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PREPARATION OF 2- AND 3-SUBSTITUTED GIBBERELLINS A_9 AND A_4 FOR BIOASSAY

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Key Word Index—Partial synthesis; 2α-,2β- and 3β-derivatives; gibberellin A_4; gibberellin A_9.

Abstract—To test the effects of preventing enzymatic 2β- and 3β-hydroxylation on the biological activities of gibberellins, the preparation of the following compounds is described: 2β-methyl- and 2,2-dimethyl-gibberellins A_4 and A_9; 2α-fluoro-, 2β-fluoro- and 2β-methoxy-gibberellin A_9; and 3β-chloro-, 3β-fluoro-, 3β-methoxy- and 3-methylene A_9.

INTRODUCTION

Gibberellin A_9 (GA_9) (**1**) and GA_4 (**2**) show similar biological activities in plant bioassays [1–3]. The biological activity of GA_9 (**1**) may therefore be the result of 3β-hydroxylation to GA_4 (**2**) in the plant bioassay system. To test this possibility several 3-substituted GA_9 derivatives, in which 3β-hydroxylation is blocked, have been prepared for bioassay.

The introduction of a 2β-hydroxyl into a biologically active gibberellin removes biological activity [2, 4]. For example, GA_{34} (**4**), GA_{51} (**5**) and GA_8 (**6**), the 2β-hydroxy derivatives of GA_4 (**2**), GA_9 (**1**) and GA_1 (**3**), are inactive in all bioassays in which they have been tested. Several 2β-derivatives of GA_9 (**1**) and GA_4 (**2**) have therefore been prepared to determine the effect, on biological activity, of preventing 2β-hydroxylation. The biological aspects of this investigation are described in the following paper. This paper is confined to the preparation of the 2- and 3-substituted derivatives of GA_4 and GA_9.

RESULTS AND DISCUSSION

The required intermediates were obtained from a mixture of 65% GA_4 (**1**) and 35% GA_7 (**7**) by the following two literature procedures. Firstly, following the method of Beale *et al.* [5], the mixture of GA_4 and GA_7 was oxidized by Jones reagent into a mixture of the corresponding 3-ketones (**9** and **10**) which was reduced by sodium borohydride and lithium bromide in di(2-methoxyethyl)ether to a mixture, mainly of the 3α-alcohol (**14**), plus some GA_4 (**2**) and 3-epiGA_7 (**8**). The latter mixture was (a) separated by chromatography into its components; (b) phenacylated and separated chromatographically into the phenacyl esters of **14**, **2** and **8**; or (c) methylated, then oxidized, to yield 3-didehydroGA_4 methyl ester (**11**). Secondly, the mixture of GA_4 (**2**) and GA_7 (**7**) was oxidized with osmium tetraoxide–sodium periodate to yield the norketone (**16**) of GA_4 (**2**) [6]. This norketone (**16**) was then converted into the phenacyl ester (**17**) or the methyl ester (**18**) which was transformed into GA_{40} methyl ester (**20**) and GA_{51} methyl ester (**19**) by the sequence described by Beeley and MacMillan [7] and Yamaguchi *et al.* [8].

3β-Substituted GA_9 derivatives

3-MethyleneGA_9 (**12**) was prepared from the 3-ketone (**11**) by reaction with salt-free methylenetriphenylphosphorane in tetrahydrofuran, followed by alkaline hydrolysis of the product (**13**). In this, and all other alkaline hydrolyses of methyl esters described in this paper, lactone opening occurred to some extent. The crude hydrolysis products were therefore heated briefly on a steam bath to bring about re-lactonization.

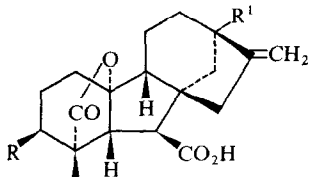
3β-MethoxyGA_9 (**23**) was prepared by treatment of GA_4 methyl ester with methyl iodide and silver oxide, followed by alkaline hydrolysis of the product (**24**).

3β-ChloroGA_9 (**25**) and 3β-fluoroGA_9 (**26**) were prepared from 3-epiGA_4 phenacyl ester (**15**). Treatment of **15** with fluoramine [diethyl-(2-chloro-1,1,2-trifluoroethyl)amine] [9] in refluxing dioxan gave a mixture of the phenacyl esters **27**, **28** and **29** which was separated into its components by repeated preparative TLC and preparative HPLC, and the isolated phenacyl esters **27** and **28** were respectively converted into 3β-chloroGA_9 (**25**) and 3β-fluoroGA_9 (**26**) by reductive removal of the phenacyl ester with zinc and acetic acid. The phenacyl esters were used to protect the carboxylic acid function since the free acids could be regenerated from them under non-alkaline conditions. When the corresponding methyl esters were hydrolysed by alkali, the 3β-chloro-substituent was, as expected, eliminated to give the 2,3-olefin and the 3β-fluoro-substituent underwent solvolysis to give the 3α-alcohol.

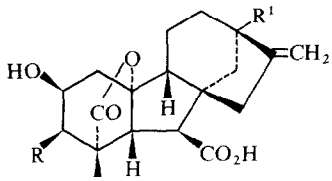
2α- and 2β-fluoro- and 2β-methoxyGA_9

2β-MethoxyGA_9 (**21**) was prepared by methylation of GA_{51} methyl ester (**19**) with methyl iodide and silver oxide, followed by alkaline hydrolysis of the product (**22**).

