteristic [4,5] of the gibb-2-enes (for nomenclature see ref. 6). Consequently, the corresponding conjugated enone is the gibb-2-ene (XX) and the unconjugated enone is the gibb-3-ene (VIII).

Unsuccessful attempts were made to confirm these conclusions by Baeyer–Villiger oxidation of the tetrahydro-derivatives (XXIII) and (XXIV) to the respective diacetates (XXIII and XXIV; OAc for Ac) of methyl tetrahydrogibberellate and of its 2-epimer; no oxidation took place and starting material was recovered.

Two possible mechanisms are indicated in the annexed scheme. It is shown below that the 2-acetyl group is equatorial and *cis* to the α-lactone bridge.[7,8] Thus, mechanism (a), which would yield initially a 2β-acetyl group, requires subsequent epimerisation at position 2; mechanism (b) gives the 2α-acetyl group directly. The allylic acetoxyl group is necessary for this reaction; the methyl esters (III) and (XIV) did not react.

Nuclear magnetic resonance spectra of (VIII) and derivatives confirm the assigned structures. In addition to the listed signals, the compounds in the Table showed three-proton singlets at τ 6·25 (OMe) and, except (XIX), at τ ~8·0 ($MeCO_2$); compounds (VIII),

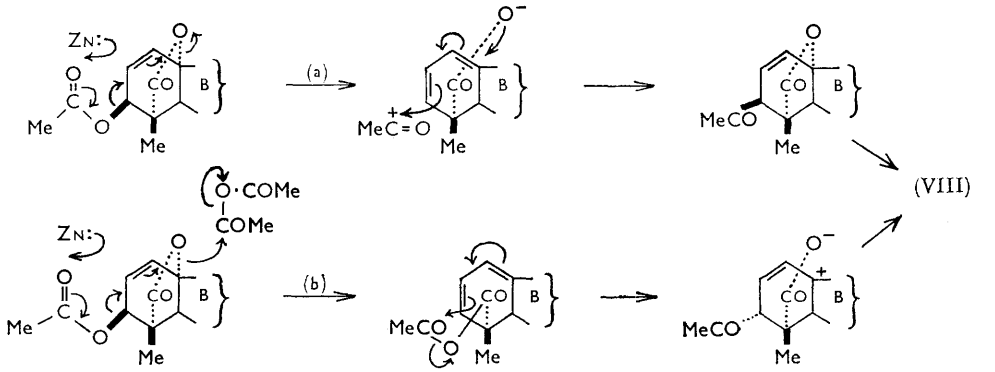
TABLE.

Chemical shifts (τ values) of protons in some derivatives of gibberellic acid.

Compound	Position of protons					Compound	Position of protons				
	H-2	H-3	H-4	2-MeCO	1-Me		H-2	H-3	H-4	2-MeCO	1-Me
(VIII)	6·93q	3·75q	3·37q	8·6	8·8	(XXII)	—	4·08t	7·52m	8·67d *	8·63
(XIX)	—	3·4t	7·37m	7·68	8·63	(XXIII)	—	—	—	8·43	8·72
(XX)	—	3·4t	7·37m	7·68	8·63	(XXIV)	—	—	—	7·83	8·98

d = doublet, t = triplet, q = quartet, m = multiplet. * Refers to MeCH·OH.

(XIX), (XX), and (XXII) showed two-proton doublets at τ 4·95 (=CH_2) replaced by three-proton peaks at τ 9·12 (MeCH<) in the tetrahydro-derivatives (XXIII) and (XXIV). The protons in (VIII) showed the following coupling constants: $J_{2,3}$ ~6 c./sec.; $J_{2,4}$ ~1 c./sec.; and $J_{3,4}$ 7 c./sec.



[4] MacMillan, Seaton, and Suter, *Tetrahedron*, 1960, **11**, 60.
[5] Moffatt, *J.*, 1963, 2595.
[6] Grove and Mulholland, *J.*, 1960, 3007.
[7] Aldridge, Grove, Speake, Tidd, and Klyne, *J.*, 1963, 143.
[8] McCapra, Scott, Sim, and Young, *Proc. Chem. Soc.*, 1962, 185.

The 2-acetyl protons in the tetrahydro-derivative (XXIII) absorb at unusually high field and must be shielded by the α-lactone carbonyl group. Such shielding requires the 2-acetyl group in (XXIII) to be *cis* to the lactone bridge and therefore α-oriented.[7,8] This conclusion agrees with the observed epimerisation of (XXIV; *ax*-2-acetyl) to (XXIII; *eq*-2-acetyl), and with the observed ease of reduction of the 2-acetyl group in (XXIV) compared to (XXIII). Similarly, it is concluded that the 2-acetyl group (τ 8·6) in (VIII) is α-oriented.

