Synthesis of Compounds related to Gibberellins. Part I. Methyl 3-Methoxy-6β-methyl-16-methylene-9α*H*-gibba-1(10),2,4-triene-4-carboxylate

By **A. J. Baker,* J. Brown,** and **R. A. Raphael,** Department of Chemistry, University of Glasgow, Glasgow W.2

Terracinoic acid (4-carboxy-5-hydroxy-3-methyl-1-oxoindan-2-ylacetic acid) (I) has been elaborated, in a stereoselective manner, to methyl 3-methoxy-6β-methyl-16-methylene-9α*H*-gibba-1(10),2,4-triene-4-carboxylate (XVI). An alternative method for removal of a C-12 carbonyl group in 12,16-dioxogibbanes involving selective reduction of the 16-oxo-function is reported.

ONE of the most promising routes to the complex problem of the synthesis of the gibberellin family of plant hormones [1] has been that starting from an indanone in an AB ⟶ C ⟶ D approach. One of the main difficulties of this approach is the unavailability of a suitably substituted indanone. However, terracinoic acid [2] (I), an indane readily available from the degradation of terramycin, was eminently suitable, by virtue of its multifunctionality, for synthesis of a tetracyclic structure appropriate for further transformation to a gibberellin. This paper describes this modification of terracinoic acid in the desired manner to give methyl 3-methoxy-6β-methyl-16-methylene-9α*H*-gibba-1(10),2,4-triene-4-carboxylate (XVI).†

Dimethyl terracinoate methyl ether (II), also readily available from terramycin [2] in 32% yield, was shown to have the *trans*-disposition of the C-2 and C-3 substituents as indicated by the coupling (J 2 Hz; $\theta \sim 115°$) of 3-H with 2-H. Annulation [3] of the ester (II) with methyl vinyl ketone in the presence of sodium methoxide smoothly afforded the tricyclic keto-acid (III; 80%) by participation of the ester function in the annulation sequence; [3] the postulated aldol lactone intermediate has been isolated in two cases.[4] The 9β–9aβ stereochemistry assigned to the acid (III) is based on the

† All asymmetric synthetic products described are racemic mixtures. Only one enantiomer is drawn for each; nomenclature is for the enantiomer depicted.

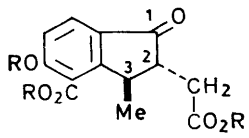
[1] N. Ya. Gregor'eva and V. F. Kucherov, *Russ. Chem. Rev.*, 1966, **35**, 850; J. van Overbeek, *Science*, 1966, **152**, 721.

[2] R. Pasternack, L. H. Conover, A. Bavley, F. A. Hochstein, G. B. Hess, and K. J. Brunings, *J. Amer. Chem. Soc.*, 1952, **74**, 1928.

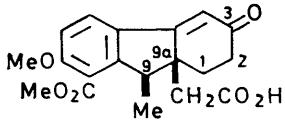
[3] (*a*) H. J. E. Loewenthal and Z. Neuwirth, *J. Org. Chem.*, 1967, **32**, 517; (*b*) K. Mori, M. Matsui, and Y. Sumiki, *Agric. and Biol. Chem. (Japan)*, 1963, **27**, 537.

[4] A. A. Shegolev and V. F. Kucherov, *Izvest. Akad. Nauk S.S.S.R., Ser. Khim.*, 1969, 1572 (*Chem. Abs.*, 1969, **71**, 112,486*k*); G. Stork and F. H. Clarke, jun., *J. Amer. Chem. Soc.*, 1961, **83**, 3114.

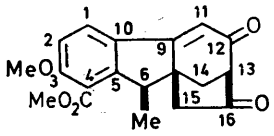
assumption that addition of the vinyl ketone to the planar anion is controlled by the 3β-methyl group in (II) and takes place from the less hindered α face of the



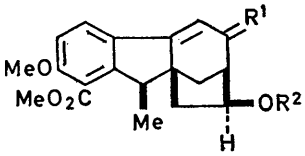
(I) R = H
(II) R = Me



(III)



(IV)



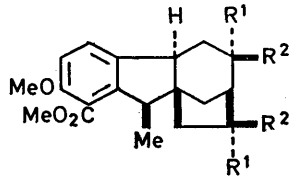
(V) R^1 = O, R^2 = H
(VI) R^1 = O, R^2 = Ac
(VII) R^1 = H, OH, R^2 = H

molecule.[5] Keto-acid (III), on treatment with naphthalenesulphonic acid in toluene,[3a] cyclised in high yield to the bridged-ring diketone (IV),[6] the structure of which followed from its spectroscopic characteristics.