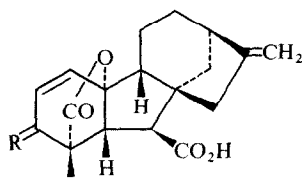
2β-FluoroGA_9 (**33**) was prepared from GA_{40} methyl ester (**20**) which, when treated with fluoramine in dioxan, gave a mixture of 2β-fluoroGA_9 methyl ester (**34**) and the 2,3-olefin (**30**). This mixture was separated by repeated preparative TLC and the 2β-fluoroGA_9 methyl ester (**34**) was hydrolysed to give the free acid (**33**), admixed with 20% of the 2,3-olefin (**32**). The 2β-fluoroGA_9 (**33**) was separated from the olefin (**32**) by preparative HPLC, but



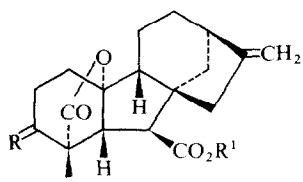
1 GA_9, R = R^1 = H
2 GA_4, R = OH, R^1 = H
3 GA_1, R = R^1 = OH



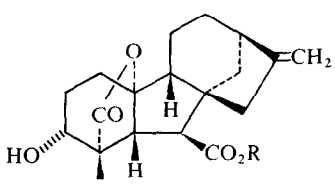
4 GA_{34}, R = OH, R^1 = H
5 GA_{51}, R = R^1 = H
6 GA_8, R = R^1 = OH



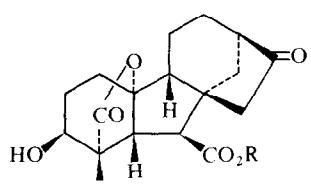
7 GA_7, R = H, β-OH
8 R = H, α-OH
9 R = O



10 R = O, R^1 = H
11 R = O, R^1 = Me
12 R = CH_2, R^1 = H
13 R = CH_2, R^1 = Me



14 R = H
15 R = CH_2COPh



16 R = H
17 R = CH_2COPh
18 R = Me

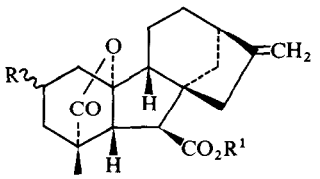
contained (GC/MS) *ca* 10% of the 15-double bond isomer.

2α-FluoroGA_9 (**35**) was prepared from the phenacyl ester (**17**) of GA_4 norketone (**16**) which was converted into the 2,3-olefin (**31**) either directly by treatment with phosphoryl chloride in pyridine or by heating the 3-toluene-*p*-sulphonate in collidine. The reaction of the olefin (**31**) with hydrogen fluoride–pyridine and *N*-bromosuccinimide in sulpholane gave the 2α-fluoro-3β-bromide (**40**) which was reduced with tri-*n*-butylstannane to give the 2α-fluoride (**41**). Formation of the corresponding free acid by reductive hydrolysis of the phenacyl ester, followed by a Wittig reaction using salt-free methylene triphenylphosphorane in tetrahydrofuran, gave the required 2α-fluoroGA_9 (**35**).

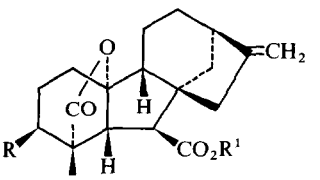
The ^{19}F NMR spectra of the esters **28**, **34**, **40** and **41** were consistent with the stereochemistry predicted for the fluoro-substituent on the basis of their method of formation. All four esters showed a J_{gem} H–F of 47 or 50 Hz. The 2β(eq)-fluoro-ester (**34**) showed two F, H vicinal couplings of 17.5 Hz and two of zero. In the 3β(ax) fluoro-ester (**28**) $J(F, H_{ax})$ and $J(F, H_{eq})$ were 50 and 18 Hz respectively. The 2α(ax) fluorobromide (**40**) showed $J(F, H_{ax})$ of 37 Hz and F, H_{eq} couplings of 21 and 16 Hz. Replacements of the bromine by hydrogen (**41**) gave J (F, H_{ax}) of 38 and 41 Hz and $J(F, H_{eq})$ of both 21 Hz.

2β-Methyl- and 2,2-dimethyl-gibberellins A_4 and A_9

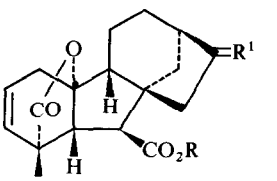
The starting point in the preparation of the 2,2-dimethyl derivatives **36** and **42** was the alkylation of 3-didehydrogibberellin A_4 methyl ester (**11**) with an excess of methyl iodide and potassium *t*-butoxide in refluxing benzene–*t*-butanol. The resulting product was separated by preparative TLC into the 2,2-dimethylketone (**43**) which, after crystallization, had the expected spectroscopic properties, and into the seco-ring A acid (**56**) which was characterized as the methyl ester (**57**). 3-Keto-gibberellins are known [10] to react with catalytic amounts of hydroxide to yield such seco-ring A acids, presumably by a retro-Claisen mechanism; all attempts to prevent formation of the acid **56**, by rigorous drying of solvents and *in situ* generation of potassium *t*-butoxide, were unsuccessful.



