The Removal of C(20) in Gibberellins

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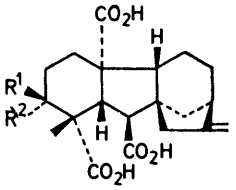
Oxidative decarboxylation of *ent*-gibberellane-19,20-dioic acids with lead tetra-acetate yields mixtures of 19,10-lactones and 20,4-lactones providing a chemical correlation between the C_{20} and C_{19} gibberellins. The oxidation of methyl *ent*-16-oxo-17-norgibberell-2-ene-7,19,20-trioate with chromium trioxide afforded a 1-ketone which underwent decarboxylation with lithium iodide to afford a 20-norgibberellane with a *trans* A–B ring fusion.

THE gibberellin plant hormones are diterpenoid substances. Whilst some of the gibberellins retain the full complement of carbon atoms, others have lost C-20 and are C_{19} compounds. The removal of the C-20 carbon atom and the formation of the γ-lactone ring represents a key step in gibberellin biosynthesis.[1] In this paper we present two chemical solutions to the removal of C-20; one of these, which has been the subject of a preliminary communication,[2] represents a direct chemical correlation between the two series of gibberellins. In view of overlapping objectives work from two laboratories is reported in this paper.

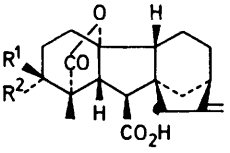
The oxidative decarboxylation of 1 : 3- and 1 : 4-dioic acids has been shown to give γ- and δ-lactones respectively.[3] The 19- and 20-carboxylic acids of the C_{20} gibberellins possess this relationship and are suitably oriented to generate γ-lactones. The oxidation of gibberellin A_{13} (1a)[4] with lead tetra-acetate in dry dimethylformamide (DMF) at room temperature overnight afforded an inseparable mixture of gibberellin A_4 (2a) and the isomeric 20 ⟶ 4-lactone (3a) (60 : 40) together with a small amount of gibberellin A_4 3-ketone and its 20 ⟶ 4 isomer. These were identified by combined gas chromatography–mass spectrometry (g.c.m.s.). The characterization of the novel isomeric lactone was effected by base-catalysed isomerization of the gibberellin A_4 to the more polar 3-epimer[5] with 2M sodium hydroxide at room temperature overnight. Subsequent preparative layer chromatography and repetition of the isomerization afforded the pure lactone (3a). Evidence for the structure of the isomeric lactone was obtained by oxidation of the mixture of lactones (2a) and (3a) to the corresponding ketones (2c) and (3c). Reduction with chromium(II) acetate in tetrahydrofuran (THF) gave unchanged gibberellin A_4 3-ketone and the 19-nor-ketone (4a). The latter was identical (g.c.m.s. of the methyl esters) with a sample prepared by the thermal decarboxylation of gibberellin A_{13} 3-ketone (1c).[4] The less-likely 4-epimeric formulations (5) for the isomeric lactone were excluded by decarboxylation of the 7-monomethyl ester which afforded the same mixture of lactones (2a) and (3a) as their methyl esters.

When the reaction was carried out under more vigorous conditions [$Pb(OAc)_4$; refluxing benzene] an intractable mixture was obtained. In part this is due to oxidation of ring D since treatment of the 19-nor-3-ketone (4b) with lead tetra-acetate under these conditions gave the 17-acetate (6). The i.r. and n.m.r. spectra of the latter lacked signals characteristic of the 17 $=CH_2$ group but contained absorptions associated with a trisubstituted double bond ($\nu_{max.}$ 807 cm^{-1}; δ 5.53) and a CH_2OAc grouping (δ 5.15 and 5.40). The 3-oxo-lactone (3c) was not formed by treatment of the corresponding acid (4a) with lead tetra-acetate.