The relatively low values (τ 8·63) of the 1-methyl protons in compounds (XIX), (XX), and (XXII), compared with methyl gibberellate (τ 8·8), are probably due to de-shielding by the oxygen function of the 2-substituent; they are not caused by the 2,3-double bond, since the 1-methyl protons in the methyl ester (XXVII) of gibberellin A_5 absorb at τ 8·8. In the ester (XXIV) the acetyl group appears to shield the 1-methyl protons.

Experimental

Nuclear magnetic resonance spectra were obtained for chloroform solutions (tetramethylsilane as internal standard) with a Varian Associates A60 spectrometer. Unless otherwise stated, infrared spectra were obtained for Nujol mulls with a Perkin-Elmer 221 spectrometer, and Woelm alumina of grade II in the " acid " form was used for chromatography. Light petroleum had b. p. 60—80°.

Methyl 2,7-Diacetyl-1-carboxy-4a-hydroxy-1-methyl-8-methylenegibbane-10-carboxylate 1→4a-Lactone (III).—Prepared by treating gibberellin A_1 methyl ester with acetic anhydride and pyridine at room temperature for 2 weeks, or at the b. p. for 6 hr., the *diacetate* formed needles, m. p. 166° (Found: C, 64·7; H, 7·3. $C_{24}H_{30}O_8$ requires C, 64·6; H, 6·8%).

Methyl 7-Acetoxy-2-acetyl-1-carboxy-4a-hydroxy-1-methyl-8-methylenegibb-3-ene-10-carboxylate 1→4a-Lactone (VIII).—Methyl 2,7-diacetylgibberellate (V) (1 g.), prepared by heating methyl gibberellate (IV) in acetic anhydride for 0·5 hr., was dissolved in refluxing acetic anhydride (25 ml.). Activated zinc (10 g.) was added, and the mixture was boiled for 1·5 hr. After filtration, acetic anhydride was removed *in vacuo*, and the residue was chromatographed in benzene on a column (12 × 2 cm.) of " neutral " alumina. Elution with benzene (300 ml.) gave the *methyl ketone* (VIII) as prisms (750 mg.), m. p. 183—184° (from benzene–light petroleum) (Found: C, 67·3; H, 6·8; Ac, 10·9. $C_{24}H_{28}O_7$ requires C, 67·3; H, 6·6; Ac, 10·0%); $\nu_{max.}$ 1783, 1747, 1735, and 1660 cm.$^{-1}$; (–$CHCl_3$) 1773, 1729, 1660, and 1603 cm.$^{-1}$.

Further elution of the column with benzene–chloroform (1 : 1) gave, after some gummy material, *methyl 7-acetoxy-1-carboxy-2-hydroxy-1-methyl-8-methylenegibb-4-ene-10-carboxylate 1→3-lactone* (XII), plates (28 mg.), m. p. 210—212° (from acetone–light petroleum) (Found: C, 65·7; H, 6·5. $C_{22}H_{26}O_7$ requires C, 65·7; H, 6·5%), $\nu_{max.}$ (Infracord) 3350, 1745, 1735, 1660, and 1652 cm.$^{-1}$. The *acetate* (XIV), prepared with warm acetic anhydride, crystallised from acetone–light petroleum as prisms, m. p. 197—198° (Found: C, 65·1; H, 6·4. $C_{24}H_{28}O_8$ requires C, 64·9; H, 6·4%), and was identical (infrared spectrum and mixed m. p.) with a specimen prepared by heating (XV) with acetic anhydride.[2] The same products were obtained by identical treatment of methyl gibberellate.

7-Acetoxy-2-acetyl-4a-hydroxy-1-methyl-8-methylenegibb-3-ene-1,10-dicarboxylic Acid 1→4a-Lactone (XI).—A solution of gibberellic acid (VII) (1·2 g.) in acetic anhydride (40 ml.) was heated under reflux for 0·5 hr. Activated zinc (12 g.) was added and the mixture was heated for a further 1·5 hr. The glass (1·3 g.), obtained by filtration and evaporation *in vacuo*, was set aside in methanol for 28 days at room temperature. Removal of the methanol gave a gum which was dissolved in ethyl acetate, and the solution was extracted with 1·5N-sodium hydrogen carbonate. Acidification of the extract, and recovery in ethyl acetate, afforded the *carboxylic acid* (XI) as needles (850 mg.), m. p. 117—120°, with setting and re-melting at 185—186° (from methanol) (Found: C, 64·0; H, 6·8. $C_{23}H_{26}O_7,H_2O$ requires C, 63·9; H, 6·5%), $\nu_{max.}$ 3400, 1770, 1755, 1724, 1705, and 1665 cm.$^{-1}$. The *anhydrous acid* (XI), obtained by prolonged drying at 100°/1 mm., had m. p. 185—186° (Found: C, 66·4; H, 6·6. $C_{23}H_{26}O_7$ requires C, 66·7; H, 6·3%).