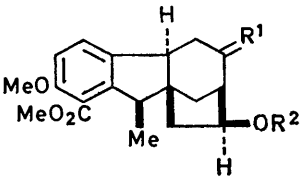
The removal of the enone system from related compounds has hitherto involved selective acetalisation of the cyclopentanone carbonyl group followed by Wolff–Kishner reduction and hydrogenation.[4,5] As in previous examples the yields in the acetalisation of (IV) were consistently poor as a result of competitive ring opening of the non-enolisable β-diketone system to afford ethylene glycol esters of the keto-acid (III).

This difficulty has been circumvented by employing an alternative scheme. Controlled reduction of diketone (IV) with sodium borohydride in dioxan effected selective reduction of the cyclopentanone carbonyl group, the reaction time for optimum yields (75%) of ketol (V) being 140 s! The unstable ketol on acetylation with acetic anhydride–pyridine gave the crystalline keto-acetate (VI) [70% from (IV)] as a single epimer, shown to be the 16β-acetate by the observation of strong intramolecular hydrogen bonding in the i.r. spectrum of ketol (V). The same keto-acetate could also be prepared by reduction of diketone (IV) with an excess of sodium borohydride to a mixture of the C-12 epimeric diols (VII), followed by oxidation with manganese dioxide to the ketol (V) and subsequent acetylation. The saturated diketone (IX) (*vide infra*), however, on reduction with sodium borohydride gave a mixture of C-12 epimeric diols in the ratio 95 : 5, the major diol, m.p. 168—168·5°, showed strong intramolecular hydrogen bonding and formed a sulphite ester in high yield and was accordingly assigned the 12β,16β-diol structure (X).

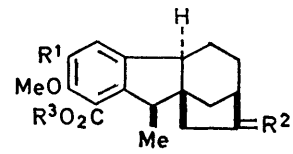
Initial attempts to remove the enone system from (VI) by thioacetalisation and obvious consequent steps failed owing to our inability to form the thioacetal. Accordingly the keto-acetate (VI) was first reduced



(IX) R^1 = R^2 = O
(X) R^1 = H, R^2 = OH



(VIII) R^1 = O, R^2 = Ac
(XI) R^1 = S·CH_2·CH_2·S, R^2 = Ac
(XII) R^1 = H_2, R^2 = Ac
(XIII) R^1 = H_2, R^2 = H

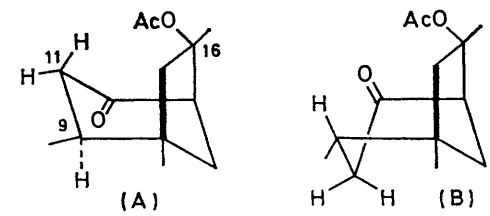


(XIV) R^1 = H, R^2 = O, R^3 = Me
(XV) R^1 = Cl, R^2 = O, R^3 = Me
(XVI) R^1 = H, R^2 = CH_2, R^3 = Me
(XVII) R^1 = R^3 = H, R^2 = O

catalytically over palladium–charcoal (30%). Under these conditions, reduction of the 12-keto-group was as rapid as that of the 9,11-double bond and accordingly the crude hydrogenation product was oxidised with Jones reagent to afford a single saturated keto-acetate (VIII) in 95% overall yield.

By analogy with the reduction of $\Delta^{9(11)}$-gibberellin derivatives which results in the epimer having 9-H *α-trans* to the 6β-carboxy-group [5,7,8] it was considered that the acetate (VIII) had the unnatural configuration at C-9, *i.e.* α-H. That the 16β-acetoxy-group in (VI) did not influence the steric course of hydrogenation followed from catalytic hydrogenation of the unsaturated diketone (IV) to the saturated diketone (IX), which was identical in all respects with (IX) prepared from keto-acetate (VIII) by methanolysis and Jones oxidation.