A number of other lead tetra-acetate decarboxylations were carried out. Gibberellin A_{25} (1b),[6] gibberellin A_{13} 3-ketone (1c), and gibberellin A_{13} 3-acetate (1d) were each treated with lead tetra-acetate in DMF at 18 °C to afford the pairs of isomeric lactones (2b) and (3b), (2c)



(1)



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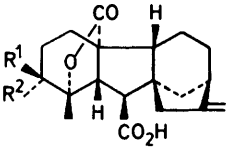

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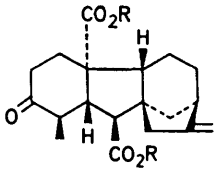
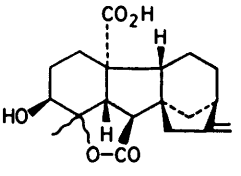


(4)
a ; R = H
b ; R = Me



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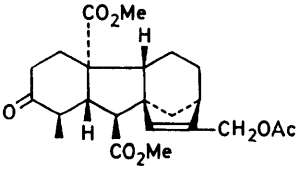

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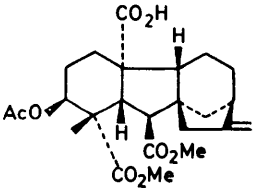


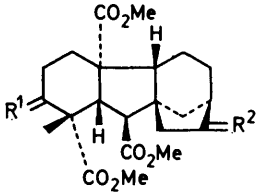
(7)

and (3c), and (2d) and (3d) in the ratios (g.c.m.s. of the methyl esters) of 50 : 50, 63 : 37, and 82 : 18 respectively. As the product ratios of the isomeric lactones formed from the 3-deoxy compound, the 3-ketone, and the 3-alcohol are comparable, this suggests that carbonium ion intermediates, particularly at C-4, are not involved in the decarboxylation. This work represents the first chemical inter-relationship of the C_{20} with the C_{19} gibberellins. After the publication of the preliminary communication, a similar approach based on the decarboxylation of the monocarboxylic acid (7) was described.[7] These approaches, whilst possessing the merit of simplicity, lacked regiospecificity. An alternative approach to the removal of C-20 was based on the decarboxylation of 1-oxo-20-acids.

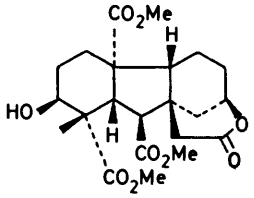
Gibberellin A_{13} trimethyl ester (8) was ozonized to afford the 17-nor-16-ketone (9).[4] The 3,16-diketone (10) [4] and the δ-lactone (11) were isolated as by-products and identified by comparison with authentic samples prepared on the one hand by 8M chromium trioxide oxidation [4] and on the other by Baeyer–Villiger oxidation of the 17-nor-16-ketone (9). The alternative method [8] of preparing the nor-ketone by oxidation with sodium periodate and a catalytic amount of osmium tetraoxide proved more satisfactory. The nor-ketone (9) was treated with phosphorus(III) trichloride oxide to afford the Δ^2-olefin (12) as the major product. Two chlorine-containing by-products were also isolated. The n.m.r. spectrum of the first of these showed an AB olefinic system characteristic of a Δ^2-olefin.[6] Thus spin decoupling and INDOR experiments showed that the octet (δ 5.76, $J_{2,1}$ 6; $J_{2,1}$ 1.5; $J_{2,3}$ 10 Hz) assigned to H-2 was coupled to the H-1 proton (δ 2.89, J 6 and 16 Hz) and to the H-1 proton (δ 1.83). The quartet (δ 5.52, $J_{3,1}$ 2.5; $J_{2,3}$ 10 Hz) assigned to H-3 showed a long-range coupling to the H-1 proton. In addition the n.m.r. spectrum contained a one-proton olefinic singlet (δ 5.77) and hence the enol–chloride structure (13) was assigned to this compound. The second dichloro-compound also possessed an olefinic signal at δ 5.85 assigned to H-15. However, in place of the olefinic ring A resonances, there was a C*H*Cl signal at δ 4.43 assigned to H-3. In view of the half-width (9 Hz) of this signal and the fact that H-5 was still deshielded (δ 2.58), the 3-chlorine atom was assigned the β-configuration (14).

