96. *Synthesis of Compounds Related to Gibberellic Acid. Part I. (±)-Gibberone.*[1]

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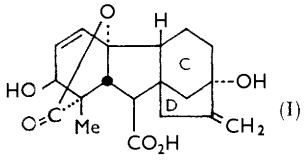
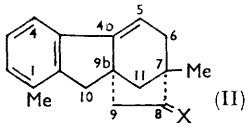
The synthesis of (±)-gibberone, a tetracyclic degradation product of gibberellic acid, is described.

The bicyclo[3,2,1]octane ring system comprising rings C and D of gibberellic acid [2] (I) is still present in the degradation product gibberone [3] (II; X = O), although here the configuration of the two-carbon bridge has been inverted during the degradation sequence by the mechanistic requirement of the change from allogibberic to gibberic acid.[4]

The same bridged-ring system occurs also in the phyllocladene group of diterpenes, and its biogenesis there has been discussed by Wenkert.[5] Previous syntheses of bicyclo-[3,2,1]octanes have been based on rearrangements of isomeric bicyclo[2,2,2]octanes [6] or, as in the case of phyllocladene itself, on the cyclisation of a dicarboxylic acid [7] which is



(I)



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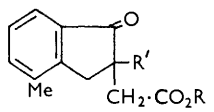


(III)

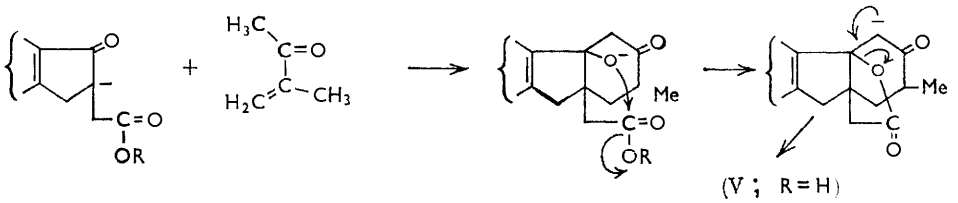
not easily accessible.[8] The elegant ring closure described by Masamune [9] should also be mentioned. Substituted bicyclo[2,2,2]octanes can be synthesised in a reasonably rational manner, but their rearrangement to substituted bicyclo[3,2,1]octanes seems to be limited in scope, because it depends on delicate stereochemical factors and there seems little to choose between the relative stabilities of the isomeric ring systems.[10]

We decided to start from 4-methyl-1-oxoindan-2-ylacetic acid (III; R = R′ = H). Attempts to alkylate 4-methylindan-1-one with methyl bromoacetate through an enamine or by reaction with the enolate of the ketone did not lead to the desired product, but reaction of the corresponding α-bromo-ketone with di-t-butyl sodiomalonate followed by acid hydrolysis and decarboxylation gave the expected keto-acid in good yield.[11] Its

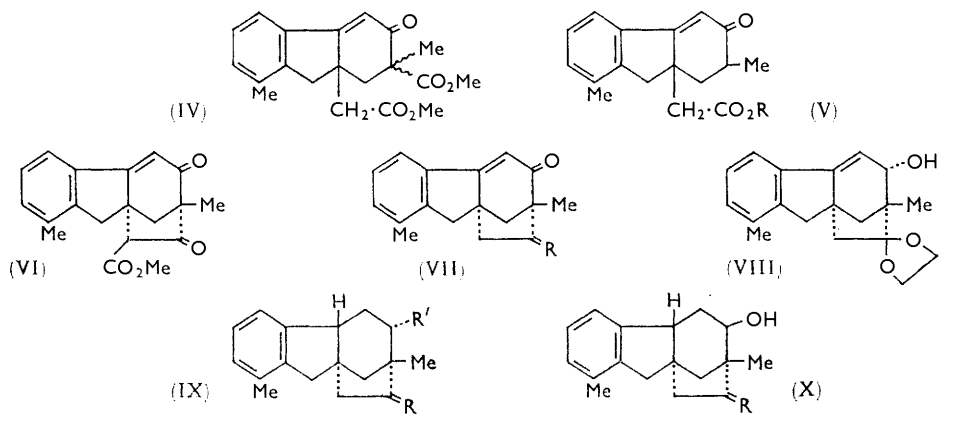
[1] Preliminary communication: Loewenthal, *Proc. Chem. Soc.*, 1960, 355.
[2] Grove, *Quart. Revs.*, 1961, **15**, 1; for *X*-ray proof of the stereochemistry see McCapra, Scott, Sim, and Young, *Proc. Chem. Soc.*, 1962, 185.
[3] Cross, Grove, MacMillan, and Mulholland, *J.*, 1958, 2320.
[4] Stork and Newman, *J. Amer. Chem. Soc.*, 1959, **81**, 3168.
[5] Wenkert, *Chem. and Ind.*, 1955, 282.
[6] Goering, Greiner, and Sloan, *J. Amer. Chem. Soc.*, 1961, **83**, 1391.
[7] Turner and Gänshirt, *Tetrahedron Letters*, 1961, 231.
[8] Turner and Shaw, *Tetrahedron Letters*, 1960, No. 18, 24; Church, Ireland, and Marshall, *ibid.*, 1960, No. 17, 1.
[9] Masamune, *J. Amer. Chem. Soc.*, 1961, **83**, 1009.
[10] Goering and Sloan, *J. Amer. Chem. Soc.*, 1961, **83**, 1397; Winstein and Carter, *ibid.*, p. 4485.
[11] Cf. Groves and Swan, *J.*, 1951, 867.