More conclusive evidence for the 9α-configuration in (VIII) and (IX) was obtained from the observed solvent



FIGURE

shifts in the n.m.r. spectra of diketone (IX) and keto-acetate (VIII). In the spectrum of the diketone (IX) in deuteriobenzene, upfield shifts were observed for, *inter*

[5] K. Mori, M. Shiozaki, N. Itaya, M. Matsui, and Y. Sumiki, *Tetrahedron*, 1969, **25**, 1293.
[6] Gibberellane numbering, M. F. Barnes, R. C. Durley, and J. MacMillan, *J. Chem. Soc.* (*C*), 1970, 1341.
[7] H. J. E. Loewenthal and S. K. Malhotra, *J. Chem. Soc.*, 1965, 990.
[8] J. F. Grove, J. MacMillan, T. P. C. Mulholland, and W. B. Turner, *J. Chem. Soc.*, 1960, 3049.

alia, the protons at C-9 (τ 6·7 ⟶ 7·44), C-11 (τ 6·0 ⟶ 8·2), C-6 (τ 6·7 ⟶ 7·3), and C-14 (τ 7·65 ⟶ 8·5). In keto-acetate (VIII) similar shifts were observed for these protons with the sole exception of one of the C-11 protons which, owing to the deshielding effect of the 16β-acetoxy-group, still resonated at τ 7·3. Such deshielding of the axial 11-H is possible only if ring C adopts a chair conformation (A) (see Figure) with the 9α-H *trans* oriented with respect to the ethano-bridge. The C-9 epimer (B) requires ring C to adopt a boat conformation in which case 9β-H and not the equatorial 11-H would have been deshielded. Removal of the 12-keto-group from keto-acetate (VIII) to furnish acetate (XII) was accomplished readily by thioacetalisation in acetic acid with ethanedithiol in the presence of boron trifluoride–ether,[9] followed by desulphurisation of the derived thioacetal (XI) with freshly prepared Raney nickel W-2 [10] in methanol–dioxan under reflux. The 16β-acetate (XII) was converted into the ketone (XIV), in high yield, by acid-catalysed methanolysis followed by Jones oxidation of the oily alcohol (XIII). In one large scale preparation of the ketone (XIV) by the above sequence from the thioacetal (XI), the chloroketone (XV) was isolated as a major by-product. This was thought to derive from carbon tetrachloride, from which the thioacetal (XI) was crystallised. The chloroketone (XV) was readily converted into the ketone (XIV) by hydrogenolysis. Reaction of the ketone (XIV) with methylenetriphenylphosphorane [11] furnished the corresponding methylene compound (XVI) in excellent yield, the structure of which was confirmed by the presence of a broad doublet (*J* 13 Hz) for the vinylic protons (τ 5·3) in its n.m.r. spectrum. The further elaboration of (XVI) toward a gibberellin structure involves manipulation to correct the BC-stereochemistry and the transformation of the 6-methyl group to a carboxy-group. Many attempts were made to functionalise the methyl group but all methods so far have proved abortive.

EXPERIMENTAL

Light petroleum refers to the fraction of b.p. 40—60°. Thin layer chromatoplates were spread with Merck Kieselgel G and developed in ethyl acetate–light petroleum. Preparative chromatoplates were spread with Merck Kieselgel HF 254. Analytical g.l.c. data were obtained on Pye Argon and Perkin-Elmer F11 chromatograms using 1% SE-30 and 1% QF-1 columns at 225°. Combined g.l.c.–m.s. analyses were obtained on an LKB 9000A spectrometer; mass spectra were determined on an AEI MS12 spectrometer. N.m.r. spectra were recorded on Perkin-Elmer R-10 and Varian HA 100 spectrometers with dilute solutions in deuteriochloroform and tetramethylsilane as internal reference. Routine i.r. spectra were run on Pye Unicam SP 200 and Perkin-Elmer 257 spectrophotometers; solution spectra were recorded with a Unicam SP 100 Mark II or Perkin-Elmer 225 spectrophotometer by Mrs. F. Lawrie. U.v. spectra were measured for methanolic solutions on a Pye Unicam SP 800 spectrophotometer. Microanalyses were by Mr. J. M. L. Cameron and his staff. All m.p.s are uncorrected.

Terracinoic Acid [2] (*4-Carboxy-5-hydroxy-3-methyl-1-oxoindan-2-ylacetic Acid*) (I).—Terramycin hydrochloride (100 g) was converted into the dihydrate of the free base, which was degraded by the method of Pasternack *et al.*[2] to yield prisms of terracinoic acid (26 g; 46%), m.p. 232—234° (decomp.; sealed tube) (from ethyl acetate), $\lambda_{max.}$ 216 (ε 12,450), 241 (12,620), and 282 nm (8950), $\nu_{max.}$ (Nujol) 3500—2500, 1710, 1680, and 1580 cm^{-1}.