The methyl ester, prepared with diazomethane, was identical (mixed m. p. and infrared spectrum) with the methyl ketone (VIII) described above.

Methyl 7-Acetoxy-2-acetyl-1-carboxy-4a-hydroxy-1-methyl-8-oxogibb-3-ene-10-carboxylate 1→4a-Lactone (IX).—The ketol [2] (VI) (100 mg.) in acetic anhydride (3 ml.) was heated under reflux for 6 hr. during the gradual addition of zinc dust (1·3 g.). After filtration and removal of the solvent *in vacuo*, the residue, in ethyl acetate, was washed with aqueous sodium hydrogen carbonate. The recovered neutral fraction (110 mg.) was chromatographed on alumina (6 × 1 cm.) in benzene (10 ml.). Elution with benzene (60 ml.) gave the *methyl ketone* (IX) (43 mg.) as needles, m. p. 196° (from ethyl acetate–light petroleum) (Found: C, 63·7, 64·6; H, 6·2, 6·1; OMe, 7·5. $C_{23}H_{26}O_8$ requires C, 64·2; H, 6·1; OMe 7·2%), $\nu_{max.}$ 1782, 1753, 1735sh, and 1725 cm.$^{-1}$, ε (mμ) 2700 (205), 1500 (210), 1000 (215), and 690 (220).

Ozonolysis of Methyl 7-Acetoxy-2-acetyl-1-carboxy-4a-hydroxy-1-methyl-8-methylenegibb-3-ene-10-carboxylate 1→4a-Lactone (VIII).—Ozonised oxygen equivalent to 24 mg. of ozone (1 mol.) was passed through ethyl acetate (10 ml.) containing the methyl ketone (VIII) (214 mg.) at −40°. Triphenylphosphine (400 mg.) was added, and the solution was kept for 24 hr. at room temperature. After extraction with sodium hydrogen carbonate solution, the recovered neutral solid was chromatographed in benzene on alumina. After starting material (128 mg.) had been eluted with benzene, benzene–ether (4 : 1; 30 ml.) furnished needles (22 mg.), m. p. 190°, identical (mixed m. p. and infrared spectra) with the nor-ketone (IX) described above.

Methyl 2-Acetyl-1-carboxy-4a,7-dihydroxy-1-methyl-8-methylenegibb-2-ene-10-carboxylate (XVI).—The methyl ketone (VIII) (1 g.) in methanol (40 ml.) and 10% aqueous potassium hydroxide (25 ml.) was boiled for 1 hr. Removal of the methanol and acidification gave the *hydroxy-acid* (XVI) which was recovered in ethyl acetate; it crystallised from ethyl acetate as prisms (770 mg.), m. p. 210—212° (Found: C, 64·6; H, 7·1; OMe, 7·2%; Equiv., 363. $C_{22}H_{28}O_7$ requires C, 65·3; H, 7·0; OMe, 7·4%; Equiv., 404); $\nu_{max.}$ (Infracord) 3420, 1760, 1735, 1690, 1660, and 1625 cm.$^{-1}$; (dimethyl sulphoxide) 1730, 1699, 1666, and 1633 cm.$^{-1}$; $\lambda_{max.}$ 227 mμ (ε 9700).

The *dimethyl ester* (XVII) was obtained in dimorphic forms from acetone–light petroleum; (*a*) large prisms, m. p. 135—137 and 164—165° (Found: C, 65·7; H, 7·3; OMe, 14·1. $C_{23}H_{30}O_7$ requires C, 66·0; H, 7·2; OMe, 14·8%); $\nu_{max.}$ (Infracord) 3500, 3450, 1725, 1700, 1660, and 1630 cm.$^{-1}$; (in chloroform) 3375, 1731, 1701, 1672, and 1629 cm.$^{-1}$; $\lambda_{max.}$ 226 mμ (ε 9400); (*b*) thin prisms, m. p. 134—136 and 164—165° (Found: C, 66·0; H, 7·4%), $\nu_{max.}$ (Infracord) 3500, 3400, 1740, 1700, 1670, and 1630 cm.$^{-1}$.