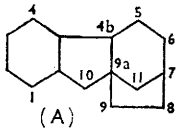
methyl ester (III; R = Me, R′ = H) was converted into a Mannich base (III; R = Me, R′ = $CH_2{\cdot}NMe_2$) from which, by reaction with the anion derived from methyl methylacetoacetate, it was hoped to obtain directly a fluorenedicarboxylic ester (IV), whose further Dieckmann cyclisation could lead (subject to the stereochemistry obtained [12] at C-2) directly to the gibbane system.* However, this Mannich base and its methiodide were most unreactive, presumably because it is of the neopentyl type.[13]

The reaction of the methyl ester (III; R = Me, R′ = H) and of the corresponding t-butyl ester with isopropenyl methyl ketone under various conditions was then studied. From the former ester, in the presence of an excess of sodium methoxide in methanol, there was obtained in high yield the unsaturated keto-acid (V; R = H).[12] This was also the only product (apart from unchanged material) from the corresponding reaction of the potassium enolate of the t-butyl ester (III; R = Bu^t, R′ = H) in benzene, which suggests that, after initial Michael addition of the vinyl ketone and aldol formation, the aldol anion attacks the ester group, giving an aldol lactone intermediate, which on addition of water is opened and dehydrated. Such a mechanism would in part correspond to that of the Stobbe condensation with di-t-butyl succinate [14] of which the ester (III; R = Bu^t, R′ = H) is formally an analogue.



Attempted internal Claisen acylation of the unsaturated keto-ester (V; R = Me) was unsuccessful, even in the presence of triphenylmethylsodium. This is not altogether surprising considering that the hoped-for β-diketone (VII; R = O) cannot be stabilised





* Nomenclature in this paper is based on the name gibbane for the fully saturated hydrocarbon (A). Aromaticity in ring A is denoted by an ending A-triene. On this system, gibberone (II; R = O) would become 1,7β-dimethylgibba-A,4b-trien-8-one. For our compounds we show the two-carbon bridge as α and specify relative configurations on this basis, but our compounds are all racemic.

[12] For an alternative synthesis of this intermediate see Money, Raphael, Scott, and Young, *J.*, 1961, 3958.

[13] Brewster and Eliel, *Org. Reactions*, 1953, **7**, 99.

[14] Johnson and Miller, *J. Amer. Chem. Soc.*, 1950, **72**, 511.

in an enolic form, though a few cases are on record [15] of the formation, in low yield, of a non-enolisable β-dicarbonyl compound by nucleophilic acylation.

Another approach consisted of the reaction of the above unsaturated keto-ester with dimethyl carbonate in the presence of an excess of sodium methoxide. This apparently proceeded by methoxycarbonylation at C-2, the reaction being sterically directed to give, after cyclisation, the bridged-ring diketo-ester (VI). This product could not, however, be utilised since all attempts to remove the methoxycarbonyl group were unsuccessful; instead, cleavage occurred between C-7 and C-8 (gibbane numbering) to return the unsaturated keto-acid (V; R = H).