Oxidation of the Δ^2-olefin (12) with chromium trioxide in t-butyl alcohol [9] afforded the 1-ketone (15) ($\lambda_{max.}$ 222 nm) (δ 6.04, J 11 Hz, H-2; δ 6.57, J 11 Hz, H-3) as the major product. The isomeric γ-lactone (16) ($\nu_{max.}$ 1 770 cm^{-1}; δ 4.68, m, H-2) and δ-lactone (17) ($\nu_{max.}$ 1 735 cm^{-1}; δ 4.83, m, H-3) formed minor products from this oxidation. These compounds showed only two methoxy-signals in their n.m.r. spectrum. Their formation is consonant with the known participation of C(20) in reactions at C-2 and C-3. Catalytic hydrogenation of the unsaturated ketone (15) afforded the 1,16-diketone (18). This compound differed in its properties from the 3,16-diketone (10) and thus the allylic oxidation of the Δ^2-olefin had proceeded without rearrangement.

Reaction of this β-oxo-ester (18) with lithium iodide in collidine and remethylation of the product with diazomethane afforded a gummy 20-nor-7,19-dimethyl ester (19) (δ 3.68 and 3.79, each 3-H). The *trans*-relationship of the H-10, H-5, and H-6 atoms was revealed by spin-decoupling experiments performed at 220 MHz. The



(8) R^1 = α–H, β–OH; R^2 = CH_2
(9) R^1 = α–H, β–OH; R^2 = O
(10) R^1 = R^2 = O



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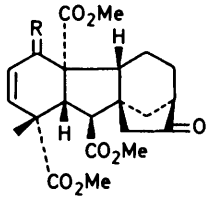
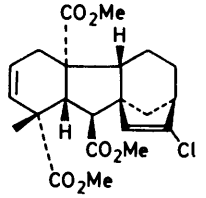


(12) R = H_2
(15) R = O



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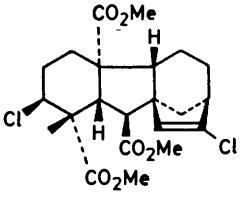

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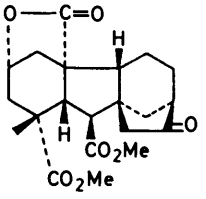

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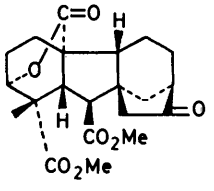

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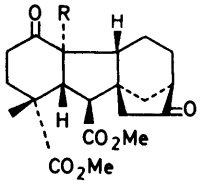

(18) R = CO_2Me
(19) R = H

key signal in this sequence was the H-6 signal which appeared as a doublet (δ 3.26, $J_{5,6}$ 10.5 Hz). Irradiation at this position collapsed the H-5 quartet (δ 2.35, J 10.5 and 13 Hz) to a doublet (J 13 Hz). Irradiation at this position then collapsed the H-10 quartet (δ 2.82, J 10.5 and 13 Hz) to a doublet (J 10.5 Hz). Thus the decarboxylation had proceeded in a regiospecific manner to afford a 20-norgibberellane with an antipodal *trans*-A–B ring fusion.

EXPERIMENTAL

General experimental details have been described previously.[6,10]

Reactions with Lead Tetra-acetate.—(a) Gibberellin A_{13} (1a) (450 mg) in dry dimethylformamide (25 ml) was treated with lead tetra-acetate (moistened with acetic acid) (800 mg) at room temperature overnight. Five drops of ethylene glycol were then added. After 0.5 h water (50 ml) was added and the mixture acidified to pH 2.5 with dil. hydrochloric acid. Extraction with ethyl acetate gave a gum (420 mg) which was purified by preparative layer chromatography on silica gel HF in ethyl acetate–light petroleum–acetic acid (80 : 20 : 2). The band with R_F 0.55 was eluted to afford a gum (177 mg) containing gibberellin A_4 (2a) and the isomer (3a) (g.c.m.s.). The mixture was stirred with 2M sodium hydroxide (5 ml) at room temperature overnight. The solution was acidified with dilute hydrochloric acid and extracted with ethyl acetate to afford a gum (154 mg) which was purified as before to afford a sample enriched in the isomer (3a) (53 mg). Repetition of the alkali treatment gave the pure *isomer* (3a) (33 mg) which crystallized from ethyl acetate–light petroleum, m.p. 207—210 °C (Found: 332.161, $C_{19}H_{24}O_5$ requires M^+ 332.162); $\nu_{max.}$ 3 350 (br), 1 730 (br), 1 660, and 880 cm^{-1}; $\delta(C_5D_5N)$ 1.65 (3 H, s, 18-H_3), 3.06 (1 H, d, *J* 11 Hz, 5-H), 3.65 (1 H, d, *J* 11 Hz, 6-H), 4.07 (1 H, t, *J* 2 Hz, 3-H), and 4.88 and 4.99 (1 H each, br, 17-H_2); *m/e* 332 (M^+) (15%), 314 (100), 296 (6), 286 (21), 271 (20), 270 (30), 105 (36), and 91 (62). The trimethylsilyl derivative of the methyl ester had *m/e* 418 (M^+) (29%), 403 (7), 390 (3), 386 (6), 362 (39), 359 (23), 328 (53), 129 (65), 116 (100), and 101 (55). G.c.m.s. analysis of the trimethylsilyl derivatives of the methyl esters of the crude reaction product showed that gibberellin A_4 (2a) and the isomer (3a) were present in the ratio 60 : 40 and indicated the presence of traces of gibberellin A_4 3-ketone (Me ester) [*m/e* 344 (M^+) (36%), 316 (16), 312 (100), 300 (20), 284 (37), 257 (21), and 240 (30)] and of the isomer (3c) [*m/e* 344 (M^+) (4%), 316 (100), 288 (86), 256 (31), 245 (82), and 228 (36)].