Dimethyl Terracinoate Methyl Ether [2] (*Methyl 5-Methoxy-4-methoxycarbonyl-3-methyl-1-oxoindan-2-ylacetate*) (II).—Terracinoic acid (I) (20·0 g) in dioxan (400 ml) was treated with a large excess of ethereal diazomethane. After 24 h, the excess of diazomethane was destroyed with acetic acid, and the solution was evaporated to dryness. Chromatography of the crude product on silica (1 kg) gave on elution with chloroform (2·2 l) the title compound (16·0 g) as needles, m.p. 85—86° (sealed tube) (from ether–light petroleum (lit.,[2] 83—84°), $\nu_{max.}$ ($CHCl_3$) 1732, 1710, and 1575 cm^{-1}, $\lambda_{max.}$ 210 (ε 15,500), 228 (22,200), 268 (15,700), and 292 nm (9050), τ 2·23 and 3·04 (2H, q, *J* 8 Hz), 6·65 (1H, octet, *J* 2 and 7 Hz), 6·09 (3H, s), 6·32 (3H, s), 7·0—7·45 (3H, complex multiplet), and 8·63 (3H, d, *J* 7 Hz) (Found: C, 63·1; H, 5·9. Calc. for $C_{16}H_{18}O_6$: C, 62·75; H, 5·9%).

[*1,2,3,9a-Tetrahydro-7-methoxy-8-methoxycarbonyl-9β-methyl-3-oxo-9aβ-fluorenyl*]*acetic Acid* (III).—Dimethyl terracinoate methyl ether (II) (3·0 g) in dry benzene (20 ml) was added to a solution of sodium (1·18 g) in dry methanol (50 ml) with stirring at 0° under nitrogen. Redistilled but-3-en-2-one (2·31 g) in methanol (5 ml) was added dropwise during 20 min, after which the mixture was left overnight to reach room temperature. After acidification with acetic acid, the mixture was evaporated almost to dryness and water and chloroform were added. The chloroform extract was extracted several times with ice-cold aqueous sodium carbonate solution (5%). The combined carbonate extracts were acidified (aq. HCl) under benzene, and twice extracted with chloroform. The combined organic extracts were washed (brine), dried, and evaporated, yielding a light yellow foam (3·17 g), which on crystallisation from methanol afforded the *acid* (III) as bright yellow prisms (2·71 g), m.p. 111—112° (sealed tube), $\nu_{max.}$ (Nujol) 3500—2600 (CO_2H), 1725 (ester CO), 1640 (enone CO), 1630, 1600, 1576, 880, and 830 cm^{-1}, $\lambda_{max.}$ 248 (ε 9700), 301sh (12,600), and 328 nm (20,400), τ 2·44 and 3·13 (2H, quartet, *J* 8 Hz), 3·60 (1H, s, 4-H), 6·11 (3H, s, OMe), 6·16 (3H, s, OMe), 6·55 (3H, s, MeOH of crystallisation; disappears on D_2O extraction), 7·85 (1H, q, *J* 7 Hz, 9-H), and 8·68 (3H, d, *J* 7 Hz, CH_3·CH) (Found: C, 64·0; H, 6·45. $C_{19}H_{20}O_6$,MeOH requires C, 63·8; H, 6·45%).

The corresponding *methyl ester* obtained by treatment of the acid (III) with ethereal diazomethane had m.p. 163—164° (M^+, 358. $C_{20}H_{20}O_6$ requires *M*, 358), $\nu_{max.}$ ($CHCl_3$) 1732, 1654·5, 1618·5, 1600, and 1576 cm^{-1}.

Methyl 3-Methoxy-6β-methyl-12,16-dioxogibba-1(10),2,4,9-tetraene-4-carboxylate (IV).—The acid (III) (1·027 g) was heated under reflux in toluene (30 ml) containing naphthalene-2-sulphonic acid (0·10 g) for 24 h with azeotropic separation of water. The cooled solution was washed with 10% aq. potassium hydrogen carbonate solution and then

[9] L. F. Fieser, *J. Amer. Chem. Soc.*, 1954, **76**, 1945.
[10] R. Mozingo, *Org. Synth.*, Col. Vol. III, 1955, 181.
[11] R. A. Bell, R. E. Ireland, and R. A. Partyka, *J. Org. Chem.*, 1966, **31**, 2530.