Finally internal electrophilic acylation of the latter acid led to the objective. In the presence of the boron trifluoride–ether complex in acetic acid–acetic anhydride the desired diketone (VII; R = O) was obtained in excellent yield, in contrast to the low yields usually obtained in this type of acylation.[16] Indeed, it is difficult to assume the mediation in the present case of a keto–enol boron complex postulated by Hauser and his co-workers,[16] though the above reaction probably does proceed by electrophilic addition of the complex cation from the carboxyl group (or its anhydride) and boron trifluoride to the double bond of the enolic form of the 3-carbonyl group. Significantly, a smaller amount of the above diketone was also formed by pyrolysis of the unsaturated keto-acid; this is reminiscent of the interconversion of 6-ketocamphor and α-campholonic acid.[17]

The β-diketone (VII; R = O) was very sensitive to hydrolytic conditions. After treatment with hot 10% sodium hydroxide, only the keto-acid (III; R = R′ = H) was isolated. This also occurred when the unsaturated keto-ester (V; R = Me) was hydrolysed by alkali, indicating a reversal of the Robinson ring annelation leading to the acid (V; R = H). The sensitivity of the above diketone was further exemplified by the course of its ketalisation with ethylene glycol, or transketalisation with dimethyldioxolan in the presence of toluene-*p*-sulphonic acid; apart from the desired monoketal [VII; R = $<(O{\cdot}CH_2)_2$] an oil was obtained which appeared to be the ethylene glycol ester of the acid (V; R = H) and was hydrolysed to the latter by acid.

In the above monoketal the 6-carbonyl group was then smoothly reduced (Wolff–Kischner), to give the ketal [II; X = $<(O{\cdot}CH_2)_2$]. Acid treatment of this gave (±)-gibberone (II; R = O) whose infrared spectrum in solution was identical with that of the dextrorotatory degradation product of gibberellic acid.

The steric course of some further reactions within the bridged-ring system of some of the compounds mentioned is of interest. The diketone (VII; R = O) absorbed 2 mol. of hydrogen catalytically, giving mainly the saturated hydroxy-ketone (IX; R = O, R′ = OH), which was accompanied by a small amount of an epimer (X; R = O). These were best separated by chromatography of their ethylene glycol ketals. Separate oxidation of the latter with chromic oxide in pyridine gave the same ketal-ketone [IX; R = $<(O{\cdot}CH_2)_2$, R′ = O], showing that the above two hydroxy-ketones differed in configuration only at C-6. The *endo*-configuration (" α ") for the hydroxyl group in the major product is given because there was slight but definite evidence of hydrogen bonding between the hydroxyl and the carbonyl group in the infrared spectrum, particularly when this was compared with the carbonyl band shown by the derived chloro-ketone (IX; R = O, R′ = Cl). This conclusion is supported by the order of elution of the hydroxy-ketals on chromatography. The stereochemistry at position 4b follows on the assumption that hydrogenation leading to the major products, at this centre and at C-6, proceeded from the same direction.

Reduction of the monoketal [VII; R = $<(O{\cdot}CH_2)_2$] with lithium aluminium hydride was also almost completely stereospecific, giving the allylic alcohol (VIII) in which the

[15] Hudson and Hauser, *J. Amer. Chem. Soc.*, 1939, **61**, 3567; Cox and McElvain, *ibid.*, 1934, **56**, 2459.

[16] Hauser, Swamer, and Adams, *Org. Reactions*, 1954, **8**, 103, 110.

[17] Komppa and Beckmann, *Ber.*, 1936, **69**, 2783.

endo-configuration (" α ") of the hydroxyl group was proved by catalytic hydrogenation to the hydroxy-ketal [IX; R = <(O·CH$_2$)$_2$, R′ = OH]. Attempts to form a toluene-*p*-sulphonate or methanesulphonate of compound (VIII), with a view to their hydrogenolysis to afford an alternative route to the ketal [II; R = <(O·CH$_2$)$_2$], were unsuccessful. Furthermore the chloro-ketal [IX; R = <(O·CH$_2$)$_2$, R′ = Cl] was resistant even to extreme conditions of dehydrohalogenation.