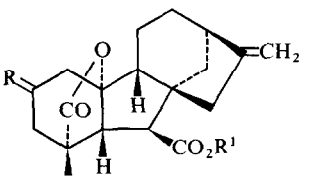
19 R = β-OH, R^1 = Me
20 R = α-OH, R^1 = Me
21 R = β-OMe, R^1 = H
22 R = β-OMe, R^1 = Me



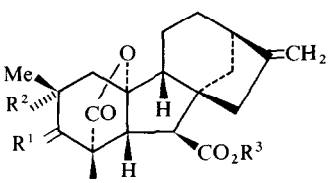
23 R = OMe, R^1 = H
24 R = OMe, R^1 = Me
25 R = Cl, R^1 = H
26 R = F, R^1 = H
27 R = Cl, R^1 = $COCH_2Ph$
28 R = F, R^1 = $COCH_2Ph$



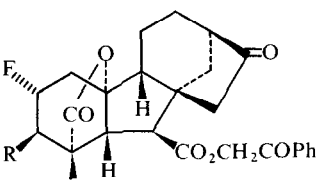
29 R = CH_2COPh, R^1 = CH_2
30 R = Me, R^1 = CH_2
31 R = CH_2COPh, R^1 = O
32 R = H, R^1 = CH_2



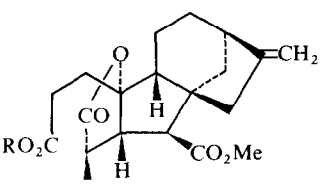
33 R = β-F, H, R^1 = H
34 R = β-F, H, R^1 = Me
35 R = α-F, H, R^1 = H
36 R = Me, Me, R^1 = H
37 R = Me, Me, R^1 = Me
38 R = β-Me, H, R^1 = H
39 R = β-Me, H, R^1 = Me



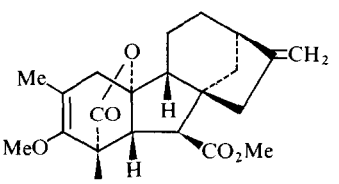
	R^1	R^2	R^3
42	β-OH,H	Me	H
43	O	Me	Me
44	α-OH,H	Me	Me
45	β-OH,H	Me	Me
46	β-OTHP,H	Me	Me
47	β-OTHP,H	Me	H
48	β-Cl,H	Me	Me
49	O	H	Me
50	α-OH,H	H	Me
51	β-OH,H	H	Me
52	β-OH,H	H	H
53	β-OTHP,H	H	Me
54	β-OTHP,H	H	H
55	β-Cl,H	H	Me



40 R = Br
41 R = H



56 R = H
57 R = Me



58

Samples of the 2,2-dimethylketone (**43**), obtained directly by preparative TLC of the methylation mixture were shown to contain 10% of the methyl enol ether (**58**) which was isolated after sodium borohydride reduction of the ketone to the 3α- and 3β-alcohols **44** and **45**. The ratio of the two epimeric alcohols depended upon the solvent; in refluxing 1,2-dimethoxyethane equal amounts were obtained and in tetrahydrofuran–methanol the 3α-alcohol **44** was the major product. The two epimeric alcohols were distinguished by their NMR spectra. In the 3β(ax)-epimer (**45**) the 5-proton signal was deshielded by 0.56 ppm compared to that in the 3α(eq)-alcohol (**44**). In both epimers the 3-proton signal was a singlet.

To obtain the free acid (**42**) from the 3β-alcohol (**45**), the 3β-alcohol was protected as the 3β-tetrahydropyranyl ether (**46**) to avoid epimerization [11, 12] at C-3. Alkaline hydrolysis of this 3-ether (**46**) gave the 3-tetrahydropyranyl acid (**47**) which was hydrolysed by acid to give 2,2-dimethylgibberellin A_4 (**42**). The 3α-alcohol (**44**) was converted into 2,2-dimethylgibberellin A_9 (**36**) via the 3β-chloro-compound (**48**) and 2,2-dimethylgibberellin A_9 methyl ester (**37**).

To obtain the 2β-methyl derivatives of gibberellins A_4 and A_9, the ketone **11** was treated at 0° with one equivalent of methyl iodide and potassium *t*-butoxide in benzene–*t*-butanol. The reaction was monitored by GLC and GC/MS showing that the initially formed monomethylketone (**49**) was rapidly converted into the 2,2-dimethylketone (**43**). Column chromatography of the product, obtained by quenching the reaction at optimum concentration of the monomethylketone (**49**), gave mixtures of the mono- and di-methylketones (**49** and **43**), starting ketone (**11**), and the seco-ring A acid (**56**). Sodium borohydride reduction of the mixtures of the methylated ketones again revealed the presence of the methyl enol ether (**58**) which was obtained admixed with the 2β-methyl-3α-alcohol (**50**), the 2β-methyl-3β-alcohol (**51**) and the 2,2-dimethyl-3α-alcohol (**44**); these products were separated by repeated preparative TLC. The expected small amounts of the 2,2-dimethyl-3β-alcohol (**45**) escaped isolation. The formation of the methyl enol ether of the 2β-methylketone (**58**), but not of the unsubstituted ketone, agrees with the observation [13] that *O*-alkylation of ketones is favoured by substituents adjacent to the carbonyl group.

The epimeric monomethyl 3α- and 3β-alcohols **50** and **51** were distinguished by their NMR spectra. In the 3β(ax)-alcohol (**51**) the 5-proton was deshielded [14] by 0.64 ppm compared to that in the 3α(eq)-alcohol (**50**). The 2β-stereochemistry for the 2-methyl group, which occurred as a doublet at δ 1.03 in both epimers, was deduced from the $J_{2,3}$ of 3 Hz for the 3β-alcohol and of 10 Hz for the 3α-alcohol. The 2β-methyl stereochemistry is consistent with the ratios of 9:1, 2:1, and 5:1 for the 3α- and 3β-alcohols, respectively, obtained by sodium borohydride reduction of the ketone **11**, the monomethylketone **49**, and the dimethylketone **43** in methanol. Thus the presence of a 2β-methyl substituent favours attack of the sodium trimethoxyborohydride at C-3 from the α-face to give a greater proportion of 3β-alcohol than is the case with either the unsubstituted or the 2,2-disubstituted ketone.

