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SYNTHESIS OF SUBSTANCES RELATED TO GIBBERELLINS—XXIV[1]

TOTAL SYNTHESIS OF (±)-EPIALLOGIBBERIC ACID

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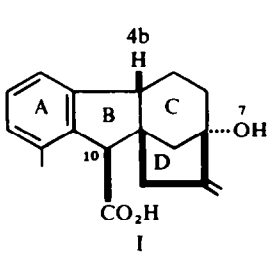
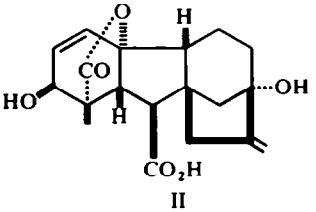
Abstract—A total synthesis of the title compound was accomplished employing a novel skeletal rearrangement.

(+)-EPIALLOGIBBERIC acid (I), which contains the characteristic C/D ring system of gibberellic acid (II), was first obtained as a degradation product of gibberellic acid[2] and later isolated as a metabolite of *Gibberella fujikuroi*.[3] After the completion of the total synthesis of some (±)-7-deoxygibberellins.[4] we turned our attention to the synthesis of this tetracyclic acid.



I



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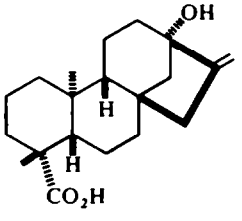
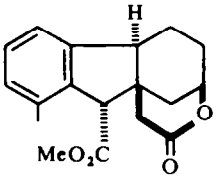
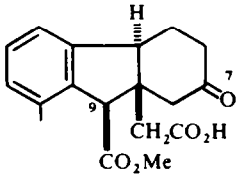


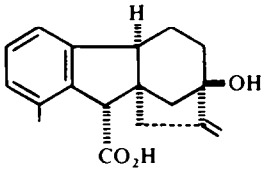
III



IVb



Vb



VI

Although the successful construction of its C/D ring system, a bicyclo [3.2.1] octane with an exocyclic methylene adjacent to a bridgehead tertiary OH group, was carried out by three independent groups employing appropriate model compounds,[5–7] a total synthesis of epiallogibberic acid (I) or related natural products such as steviol (III) was not achieved. We recently devised a new method for the C/D ring construction[8–10] and this paper described the total synthesis of (±)-epiallogibberic acid (I) reported in preliminary form.[1,8]

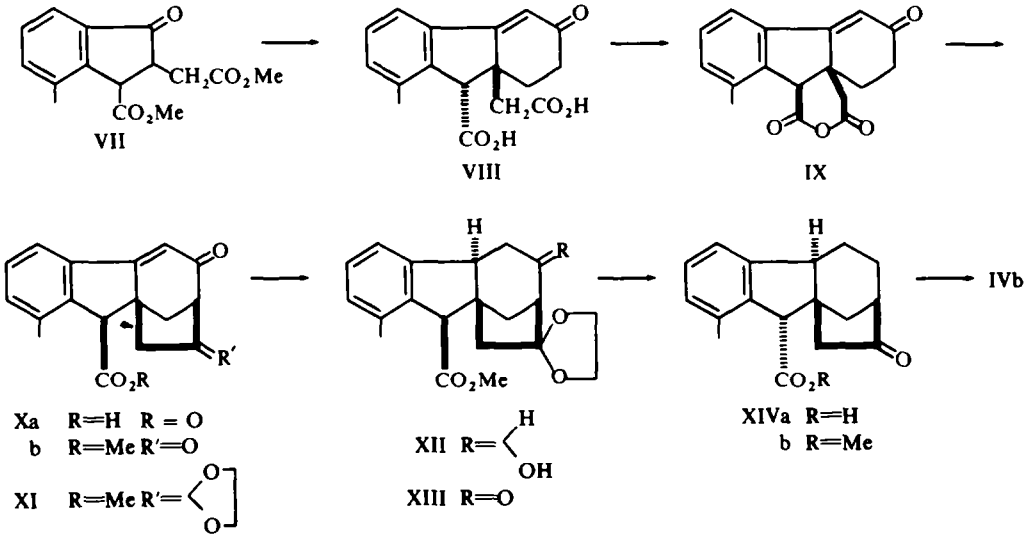
The synthesis can be divided into three stages: (i) synthesis of a racemic lactone (IVb)* from *o*-xylene[1] (ii) conversion of the optically active lactone (IVb) into the

* Although the formulas depicted represent only one enantiomer, they are taken to mean a racemate in the case of totally synthetic material.

known keto acid (Vb)[1] (iii) a partial synthesis of (−)-epiallogibberic acid (VI) from the keto acid (Vb).[8]

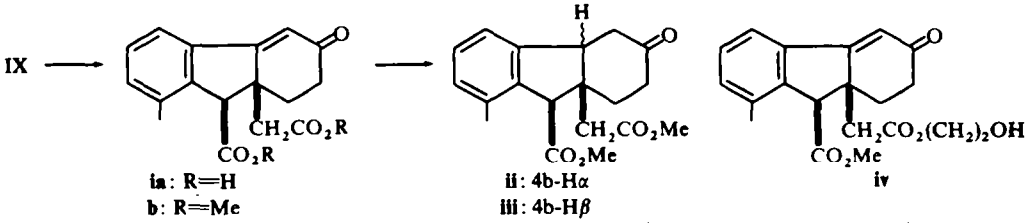
Synthesis of the lactone (IVb). A stereoselective synthesis of the lactone (IVb) was achieved *via* a tetracyclic keto acid (XIVa) which could be prepared in an analogous manner as described.[11,12]

A keto diester (VII)[13,cf.4] was synthesized from *o*-xylene. The Robinson annelation of the ketone (VII) with methyl vinyl ketone gave an acid (VIII) after alkaline hydrolysis. This *trans*-dicarboxylic acid was heated with acetic anhydride to yield the anhydride (IX) of *cis*-dicarboxylic acid (ia).* Intramolecular acylation was effected with boron



trifluoride etherate to give a tetracyclic diketo acid (Xa). The corresponding methyl ester (Xb) was heated with ethylene glycol and *p*-toluenesulfonic acid to give a ketal (XI).† This was hydrogenated to afford a hydroxy ester (XII). This step was proved to be highly stereoselective giving only the desired product. The alcohol (XII) was oxidized to a keto ester (XIII). This gave (±)-7-demethylepigibberic acid (XIVa) upon reduction with concomitant epimerization at C-10 (gibbane numbering). The Baeyer-Villiger oxidation of the corresponding methyl ester (XIVb) was effected

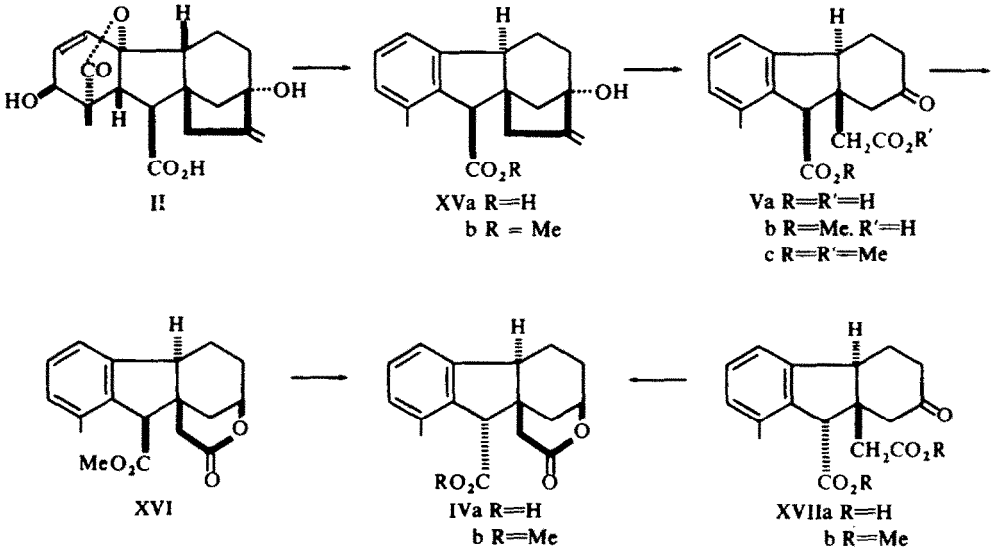
* An attempt was made to obtain a B/C-*trans*-fused keto ester (ii) by hydrogenating the *cis*-diester (ib) over Raney nickel followed by the Jones chromic acid oxidation. The product, however, was an inseparable crystalline mixture of ii and its stereoisomer (iii). This lack of stereoselectivity was in accord with the result reported by House and co-workers.[14]