Finally the ultraviolet spectra of some of the above-mentioned compounds, which are shown in the accompanying Table, are worthy of note. The unsaturated keto-ester (V;

Ultraviolet spectra (mμ) (sh = shoulder).

	In MeOH		In " iso-octane "			In MeOH		In " iso-octane "	
Compound	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε	Compound	$\lambda_{max.}$	ε	$\lambda_{max.}$	ε
(V; R = Me)	215	10,400			(II; R = O)	259	14,500	227sh	12,300
	230	8100				268	12,200	258·5	16,400
	237	8100				290	4100	268·5	14,700
	298	18,300				300	4000	289·5	4500
(VII; R = O)	238	7400						301	4300
	300	19,000			[II; R =	228sh	9700	222sh	6000
	330	15,300			<(O·CH$_2$)$_2$]	259	15,700	230	4200
[VII; R =	229	9300	227·5	13,100		268·5	13,600	259	15,200
<(O·CH$_2$)$_2$]	235	10,000	234	11,300		291	4000	269	13,000
	299	18,400	279	18,800		302	3800	291	4100
	316sh	15,900	291	21,500				302	3900
			303	15,400	(VIII)	260	13,000		
			315·5	14,100		268	11,500		
VI)	238	7600				290	4400		
	300·5	18,400				300	3600		
	331	15,900							

R = Me) shows absorption expected for its chromophoric system,[18] but on formation of the bridged-ring system the spectrum increases in complexity. Compounds (VI) and (VII; R = O) show an additional high-intensity band at 330 mμ; the same tendency is shown by the monoketal [VII; R = <(O·CH$_2$)$_2$]. In addition, the ketal of (±)-gibberone has a spectrum which is almost identical with that of the parent ketone (in methanol and in " iso-octane "), both showing the reported [19] abnormally intense bands at *ca.* 290 and 300 mμ. These facts are difficult to interpret on the basis of an interaction (*e.g.*, π-orbital overlap) between two isolated chromophores in a bridged-ring system.[19,20] Professor R. C. Cookson [21] has suggested that the additional bands shown in the bridged-ring system are due to the rigidity imposed on the chromophore, the vibrational energy then being concentrated in fewer modes with the development of conspicuous fine structure [22] (we are grateful for this suggestion).

Experimental

Infrared spectra refer to $CHCl_3$ solutions unless otherwise stated.

2-Bromo-4-methylindan-1-one.—4-Methylindan-1-one was brominated in ether–chloroform as described for indan-1-one.[11] The crude bromo-ketone was used directly for the next step; a sample, recrystallised from ether–methanol, had m. p. 85·5—86° (Found: C, 53·45; H, 4·2; Br, 35·75. $C_{10}H_9BrO$ requires C, 53·2; H, 4·05; Br, 35·5%).

4-Methyl-1-oxoindan-2-ylacetic Acid (III; R = R′ = H).—The above crude bromo-ketone (from 14·6 g. of 4-methylindan-1-one) in toluene (20 ml.) was added under nitrogen with stirring to a suspension of di-t-butyl sodiomalonate, prepared from the ester (32 g.) and sodium hydride (3·1 g.) in benzene (100 ml.). The mixture was refluxed for 12 hr., then cooled, and water

[18] Wilds, Beck, Djerassi, Johnson, Johnson, and Shunk, *J. Amer. Chem. Soc.*, 1947, **69**, 1985.
[19] Birnbaum, Cookson, and Lewin, *J.*, 1961, 1224.
[20] Winstein, De Vries, and Orloski, *J. Amer. Chem. Soc.*, 1961, **83**, 2020.
[21] Cookson, personal communication.
[22] Lewis and Calvin, *Chem. Rev.*, 1939, **25**, 318; Jones, *J. Amer. Chem. Soc.*, 1945, **67**, 2127.