2β-Methylgibberellin A_4 (**52**) was prepared from the 2β-methyl-3β-alcohol (**51**) via the 3β-tetrahydropyranyl ethers **53** and **54**, and 2β-methylgibberellin A_9 (**38**) was obtained from the 2β-methyl-3α-alcohol (**50**) via the 3β-chloro-compound (**55**) and 2β-methylgibberellin A_9 methyl ester (**39**).

EXPERIMENTAL

For general procedures see ref. [15].

Methyl ent-10β-*hydroxy*-3-*methylene*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**13**). 3-Oxogibberellin A_9 Me ester [5] (**11**) (100 mg) was treated for 1 hr at room temp. with 5 ml of a soln prepared from methyltriphenylphosphonium bromide (4.8 g), NaH (1.78 g of a 60% dispersion in oil, washed with petrol) in THF (80 ml). Me_2CO (1 ml) was added and the solvents were removed in a stream of N_2. The residue was partitioned between EtOAc and H_2O. Recovery from the organic layer yielded the crude product which was purified by prep. TLC on Si gel using EtOAc–petrol (1:4). The band at R_f 0.4 gave the required 3-methyleneGA$_9$ methyl ester (**13**) (64 mg), m.p. 118–119° (from MeOH) (Found: C, 73.4; H, 7.9. $C_{21}H_{26}O_4$ requires: C, 73.7; H, 7.65%): ν_{max} 1784, 1733, 1660, 1649, 865 cm^{-1}; δ 1.23 (*s*, 18-H_3), 2.70 (*d*, J = 10 Hz, 5-H), 2.82 (*d*, J = 10 Hz, 6-H), 3.75 (*s*, CO_2Me), 4.86 and 5.95 (both *br.* 17-H_2 and 3 = CH_2); *m/z* 342 (M^+, 0.3%), 311 (8), 298 (100), 283 (12), 269 (33), 255 (15), 239 (43), 240 (48), 91 (24), 58 (29).

ent-10β-*Hydroxy*-3-*methylene*-20-*norgibberell*-16-*en*-7,19-*dioic acid* 19,10-*lactone* (**12**). A soln of the Me ester (**13**) (60 mg), from the previous experiment, in MeOH (30 ml) and 2 M NaOH (30 ml) was heated under reflux for 24 hr. After the usual work-up, the recovered product was heated on a steam bath for 0.5 hr to re-lactonize and then was partitioned between EtOAc and 2 M NaOH. Acidification of the alkaline layer and recovery in EtOAc yielded the required 3-methylene GA$_9$ (**12**) (23 mg); *m/z* 328.165 (M^+, 1%, $C_{20}H_{24}O_4$ requires M^+ 328.167), 284 (100), 269 (19), 255 (46), 241 (22), 239 (34), 215 (20) and 91 (41).

Methyl ent-10β-*hydroxy*-3α-*methoxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**24**). GA_4 Me ester (85 mg), MeI (5 ml, freshly distilled from P_2O_5), and Ag_2O (200 mg) were refluxed for 16 hr. After filtration the excess MeI was removed in a stream of N_2. Preparative TLC of the residue on Si gel with Me_2CO–petrol (1:3) gave, from R_f 0.5, the required Me ether (**24**) as an intractable gum (77 mg) (Found: M^+ 360.192. $C_{21}H_{28}O_5$ requires M^+ 360.194): $\nu_{max}^{CH_2Cl_2}$ 1770, 1732, 1660 and 920 cm^{-1}; δ 1.14 (*s*, 18-H_3), 2.60 (*br.*, $W_{1/2}$ = 16 Hz, 13-H), 2.63 and 3.14 (each *d*, J = 10 Hz, 6- and 5-H), 3.20 (*br.*, $W_{1/2}$ = 7 Hz, 3-H), 3.36 (*s*, OMe), 3.68 (*s*, CO_2Me), 4.82 and 4.94 (each *br.*, 17-H_2); *m/z* 360 (M^+, 15%), 342 (3), 328 (69), 300 (42), 289 (36), 284 (100), 225 (60), 224 (89), 105 (22), 91 (25), 71 (93), 43 (78).

ent-10β-*Hydroxy*-3α-*methoxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**23**). The Me ester (**24**) (100 mg), in MeOH (40 ml), and 2 M NaOH (40 ml) were refluxed for 20 hr. The product, recovered in the usual way, was heated on a steam bath for 0.5 hr (TLC monitoring) to cause re-lactonization and then partitioned between EtOAc and 2 M NaOH. Evapn of the EtOAc gave unchanged Me ester (34 mg). Acidification of the alkaline layer and recovery in EtOAc yielded the required 3β-methoxyGA$_9$ (**23**) (65 mg), mp 215–220° (dec.) (Found: M^+ 346.177. $C_{20}H_{26}O_5$ requires M^+ 346.178); ν_{max} 3300–2500, 1770, 1740, 1658 and 887 cm^{-1}; *m/z* 346 (M^+, 27%), 328 (24), 300 (36), 270 (100), 268 (30), 225 (39) and 91 (90).