† The crude product contained the ketal (XI) and an ester (IV). These could be separated by chromatography over alumina.

with trifluoroperacetic acid to give a racemic lactonic ester (IVb). Its IR. NMR and mass spectra are identical with those of the optically active lactone (IVb).[2]

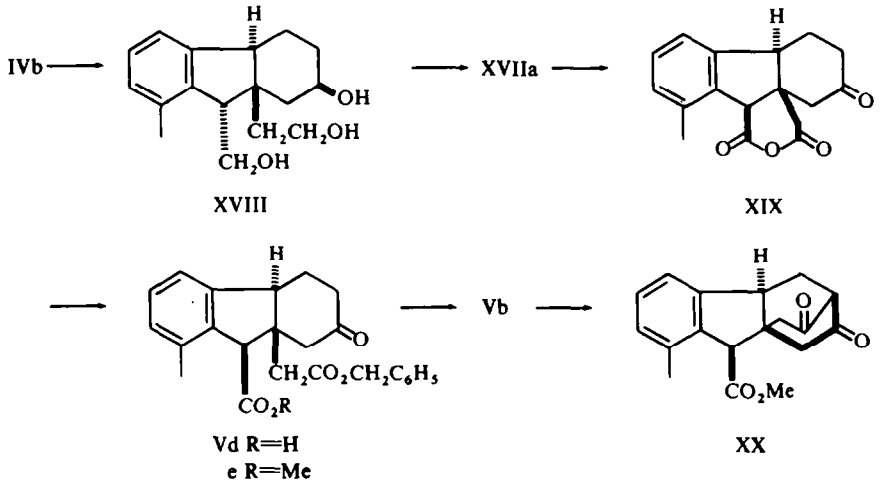
This lactone (IVb) was prepared from gibberellic acid (II) as described and served as a relay compound in the present synthesis. Gibberellic acid (II) was converted into allogibberic acid (XVa)[15,16]. The corresponding methyl ester (XVb) was oxidized to give a seco-acid (Vb) previously obtained by ozonolysis of methyl allogibberate (XVb).[17] A diester (Vc) derived from the seco-acid (Vb) was hydrogenated to yield a



lactone (XVI).[2] This was hydrolyzed to give a new lactonic acid (IVa) with concomitant epimerization at C-9 (fluorene numbering). This could also be obtained by hydrogenating a seco-acid (XVIIa) but only in poor yield. The *trans*-seco-acid (XVIIa) was prepared by alkaline hydrolysis of the seco- half ester (Vb).[2,17] Grove and Mulholland originally prepared the lactonic ester (IVb) by reduction of *trans*-diester (XVIIb).[2] In our hands. however. their method was unsatisfactory for the preparation of sufficient material.

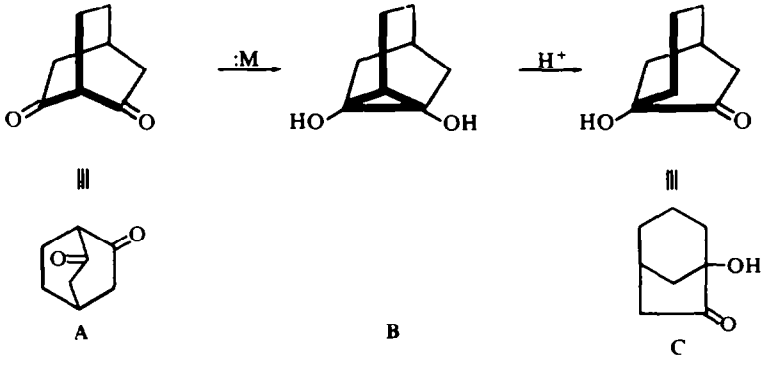
Synthesis of the keto acid (Vb). Conversion of the lactone (IVb) into the keto acid (Vb) requires both epimerization at C-9 and oxidation at C-7 (fluorene numbering). For this purpose the lactone (IVb) was reduced with LAH to a highly crystalline triol (XVIII). This was oxidized to a mixture of the *trans*-seco acid (XVIIa) and the lactonic acid (IVa) which could easily be separated by chromatography. A similar combination of reduction-oxidation steps was recorded for phyllocladene[18] and kaurene.[19] Epimerization at C-9 of the *trans*-seco-acid yielded an anhydride (XIX)[2,17] of the *cis*-seco-acid (Va). This was boiled with benzyl alcohol to give a half ester (Vd). The corresponding gummy methyl ester (Ve) was hydrogenated to remove the benzyl protective group. The product was chromatographed to give pure keto acid (Vb). This was identified with an authentic sample by mixed m.p.. IR. MS and TLC.

Synthesis of (−)-*epiallogibberic acid* (VI). For the construction of the C/D ring system of the final product. the key reaction is the conversion of bicyclo[2.2.2]octane-



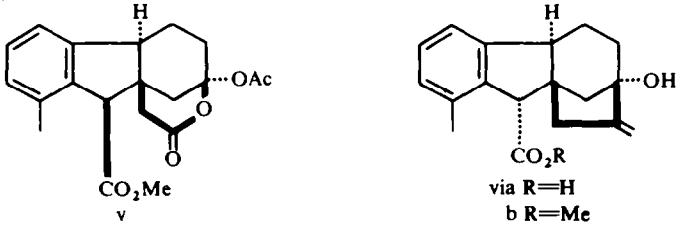
2.6-dione (A) into bicyclo[3.2.1] octan-1-ol-7-one (C) *via* a cyclopropanediol (B) as a possible intermediate.*

The required starting material (XX) was prepared from the keto acid (Vb) as described.[21]† This was reduced to give three reduction products: XXI (48% yield). XXII (6·6%) and XXIII (1·5%). The major product (XXI) crystallized directly from the



crude gummy reaction mixture. A chemical proof of the structure (XXI) was provided by its periodate oxidation to a keto acid (XXIVa). This, upon alkaline hydrolysis.

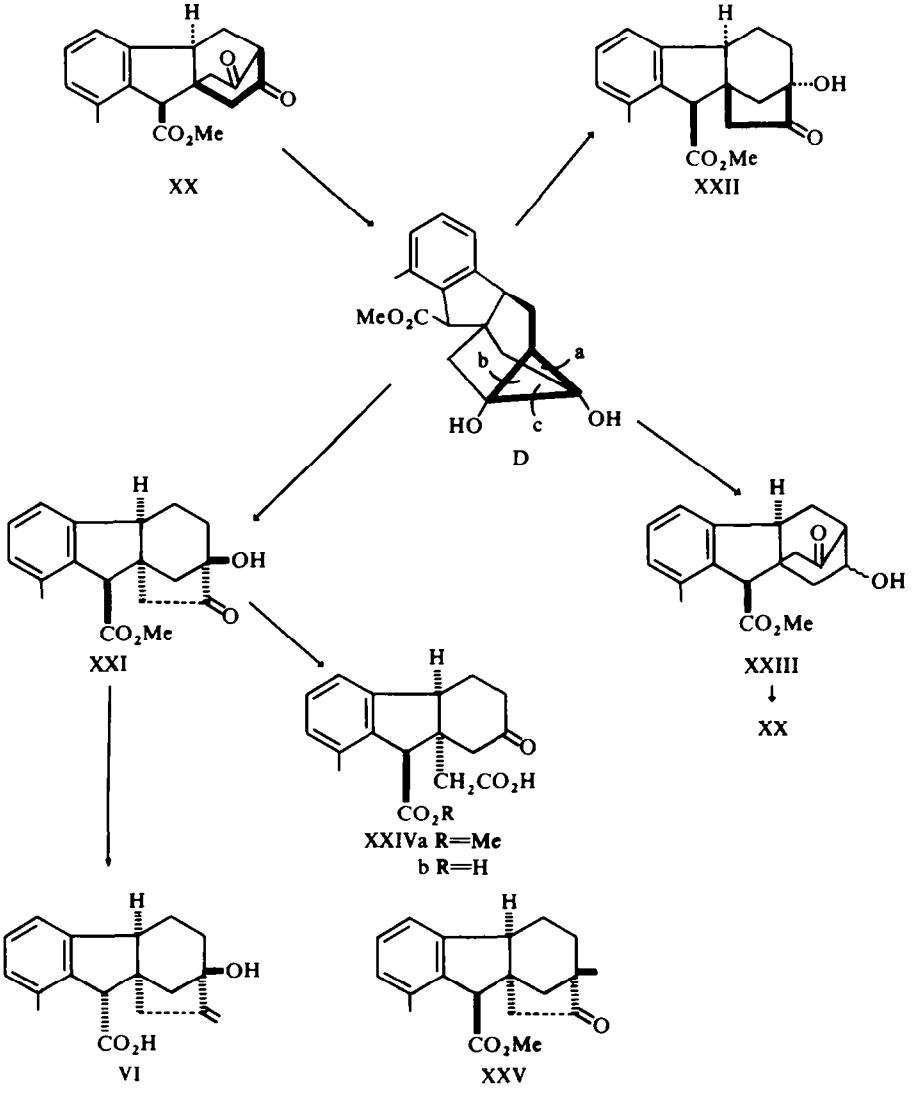
* This reductive rearrangement of the simple diketone (A) into the ketol (C) will be described in our forthcoming paper.[20]