was added. The organic layer was separated and concentrated *in vacuo*. The residue was refluxed with acetic acid (150 ml.), water (50 ml.), and hydrochloric acid (10 ml.) for 6 hr., after which the solvents were removed under reduced pressure. The residue was heated at 180—200° until gas evolution ceased (20 min.), after which it was cooled, taken up in ether–benzene, and extracted several times with 5% aqueous sodium carbonate. Acidification of the extracts and isolation with ether gave the crude *acid* (15·5 g.), which had m. p. 137° after crystallisation from isopropyl ether (Found: C, 70·7; H, 5·85%; equiv., 202. $C_{12}H_{12}O_3$ requires C, 70·55; H, 5·9%, equiv., 204), $\nu_{max.}$ 5·75, 5·85, 6·21, and 6·26 μ. The *methyl ester* (III; R = Me, R′ = H), prepared with diazomethane, had m. p. 84·5—85° (from hexane) (Found: C, 71·65; H, 6·6. $C_{13}H_{14}O_3$ requires C, 71·55; H, 6·45%), $\nu_{max.}$ 5·80, 5·85, 6·21, and 6·26 μ. The *t-butyl ester* (III; R = Bu^t, R′ = H) was prepared by shaking the acid (4·5 g.) in dioxan (12 ml.) in a pressure-bottle at room temperature with isobutene (15 ml.) and sulphuric acid (0·9 ml.) until it had dissolved (5 hr.); 5% sodium carbonate solution was added and the neutral product isolated with ether; after recrystallisation from methanol the ester had m. p. 90—91° (4·2 g.) (Found: C, 73·65; H, 7·6. $C_{16}H_{20}O_3$ requires C, 73·8; H, 7·75%).

Methyl 2-Dimethylaminomethyl-4-methyl-1-oxoindan-2-ylacetate (III; R = Me, R′ = CH_2·NMe_2).—The above methyl ester (3·0 g.) was stirred at room temperature with 2·5N-methanolic dimethylamine (7·5 ml.) and paraformaldehyde (0·45 g.) until a clear solution was obtained (0·5 hr.). More paraformaldehyde (0·3 g.) and dimethylamine hydrochloride (2·4 g.) were then added and the mixture was refluxed for 2 hr. It was then cooled to 0°, an excess of 20% sodium hydroxide was added, and the product was extracted with ether. The ether layer was repeatedly extracted with ice-cold 5% hydrochloric acid, and the extracts were basified with 20% aqueous sodium hydroxide under a layer of ether. The ether layer was dried ($MgSO_4$) and the solvent removed. Crystallisation of the residue from pentane at 0° gave the *amino-keto-ester* (3·1 g.), m. p. 53° (Found: C, 69·5; H, 7·45; N, 5·25. $C_{16}H_{21}NO_3$ requires C, 69·8; H, 7·7; N, 5·1%), $\nu_{max.}$ 3·38, 3·52, 3·60, 5·79, and 5·85 μ.

All attempts to condense this compound or its methiodide with methyl sodiomethylacetoacetate failed; in all cases only the amino-keto-ester was recovered.

1,2,3,10-Tetrahydro-2,8-dimethyl-3-oxofluoren-10-ylacetic Acid (V; R = H).—The methyl ester (III; R = Me, R′ = H) (8·72 g.) in benzene (20 ml.) was added at 5° under nitrogen (with stirring) to a solution of sodium (2·3 g.) in methanol (80 ml.). To the resulting solution, isopropenyl methyl ketone (5·05 g.) in methanol (5 ml.) was added during 20 min., after which the mixture was allowed to reach room temperature overnight. It was then acidified with acetic acid and concentrated *in vacuo* to one-third of its volume. Water and ether–chloroform were added and the organic layer was extracted several times with ice-cold 5% aqueous sodium carbonate. The extracts were acidified under a layer of benzene, and the benzene layer was washed, dried ($MgSO_4$), and evaporated. Crystallisation of the residue from isopropyl ether gave the unsaturated *keto-acid* (8·80 g.), m. p. 172·5—173° (Found: C, 75·2; H, 6·65%; equiv., 279. $C_{17}H_{18}O_3$ requires C, 75·55; H, 6·7%; equiv., 270), $\nu_{max.}$ 5·85, 6·05, 6·14, 6·25 μ.