2-Acetyl-4a,7-dihydroxy-1-methyl-8-methylenegibb-2-ene-1,10-dicarboxylic Acid (XVIII).—Using the procedure described above, the acid (XI) (150 mg.) was converted into the *dicarboxylic acid* (XVIII) (110 mg.), prisms, m. p. 225—229° (from acetone) (Found: C, 64·3; H, 6·9. $C_{21}H_{26}O_7$ requires C, 64·6; H, 6·7%), $\nu_{max.}$ (Infracord) 3350, 1745, 1695, 1680, and 1630 cm.$^{-1}$. Methylation of (XVIII) with ethereal diazomethane gave the dimethyl ester (XVII).

Methyl 2-Acetyl-1-carboxy-4a,7-dihydroxy-1-methyl-8-methylenegibb-2-ene-10-carboxylate 1→4a-Lactone (XIX).—The acid (XVI) (500 mg.) in glacial acetic acid (20 ml.) was heated under reflux for 0·5 hr., and the solvent was evaporated under reduced pressure. The residue, in ethyl acetate, was washed with 2N-sodium hydrogen carbonate (10 ml.) and water (10 ml.), and recrystallised from benzene–light petroleum, giving the *lactone* (XIX) (442 mg.) as plates, m. p. 200—202° (Found: C, 68·3; H, 6·8; OMe, 8·1. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·8; OMe, 8·0%); $\lambda_{max.}$ 224 and 234 mμ (ε 6180 and 5630); $\nu_{max.}$ (Infracord) 3430, 1770, 1735, 1680, and 1603 cm.$^{-1}$; (chloroform) 1779, 1721, 1684, and 1603 cm.$^{-1}$. By the same procedure, the dimethyl ester (XVII) was converted into the lactone (XIX), identified by mixed m. p. and infrared spectrum.

The *acetate* (XX), prepared by heating (XIX) with acetic anhydride for 2 hr., crystallised from acetone–light petroleum as plates, m. p. 175—177° (Found: C, 67·2; H, 6·7. $C_{24}H_{28}O_7$ requires C, 67·3; H, 6·6%), $\lambda_{max.}$ 224 and 234 mμ (ε 6200 and 5680), $\nu_{max.}$ (Infracord) 1780, 1720, 1680, 1660, and 1605 cm.$^{-1}$. The acetate (XX) (80 mg.) was also formed on heating the ester (XVII) (100 mg.) with acetic anhydride for 2·5 hr.

2-Acetyl-4a,7-dihydroxy-1-methyl-8-methylene-gibb-2-ene-1,10-dicarboxylic Acid 1→4a-lactone (XXI).—By boiling with acetic acid for 1 hr., the acid (XVIII) (100 mg.) was converted into the *lactone* (XXI) (87 mg.), prisms, m. p. 223—225° (from acetone) (Found: C, 66·5; H, 6·6. $C_{21}H_{24}O_6,\frac{1}{2}H_2O$ requires C, 66·2; H, 6·6%), $\nu_{max.}$ (Infracord) 3330, 1770, 1730, 1680, 1660, and 1603 cm.$^{-1}$. Treatment of the acid (XXI) with ethereal diazomethane gave the ester (XIX), identified by mixed m. p. and infrared spectrum.

The *acetate*, prepared by heating the acid (XXI) with acetic anhydride for 2·5 hr., followed

by methanolysis, crystallised from ethyl acetate as prisms, m. p. 224—228° (Found: C, 66·5; H, 6·4. $C_{23}H_{26}O_7$ requires C, 66·7; H, 6·3%), $\nu_{max.}$ (Infracord) 3200, 1750, 1725, 1680, and 1603 cm.$^{-1}$; this acetate with ethereal diazomethane gave the ester (XX), identified by mixed m. p. and infrared spectrum.

Treatment of the acid (XXI) (100 mg.), in 2N-sodium hydroxide (1 ml.) at 60°, with a few drops of a solution of iodine (1 g.) and potassium iodide (2 g.) in water (4 ml.), setting aside at 60° for 5 min., and dilution with water gave a precipitate of iodoform (40 mg.) which, on sublimation, gave hexagonal prisms, m. p. and mixed m. p. 121°.