† When the keto acid (Vb) was treated with boron trifluoride in acetic acid, an acetoxy lactol (v) was obtained in good yield instead of the β-diketone (XX).

yielded a known dicarboxylic acid (XXIVb) identified by mixed m.p. and IR with an authentic sample prepared from the diketone (XX).[21] The proposed stereochemistry (XXI) was also supported by the comparison of the ORD and CD measurements of the ketol (XXI) with those of the known ketol (XXII)[17] and methyl gibberate (XXV).[15] Negative Cotton effect curves were observed for the ketol (XXI) and methyl gibberate (XXV) while the isomeric ketol (XXII) exhibited a positive Cotton effect curve.

The mother liquor obtained after removing the crystalline ketol (XXI) was chromatographed to give two additional products. The earlier eluates gave the isomeric ketol (XXII). identified with an authentic sample by mixed m.p.. IR and NMR.



Another product was shown to be XXIII. since it gave the β-diketone (XX) when oxidized. This ketol (XXIII) showed a complex negative Cotton effect ORD curve

which was difficult to interpret. IR measurement of its dilute $CHCl_3$ solution was carried out to determine the configuration of the OH group but it did not give useful results. The stereochemistry of XXIII. therefore. remains to be determined.

This skeletal rearrangement probably involves a cyclopropane diol (D). generated by the intramolecular pinacol condensation. as the intermediate. Cleavage of the bonds a. b and c as depicted in the formula (D) will afford the three ketols XXI. XXII and XXIII. respectively. A similar rearrangement under the Clemmensen condition was observed with a simple monoterpene system almost at the same time when our work was completed.[22]

Finally the ketol (XXI) was converted into (−)-epiallogibberic acid (VI) by treatment with triphenylmethylene phosphorane followed by alkaline hydrolysis.* Epimerization of the carboxyl group took place during the hydrolysis. The IR and mass spectra of the synthetic acid (VI) was identical in every detail with that of the (+)-acid (I) prepared from gibberellic acid (II).[2] The two acids (I and VI) were also indistinguishable by TLC. The ORD curve of the synthetic acid. however. was antipodal to that of the (+)-acid (I) in accord with the assigned stereochemistry. This completed the total synthesis of (±)-epiallogibberic acid in view of the omission of the optical resolution of the racemic lactone (IVb).

EXPERIMENTAL

All m.ps were uncorrected. IR spectra refer to Nujol mulls for crystalline samples and films for gums unless otherwise stated and were measured with a JASCO IR-E spectrometer. NMR spectra were measured with a JEOL NM-4H 100 spectrometer at 100 MHz in $CDCl_3$ with TMS as an internal standard.

(±)-1-*Methyl*-8aβ-*carboxymethyl*-9α-*carboxy*-6.7.8.8a-*tetrahydrofluoren*-6-*one* (VIII)

Compound VII (70 g) in dry THF (200 ml) was added with stirring to a soln of NaOMe (from 18 g of Na) in MeOH (500 ml) at room temp. After the addition the mixture was cooled with a Dry Ice-acetone bath. To this soln methyl vinyl ketone (18 g) in MeOH (200 ml) was added dropwise during 1 hr at −50° ~ −40°. Then the bath was removed and the mixture was stirred for 2·5 hr. Alter the addition of NaOHaq (60 g in 300 ml) the mixture was stirred and heated under reflux for 2·5 hr and left to stand overnight at room temp. The mixture was concentrated *in vacuo*. acidified with ice-cooled dil HCl and extracted with EtOAc. The extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 52·3 g (68%) of crystalline VIII. Recrystallization from EtOAc-light petroleum gave prisms. m.p. 243–244° (dec); ν_{max} 1730, 1700, 1650, 1630, 1610, 790 cm^{-1}. (Found: C. 67·64; H. 5·43. $C_{17}H_{16}O_5$ requires: C. 67·99; H. 5·37%).

The anhydride (IX) *of* (±)-1-*methyl*-8aβ-*carboxymethyl*-9β-*carboxy*-6.7.8.8a-*tetrahydrofluoren*-6-*one* (**Ia**)

The acid VIII (52·2 g) was mixed with Ac_2O (500 ml) and the mixture was heated under reflux for 2·5 hr. After the removal of the solvent *in vacuo*. the residue was triturated with ether to give 30·6 g (62%) of crystalline IX. Recrystallization from $CHCl_3$-light petroelum gave prisms. m.p. 212–213°; ν_{max} 1815. 1760. 1660. 1625 cm^{-1}. (Found: C. 72·30; H. 5·01. $C_{17}H_{14}O_4$ requires: C. 72·33; H. 5·00%).

(±)-1-*Methyl*-8aβ-*carboxymethyl*-9β-*carboxy*-6,7. 8,8a-*tetrahydroiluoren*-6-*one* (via)

A mixture of the anhydride IX (15·0 g) and KOHaq (10 g in 250 ml) was stirred and heated at 50–60° for 15 min. It was acidified with ice-cooled dil HCl. The crystalline diacid **Ia** was collected on a Buchner

* When the reaction sequence was reversed, that is, if the ketol (XXI) was first hydrolyzed with base and then treated with the Wittig reagent. another acid (via) was obtained as a gum together with a small amount of the crystalline (−)-epiallogibberic acid (VI). This was due to the inversion of the D ring of the ketol (XXI) induced by base as observed in the case of steviol methyl ester nor-ketone.[23] Authentic samples of the C-10 epimer of allogibberic acid (via) and its methyl ester (vib) were prepared from allogibberic acid (XVa) as reported by Grove and Mulholland.[2]

funnel and washed with a small amount of ether. The *cis*-diacid (16·0 g. 99%) was recrystallized from EtOAc-light petroleum to give prisms. m.p. 234–235°; ν_{max} ~ 3500–~2600. 1700. 1655. 1630. 790 cm^{-1}. (Found: C. 67·26; H. 5·34. $C_{17}H_{16}O_5$ requires: 67·99; H. 5·37%).

(±)-1-*Methyl*-8aβ-*carbomethoxymethyl*-9β-*carbomethoxy*-6,7,8,8a-*tetrahydrofluoren*-6-*one* (ib)

The acid **ia** was esterified with ethereal diazomethane and the resulting **ib** was recrystallized from EtOAc-light petroleum to give needles. m.p. 159–160°; ν_{max} 1745. 1735 (sh). 1655, 1630. 805 cm^{-1}; δ 2·17 (3H. s). 3·60 (3H. s). 3·76 (3H. s). 3·88 (1H. s). 6·16 (1H. s) ppm. (Found: C. 69·14; H. 6·09. $C_{19}H_{20}O_5$ requires: C. 69·50; H. 6·14%).