Addition of isopropenyl methyl ketone to the potassium enolate of the t-butyl ester (III; R = Bu^t, R′ = H), prepared with 1·1 mol. of dry potassium t-butoxide in benzene, as previously reported,[1] gave only a 45% yield of the unsaturated keto-acid. From the neutral portion of the product, only unchanged t-butyl ester was isolated.

The *methyl ester* (V; R = Me), prepared with diazomethane, had m. p. 110—110·5° (from cyclohexane) (Found: C, 75·9; H, 6·9. $C_{18}H_{20}O_3$ requires C, 76·05; H, 7·1%), $\nu_{max.}$ 5·80, 6·05, 6·13, and 6·25 μ. After hydrolysis of this ester by boiling 10% potassium hydroxide solution for 2 hr., only the keto-acid (III; R = R′ = H) was isolated.

(±)-*Methyl 1,7β-Dimethyl-6,8-dioxogibba-*A,4b*-tetraene-9-carboxylate* (VI).—The above methyl ester (1·0 g.) was added under nitrogen to a suspension of dry sodium methoxide (from 0·37 g. of sodium) in dimethyl carbonate (distilled from sodium hydride, 30 ml.), and the mixture was slowly distilled through a short column during 6 hr. so that the volume decreased to *ca.* 10 ml. It was then cooled, and dilute acetic acid and ether–chloroform were added. The organic layer was washed with water, dried ($MgSO_4$), and concentrated. The residue crystallised slowly on contact with ether to give the *diketo-ester* (0·30 g.) which after recrystallisation from chloroform–isopropyl ether had m. p. 195—197° (decomp.) (Found: C, 73·4; H, 6·05. $C_{19}H_{18}O_4$ requires C, 73·55; H, 5·85%). It gave a strong colour with methanolic ferric chloride and $\nu_{max.}$ 5·65, 5·76, 5·99, and 6·13 μ.

Refluxing this compound with acetic acid–water–hydrochloric acid (5 : 1 : 1) gave only traces of neutral material. The crystalline acidic product was identified (m. p., mixed m. p., and infrared spectrum) as the unsaturated keto-acid (V; R = H). Similar results were obtained by refluxing it with a trace of toluene-*p*-sulphonic acid in acetic acid or in acetic acid–acetic anhydride.

(±)-1,7β-*Dimethylgibba*-A,4b-*tetraene*-6,8-*dione* (VII; R = O).—(*a*) The unsaturated keto-acid (V; R = H) (8·0 g.) was dissolved in warm acetic acid (40 ml.) and acetic anhydride (8 ml.). To the cooled solution boron trifluoride–ether complex (redistilled; 9 ml.) was added and the red solution set aside for 24 hr., after which some of the product had crystallised. Water was added and the product taken up in chloroform. The chloroform solution was washed with water, 5% sodium carbonate solution, and again with water, dried ($MgSO_4$), and concentrated. Crystallisation of the residue from chloroform–isopropyl ether gave the *diketone* (7·05 g.), m. p. 207° (Found: C, 80·45; H, 6·45. $C_{17}H_{16}O_2$ requires C, 80·9; H, 6·4%), $\nu_{max.}$ 5·74, 6·02, 6·17, and 6·26 μ.

(*b*) The unsaturated keto-acid (V; R = H) (287 mg.) was heated at 170—180°/3 mm. for 10 hr. The sublimed material was separated into recovered acid (123 mg.) and neutral (176 mg.) fractions. The latter, on crystallisation from ether, gave the above diketone (110 mg.), identical (mixed m. p. and infrared spectrum) with the material obtained as under (*a*).

(±)-8,8-*Ethylenedioxy*-1,7β-*dimethylgibba*-A,4b-*tetraen*-6-*one* [VII; R = $<(O{\cdot}CH_2)_2$].—The diketone (VII; R = O) (1·30 g.) was refluxed (azeotropic removal of water) with ethylene glycol (10 ml.) and toluene-*p*-sulphonic acid (0·12 g.) in benzene (60 ml.) for 12 hr. The neutral product obtained after the usual working-up was chromatographed on alumina (Alcoa F-20; 35 g.). Hexane–methylene chloride and methylene chloride eluted the *monoketal* (0·59 g.), m. p. 177—177·5° (from methylene chloride–isopropyl ether) (Found: C, 76·8; H, 6·8. $C_{19}H_{20}O_3$ requires C, 77·0; H, 6·8%), $\nu_{max.}$ 6·03, 6·14, and 6·25 μ. Elution with chloroform gave an oil which appeared to be a mixture ($\nu_{max.}$ 2·75—2·90, 5·79, 6·05, and 6·15 μ) of the mono(and possibly bis)ethylene glycol esters of the acid (V; R = H), from which the acid was obtained almost quantitatively by hydrolysis with acetic and hydrochloric acid.