(b) Gibberellin A_{13} 3-acetate (1d) (5 mg) in dimethylformamide (0.5 ml) was treated with a solution of lead tetra-acetate (150 μl; 110 mg ml^{-1}) in the same solvent at room temperature overnight. The solution was worked-up as above, methylated, and analysed by g.c.m.s. to afford acetylgibberellin A_4 methyl ester [*m/e* 388 (M^+) (1%), 356 (4), 357 (3), 328 (11), 284 (100), 269 (13), 255 (79), 224 (100), and 43 (40)] and the isomer (3d) [*m/e* 388 (M^+) (2%), 370 (9), 328 (8), 310 (15), 300 (13), 296 (100), 284 (61), 283 (51), 225 (30), and 43 (77)] in the ratio of 82 : 18. Under the same conditions, gibberellin A_{25} (1b) gave gibberellin A_9 methyl ester (2b) and the isomer (3b) [*m/e* 330 (M^+) (16%), 298 (100), 286 (29), 284 (18) 270 (79), 255 (20), 253 (24), 244 (61), 227 (80), 226 (76), 225 (54), and 217 (52)] (as its methyl ester), in the ratio 1 : 1; gibberellin A_{13} 3-ketone (1c) gave gibberellin A_4 3-ketone (as its methyl ester) and the isomer (3c) as its methyl ester (m.s. as above), in the ratio 63 : 37. Gibberellin A_{13} 7-methyl ester gave the same ratio of methyl esters as described in (a).

(c) Dimethyl *ent*-3-oxo-19-norgibberell-16-ene-7,20-dioate (4b) (1 g) was treated with lead tetra-acetate (3.16 g) in refluxing benzene (50 ml) overnight. Water (30 ml) was added and the solution filtered. The organic product was recovered in chloroform and purified by preparative layer chromatography in ethyl acetate–light petroleum (1 : 1) to afford *dimethyl* ent-17-*acetoxy*-3-*oxo*-19-*norgibberell*-15-*ene*-7,20-*dioate* (6) (83 mg) as needles, m.p. 227—229 °C (Found: C, 66.4; H, 7.0. $C_{23}H_{30}O_7$ requires C, 66.0; H, 7.2%); $\nu_{max.}$ 1 740, 1 725, 1 710, 1 670, 821, and 807 cm^{-1} δ 0.95 (3 H, d, *J* 6 Hz), 1.97 (3 H, s), 3.70 (1 H, d, *J* 12 Hz), 3.63 and 3.83 (each 3 H, s), and 5.15, 5.40, and 5.53 (each 1 H, br s).

Oxidation of the Mixed Lactones (2a) *and* (3a).—An aliquot portion (10 mg) of the crude product from the lead tetra-acetate oxidation (a) was dissolved in acetone (2 ml). It was treated with excess of the 8M chromium trioxide reagent at 0 °C for 10 min. Methanol and water were added. The solution was extracted with ethyl acetate, and the extract washed with water, dried, and evaporated to afford a gum (9 mg). The gum was methylated with diazomethane and analysed by g.c.m.s. It was shown to contain a mixture of the methyl ester of gibberellin A_4 3-ketone and the methyl ester of the isomer (3c).