An epimeric mixture at C-4b *of* (±)-1-*methyl*-8aβ-*carbomethoxymethyl*-9β-*carbomethoxy*-4b. 5,6,7,8,8a-*hexahydrofluoren*-6-*ones* (**ii** *and* **iii**)

The diester **ib** (10·0 g) dissolved in dioxan (150 ml) was hydrogenated over Raney nickel W-7 (20g) at 80° and an initial press of 50 kg/cm^2 for 8 hr. Removal of the catalyst and the solvent gave an oil. ν_{max} ~ 3500. 1735. 1600. 860 cm^{-1}. This oil (9·0 g) in acetone (200 ml) was treated with the Jones chromic acid (10 ml) under ice-cooling. The mixture was left to stand at room temp for 10 min. MeOH (30 ml) was added and the mixture was concentrated *in vacuo*. The residue was diluted with water and extracted with EtOAc. The extract was washed with water. sat $NaHCO_3$ aq and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 8·2 g (82%) of crystalline product as fine prisms. m.p. 104–109°; ν_{max} 1730. 1705. 1600. 780 cm^{-1}; δ 2·14 (~ 1H. C-1 Me). 2·28 (~ 2H. C-1 Me). 3·58. 3·68. 3·74 (total 6H. —CO_2Me) ppm. (Found: C. 69·09; H. 6·75. $C_{19}H_{22}O_5$ requires: C. 69·07; H. 6·71%).

(±)-1-*Methyl*-6.8-*dioxogibba*-A.4b-*tetraene*-10β-*carboxylic acid* (Xa)

The anhydride IX (17·3 g) dissolved in AcOH (160 ml) containing Ac_2O (3 ml) was mixed with BF_3-etherate (20 ml). The mixture was refluxed for 40 min. cooled. poured into ice-water (1l) and extracted with EtOAc. The extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 10·0 g (58%) of crystalline Xa. Recrystallization from EtOAc-MeOH gave small needles. mp. 247–248°; ν_{max} ~ 3200–~2600. 1750. 1725. 1635. 1620. 1605 cm^{-1}. (Found: C. 71·85; H. 4·91. $C_{17}H_{14}O_4$ requires: C. 72·33; H. 5·00%).

Methyl (±)-1-*methyl*-6.8-*dioxogibba*-*A*.4b-*tetraene*-10β-*carboxylate* (Xb)

The acid Xa (9·0 g) was esterified with ethereal CH_2N_2 to give 9·0 g (98%) of Xb. Recrystallization from EtOAc-light petroleum gave rods, m.p. 154–155°; ν_{max} 1740 (sh). 1735, 1660, 1615, 790 cm^{-1}; δ 2·26 (3H, s). 3·60 (1H. br. s). 4·23 (1H. s. C-10H). 6·14 (1H. s. C-5H). 7·20–7·45 (3H. aromatic H) ppm. (Found: C. 73·01; H. 5·44. $C_{18}H_{16}O_4$ requires: C. 72·96; H. 5·44%).

Methyl (±)-1-*methyl*-6-*oxo*-8-*ethylenedioxygibba*-A. 4b- *tetraene*-10β-*carboxylate* (XI)

To a soln of Xb (8·5 g) in dichloroethane (300 ml). ethylene glycol (20 ml) and *p*-TsOH (0·4 g) were added and the mixture was stirred and heated under reflux for 3 hr. During that period anhyd dichloroethane (600 ml) was gradually added while an equal amount of the water-containing solvent was distilled from it. After cooling, the soln was washed with K_2CO_3 aq, dried (K_2CO_3) and concentrated *in vacuo*. The residue dissolved in EtOAc (19 ml) was chromatographed over alumina (17 × 2·5 cm) in light petroleum. Elution with EtOAc-light petroleum (1:9, 1 l) gave 2·015 g (21%) of XI. Recrystallization from EtOAc-light petroleum gave needles. m.p. 196–197°; ν_{max} 1730. 1670. 1620. 1590 cm^{-1} (or 1745. 1715. 1655. 1620; polymorphism); δ 2·22 (3H. s). 3·78 (3H. s). 3·92 (4H. br. s). 4·11 (1H. s. C-10H). 6·14 (1H. s. C-5H). 7·15–7·45 (3H. aromatic H) ppm. (Found: C. 70·54; H. 5·96. $C_{20}H_{20}O_5$ requires: C. 70·57; H. 5·92%). Further elution with EtOAc gave 3·8 g (37%) of an *ester* **iv**. Recrystallization from EtOAc-light petroleum gave rods. m.p. 122–123°; ν_{max} 3650. 1725. 1655. 1625. 1600. 800. 790 cm^{-1}. (Found: C. 66·82; H. 6·22. $C_{20}H_{22}O_6$ requires: C. 67·02; H. 6·19%).

Methyl (±)-1-*methyl*-6ξ-*hydroxy*-8-*ethylenedioxy*-4bα-*gibba*-A-*triene*-10β-*carboxylate* (XII)

The ketal ester XI (842 mg) dissolved in EtOAc (80 ml) was hydrogenated over Raney nickel W-7 (3g) at 70° and an initial press of 40 kg/cm^2 for 7 hr. After cooling. the catalyst was removed by filtration and the filtrate was concentrated *in vacuo*. The residual oil (810 mg. 96%) crystallized after having left to stand overnight. Recrystallization from EtOAc-light petroleum gave needles. m.p. 113–114°; ν_{max} 3600. 1740. 1600. 780 cm^{-1}; δ 2·15 (3H. s). 3·80 (3H. s) ppm. (Found: C. 69·33; H. 7·03. $C_{20}H_{24}O_5$ requires: C. 69·75; H. 7·02%).

Methyl (±)-1-*methyl*-6-*oxo*-8-*ethylenedioxy*-4bα-*gibba*-A-*triene*-10β-*carboxylate* (XIII)

The alcohol XII (690 mg) dissolved in dry pyridine (10 ml) was added to the Sarett reagent prepared from CrO_3 (800 mg) and pyridine (10 ml). The mixture was left to stand overnight at room temp. poured into ice-water and extracted with C_6H_6-ether (1:1). The extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 467 mg (68%) of crystalline XIII. Recrystallization from EtOAc-light petroleum gave elongated prisms. m.p. 167–168°; ν_{max} 1740. 1705 cm^{-1}; δ 2·15 (3H. s). 3·78 (7H. br. s). 3·92 (1H. s). 6·80–7·30 (3H aromatic H) ppm. (Found: C. 70·19; H. 6·49. $C_{20}H_{22}O_5$ requires: C. 70·16; H. 6·48%).

(±)-1-*Methyl*-8-*oxo*-4bα-*gibba*-A-*triene*-10α-*carboxylic acid* [=(±)-7-*demethylepigibberic acid*, XIVa]

To a soln of XIII (420 mg) in diethylene glycol (20 ml). KOH aq (2g in 2 ml) and $N_2H_4.H_2O$ (2 ml) were added. The mixture was heated under reflux for 30 min. Then water and excess hydrazine were distilled off and the bath temp was gradually raised to 200° and kept there for 2·5 hr. After cooling. the mixture was diluted with water and extracted with ether to remove neutral by-products. The aqueous layer was acidified with dil HCl and heated on a boiling water bath for 10 min. After cooling, the ppt (XIVa) was collected on a filter (237 mg. 72%). Recrystallization from EtOAc-light petroleum gave prisms. m.p. 234–236°; ν_{max} ~3400–~2600. 1740 (br). 1600. 750 cm^{-1}; δ 2·28 (3H. s). ~3·60 (1H. m). 3·76 (1H. s. C-10 H). 6·85–7·15 (3H. aromatic H) ppm. (Found: C. 74·95; H. 6·81. $C_{17}H_{18}O_3$ requires: C. 75·53; H. 6·71%).