Benzoylmethyl ent-3β,10β-*dihydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,2-*lactone* (**15**). To dry $(MeOCH_2CH_2)_2O$ (20 ml) at 0° was added $NaBH_4$ (300 mg) and LiBr (700 mg). After 5 min with stirring, a mixture (2 g) of 3-didehydroGA$_7$ (**9**, 35%) and 3-didehydroGA$_4$ (**10**, 65%) was added. After 1.5 hr at 0°, the reaction mixture was poured into ice–H_2O which was adjusted to pH 2.5 with 10 M HCl and was extracted with EtOAc. The EtOAc was extracted with satd aq. $NaHCO_3$ which was

acidified and extracted with EtOAc to yield crude 3-epiGA_4 (**14**) as an oil containing residual $(MeOCH_2CH_2)_2O$.

To this product in MeCN (70 ml) was added $PhCOCH_2Br$ (1.6 g), 18-crown-6-ether (200 mg) and $KHCO_3$ (2.2 g). After refluxing the mixture for 1 hr, the solvent was evapd *in vacuo* and the residue was partitioned between H_2O and EtOAc. The oil, recovered from the organic layer, was adsorbed on Si gel which was placed on a column (36.0 × 3.5 cm) of Si gel (200 g), prepared in petrol. The column was eluted with petrol containing increasing percentages of EtOAc. With 5% EtOAc (1 l.) and 10, 15 and 20% EtOAc (500 ml each), $(MeOCH_2CH_2)_2O$ and unreacted $PhCOCH_2Br$ were eluted and discarded. The material, eluted with 50% (500 ml), 70% (1 l.), and 100% (25 ml) EtOAc, was combined and purified by prep. TLC on Si gel developed twice with EtOAc–petrol (1:1). The band at R_f 0.4 yielded 3-epiGA_4 phenacyl ester (**15**) (1.0 g), mp 139–140° (from C_6H_6–MeOH) (Found: C, 71.8; H, 7.0. $C_{27}H_{30}O_6$ requires: C, 72.0; H, 6.7%); ν_{max} 3450 (br.) 1784, 1754, 1738, 1704, 1658, 1601, 1451, 880, 754, 746 and 690 cm^{-1}; δ 1.29 (*s*, 18-H_3), 1.93 (*s*, OH, removed with D_2O), 2.58 and 2.97 (each *d*, J = 10 Hz, 5- and 6-H), 3.70 (*dd*, J = 6 and 10 Hz, 3-H), 4.98 and 4.88 (each *br.* 17-H_2), 5.36 (*s*, CO_2CH_2Ph), 7.50 (*m*, 3 × ArH) and 7.88 (*dd*, J = 2 and 8 Hz, 2 × ArH); *m/z* 450 (M^+, 20%), 432 (3), 417 (4), 404 (5), 331 (10), 314 (60), 296 (21), 286 (73), 268 (30), 120 (34), 105 (100), 91 (57) and 77 (60).

The material (285 mg), recovered from the band at R_f 0.5 was subjected to prep. TLC with Me_2CO–petrol (2:3) to yield: (a) at R_f 0.5, 3-epiGA_7 phenacyl ester (60 mg) as a gum (Found: M^+ 448.185. $C_{27}H_{28}O_6$ requires M^+ 448.189); $\nu_{max}^{CH_2Cl_2}$ 3560, 1767, 1740, 1705, 1655, 1600, 1448, and 885 cm^{-1}; δ 1.40 (*s*, 18-H_3), 3.36 (*br.*, OH, removed by D_2O), 2.96 (*s*, 5- and 6-H), 4.30 (*br.*, $W_{1/2}$ = 7 Hz, 3-H), 4.90 and 5.01 (both *br.*, 17-H_2), 5.38 (*s*, CO_2CH_2COPh), 5.87 (*dd*, J = 3 and 10 Hz, 2-H), 6.24 (*dd*, J = 2 and 10 Hz, 1-H), 7.52 (*m*, 3 × ArH), and 7.92 (*dd*, J = 2 and 8 Hz, 2 × ArH); *m/z* 448 (M^+, 1%), 430 (2), 404 (2), 385 (5), 372 (10), 294 (11), 120 (21), 105 (100), 91 (38), 77 (71); (b) at R_f 0.65, GA_4 phenacyl ester (164 mg), mp 147–148° (from EtOH–petrol) (Found: C, 72.4; H, 7.1. $C_{27}H_{30}O_6$ requires: C, 72.0; H, 6.7%); ν_{max} 3410 (br.), 1772, 1755, 1705, 1658, 1603, 1450, 895, 752, 745, and 690 cm^{-1}; δ 1.27 (*s*, 18-H_3), 2.10 (*br.*, OH, removed by D_2O), 2.68 (*br.*, $W_{1/2}$ = 12 Hz, 13-H), 2.90 and 3.26 (each *d*, J = 10 Hz, 6- and 5-H), 3.88 (*br.*, $W_{1/2}$ = 7 Hz, 3-H), 4.90 and 5.00 (each *br.*, 17-H_2), 5.36 (*s*, CO_2CH_2COPh), 7.52 (*m*, 3 × ArH) and 7.90 (*dd*, J = 2 and 8 Hz, 2 × ArH).