Methyl 7-Acetoxy-1-carboxy-4a-hydroxy-2-(1′-hydroxyethyl)-1-methyl-8-methylenegibb-2-ene-10-carboxylate 1→4a-*Lactone* (XXII).—Sodium borohydride (200 mg.) was added to the ketone (XX) (200 mg.) in ethanol (20 ml.), and the mixture was set aside at 18° for 4 hr. After the addition of acetic acid (1 ml.) and water (25 ml.), the solution was extracted with ethyl acetate (6 × 30 ml.), and the extract washed with 2N-sodium hydrogen carbonate (2 × 10 ml.) and water (10 ml.). Evaporation of the dried solution gave a glass which was adsorbed on a column (15 × 1 cm.) of alumina. Elution with benzene–chloroform (5 : 1) gave gummy material (84 mg.) and then the *allylic alcohol* (XXII) (75 mg.), which crystallised from benzene–light petroleum as prisms, m. p. 164—166° (Found: C, 67·0; H, 7·1. $C_{24}H_{30}O_7$ requires C, 67·0; H, 7·0%), $\lambda_{max.}$ 224 mμ (ε 1820), $\nu_{max.}$ (Infracord) 3570, 1786, 1739, and 1660 cm.$^{-1}$.

Methyl 7-Acetoxy-2(α)-acetyl-1-carboxy-4a-hydroxy-1,8-dimethylgibbane-10-carboxylate 1→4a-*Lactone* (XXIII).—A solution of (VIII) (340 mg.) in ethyl acetate (25 ml.) was shaken with 10% palladium–charcoal (200 mg.) in hydrogen at 19° until absorption ceased (2 moles; 3 min.). The filtered solution was evaporated, and the residue, in benzene, was adsorbed on a column of alumina (15 × 1 cm.) and the column eluted in 15 ml. fractions with benzene–chloroform (10 : 1). Fractions 6—12 gave an 8-*epimer* (A) of the gibbane (XXIII) (175 mg.) as thin rods, m. p. 129—130° (from benzene–light petroleum) (Found: C, 66·8; H, 7·4. $C_{24}H_{32}O_7$ requires C, 66·65; H, 7·5%); $\nu_{max.}$ (Infracord), 1775 and 1730 cm.$^{-1}$; (in chloroform), 1779 and 1729 cm.$^{-1}$. Fractions 17—19 gave an 8-*epimer* (B) of the gibbane (XXIII) (20 mg.) as fine needles, m. p. 167—168° (from benzene–light petroleum) (Found: C, 67·0; H, 7·6%), $\nu_{max.}$ (Infracord) 1775, 1740sh, and 1730 cm.$^{-1}$. Fractions 13—16 gave a mixture of epimers (A) and (B) (100 mg.).

Methyl 7-Acetoxy-2(β)-acetyl-1-carboxy-4a-hydroxy-1,8-dimethylgibbane-10-carboxylate 1→4a-*Lactone* (XXIV).—The ketone (XIX) (300 mg.) in ethyl acetate (30 ml.) was shaken with 10% palladium–charcoal (150 mg.) in hydrogen at 19° until absorption ceased (2 moles; 5 min.). The filtered solution was evaporated, and the residue, in benzene, adsorbed on alumina (10 × 1·5 cm.) and the column eluted in 10 ml. fractions with benzene–chloroform (10 : 1). Fractions 4—6 gave a mixture of isomers of a tetrahydro-derivative (170 mg.) as prisms, m. p. 130—132° (from acetone–light petroleum) (Found: 66·8; H, 7·5%), $\nu_{max.}$ 1770, 1732, 1722, and 1710 cm.$^{-1}$; this substance was probably stereochemically impure at C-2, as judged by the infrared spectra. Fractions 9—17 gave an 8-*epimer* (C) of the gibbane (XXIV) (141 mg.) as large prisms, m. p. 155—157° (from acetone–light petroleum) (Found: C, 66·6; H, 7·5. $C_{24}H_{32}O_7$ requires C, 66·7; H, 7·5%); $\nu_{max.}$ 1773, 1741, 1734, and 1720 cm.$^{-1}$; ($CHCl_3$) 1774, 1732, and 1724 cm.$^{-1}$.