(±)-1-*Methyl*-7β-*hydroxy*-8aβ-*carboxymethyl*-9α-*carbomethoxy*-4bα, 5,6,7,8,8a-*hexahydrofluorene lactone* (IVb)

The acid XIVa (112 mg) was esterified with ethereal CH_2N_2 to give a methyl ester XIVb. ν_{max} 1730. 1600. 830 cm^{-1}. A soln of CF_3CO_3H was prepared from $(CF_3CO)_2O$ (1·3 ml) and 90% H_2O_2 (0·2 ml) in CH_2Cl_2 (2 ml). One ml of this soln was added to a mixture of Na_2HPO_4 (300 mg) and the ester XIVb (from 112 mg of XIVa) in CH_2Cl_2 (5 ml). The mixture was stirred and heated under reflux for 1 hr. After cooling, the mixture was diluted with CH_2Cl_2, washed with water, sat $NaHCO_3$ aq and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 27 mg of crystalline IVb. The mother liquor was chromatographed over alumina (8 × 1·5 cm) in ether. Elution with ether gave 44 mg of IVb. The total yield was 71 mg (61%). Recrystallization from EtOAc-light petroleum gave rods. m.p. 166–167°; ν_{max}(Nujol) 1720 (vs). 1600 (w). 1360 (m). 1340 (m), 1320 (m). 1300 (w). 1275 (w). 1210 (s). 1195 (s), 1180 (s), 1150 (s), 1095 (m), 1060 (m), 990 (s), 965 (m), 910 (w), 855 (w), 825 (w). 795 (m), 760 (m), 730 (w), 690 (w) cm^{-1}. This is very similar to but slightly different from that of the optically active IVb. ν_{max}($CHCl_3$) 1732 (vs). 1600 (w). 1370 (m). 1330 (m). 1310 (m). 1105 (w). 1090 (m) 990 (s). 965 (w) cm^{-1}. This is entirely identical with that of the optically active IVb. δ 2·22 (3H. s). 3·53 (1H, s). 3·69 (3H. s). 4·85 (1H. $W_{\frac{1}{2}}$ = 7Hz. C-7H). 6·85–7·30 (3H. aromatic H) ppm; MS (measured with a Hitachi RMU—6L spectrometer) 300 (M^+), 282, 241, 240, 199, 181, 156; TLC (Kieselegel G nach Stahl, EtOAc—C_6H_6 (1:9) as the solvent) R_f 0·12. The NMR. MS and TLC were identical with those of the optically active form. (Found: C. 71·87; H. 6·69. $C_{18}H_{20}O_4$ requires: C. 71·98; H. 6·71%).

Allogibberic acid (XVa). A suspension of II (15 g) in dil HCl (1:10, 200 ml) was vigorously stirred with a magnetic stirrer and heated at 55–65° for 2·25 hr. This vigorous stirring caused a remarkable increase in the yield of XVa.[cf 15] After cooling. the crystalline XVa was collected, washed with water and dried to give almost pure XVa hydrate (10·6 g. 80·6%). m.p. 125–130°. ν_{max} 3400, 2700, 2600. 2000. 1690. 1630. 1595. 900. 880 cm^{-1}. The IR spectrum was superimposable on that reported by Brian *et al.*[16]

Methyl allogibberate (XVb). This gummy ester was obtained from XVa by esterification with ethereal CH_2N_2. ν_{max} ~ 3400. 1735. 1660. 1595. 880 cm^{-1}; δ 2·18 (3H. s). 2·80 (1H. m). 3·77 (3H. s). 3·96 (1H. s. C-10 H). 4·80 (1H. s). 5·03 (1H. s). 6·92–7·20 (3H. m. aromatic H) ppm.

1-*Methyl*-8aβ-*carboxymethyl*-9β-*carbomethoxy*-4bα,5,6,7,8,8a-*hexahydrofluoren*-7-*one* (Vb)

(a) To a soln of XVb (10 g) in THF (280 ml)-water (95 ml), OsO_4 (200 mg) was added. After stirring for 5 min. finely powdered $NaIO_4$ (27·2 g) was added portionwise. The mixture was stirred at room temp for 2 days and filtered. The filtrate was extracted with benzene. The extract was concentrated *in vacuo*. The residue was dissolved in MeOH (400 ml) and mixed with $NaIO_4$ (20 g) in water (200 ml). The mixture was stirred at room temp for a day. concentrated *in vacuo*. diluted with water and extracted with benzene-ether (1:1). The product partly crystallized during the extraction and was collected on a Buchner funnel (2·3 g). The extract was washed with water and sat NaCl aq and concentrated *in vacuo* to give 3·3 g of Vb. The total yield of Vb was 5·6 g (53 %). Recrystallization from acetone-light petroleum gave prisms, m.p. 246–247°

(lit.[17] 239–241°); ν_{max} 3350. 1745. 1690. 1595 cm^{-1}; δ 2·17 (3H, s). 3·80 (3H. s). 3·82 (1H. s C-9H) ppm. (Found: C. 67·90; H. 6·42. Calcd. for $C_{18}H_{20}O_5$: 68·34; H. 6·37%).

(b). A mixture of XVb (1·0 g). OsO_4 (70 mg). $NaIO_4$ (7·0 g). MeOH (150 ml) and water (75 ml) was stirred for 5 days at room temp. Subsequent treatments gave 296 mg (28 %) of Vb. When this oxidation was carried out in THF-water. Vb could not be obtained.

1-*Methyl*-8aβ-*carbomethoxymethyl*-9β-*carbomethoxy*-4bα.5.6.7.8.8a-*hexahydrofluoren*-7-*one* (Vc)

The acid Vb was esterified with ethereal CH_2N_2. Recrystallization from EtOAc-light petroleum gave prisms, m.p. 210–212° (lit.[2,17] 205–207°); ν_{max} 1745, 1700, 1590, 1270, 1200, 1010 cm^{-1}; δ 2·15 (3H, s), 3·55 (3H. s). 3·74 (3H. s). 6·85–7·20 (3H. aromatic H) ppm. (Found: C. 69·34; H. 6·77. Calcd. for $C_{19}H_{22}O_5$: C. 69·07; H. 6·71%).

1-*Methyl*-7β-*hydroxy*-8aβ-*carboxymethyl*-9β-*carbomethoxy*-4bα.5.6.7.8.8a-*hexahydrofluorene lactone* (XVI)

The diester Vc (732 mg) dissolved in AcOH (75 ml) was hydrogenated over Adams's PtO_2 (250 mg) under atmospheric press at room temp for 6 hr. The mixture was left to stand overnight at room temp and filtered. The filtrate was concentrated *in vacuo*. The residue was triturated with MeOH to give 528 mg (80 %)of XVI. Recrystallization from EtOAc-light petroleum gave needles. m.p. 203–204° (lit.[2] 202–204°); ν_{max} 1730. 1590. 1215. 1200. 1180. 1150. 1110. 1000. 980. 780. 760 cm^{-1}; δ 2·18 (3H. s). 3·55 (1H. s. C-9H). 4·80 1H. s. $W_{\frac{1}{2}}$ = 7Hz, C-7 H), 6·85–7·20 (3H, aromatic H) ppm. (Found: C, 71·99; H, 6·70. Calcd. for $C_{18}H_{20}O_4$: C, 71·98; H. 6·71%).

1-*Methyl*-7β-*hydroxy*-8aβ-*carboxymethyl*-9α-*carboxy*-4bα.5.6.7.8.8a-*hexahydrofluorene lactone* (IVa)

(a). *By hydrolysis of* XVI. The lactonic ester XVI (200 mg) was suspended in NaOHaq (1·2 g in 15 ml) and the suspension was heated under reflux for 3 hr. The resulting homogeneous soln was cooled. acidified with dil HCl and extracted with ether. The ethereal extract was washed with sat NaCl aq. dried ($MgSO_4$) and concentrated to give 154 mg (81%) of crystalline IVa. Recrystallization from MeOH-EtOAc gave rods. m.p. 297–299°; ν_{max} ~3450–~2600. 1735. 1680. 1600. 1250. 1170. 1160. 1095. 1000. 780. 765 cm^{-1}. (Found: C. 70·82: H. 6·26. $C_{17}H_{18}O_4$ requires: C. 71·31; H. 6·34%).