Benzoylmethyl ent-3α-*chloro- and* 3α-*fluoro*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactones* (**27** *and* **28**). 3-epiGA_4 phenacyl ester (**15**) (850 mg), in dry dioxan (50 ml), was treated with fluoramine [9] (4 ml) and the soln was refluxed for 50 min in an atmosphere of N_2. The mixture was then poured into H_2O which was extracted with EtOAc. The material recovered from the EtOAc was separated by prep. TLC on Si gel and developed twice with Me_2CO–petrol (2:3) into two major fractions: (A) 510 mg (R_f 0.45) and (B) 178 mg (R_f 0.40).

Re-chromatography of fraction (A) on Si gel, developed 4 × with Me_2CO–petrol (1:5) yielded (a) at R_f 0.40, 2,3-didehydroGA_9 phenacyl ester (**29**) (108 mg), identified from the following ^1H NMR data: δ 1.35 (*s*, 18-H_3), 2.86 (*s*, 5- and 6-H), 4.91 and 5.01 (both *br.*, 17-H_2), 5.39 (*s*, CO_2CH_2COPh), 5.73 (*m*, 2- and 3-H), 7.52 (*m*, 3 × ArH) and 7.92 (*dd*, J = 2 and 8 Hz, 2 × ArH); and (b) at R_f 0.45 a mixture (252 mg) containing 2,3-didehydro- (**29**), 3β-chloro- (**27**), and 3β-fluoroGA_9 (**28**) phenacyl esters in the ratio of 1:25:10 by GLC. Re-chromatography of fraction (B), as for fraction (A), gave: (c) at R_f 0.30, 3-chlorofluoroacetyl 3-epiGA_4 phenacyl ester (97 mg), identified by its NMR spectrum (δ 6.30, *d*, J_{HF} = 50 Hz, ClFCHCOO-) and MS (M^+ 544); (d) at R_f 0.40, 2,3-didehydroGA_9 phenacyl ester (**29**) (12 mg); and (e) at R_f 0.45 a mixture (10 mg) of 3β-chloro- and 3β-fluoroGA_9 phenacyl esters (**27** and **28**) in the ratio of 5:2 by GLC.

Fractions (b) and (e) were combined and subjected to HPLC on a column (25 × 0.8 cm) of Hypersil (5 μm) with MeOH–H_2O (3:1) at a flow-rate of 5 ml/min. The mixture (233 mg) was dissolved in MeOH–H_2O (9:1) and aliquots (0.7–1.0 ml) were injected. The following fractions were collected, using UV detection at 280 nm: (i) R_t 9.5 min, 2,3-didehydroGA_9 phenacyl ester (**29**); (ii) R_t 10.7 min, 3β-fluoroGA_9 phenacyl ester (**28**) (48 mg) which crystallized on trituration with MeOH–H_2O with mp 75–78° (Found: C, 71.7; H, 6.5. $C_{27}H_{29}FO_5$ requires: C, 71.1; H, 6.7%); δ (^1H NMR) 1.33 (*s*, 18-H_3), 2.67 (*m*, 13-H), 2.90 and 3.17 (each *d*, J = 10 Hz, 6- and 5-H), 4.59 (*br. d*, J_{HF} = 50 Hz, 3-H), 4.89 and 4.99 (each *br.*, 17-H_2), 5.37 (*s*, CO_2CH_2COPh), 7.49 (*m*, 3 × ArH), and 7.90 (*dd*, J = 2 and 8 Hz, 2 × ArH); Φ* (^{19}F NMR) 192.8 (J_1 = 50, J_2 = 50 and J_3 = 18 Hz); *m/* 452 (M^+, 8%), 288 (31), 136 (20), 120 (40), 105 (100), 91 (30), 77 (52); (iii) R_t 15.5 min, 3β-chloroGA_9 phenacyl ester (**27**) (123 mg), mp 142–143° (from MeOH–H_2O) (Found: C, 69.45; H, 6.6. $C_{27}H_{29}ClO_5$ requires: C, 69.15; H, 6.3%); ν_{max} 1778, 1750, 1710, 1658, 1600, 892, 885, 740, and 688 cm^{-1}; δ 1.31 (*s*, 18-H_3), 2.68 (*br.*, $W_{1/2}$ 15 Hz, 13-H), 2.90 and 3.31 (each *d*, J = 10 Hz, 6- and 5-H), 4.14 (*br.* $W_{1/2}$ = 6 Hz, 3-H), 4.91 and 5.00 (both *br.*, 17-H_2), 5.37 (*s*, CO_2CH_2COPh), 7.52 (*m*, 3 × ArH), and 7.90 (*dd*, J = 2 and 8 Hz, 2 × ArH); *m/z* 470 (M^+ + 2, 19%), 468 (M^+, 47), 304 (48), 269 (23), 225 (26), 169 (35), 120 (68), 105 (100), 91 (40), and 77 (38).

ent-3α-*Fluoro*-10β-*hydroxy*-20-*norgibberell*-16-*ene*,7,19-*dioic acid* 19,10-*lactone* (**26**). 3β-FluoroGA_9 phenacyl ester (**28**) (35 mg) in $MeCO_2H$ (1.5 ml) was treated with freshly activated Zn dust (350 mg) for 1.5 hr at room temp. The reaction mixture was filtered and the filtrate was evapd *in vacuo*. The residue was partitioned between EtOAc and satd aq. $NaHCO_3$. The alkaline phase was acidified and extracted with EtOAc to yield 3β-fluoroGA_9 (**26**) (20 mg), mp 241–245° (dec.) (from Me_2CO) (Found: M^+ 334.157. $C_{19}H_{23}FO_4$ requires M^+ 334.158); *m/z* 334 (M^+, 26%), 316 (100), 288 (84), 270 (78), 227 (29), 225 (24), 105 (28), and 91 (52).

ent-3α-*Chloro*-10β-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**25**). 3β-ChloroGA_9 phenacyl ester (**27**) (85 mg) in $MeCO_2H$ (3 ml) was treated with Zn dust (850 mg) as in the previous experiment to yield 3β-chloroGA_9 (**25**) (45 mg), mp 252–255° (from Me_2CO) (Found: M^+ 350.129. $C_{19}H_{23}ClO_4$ requires M^+ 350.129); *m/z* 352 (M^+ + 2, 4%), 350 (M^+, 11%), 332 (42), 304 (32), 270 (100), 225 (22) and 91 (30).