Alkaline Hydrolysis of Gibbanes (XXIII) and (XXIV).—Epimer (C) of (XXIV) (50 mg.), in methanol (3 ml.), and 10% aqueous potassium hydroxide (1 ml.) were boiled for 0·5 hr. After removal of methanol, the solution was acidified, and extracted with ethyl acetate (3 × 10 ml.). Recovery (washing with 2N-sodium hydrogen carbonate) gave the alcohol (XXIII; OH for OAc) as microneedles (47 mg.), m. p. 160—162° (from ethyl acetate–light petroleum), $\nu_{max.}$ 3485, 3380, 1772, 1727, and 1716 cm.$^{-1}$. The same alcohol (43 mg.) was also produced by a similar alkaline hydrolysis of epimer (A) of (XXIII) (50 mg.), and the alcohol (40 mg.), boiled with acetic anhydride (5 ml.), gave epimer (A) of (XXIII) (46 mg.), identified by mixed m. p. and infrared spectrum.

Reductions with Sodium Borohydride.—(*a*) *Reduction of epimer* (C) *of* (XXIV). Sodium borohydride (140 mg.) was added to epimer (C) of (XXIV) (140 mg.) in ethanol (10 ml.), and the mixture was set aside at 18° for 24 hr. Acetic acid (1 ml.) and water (15 ml.) were added; extraction with ethyl acetate and recovery (washing with 2N-sodium hydrogen carbonate) gave a gum which was adsorbed on a column (10 × 1 cm.) of alumina. Elution with chloroform gave the *hydroxy-hemiacetal* (XXVI) (75 mg.) as prisms, m. p. 176—178° (from acetone–light petroleum) (Found: C, 65·9; H, 8·8; OMe, 7·4. $C_{24}H_{36}O_7$ requires C, 66·0; H, 8·3; OMe, 7·1%), $\nu_{max.}$ 3272, 3143, 1732, and 1728 cm.$^{-1}$.

(*b*) *Reduction of the mixed* 8-*epimers* (A) *and* (B) *of* (XXIII). The mixture of C-8 epimers of

(XXIII) (330 mg.) was reduced by sodium borohydride (300 mg.) in ethanol (15 ml.) as in (*a*), The product was adsorbed on alumina (12 × 1 cm.) and the column was eluted in 10 ml. fractions with benzene–chloroform (10 : 1). Fractions 2—14 gave an 8-*epimer* (A) of the hemiacetal (XXV) (232 mg.) as prisms, m. p. 185—187° (from benzene–light petroleum) (Found: C, 66·6; H, 7·9; OMe, 7·2. $C_{24}H_{34}O_7$ requires C, 66·3; H, 7·9; OMe, 7·2%), $\nu_{max.}$ 3519, 1728, and 1720sh cm.$^{-1}$. Fractions 19—21 gave an 8-*epimer* (B) of the hemiacetal (XXV) (48 mg.) as prisms, m. p. 173° (from benzene–light petroleum) (Found: C, 66·3; H, 7·9; OMe, 7·6%), $\nu_{max.}$ 3468, 1728, and 1715 cm.$^{-1}$. Further elution of the column with chloroform gave a glass (64 mg.).

Oxidations with Manganese Dioxide.—(*a*). Epimer (A) of (XXV) (25 mg.) in chloroform (10 ml.) was shaken with manganese dioxide [9] (200 mg.) at 18° for 340 hr. After filtration and recovery, the residue was adsorbed on alumina (7 × 0·5 cm.) which was eluted in 10 ml. fractions with benzene–chloroform (10 : 1). Fractions 1—3 gave the epimer (A) of the gibbane (XXIII) (7 mg.), identified by mixed m. p. and infrared spectrum. Further elution with chloroform gave unreacted (XXV) (12 mg.).

(*b*) Epimer (B) of (XXV) (5 mg.) similarly gave epimer (B) of (XXIII) (1·8 mg.), identified by mixed m. p. and infrared spectrum, and unreacted (XXV) (2·2 mg.).

Attempted Bayer–Villiger Oxidations.—The ketone (XXIII) (330 mg.) in methylene dichloride (12 ml.) was added dropwise to trifluoroacetic anhydride (0·3 ml.) and 90% hydrogen peroxide (0·03 ml.) in methylene dichloride (12 ml.). The solution was set aside at 0° for 14 days, heated under reflux for 5 hr., diluted with chloroform (50 ml.), and washed successively with 10% aqueous ferrous sulphate (2 × 10 ml.), water (10 ml.), 2N-sodium hydrogen carbonate (10 ml.), and water (10 ml.). Recovery, and crystallisation of the product from benzene–light petroleum, gave starting material (327 mg.) identified by mixed m. p. and infrared spectrum. A similar oxidation of (XXIV) (200 mg.) also gave starting material (196 mg.).

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[9] Haslam and Quibell, *J.*, 1957, 4911.