brine, dried, and the toluene was removed under reduced pressure to yield the ester (IV) (0·827 g). Recrystallisation from dichloromethane–di-isopropyl ether afforded the pure *diketone* (IV) as pale yellow needles, m.p. 249—250° (sealed tube), $\nu_{max.}$ ($CHCl_3$) 1750, 1662, 1620, 1600, and 1584 cm^{-1}, $\lambda_{max.}$ 250 (ε 8800), 308 (12,300), and 340 nm (21,800), τ 2·46 and 3·04 (2H, q, *J* 8 Hz), 3·93 (1H, s, 11-H), 6·43 (1H, t, $J<2$ Hz; collapses to a singlet on irradiation at τ 7·49, 13-H), 6·47 (1H, q, *J* 7 Hz, collapses to a singlet on irradiation at τ 8·76, 6-H), 7·49 (2H, t, $J<2$ Hz, collapses to a singlet on irradiation at τ 6·43, 15-H_2), 7·74 (2H, q, *J* 16 Hz, 15-H_2), 8·76 (3H, d, *J* 7 Hz, collapses to a singlet on irradiation at τ 6·47, 6-Me), 6·06 (3H, s, OMe), and 6·09 (3H, s, OMe) [Found: C, 69·65; H, 5·7%; *M* (mass spectrum), 326. $C_{19}H_{18}O_5$ requires C, 69·9; H, 5·55%; *M*, 326].

Methyl 16β-*Acetoxy*-3-*methoxy*-6β-*methyl*-12-*oxogibba*-1(10),2,4,9-*tetraene*-4-*carboxylate* (VI).—To a stirred solution of diketone (IV) (1·0 g) in dioxan–water (1 : 1; 2·0 l) at 0° sodium borohydride (2·0 g) was added in one portion. The reaction was quenched with dil. sulphuric acid after 140 s and the mixture was extracted with chloroform and dried. G.l.c. examination (1% QF-1 at 225°) of the organic material obtained after removal of the solvent indicated a mixture of ketol (V), diketone (IV), and diol (VII) in the ratio 93 : 6 : 1. A pure sample of ketol (V) obtained by preparative t.l.c. showed $\nu_{max.}$ (CCl_4) 3620 and 3520 cm^{-1} and *m/e* 310 [M^+ (328) — H_2O] in its mass spectrum. The crude ketol (V) was acetylated (pyridine–acetic anhydride at 0° during 24 h) to afford the *keto-acetate* (VI) (0·736 g) as pale yellow prisms, m.p. 222·5—224° (from ethyl acetate–light petroleum) (sealed tube), $\nu_{max.}$ ($CHCl_3$) 1730, 1655, 1620, and 1240 cm^{-1}, $\lambda_{max.}$ 248 (ε 11,250), 300 (15,800), and 328·5 nm (23,000), τ 2·32 and 3·00 (2H, q, *J* 8·5 Hz), 3·77 (1H, d, *J* 1 Hz, collapses to a singlet on irradiation of 13-H at τ 6·60, 11-H), 4·40 (1H, octet, $J_{13.16\alpha}$ 6, $J_{15\alpha.16\alpha}$ 10, and $J_{15\beta.16\alpha}$ 5 Hz, 16α-H), 6·06 (3H, s, OMe), 6·08 (3H, s, OMe), 8·02 (3H, s, OAc), and 8·76 (3H, d, *J* 7 Hz, CH_3·CH) [Found: C, 67·95; H, 6·05%; *M* (mass spectrum), 370. $C_{21}H_{22}O_6$ requires C, 68·0; H, 6·0%; *M*, 370].

Methyl 16β-*Acetoxy*-3-*methoxy*-6β-*methyl*-12-*oxo*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (VIII).—Keto-acetate (VI) (50 mg) in methyl acetate was hydrogenated in the presence of palladium–charcoal (30%, 50 mg). After 12 h, when the uptake of hydrogen was complete (110% of theoretical), the product was isolated in the normal manner and treated with Jones reagent (to regenerate reduced ketone). *Keto-acetate* (VIII), obtained as an off-white solid (50 mg), was recrystallised from ethyl acetate–light petroleum to give needles, m.p. 229—230° (sealed tube), $\nu_{max.}$ ($CHCl_3$) 1735, 1720, 1590, and 1240 cm^{-1}, $\lambda_{max.}$ 229 (ε 6150) and 288 nm (2260), τ 2·89 and 3·18 (2H, q, *J* 8 Hz), 4·70 (1H, m, 16α-H), 6·06 (3H, s, OMe), 6·16 (3H, s, OMe), 6·10 (1H, m, 13-H), 6·7—7·4 (4H, m, 6-, 9-, 11α-, and 11β-H), 7·7—8·1 (3H, m, 14α, 14β-, and 15β-H), 8·8 (1H, m, 15α-H), and 8·75 (3H, d, *J* 7 Hz, 6-Me) [Found: C, 67·85; H, 6·6%; *M* (mass spectrum), 372. $C_{21}H_{24}O_6$ requires C, 67·75; H, 6·5%; *M*, 372].