(b). *By hydrogenation of* XVIIa. The diacid XVIIa (153 mg) dissolved in AcOH (20 ml) was hydrogenated over Adams's PtO_2 (100 mg) under atmospheric press at room temp for 6hr. Removal of the catalyst and the solvent gave a gum which gave 15 mg (10%) of IVa after trituration with ether. The identity was proved by mixed m.p. and IR.

1-*Methyl*-7β-*hydroxy*-8aβ-*carboxymethyl*-9α-*carbomethoxy*-4bα.5.6.7.8.8a-*hexahydrofluorene lactone* (IVb)

The acid IVa prepared from 528 mg of XVI was esterified with ethereal CH_2N_2 to give 468 mg (89 %) of IVb. Recrystallization from EtOAc-light petroleum gave prisms. m.p. 164–166° (lit.[2] 167–168°); ν_{max} 1725 (vs), 1600 (w), 1215 (s), 1210 (s), 1200 (s), 1000 (s), 780 (m) cm^{-1}. Other spectral data were identical with those of the racemate (Found: C. 72·10; H. 6·70. Calcd. for $C_{18}H_{20}O_4$: C. 71·98; H. 6·71 %).

1-*Methyl*-7β-*hydroxy*-8aβ-(β-*hydroxyethyl*)-9α-*hydroxymethyl*-4bα.5.6.7.8.8a-*hexahydrofluorene* (XVIII)

LAH (200 mg) was added to a soln of IVb (202 mg) in dry THF (15 ml). The mixture was stirred and heated under reflux for 1·5 hr. and stirred overnight at 30–40°. EtOAc was added to destroy the excess of LAH. After the addition of a small amount of sat NH_4Cl aq. the mixture was concentrated *in vacuo*. The residue was acidified with ice-cooled dil HCl and extracted with EtOAc (500 ml). The extract was washed with sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo* to give 135 mg (72%) of XVIII. Recrystallization from MeOH-EtOAc gave prisms. m.p. 229–230°; ν_{max} 3300. 1595. 1050. 1020. 950. 890. 750. 720 cm^{-1}. (Found: C. 73·60; H. 8·60. $C_{17}H_{24}O_3$ requires: C. 73·88; H. 8·75%).

1-*Methyl*-8aβ-*carboxymethyl*-9α-*carboxy*-4bα.5.6.7.8.8a-*hexahydrofluorene*-7-*one* (XVIIa)

(a) *By hydrolysis of* Vb. The half ester Vb (650 mg) was dissolved in KOH aq (5g in 25 ml) and left to stand at room temp for 2 days. Then the soln was acidified with dil HCl and extracted with ether. The extract was washed with water. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 410 mg (66 %) of XVIIa. Recrystallization from EtOAc-ether-light petroleum gave prisms, m.p. 260–263° dec. (lit.[17] 247–249°; lit.[2] 252–255°); ν_{max} 3450. ~2600. 1745. 1705. 1680. 1225. 1205. 1175. 1150. 1140. 795. 765 cm^{-1}; MS: 302 (M^+); TLC (Kieselgel G nach Stahl. C_6H_6-n-BuOH-AcOH. 70 : 25 :5) R_f 0·63. (Found: C. 67·25; H. 6·06. Calcd. for $C_{17}H_{18}O_5$: C. 67·54; H. 6·00%).

(b) *By oxidation of* XVIII. The Jones chromic acid (0·5 ml) was added to a soln of XVIII (103 mg) in acetone

(250 ml) at room temp. After 1 hr an additional amount of Jones chromic acid (0·1 ml) was added and the mixture was left to stand at room temp for 10 min. MeOH was added to destroy the excess oxidant. The mixture was concentrated *in vacuo*. The residue was diluted with water and extracated with EtOAc. The extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residual gum in $CHCl_3$ (5 ml) was chromatographed over silicic acid (Mallinckrodt. AR 100 mesh, 9·5 × 1·5 cm) in benzene to give the following fractions (50 ml each). No. 1–4 ($CHCl_3$–C_6H_6, 1:1): none. No. 5–10 ($CHCl_3$): 19 mg of IVa. No. 11, 12 ($CHCl_3$–AcOH, 99:1); 10 mg of IVa. No. 13–15 ($CHCl_3$–AcOH, 99:1); none. No. 16–21 ($CHCl_3$–AcOH, 99:1) 53 mg of XVIIa. This was identified with an authentic sample by mixed m.p., IR, MS and TLC.

The anhydride (XIX) *of* 1-*methyl*-8aβ-*carboxymethyl*-9β-*carboxy*-4bα.5.6.7.8.8a-*hexahydrofluoren*-7-*one* (Va)

(a) *From* Va. The procedure described[17] was exactly followed to yield XIX. Recrystallization from acetone-EtOAc gave prisms. m.p. 288–290° dec (lit.[17] 285-287°); ν_{max} 1815. 1765. 1705. 1595. 1120. 1100. 1070. 930 cm^{-1}. TLC (Kieselgel G. CH_2Cl_2) R_f 0·52. (Found: C. 71·71; H. 5·72. Calcd. for $C_{17}H_{16}O_4$: C. 71·82; H. 5·67%).

(b) *From* XVIIa. A soln of XVIIa (1·173 g) in Ac_2O (20 ml) was heated under reflux for 3·5 hr. The soln was concentrated *in vacuo*. The residue dissolved in acetone-ether slowly deposited XIX (38 mg). This was recrystallized from acetone-EtOAc and identified with an authentic sample by mixed m.p., IR and TLC. Grove and Mulholland obtained 11 mg of XIX from 75 mg of XVIIIa.[2]

Benzyl 1-*methyl*-7-*oxo*-9β-*carboxy*-4bα.5.6.7.8.8a-*hexahydrofluoroen*-8aβ-*ylacetate* (Vd)

A suspension of XIX (51 mg) in benzyl alcohol (3 ml) was heated under reflux for 15 min. The resulting soln was concentrated *in vacuo* to yield gummy Vd. ν_{max} ~3400–~2600. 1735. 1700 cm^{-1}. This was employed for the next step without further purification.

Benzyl 1-*methyl*-7-*oxo*-9β-*carbomethoxy*-4bα.5.6.7.8.8a-*hexahydrofluoren*-8aβ-*ylacetate* (Ve)

The acid Vd (from 51 mg of XIX) was esterified with ethereal CH_2N_2 and the product was chromatographed over Al_2O_3 (5·5 × 1·5 cm) in light petroleum. Elution with light petroleum EtOAc (9:1) gave 48 mg (64% from XIX) of Ve as a gum. ν_{max} 1735, 1705, 1595, 1195, 1150, 730 cm; δ 2·13 (3H, s), 3·65 (3H, s), 4·67, 4·95 (2H, s), 6·85–7·20 (3H, m, aromatic H), 7·30 (5H, s) ppm. This was employed for the next step without further purification.

1-*Methyl*-8aβ-*carboxymethyl*-9β-*carbomethoxy*-4bα.5.6.7.8.8a-*hexahydrofluoren*-7-*one* (Vb)

The gummy ester Ve (47 mg) dissolved in EtOAc (20 ml) was hydrogenated over 10% Pd-C (300 mg) under atmospheric pressure for 2·5 hr at room temp. The catalyst was removed by filtration and the filtrate was concentrated *in vacuo* to give 27 mg of semi-solid mass. This was dissolved in EtOAc (1 ml) and chromatographed over silicic acid (Mallinckrodt AR 100 mesh, 5 × 1·0 cm) in $CHCl_3$. Elution with $CHCl_3$ (80 ml) gave 16 mg (46%) of pure crystalline Vb. This was recrystallized from EtOAc-light petroleum and identified with an authentic sample by mixed m.p. and IR. The following MS and TLC data were also identical with those of authentic Vb. MS: 316 (M^+); TLC (Kieselgel G nach Stahl. C_6H_6-n-BuOH-AcOH. 70:25:5) R_f 0·66.