Chromium(II) *Acetate Reduction of the Mixed Ketones* (2c) *and* (3c).—The product from the foregoing oxidation was dissolved in tetrahydrofuran (oxygen free) (4 ml). It was treated with chromium(II) acetate (300 mg) at room temperature for 24 h. Water was added and the solution was acidified to pH 2.5. The product was recovered in ethyl acetate to afford a gum (7 mg) which was analysed by g.c.m.s. of the methyl esters. It contained both starting ketones and dimethyl *ent*-3-oxo-19-norgibberell-16-ene-7,20-dioate [*m/e* 360 (M^+) (53%), 332 (6), 328 (63), 310 (20), 300 (100), 283 (18), 272 (29), 269 (83), 244 (29), and 241 (57)]. This was identical with an authentic sample prepared by the oxidation, decarboxylation, and methylation of gibberellin A_{13}.[4]

Ozonolysis of Gibberellin A_{13} Trimethyl Ester (8).—Ozonised oxygen was passed through the trimethyl ester (8) [4] (1 g) in ethyl acetate (50 ml) at −70 °C until the solution became blue. The solution was allowed to warm to room temperature and then a stream of nitrogen was passed through. The solvent was removed *in vacuo* and the residue was stirred with water for 5 h. The product was recovered in ethyl acetate and chromatographed on silica. Elution with 20% ethyl acetate–light petroleum gave trimethyl *ent*-3,16-dioxo-17-norgibberellane-7,19,20-trioate (93 mg) which crystallized as plates, m.p. 189—180 °C (lit.,[4] 181—184 °C); $\nu_{max.}$ 1 745, 1 720, 1 705, and 1 698 cm^{-1}; δ 1.24 (3 H, s), 2.45 (1 H, d, *J* 12.5 Hz), 3.61 (3 H, s), 3.68 (6 H, s), and 3.98 (1 H, d, *J* 12.5 Hz). Elution of the column with increasing amounts of ethyl acetate in light petroleum gave trimethyl *ent*-3α-hydroxy-16-oxo-17-norgibberellane-7,19,20-trioate (9) (560 mg) which crystallized from ethyl acetate–light petroleum as needles, m.p. 188—190 °C (lit.,[4] 186—189 °C); $\nu_{max.}$ 3 510, 1 745, 1 720, and 1 710 cm^{-1}; δ 1.22 (3 H, s), 2.56 (1 H, d, *J* 12.5 Hz), 3.57, 3.61, and 3.68 (each 3 H, s), and 3.94 (1 H, d, *J* 12.5 Hz). Further elution gave the *δ-lactone* (11) (62 mg) which crystallized from aqueous ethanol as plates, m.p. 194—195 °C (Found: C, 60.6; H, 6.7. $C_{22}H_{30}O_9$ requires C, 60.3; H, 6.9%); $\nu_{max.}$ 3 545, 1 740, and 1 720 cm^{-1}; δ 1.15 (3 H, s), 2.41 (1 H, d, *J* 12.5 Hz), 3.58, 3.63, and 3.69 (each 3 H, s), 3.53 (1 H, d, *J* 12.5 Hz), 3.94 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz), and 4.64 (1 H, m, $W_{\frac{1}{2}}$ 12 Hz).

Baeyer–Villiger Oxidation of the Ketone (9).—*m*-Chloroperbenzoic acid (80 mg) in chloroform (10 ml) was added at 0 °C to the norketone (9) (120 mg) in chloroform (10 ml). The mixture was left overnight at 5 °C. The solution was washed with aqueous iron(II) sulphate, water, aqueous sodium hydrogen carbonate, and water, and dried. The

solvent was evaporated off and the residue chromatographed on silica to afford the δ-lactone (11) (48 mg) identical (i.r. and n.m.r.) to the material obtained above.