Methyl ent-3α-*fluoro*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**26**, R^1 = Me). 3-epiGA_4 Me ester (760 mg) and fluoramine (3.2 ml) in dry dioxan (48 ml) were refluxed for 40 min in an atmosphere of N_2. The soln was poured into H_2O and the product, recovered in EtOAc, was shown by GLC and GC/MS to contain 2,3-didehydro-, 3β-fluoro-, and 3β-chloroGA_9 Me esters. Prep. TLC of this mixture on Si gel, developed 3 × with Me_2CO–petrol (1:8) gave three fractions: (i) from R_f 0.31–0.38, a mixture (330 mg) of 2,3-dehydroHA_9 Me ester (85%) and 3β-fluoroGA_9 Me ester (15%); (ii) from R_f 0.38–0.45, a mixture (206 mg) of the same compounds containing 90% of the 3β-fluoro-derivative; and (iii) from R_f 0.45–0.50 a mixture (73 mg) of the 3β-chloro- and 3β-fluoroGA_9 Me esters in the ratio of 3:1.

Re-chromatography of fraction (iii) under the same conditions gave pure 3β-chloroGA_9 Me ester (**25**, R^1 = Me) (51 mg), identified by direct comparison with an authentic specimen, and pure 3β-fluoroGA_9 Me ester (**26**, R^1 = Me) (17 mg), mp 114–115° (from Me_2CO–petrol) (Found: C, 68.7; H, 7.5. $C_{20}H_{25}O_4F$ requires C, 68.9; H, 7.2%); ν_{max} 1779, 1742, 1658 and

885 cm^{-1}; δ (^{1}H NMR) 1.20 (*s*, 18-H_3), 2.68 and 3.14 (each *d*, J = 10 Hz, 6- and 5-H), 3.72 (*s*, CO_2Me), 4.58 (*d*, J_{HF} = 50 Hz, 3-H), 4.87 and 4.99 (each *br*., 17-H_2); Φ* (^{19}F NMR) 192.9 (J_1 = 50, J_2 = 50 and J_3 = 18 Hz); *m/z* 348 (M^+, 6%), 316 (93), 302 (2), 288 (100), 248 (18), 243 (14) and 169 (20).

Repeated prep. TLC of fraction (ii) on Si gel, developed twice with Me_2CO–petrol (1:10) yielded pure 3β-fluoroGA$_9$ Me ester (126 mg) and a mixture (56 mg) of the 3β-fluoro- and 2,3-didehydroGA$_9$ Me esters in the ratio 1:1.5.

Repeated prep. TLC of fraction (*i*), plus the mixture from fraction (ii) on Si gel, developed 3× with Me_2CO–petrol (1:10) afforded pure 3β-fluoroGA$_9$ Me ester (34 mg) and pure 2,3-didehydroGA$_9$ Me ester (**30**) (174 mg), identified by direct comparison with an authentic specimen.

Methyl ent-2α,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7-*oate*-19-*oic acid* 19,10-*lactone* (**19**). To GA$_{40}$ Me ester (**20**) (180 mg) in Me_2CO (3 ml) at 0° was added excess Jones reagent. After 5 min, MeOH was added and the soln was added to H_2O. A product less polar than starting material by TLC, was recovered in EtOAc. It was dissolved in EtOH (20 ml) and treated for 2 hr at room temp. with $NaBH_4$. Removal of the solvent *in vacuo* and partitioning of the residue between EtOAc and 2 M HCl gave, from the organic layer, a 1:1 mixture (GLC) of GA$_{40}$ Me ester (**20**) and GA$_{51}$ Me ester (**19**). This mixture, plus the product from the identical oxidation of GA$_{40}$ Me ester (380 mg) and reduction of the product, was subjected to prep. TLC on Si gel with EtOAc–petrol (3:2). The band at R_f 0.35 yielded GA$_{51}$ Me ester (**19**) (135 mg) which crystallized from CH_2Cl_2–petrol with mp 140–142° (Found: C, 69.1; H, 8.0. $C_{20}H_{26}O_5$ requires: C, 69.35; H, 7.6%); ν_{max} 3525, 1782, 1715, and 1660 cm^{-1}.

Methyl ent-2α-*fluoro*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**34**). GA$_{40}$ Me ester (**20**) (200 mg) and fluoramine (0.67 ml) in dioxan (10 ml) were left for 1 hr at room temp., then heated at 60° for 25 min. The reaction mixture was added to H_2O and the product, recovered in EtOAc, was shown by GC/MS to contain 2β-fluoroGA$_9$ Me ester and 2,3-didehydroGA$_9$ Me ester in the ratio 11:9. Prep. TLC of this mixture on Si gel, developed × 4 with Me_2CO–petrol (1:25) gave only one visible band from which the original mixture (151 mg) was obtained. Repeated prep. TLC developing 6× with Me_2CO–petrol (1:10) gave a partial separation. The upper band (84 mg) gave the 2β-fluoro-ester (**34**), admixed with 25% of the 2,3-olefin (**30**) and the lower band gave a mixture (31 mg) containing 80% of the olefin (**30**).