The diketone (XX)

A suspension of Vb (5·4 g) in Ac_2O (260 ml) was stirred and heated under reflux for 3·5 hr. The resulting soln was concentrated *in vacuo*. The residual semi-solid was dissolved in EtOAc. The EtOAc soln was washed with sat $NaHCO_3$ aq and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 3·5 g (69%) of XX. The highest yield was 97% (713 mg of XX from 773 mg of Vb). Recrystallization from EtOAc-light petroleum gave rhombs. m.p. 192–194° (lit.[21] 191–193°); ν_{max} 1735. 1720. 1705. 1275. 1260. 1235. 1210. 1045. 1010. 785 cm^{-1}; δ 2·19 (3H. s). 2·4–3·0 (4H. m). ~3·25 (2H. m). 3·80 (3H. s). 3·96 (1H. s. C-10 H). 7·0–7·3 (3H. m. aromatic H) ppm; ORD: negative Cotton effect curve. $[\phi]_{332nm}$ −3400°. peak; $[\phi]_{288}$ +3400°. trough; $[\phi]_{230}$ +5300°. trough. CD: $[\theta]_{314nm}$ −2700 (EtOH soln. c=0·06). (Found: C. 72·16; H. 6·09. Calcd. for $C_{18}H_{18}O_4$: C. 72.46; H. 6·08%).

The acetoxy lactol (v)

BF_3-etherate (0·2 ml) was added to a soln of Vb (505 mg) in AcOH (20 ml) containing Ac_2O (2 ml) and the soln was left to stand overnight at room temp. The mixture was poured into water and extracted with

ether. The ethereal extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo* to give 492 mg (84%) of v. Recrystallization from EtOAc gave needles. m.p. 175–176°; ν_{max} 1745 (sh). 1740. 1730. 1240. 1220. 1205. 1125. 1115. 1000. 772 cm^{-1}; δ 2·13 (3H. s). 2·18 (3H. s). 3·82 (3H. s). 3·84 (1H. s). 6·95–7·22 (3H. m. aromatic H) ppm. (Found: C. 67·08; H. 6·22. $C_{20}H_{22}O_6$ requires: C. 67·02; H. 6·19%).

Zinc-acetie acid reduction of XX

Production of methyl 1-methyl-7β-hydroxy-8-oxo-4bα.7α-gibba-A-triene-10β-carboxylate (XXI). *methyl 1-methyl-7α-hydroxy-8-oxo-4bα-gibba-A-triene-10β-carboxylate* (XXII) *and a ketol* (XXIII). Zn dust (120 g) was added portionwise to a stirred and refluxing soln of XX (3·4 g) in AcOH (360 ml) containing water (12 ml) during 2 hr. After the addition. the mixture was stirred and heated under reflux for 1·5 hr. The hot mixture was filtered and the solid [Zn and $Zn(OAc)_2$] remaining was thoroughly washed with EtOAc. The combined filtrate and washings were concentrated *in vacuo*. The residue was diluted with water and extracted with ether. The ethereal soln was washed with water. sat $NaHCO_3$ aq and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. Trituration of the residue with ether gave 1·6 g (47%) of crystalline XXI. Recrystallization from ether-light petroleum gave prisms. m.p. 145–146°; ν_{max} 3520. 1740. 1600. 1150. 1110 cm^{-1}; δ 1·38. 1·50. 2·00. 2·04. 2·20 (3H. s). 2·27. 2·35. 2·39. 2·45. 2·63. 2·66. 2·75 (1H. s. –OH. area decreased after D_2O addition). 3·05 (1H. br. m). 3·80 (3H. s). 4·18 (1H. s. C-10H). 7·02–7·25 (3H. m. aromatic H) ppm; ORD: negative Cotton effect curve. $[\phi]_{328nm}$ −800°. peak; $[\phi]_{286}$ +1260°. trough; $[\phi]_{228}$ +3200°. second trough. CD: $[\theta]_{310nm}$ −830 (EtOH soln. c = 0·07). (Found: C. 71·57; H. 6·75. $C_{18}H_{20}O_4$ requires: C. 71·98; H. 6·71%).

The mother liquor (1·8 g) was chromatographed over alumina (20 × 2·5 cm) in benzene to give the following fractions (200 ml each). No. 1,2 (C_6H_6): oil (9 mg). No. 3 (C_6H_6-MeOH. 100:1) oil (26 mg). No. 4 (C_6H_6-MeOH. 100:1): gum (1·427 g). No. 5 (C_6H_6-MeOH. 50:1): gum (161 mg). No. 6 (C_6H_6-MeOH. 50:1): oil (62 mg). No. 7 (C_6H_6-MeOH, 50:1): oil (23 mg). Trituration of the 4th fraction (1·427 g) with ether gave 225 mg (6·6%) of crystalline XXII. Recrystallization from ether gave needles. m.p. 130–132° (lit.[17] 130–132°); ν_{max} 3520. 1745. 1715. 1280. 1270. 1010 cm^{-1}; δ 1·48–2·15 (6H. m) 2·19 (3H. s). ~2·30 (2H. m). 2·95 (1H. s. –OH. area decreased after D_2O addition). 3·05 (1H. br. m). 3·81 (3H. s). 4·05 (1H. s. C-10 H). 6·96–7·25 (3H, m. aromatic H) ppm; ORD: positive Cotton effect curve, $[\phi]_{324nm}$ + 2400°, peak; $[\phi]_{275}$ − 7000°. trough. CD: $[\theta]_{307nm}$ + 3500 (EtOH soln. c = 0·07). This was identified with an authentic sample by mixed m.p. and IR. (Found: C. 71·63; H. 6·69. Calcd. for $C_{18}H_{20}O_4$: C. 71·98; H. 6·71%). The mother liquor obtained after removal of XXII slowly deposited 39 mg (1·1%) of XXI. identified with an authentic sample by mixed m.p. and IR. Trituration of the 5th fraction (161 mg) with ether gave 51 mg (1·5%) of XXIII. Recrystallization from EtOAc-light petroleum gave rhombs. m.p. 193–194°; ν_{max} 3500. 1730. 1710. 1585. 1190. 1160. 1010. 795 cm^{-1}; δ ~1·60–~2·10 (4H. m). 2·18 (3H. s). ~2·25–~2·80 (3H. m). 3·05 (1H. m). 3·78 (3H. s). ~3·78 (1H. C-10 H). 4·50 (1H. m. J = 18 Hz). 6·97–7·25 (3H. m) ppm; CD: $[\theta]_{300nm}$ −330; $[\theta]_{228}$ +2100 (EtOH soln. c = 0·07). (Found: C. 71·97; H. 6·70. $C_{18}H_{20}O_4$ requires: C. 71·98; H. 6·71%).

Periodate oxidation of the ketol (XXI)

$NaIO_4$ aq (1 g in 20 ml) was added to a soln of XXI (104 mg) in MeOH (40 ml) and the mixture was stirred overnight at room temp. MeOH was removed *in vacuo* and the residue was extracted with ether. The ethereal extract was washed with water and sat $NaHCO_3$ aq. dried ($MgSO_4$) and concentrated *in vacuo* to give a neutral gum (16 mg). $NaHCO_3$ aq. dried ($MgSO_4$) and concentrated *in vacuo* to give a neutral gum (16 mg). $NaHCO_3$ soln was acidified with dil HCl and extracted with ether. The extract was washed with water and sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo* to give a gum (76 mg). This was triturated with ether to give 40 mg (37%) of *1-methyl-8aα-carboxymethyl-9β-carbomethoxy-4bα.5.6.7.8.8a-hexahydrofluoren-7-one* (XXXIVa). Recrystallization from EtOAc-light petroleum gave rods. m.p. 154–155°; ν_{max} ~3400. 2600. 1715. 1685. 1595. 1210. 1195. 1160. 775 cm^{-1}; δ 2·19 (3H. s). ~2·25–~2·80 (8H). 3·38 (1H. m). 3·72 (3H. s). 4·25 (1H. s. C–9 H). 7·05–7·30 (3H. m. aromatic H). ~8·1 (1H. br) ppm. (Found: C. 68·55; H. 6·42. $C_{18}H_{20}O_5$ requires: C. 68·34; H. 6·37%).