(±)-8,8-*Ethylenedioxy*-1,7β-*dimethylgibba*-A,4b-*tetraen*-6α-*ol* (VIII).—The above monoketal (0·40 g.) was treated in dry tetrahydrofuran (5 ml.) with lithium aluminium hydride (0·15 g.) at 0° for 4 hr. The mixture was decomposed with ethyl acetate and Rochelle salt solution, and the product isolated with ether. It was purified by chromatography on alumina (Alcoa F-20) and crystallised from ether–hexane to give the allylic *alcohol* (0·31 g.), m. p. 140° and 149·5—150° (only the latter m. p. was shown after crystallisation from dilute methanol) (Found: C, 76·4; H, 7·45. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·45%), $\nu_{max.}$ 2·82 (sharp), 6·0 (weak), 6·13, and 6·25 μ.

Attempts to form a methanesulphonate or a toluene-*p*-sulphonate of this alcohol were unsuccessful.[23]

Catalytic reduction of this alcohol in methanol in the presence of 7% palladium–strontium carbonate gave in high yield the hydroxy-ketal [IX; R = $<(O{\cdot}CH_2)_2$, R′ = OH] (see below), identified by mixed m. p. and infrared spectrum.

(±)-*Gibberone* (II; R = O).—The monoketal [VII; R = $<(O{\cdot}CH_2)_2$] (0·30 g.) was refluxed with hydrazine hydrate (0·7 ml.) in ethylene glycol (5 ml.) for 3 hr., after which the mixture was distilled until the temperature reached 180°. It was then cooled and potassium hydroxide (0·7 g.) was added, after which refluxing was resumed for 2 hr. To the cooled solution water and ether–benzene were added; the organic layer was washed with water, dried ($MgSO_4$), and evaporated. The residue recrystallised from benzene–methanol to give the *ketal* of (±)-gibberone (0·22 g.), m. p. 151·5—152° (Found: C, 80·75; H, 7·7. $C_{19}H_{22}O_2$ requires C, 80·8; H, 7·85%), $\nu_{max.}$ at 5·97 (weak) and 6·26 μ.

The ketal (0·25 g.) was refluxed with toluene-*p*-sulphonic acid (0·10 g.) in acetone (5 ml.) for 2 hr. Removal of the acetone and isolation with ether gave the *ketone* (0·15 g.), m. p. 118—118·5° (from benzene–methanol) (Found: C, 85·5; H, 7·8. $C_{17}H_{18}O$ requires C, 85·65; H, 7·85%), $\nu_{max.}$ 5·77 μ. The 2,4-*dinitrophenylhydrazone* formed orange needles (from chloroform–methanol), m. p. 244—245° (decomp.) (Found: C, 65·9; H, 5·25; N, 13·4. $C_{23}H_{22}N_4O_4$ requires C, 66·0; H, 5·3; N, 13·4%).

Comparison of the infrared spectrum, in hexane solution, of this ketone and of authentic

[23] Rapoport and Bonner, *J. Amer. Chem. Soc.*, 1951, **73**, 2872.

(+)-gibberone, kindly undertaken by Mr. J. F. Grove (Imperial Chemical Industries Limited) through the help of Professor R. A. Raphael (University of Glasgow), showed them to be identical.

Catalytic Reduction of the Diketone (VII; R = O).—The diketone (756 mg.), on being shaken with 7% palladium–strontium carbonate (100 mg.) and 10% palladium–carbon (100 mg.) in ethyl acetate–ethanol, absorbed 2·0 mol. of hydrogen in *ca.* 1 hr. The crystalline product obtained after filtration and removal of solvent was twice recrystallised from chloroform–benzene, to give (±)-6α-*hydroxy*-1,7β-*dimethyl*-4bβ*H*-*gibba*-A-*trien*-8-*one* (IX; R = O, R′ = OH) (360 mg.), m. p. 207—209°, which after further crystallisation had m. p. 215·5—217° (decomp.) (Found: C, 79·65; H, 8·05. $C_{17}H_{20}O_2$ requires C, 79·65; H, 7·85%), $\nu_{max.}$ 2·77—2·85 and 5·77 μ.