Methyl 3-*Methoxy*-6β-*methyl*-12,16-*dioxo*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (IX).—(*a*) Diketone (IV) (50 mg) in methanol was hydrogenated in the presence of palladium–charcoal (30%, 20 mg) during 20 h by which time uptake of hydrogen was 105% of the theoretical. The hydrogenation product (50 mg) in acetone at 0° was treated with Jones reagent (to reoxidise the carbonyl-reduced material) and worked up in the normal way to afford a crystalline product (47 mg) shown by g.l.c.–m.s. to contain five compounds (2 : 2 : 5 : 5 : 85), the major product (M^+, 328) being the title compound. Recrystallisation from ethyl acetate gave *diketone* (IX) (42 mg) as microprisms, m.p. 236—236·5° (decomp.) (sealed tube), $\nu_{max.}$ ($CHCl_3$) 1752·5, 1733·5, and 1721 cm^{-1}, $\lambda_{max.}$ 239 (ε 3500), 290 (3620), and 335 nm (1890), τ (deuteriobenzene), 3·49 and 3·67 (2H, q, *J* 8 Hz), 6·39 (3H, s, OMe), 6·71 (3H, s, OMe), 6·83 (1H, br s, 13-H), 7·37 (1H, q, *J* 7 Hz, 6-H), 7·44 (1H, m, 9-H), 8·24 (2H, m, 11-H_2), 8·34 [2H, s, 15-H_2 (accidental equivalence)], 8·54 (2H, m, 14-H_2), and 9·10 (3H, d, *J* 7 Hz, CH_3·CH) [Found: C, 69·6; H, 6·0%; *M* (mass spectrum), 328. $C_{19}H_{20}O_5$ requires C, 69·5; H, 6·15%; *M*, 328].

(*b*) Diketone (IV) (100 mg) in dioxan–water (10 : 1) was treated portionwise with stirring with sodium borohydride (30 mg) and after addition was complete, the mixture was stirred at room temperature for 4 h. The mixture was neutralised (pH 7) with dilute sulphuric acid, poured into ammonium sulphate solution, and extracted with chloroform. Evaporation of solvent from the dried solution gave an oily mixture (98 mg) [$\nu_{max.}$ (CCl_4) 3620, 2540, and 1735 cm^{-1}] of two epimeric diols (VII). This material (96 mg) in methanol was hydrogenated in the presence of palladium–charcoal (30%) and glacial acetic acid (1 ml) during 3 h. Jones oxidation of the product afforded the diketone (IX) (86 mg) identical with that from preparation (*a*).

The mixture of epimeric diols (VII) (2 mg) in chloroform (20 ml) and manganese dioxide (200 mg) was stirred for 24 h at room temperature, after which the solution was filtered and evaporated to dryness. The resulting oil on acetylation (acetic anhydride–pyridine) gave a single keto-acetate (VI) (0·92 mg) identical in all respects with an authentic sample (see before).

Methyl 12β,16β-*Dihydroxy*-3-*methoxy*-6β-*methyl*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (X).—The diketone (IX, 25 mg) in dioxan–water (10 : 1) was treated portionwise with an excess of sodium borohydride (30 mg) with stirring. After 6 h at room temperature, the mixture was acidified to pH 6 with dilute sulphuric acid, poured into ammonium sulphate solution, and extracted with chloroform. The combined extracts were washed (brine), dried, and evaporated to yield a crystalline mixture of diols (25 mg), from which the 12β,16β-diol (X) (20 mg) was obtained as a crystalline solid, m.p. 168—168·5° (sealed tube) (from ethyl acetate–light petroleum), $\nu_{max.}$ ($CHCl_3$) 3520, 3440, and 1729 cm^{-1}, $\lambda_{max.}$ 235 (ε 5100) and 288 nm (3630) [Found: C, 68·9; H, 7·4%; *M* (mass spectrum), 332. $C_{19}H_{24}O_5$ requires C, 68·65; H, 7·3%; *M*, 332].