Reaction of the Ketone (9) *with Phosphorus Trichloride Oxide*.—The norketone (9) (1 g) in pyridine (20 ml) was treated with phosphorus trichloride oxide (2 ml) at 20 °C overnight and then heated under reflux for 3 h. The solution was poured into water and extracted with ethyl acetate, and the extract washed with diluted hydrochloric acid, aqueous sodium hydrogen carbonate, and water, and dried. Evaporation gave a gum which was chromatographed on silica. Elution with 20% ethyl acetate–light petroleum gave trimethyl *ent*-16-oxo-17-norgibberell-2-ene-7,19,20-trioate (12) (640 mg), m.p. 165—167 °C (lit.,[6] 164—165 °C) (Found: C, 65.7; H, 6.7. Calc. for $C_{22}H_{28}O_7$: C, 65.3; H, 7.0%); $\nu_{max.}$ 3 025, 1 740, and 1 728 cm^{-1}, n.m.r. spectrum identical to that in ref. 6. Elution with 30% ethyl acetate–light petroleum gave *trimethyl* ent-16-*chloro*-17-*norgibberella*-2,15-*diene*-7,19,20-*trioate* (13) (175 mg) which crystallized from ethyl acetate–light petroleum as needles, m.p. 150—152 °C (Found: C, 62.1; H, 6.6. $C_{22}H_{27}ClO_6$ requires C, 62.5; H, 6.4%); $\nu_{max.}$ 1 735 and 1 653 cm^{-1}, δ 1.24 (3 H, s), 2.32 (1 H, d, *J* 12.5 Hz), 2.89 (1 H, q, *J* 6 and 16 Hz), 3.52, 3.58, and 3.68 (each 3 H, s), 3.76 (1 H, d, *J* 12.5 Hz), 5.52 (1 H, q, *J* 2.5 and 10 Hz), 5.76 (1 H, octet, *J* 1.5, 6, and 10 Hz), and 5.77 (1 H, s). Elution with 40% ethyl acetate–light petroleum gave *trimethyl* ent-3,16-*dichloro*-17-*norgibberell*-15-*ene*-7,19,20-*trioate* (14) (38 mg) which crystallized from ethyl acetate–light petroleum as plates, m.p. 138—141 °C (Found: C, 57.4; H, 6.3. $C_{22}H_{28}Cl_2O_6$ requires C, 57.5; H, 6.1%); $\nu_{max.}$ 1 740 and 1 662 cm^{-1}; δ 1.28 (3 H, s), 2.58 (1 H, d, *J* 12.5 Hz), 3.54, 3.61, and 3.64 (each 3 H, s), 3.81 (1 H, d, *J* 12.5 Hz), 4.43 (1 H, m, $W_{\frac{1}{2}}$ 9 Hz), and 5.85 (1 H, s).