1-Methyl-8aα-carboxymethyl-9β-carboxy-4bα.5.6.7.8.8a-hexahydrofluoren-7-one (XXIVb)

(a) *From* XXIVa. The half ester XXIVa (68 mg) was dissolved in NaOH aq (0·6 g in 5 ml) and the soln was stirred and heated under reflux for 2 hr. It was diluted with water. acidified with dil HCl and extracted with ether. The extract was washed with sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was triturated with ether to give 36 mg of XXIVb. Recrystallization from acetone-light petroleum gave prisms. m.p. 216–218°; ν_{max} ~3200. ~2600. 1725. 1670. 1290. 1160. 790. 680 cm^{-1}. This was identified with an

authentic sample prepared as described below by mixed m.p. and IR. (Found: C, 67·23; H, 6·15, Calcd. for $C_{17}H_{18}O_5$: C. 67·54; H. 6·00%).

(b) *From* XX. According to the procedure reported by Cross *et al.*[21] XX (99 mg) was treated with base to give 61 mg of XXIVb. Recrystallization from acetone-light petroleum gave a pure sample. m.p. 214–215° (lit.[21] 214–216°).

Methyl gibberate (XXV)

This was prepared by the method of Cross[15]. m.p. 112–113° (lit.[15] 113–115°): ν_{max} 1735. 1720. 1595. 1260. 1030. 760. 730. 690 cm^{-1}; δ 1·08 (3H. s). 1·16. 1·29. ~1·60–~2·15 (~6H). 2·18 (3H. s). ~2·60 (2H. br). 3·02 (1H. br). 3·80 (3H. s). 4·17 (1H. s. C-10 H). 7·00–7·26 (3H. m. aromatic H) ppm; ORD: negative Cotton effect curve. $[\phi]_{324nm}$ −5300°. peak; $[\phi]_{280}$ + 8700°. trough; $[\phi]_{228}$ + 23000°. trough. CD: $[\theta]_{300nm}$ −5700 (EtOH soln. c = 0·08).

Oxidation of the ketol (XXIII) to the diketone (XX)

Jones chromic acid reagent (0·05 ml) was added to a soln of XX (24 mg) in acetone (3 ml). After 3 min at room temp. MeOH was added to destroy the excess of the oxidant. The mixture was concentrated *in vacuo*. The residue was diluted with water and extracted with EtOAc. The extract was washed with sat NaCl aq, dried ($MgSO_4$) and concentrated to give mg (79%) of XX. This was identified with an authentic sample by mixed m.p. and IR.

(—)-*Epiallogibberic acid* (VI)

A soln of triphenylmethylene phosphorane was prepared from triphenylmethylphosphonium bromide (5·2 g) and t-BuOK (from 0·5 g of K) in dry THF (40 ml) and t-BuOH (20 ml) by stirring and heating under reflux under N_2. A soln of XXI (501 mg) in dry THF (10 ml) was added to the cooled and stirred Wittig reagent. After the addition the mixture was stirred and heated under reflux for 3 hr. Then it was concentrated *in vacuo*. The residue was dissolved in MeOH (30 ml) and mixed with NaOH aq (3·0 g in 30 ml). The soln was stirred and heated under reflux for 2 hr. concentrated *in vacuo*. diluted with water and extracted with benzene. The benzene layer was extracted with dil NaOH aq. The combined alkaline aqueous extract was acidified with dil HCl and extracted with EtOAc. The extract was washed with sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo* to give a gum (146 mg). This was triturated with ether to afford 43 mg (8·6%) of crystalline VI. Recrystallization from MeOH gave prisms. m.p. 240–242° (dec); ν_{max} 3450 (s). ~3200–~2600. 1680 (s). 1595 (w). 1340 (m). 1290 (w). 1250 (m). 1220 (s). 1205 (s). 1190 (m). 1160 (m). 1150 (m). 1140 (w). 1115 (m). 1090 (m). 1080 (w). 1060 (m). 1050 (m). 1020 (w). 1000 (w). 970 (w). 950 (w). 900 (s). 800 (m). 760 (m) cm^{-1}; MS: 284 (M^+). 268. 255. 239. 238. 223. 221. 209. 195. 181. 180. 179. 169. 165. 155; ORD: plain negative curve with a minimum at 236 nm. $[\phi]_{236nm}$ − 24000°; CD: $[\theta]_{230nm}$ − 20000 (EtOH soln. c = 0·02); TLC (Kieselgel G nach Stahl. C_6H_6-*n*-BuOH-AcOH, 70:25:5) R_f 0·64. (Found: C. 76·67; H. 7·35. $C_{18}H_{22}O_3$ requires: C. 76·48; H. 7·43%).

(+)-*Epiallogibberic acid* (I)

This was prepared from II[2]. Recrystallization from MeOH gave prisms. m.p. 242–244° (lit.[17] 244°); ORD: plain positive curve with a minimum at 236nm. $[\phi]_{236nm}$ + 16000°; CD: $[\theta]_{230nm}$ + 15000 (EtOH soln. c = 0·13). The IR. MS and TLC were identical with those of the (−)-isomer. (Found: C. 75·80; H. 7·20. Calcd. for $C_{19}H_{22}O_3$: C. 76·48; H. 7·43%).

Methyl (+)-*epiallogibberate* (I. CO_2Me *instead of* CO_2H)

This gummy ester was prepared from I by esterification with CH_2N_2: ν_{max} ~3500. 1725. 1660. 1600. 1240. 1150, 920. 890. 800. 760. 725 cm^{-1}; δ 1·08–2·15 (6H, m), 2·25 (3H, s), 2·40–2·90 (2H, m), 3·42 (1H, m), 3·65 (3H, s), ~3·65 (1H. s. C-10 H). 5·08 (1H. br. s). 5·20 (1H. br. s). 7·00–7·25 (3H. m. aromatic H) ppm.

C-10 *Epimer* (via) *of allogibberic acid*

(a) *From* XXI. To a soln of XXI (500 mg) in MeOH (15 ml). NaOH aq (3·6 g in 15 ml) was added and the mixture was left to stand overnight at room temp. MeOH was removed *in vacuo*. The residue was acidified with dil HCl and extracted with EtOAc. The EtOAc soln was washed with sat NaCl aq. dried ($MgSO_4$) and concentrated *in vacuo*. The residue was dissolved in dry C_6H_6 and concentrated to remove the remaining trace of water. This gummy acid. ν_{max} ~3500. ~2600. 1750. 1700. 1600 cm^{-1}. dissolved in dry THF (10 ml) was added to a Wittig reagent prepared from triphenylmethylphosphonium bromide (5·2 g) and t-BuOK

(from 0·5 g of K) in t-BuOH (20 ml)-dry THF (40 ml). The mixture was stirred and heated under reflux for 3 hr and then concentrated *in vacuo*. Benzene and sat $NaHCO_3$ aq were added to the residue with shaking. The aqueous layer was separated, acidified with dil HCl and extracted with EtOAc. The extract was washed with sat NaCl aq, dried ($MgSO_4$) and concentrated *in vacuo* to give 382 mg of crude oily product. This was chromatographed over silicic acid (Mallinckrodt AR 100 mesh, 15 × 1·5 cm) to give the following fractions (50 ml each). No. 1–4 ($CHCl_3$): none. No. 5–7 ($CHCl_3$-EtOAc, 9:1): gum (12 mg). No. 8 (same eluant): semi-solid (5 mg). No. 9.10 (same eluant): crystalline mass (23 mg). This was identified as (−)-epiallogibberic acid (VI) by mixed m.p. and IR. No. 11–16 (same eluant): gum (146 mg). ν_{max} ~3500, ~2600, 1705, 1600, 1040, 890 cm^{-1}. This IR was almost identical with that of an authentic sample of via. The corresponding *methyl ester* vib was also a gum, ν_{max} 3500, 1725, 1665, 1600, 1340, 1240, 1200, 1160, 1050, 880 cm^{-1}; δ 2·25 (3H, s), 3.35 (1H, br.) 3·65 (1H, s, C-10 H), 3·69 (3H, s), 4·78 (1H, br, s), 5·04 (1H, br, s), 6·95–7·22 (3H, m, aromatic H) ppm. These IR and NMR data were identical with those of an authentic sample of vib except for some small differences in weak absorptions.

(b) *From* XVb. According to the reported procedure,[2] XVb was hydrolyzed with base to give gummy **via**. This was esterified with CH_2N_2 to give gummy **vib**.

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