The 12β,16β-*sulphite ester* (13·9 mg) was obtained from diol (X) (12·5 mg) on treatment with thionyl chloride (0·1 ml) in chloroform. Recrystallisation from benzene–light petroleum gave the *sulphite ester* (9·0 mg), needles, m.p. 196—198° (decomp.) (sealed tube), $\nu_{max.}$ ($CHCl_3$) 1729 cm^{-1}, $\lambda_{max.}$ 230 (ε 7600) and 288 nm (3450) [Found: C, 60·55; H, 5·8%; *M* (mass spectrum), 378. $C_{19}H_{22}O_6S$ requires C, 60·3; H, 5·85%; *M*, 378].

Methyl 16β-*Acetoxy*-12,12-*ethylenedithio*-3-*methoxy*-6β-*methyl*-9aH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (XI).—Ethanedithiol (5 ml) and freshly distilled boron trifluoride–ether (2·5 ml) were added sequentially to a stirred solution of keto-acetate (VIII) (125 mg) in glacial acetic acid (20 ml) under nitrogen and the resulting solution kept at room temperature for 40 h. After addition of water (40 ml), the

solution was extracted with chloroform, the chloroform extracts were washed with N-NaOH solution and brine, and dried. Removal of solvent afforded the *dithioacetal* (135 mg; 90%) which, on recrystallisation from carbon tetrachloride–light petroleum, afforded prisms, m.p. 204·5—205·5°, $\nu_{max.}$ ($CHCl_3$) 1730 cm^{-1}, $\lambda_{max.}$ 229 (ε 8100) and 286 nm (2850), τ 6·5—7·0 (4H, m, S·CH_2·CH_2·S) [Found: C, 61·85; H, 6·25%; *M* (mass spectrum), 448. $C_{23}H_{28}O_5S_2$ requires C, 61·6; H, 6·3%; *M*, 448].

Methyl 16β-*Acetoxy*-3-*methoxy*-6β-*methyl*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (XII).—Thioacetal (XI) (149 mg) and a large excess of Raney nickel W-2 in methanol–dioxan (2·5 : 1; 40 ml) were heated under reflux with stirring for 16 h. The cooled solution was filtered and the nickel was washed with chloroform. The combined filtrates were washed with brine, dried, and evaporated. The crude product (108 mg), on preparative t.l.c., yielded the *acetate* (XII) (97 mg) as prisms, m.p. 148—149° (from carbon tetrachloride–light petroleum), $\nu_{max.}$ ($CHCl_3$) 1735, 1590, and 1240 cm^{-1}, $\lambda_{max.}$ 231 (ε 6500) and 288 nm (2950), τ 2·95 and 3·27 (2H, q, *J* 8 Hz), 6·13 (3H, s, OMe), 6·22 (3H, s, OMe), 8·20 (3H, s, Ac), and 8·89 (3H, d, *J* 7 Hz, CH_3·CH) [Found: C, 70·4; H, 7·35%; *M* (mass spectrum), 358. $C_{21}H_{26}O_5$ requires C, 70·35; H, 7·3%; *M*, 358].

Methyl 2-*Chloro*-3-*methoxy*-6β-*methyl*-16-*oxo*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (XV).—Desulphurisation of the above thioacetal (1·45 g) (which had been recrystallised from carbon tetrachloride–light petroleum) by an identical procedure gave, after the usual work-up, an off-white solid (1·0 g), which although homogeneous on t.l.c. was shown by g.l.c. to contain seven components (50 : 15 : 15 : 1 : 1 : 2). Catalytic reduction (Pd–C 10%) followed by methanolysis (MeOH–dioxan–HCl) and Jones oxidation (see later) afforded an off-white solid (510 mg) after preparative t.l.c., shown by g.l.c. to consist of two components (2·1 : 1). Separation was effected by fractional crystallisation followed by preparative t.l.c. of the mother liquors. This procedure afforded ketone (XIV) (302 mg) (see later) and the *chloro-ketone* (XV) (136·5 mg) as prisms, m.p. 149—151° (from ethyl acetate–light petroleum), $\nu_{max.}$ (CCl_4) 1740 and 1735 cm^{-1}, $\lambda_{max.}$ 228 (ε 10,800) and 285 nm (4050), τ 2·92 (1H, s, aromatic H) [Found: C, 64·5; H, 5·9%; *M* (mass spectrum), 348 and 350 (3 : 1). $C_{19}H_{21}ClO_4$ requires C, 65·25; H, 6·05%; *M*, 348 and 350 (3 : 1)].