Oxidation of the Olefin (12) *with Chromium Trioxide*.—Chromium trioxide (18.5 g) was added in portions with stirring to t-butyl alcohol (46.8 ml). The solution was stirred for a further 5 min and then transferred to a separating funnel and diluted with carbon tetrachloride (130 ml). The aqueous phase was separated off and the organic phase was dried over sodium sulphate. The drying agent was filtered off and washed with carbon tetrachloride (80 ml). The combined organic phases were concentrated to 100 ml *in vacuo* below 45 °C. The olefin (12) (400 mg) in refluxing carbon tetrachloride (30 ml) was treated with the foregoing solution (20 ml), and acetic acid (7 ml) and acetic anhydride (3 ml) dropwise over 30 min. The mixture was heated under reflux overnight and then treated with oxalic acid (1.2 g) in water (70 ml) for 3 h. The organic phase was separated off, the aqueous phase extracted with carbon tetrachloride, and the combined extracts were washed with water, aqueous sodium hydrogen carbonate, and water, and dried. Evaporation gave a gum which was chromatographed on silica. Elution with 25% ethyl acetate–light petroleum gave *trimethyl* ent-1,16-*dioxo*-17-*norgibberell*-2-*ene*-7,19,20-*trioate* (15) (255 mg) which crystallized from ethyl acetate–light petroleum as needles, m.p. 134—136 °C (Found: C, 63.2; H, 6.3. $C_{22}H_{26}O_8$ requires C, 63.15; H, 6.2%); $\nu_{max.}$ 1 760, 1 745, 1 725, and 1 688 cm^{-1}; $\lambda_{max.}$ 222 nm, (ε 6 300); δ 1.38 (3 H, s), 2.67 (1 H, d, *J* 12.5 Hz), 3.57, 3.67, and 3.73 (each 3 H, s), 4.03 (1 H, d, *J* 12.5 Hz), 6.04 (1 H, d, *J* 11 Hz), and 6.57 (1 H, d, *J* 11 Hz). Further elution with ethyl acetate–light petroleum gave a mixture of lactones which were purified by preparative layer chromatography on silica in 25% ethyl acetate–light petroleum. The less polar band afforded ent-3β-*hydroxy*-16-*oxo*-17-*norgibberellane*-7,19,20-*trioic acid* 20,3-*lactone* 7,-19-*dimethyl ester* (17) which crystallized from ethyl acetate–light petroleum as needles, m.p. 156—158 °C (Found: C, 65.2; H, 6.8. $C_{21}H_{26}O_7$ requires C, 64.6; H, 6.7%); $\nu_{max.}$ 1 745, 1 735, and 1 728 cm^{-1}; δ 1.45 (3 H, s,), 2.32 (1 H, d, *J* 12.5 Hz), 3.04 (1 H, d, *J* 12.5 Hz), 3.64 and 3.68 (each 3 H, s), and 4.83 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz). The more polar band afforded ent-2β-*hydroxy*-16-*oxo*-17-*norgibberellane*-7,19,20-*trioic acid* 20,2-*lactone* 7,19-*dimethyl ester* (16) which crystallized from ethyl acetate–light petroleum as needles, m.p. 225—227 °C (Found: C, 63.7; H, 6.8. $C_{21}H_{26}O_7$ requires C, 64.6; H, 6.7%); $\nu_{max.}$ 1 770, 1 745, 1 737, and 1 723 cm^{-1}; δ 1.32 (3 H, s), 2.45 (1 H, d, *J* 12.5 Hz), 3.06 (1 H, d, *J* 12.5 Hz), 3.64 and 3.68 (each 3 H, s), and 4.68 (1 H, m, $W_{\frac{1}{2}}$ 13 Hz).

Hydrogenation of the Unsaturated Ketone (15).—The unsaturated ketone (15) (250 mg) in ethanol (20 ml) was hydrogenated over 10% palladium on charcoal (150 mg) at room temperature and pressure for 3 h. The solvent was evaporated off and the residue chromatographed on silica to afford *trimethyl* ent-1,16-*dioxo*-17-*norgibberellane*-7,19,20-*trioate* (18) as a gum (Found: C, 63.5; H, 6.4. $C_{22}H_{28}O_8$ requires C, 62.9; H, 6.7%); $\nu_{max.}$ 1 744 and 1 715 cm^{-1}; δ 1.25 (3 H, s), 2.35 (1 H, d, *J* 12.5 Hz), 3.62, 3.67, and 3.69 (each 3 H, s), and 3.91 (1 H, d, *J* 12.5 Hz).

Reaction of the Ester (18) *with Lithium Iodide*.—A solution of the ester (11) (200 mg) and freshly dried lithium iodide (800 mg) in freshly distilled collidine (20 ml) was heated under reflux under nitrogen for 65 h. The solution was cooled and diluted with ethyl acetate (50 ml). The solution was washed thoroughly with diluted hydrochloric acid and water, dried, and evaporated to give a gum which was methylated with diazomethane in ether. The solvent was evaporated off to give a gum which was chromatographed on silica. Elution with 20% ethyl acetate–light petroleum gave *dimethyl* ent-1,16-*dioxo*-17,20-*dinorgibberellane*-7,19-*dioate* as a gum (homogeneous by t.l.c. on silica) (Found: M^+ 362.173. $C_{20}H_{26}O_6$ requires 362.173); $\nu_{max.}$ 1 740 and 1 720 cm^{-1}; δ (220 MHz) 1.20 (3 H, s), 2.35 (1 H, q, *J* 10.5 and 13 Hz), 2.82 (1 H, q, *J* 10.5 and 13 Hz), 3.26 (1 H, d, *J* 10.5 Hz), 3.68 (3 H, s), and 3.79 (3 H, s).

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