The mother-liquors were combined and ketalised as described for the diketone (VII; R = O) (see above). The mixture of ketals obtained was chromatographed on alumina (Alcoa F-20; 10 g.) with hexane and hexane–methylene chloride as eluants. After a small amount of a very soluble oil there were obtained (in order of elution): (*a*) the *hydroxy-ketal* [IX; R = $<(O{\cdot}CH_2)_2$, R′ = OH] (173 mg.), m. p. 145—146° (from hexane) (Found: C, 76·1; H, 8·2. $C_{19}H_{24}O_3$ requires C, 75·95; H, 8·05%), $\nu_{max.}$ 2·80 μ (sharp), whose cleavage with toluene-*p*-sulphonic acid in acetone gave the hydroxy-ketone (IX; R = O, R′ = OH), identified by m. p. and mixed m. p.; (*b*) an intermediate fraction (30 mg.); and (*c*) the *hydroxy-ketal* [X; R = $<(O{\cdot}CH_2)_2$] (100 mg.), m. p. 137·5° and 141·5—142° (from hexane) (Found: C, 75·85; H, 8·0%), $\nu_{max.}$ 2·74 (sharp) and 2·88 μ (broad), whose cleavage gave 6β-*hydroxy*-1,7β-*dimethyl*-4bβ*H*-*gibba*-A-*trien*-8-*one* (X; R = O); after crystallisation from dilute methanol this had m. p. 128·5—129·5° (Found: C, 75·05; H, 8·0. $C_{17}H_{20}O_2,CH_3{\cdot}OH$ requires C, 74·95; H, 8·4%), $\nu_{max.}$ (sublimed sample) at 2·73 (sharp) and 5·75 μ.

Oxidation of the hydroxy-ketal [X; R = $<(O{\cdot}CH_2)_2$] with chromic oxide in pyridine gave the *ketal-ketone* [IX; R = $<(O{\cdot}CH_2)_2$, R′ = O], m. p. 163·5—165° (from hexane) (Found: C, 76·35; H, 7·4. $C_{19}H_{22}O_3$ requires C, 76·5; H, 7·45%), $\nu_{max.}$ at 5·86 μ. Oxidation of the epimeric hydroxy-ketal [IX; R = $<(O{\cdot}CH_2)_2$, R′ = OH] under the same conditions was incomplete; it gave a mixture of the same ketal-ketone (identified by m. p., mixed m. p., and infrared spectrum) and starting material which was separated by chromatography.

6ξ-*Chloro*-1,7β-*dimethyl*-4bβ*H*-*gibba*-A-*trien*-8-*one* (IX; R = O, R′ = Cl).—The hydroxy-ketone (IX; R = O, R′ = OH) (0·45 g.) in pyridine (4·5 ml.) was treated with phosphorus oxychloride (0·45 ml.) at 100° for 0·5 hr. The customary working-up gave the *chloro-ketone* (0·30 g.) which after recrystallisation from ether–methanol had m. p. 137—137·5° (Found: C, 74·45; H, 7·05. $C_{17}H_{19}ClO$ requires C, 74·3; H, 6·95%), $\nu_{max.}$ 5·73 μ.

Ketalisation of this compound (300 mg.) as described for the diketone (VII; R = O) (see above), followed by chromatography, gave the *chloro-ketal* [IX; R = $<(O{\cdot}CH_2)_2$, R′ = Cl] (200 mg.), m. p. 117·5—118° (from ether–methanol) (Found: C, 71·5; H, 7·2; Cl, 11·4. $C_{19}H_{23}ClO_2$ requires C, 71·6; H, 7·25; Cl, 11·15%). Further elution of the chromatogram gave unchanged starting material.

This chloro-ketal was recovered unchanged after being boiled with 2,4,6-trimethylpyridine or with potassium t-butoxide in toluene.

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