Methyl 3-*Methoxy*-6β-*methyl*-16-*oxo*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (XIV).—(*a*) The acetate (XII) (55 mg) in methanol–dioxan (6 : 1; 35 ml) containing dilute hydrochloric acid (2 ml) was heated under reflux for 16 h. The cooled solution was diluted with water and extracted with chloroform. The chloroform extract was washed with brine, dried, and evaporated to an oil (47 mg), homogeneous on t.l.c. and g.l.c., $\nu_{max.}$ (CCl_4) 3630, 3580, and 1740 cm^{-1}. The oil was oxidised with Jones reagent and the product was purified by preparative t.l.c. to afford the *ketone* (XIV) (27·6 mg) as prisms, m.p. 173·5—175° (from benzene–light petroleum), $\nu_{max.}$ (CCl_4) 1746 and 1735 cm^{-1}, $\lambda_{max.}$ 232 (ε 7550) and 294·5 nm (3450) [Found: C, 72·75; H, 7·1%; *M* (mass spectrum), 314. $C_{19}B_{22}O_4$ requires C, 72·8; H, 7·05%; *M*, 314].

(*b*) The ketone (XIV) was also obtained from the chloro-ketone (XV) by hydrogenolysis in the presence of palladium–charcoal (30%).

3-*Methoxy*-6β-*methyl*-16-*oxo*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylic Acid* (XVII).—The keto-ester (XIV) (32 mg) was heated under reflux in 1N-NaOH (10 ml) containing dioxan (3 ml) for 16 h. After washing the cooled solution with ethyl acetate, the aqueous solution was acidified (HCl) and extracted thoroughly with ethyl acetate. After the usual work up the *keto-acid* (XVII) was obtained as an off-white powder (23 mg), which afforded microprisms, m.p. 271—272° (from ethyl acetate), $\nu_{max.}$ (KBr) 3300—2800, 1730, and 1710 cm^{-1}, $\lambda_{max.}$ 230 (ε 7100) and 285 nm (2500), τ 2·97 and 3·20 (2H, q, *J* 8 Hz), 6·33 (3H, s, OMe), 6·85 (1H, q, *J* 7 Hz), 7·3 (1H, m, 9α-H), 7·5 (1H, m, 13-H), 7·8—8·6 (8H, m, 11-, 12-, 14-, and 15-H_8), and 8·55 (3H, d, *J* 7 Hz, CH_3·CH) (Found: C, 72·0; H, 6·6. $C_{18}H_{20}O_4$ requires C, 72·0; H, 6·7%).

Methyl 3-*Methoxy*-6β-*methyl*-16-*methylene*-9αH-*gibba*-1(10),2,4-*triene*-4-*carboxylate* (XVI).—To a stirred suspension of triphenylmethylphosphonium bromide (400 mg; 4 : 1 molar excess) in dry ether (10 ml) under nitrogen at room temperature a 0·8M solution of potassium t-butoxide in t-butyl alcohol (1·6 ml) was added. After 30 min, ketone (XIV) (87·4 mg; in the minimum volume of dry benzene) was added to the yellow suspension and the resulting mixture stirred for 16 h. Water was added, the layers were separated, and the aqueous phase was extracted with ether–pentane (1 : 1). The combined organic extracts were washed (water), dried, and evaporated to afford crystalline material, which on preparative t.l.c. gave the *olefin* (XVI) (77·2 mg). Recrystallisation from pentane at −10° afforded clusters of needles, m.p. 128—129°, $\nu_{max.}$ (CCl_4) 1720, 1595, and 880 cm^{-1}, $\lambda_{max.}$ 232 (ε 6000) and 289 nm (2500), τ 3·05 and 3·29 (2H, q, *J* 8 Hz), 5·33 (2H, d, *J* 13 Hz, 17-H_2), 6·17 (3H, s, OMe), 6·26 (3H, s, OMe), 6·95 (1H, q, *J* 7 Hz, 6-H), 7·3 (2H, m, 9- and 13-H_2), 7·8—8·8 (8H, complex 12-, 13-, 14-, and 15-H_8), and 8·90 (3H, d, *J* 6 Hz, CH_3·CH) [Found: C, 76·8; H, 7·8%; *M* (mass spectrum), 312. $C_{20}H_{24}O_3$ requires C, 76·9; H, 7·75%; *M*, 312].

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