Repeated prep. TLC of the upper band with Me_2CO–petrol (1:12.5, 6 developments) yielded pure 2β-fluoroGA$_9$ Me ester (**34**) (54 mg), mp 100–105° (by trituration with MeOH–H_2O) (Found: C, 68.8; H, 7.3. $C_{20}H_{25}O_4F$ requires: C, 68.9; H, 7.2%); δ (^{1}H NMR) 1.15 (*s*, 18-H_3), 2.60 and 2.80 (each *d*, J = 10 Hz, 6- and 5-H), 3.74 (*s*, CO_2Me), 4.82 (*d* of *m*, J = 50 Hz, 2-H), 4.88 and 5.00 (both *br*. 17-H_2); Φ* (^{19}F NMR) 183.8 (*dt*, J = 50, 17.5 and 17.5 Hz); *m/z* 348 (M^+, 8%), 316 (100), 296 (6), 288 (79), 284 (14), 261 (14), 245 (20), 244 (29) and 243 (18).

ent-2α-*Fluoro*-10β-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**33**). The Me ester (**34**) (30 mg) in MeOH (11 ml) and 2 M NaOH (11 ml) was refluxed for 20 hr. After the usual work-up and heating at 60° to reform the lactone, the product was extracted from EtOAc by satd aq. $NaHCO_3$. Acidification of the alkaline extract and recovery in EtOAc gave an oil which was purified by prep. TLC on Si gel with EtOAc–petrol–$MeCO_2H$ (50:50:1) to give 2β-fluoroGA$_9$ (**33**) (10 mg) admixed with *ca* 20% of the olefin (**32**) (by NMR). These were separated by prep. HPLC on a Shandon Hypersil ODS semi-preparative column with K-Pi buffer (pH 3)–MeOH (2:3) as eluant (2 ml/min). Detection was by UV at 204 nm. R_t (olefin, **32**) = 32.5 min and R_t (2β-fluoroGA$_9$, **33**) = 37 min. 2β-FluoroGA$_9$ (6.2 mg), was recovered from the relevant fractions by adding $NaHCO_3$ until alkaline, removal of the MeOH *in vacuo*, acidification and recovery in EtOAc. It contained *ca* 10% of the 15-double bond isomer (GC/MS).

Methyl ent-10β-*hydroxy*-2α-*methoxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**22**). GA$_{51}$ Me ester (**19**) (140 mg) and MeI (10 ml, distilled from P_2O_5) were refluxed for 16 hr with freshly prepared Ag_2O (600 mg). The filtrate from the reaction mixture was diluted by EtOAc and washed with H_2O. Recovery from the EtOAc, by evapn, furnished the required 2β-methoxyGA$_9$ Me ester (**22**) (155 mg), mp 165–167° (from Me_2CO–petrol) (Found: C, 69.4; H, 8.3. $C_{21}H_{28}O_5$ requires: C, 70.0; H, 7.8%); ν_{max} 1767, 1736, 1657, 885 cm^{-1}; δ 1.12 (*s*, 18-H_3), 2.67 (*s*, 5- and 6-H), 3.32 (*s*, OMe), 3.50 (*m*, 2-H), 3.72 (*s*, CO_2Me), 4.85 and 4.97 (both *br*., 17-H_2); *m/z* 360 (M^+, 14%), 328 (87), 284 (83), 268 (100), 256 (38), 227 (59), 225 (86) and 224 (56).

ent-10β-*Hydroxy*-2α-*methoxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**21**). The Me ester (**22**) (140 mg), MeOH (50 ml) and 2 M NaOH (50 ml) were refluxed for 20 hr. The crude product, obtained by the usual work-up, was heated at 60° for 30 min, then partitioned between EtOAc and satd aq. $NaHCO_3$. Recovery from the organic layer gave unreacted Me ester (**22**) (60 mg). Recovery from the alkaline layer yielded the required 2β-methoxyGA$_9$ (**21**) (69 mg) as a gum (Found: M^+ 346.177. $C_{20}H_{26}O_5$ requires M^+ 346.178); *m/z* 346 (M^+, 17%), 328 (17), 270 (100), 268 (26), 256 (95), 225 (83), and 183 (45).

Benzoylmethyl ent-3α,10β-*dihydroxy*-17,20-*bisnor*-16-*oxogibberellane*-7-*oate*-19-*oic acid* 19,10-*lactone* (**17**). A mixture (3.0 g) containing 65% GA$_4$ and 35% GA$_7$ in THF–H_2O (1:1, 100 ml) was treated at room temp. overnight with OsO_4 (20 mg) and $NaIO_4$ (4.8 g). The THF was removed *in vacuo* and the residual aq. layer was extracted with ErOAc. The crude norketone (**16**) recovered from the EtOAc was dissolved in MeCN (100 ml) and refluxed for 1 hr with $PhCOCH_2Br$ (2.4 g), 18-crown-6-ether (300 mg) and $KHCO_3$ (3.3 g). The solvent was removed *in vacuo* and the residue was partitioned between EtOAc and H_2O. Recovery from EtOAc yielded an oil which was chromatographed on a column (32.0 × 3.5 cm) of Si gel (200 g), made up in petrol. Elution with 5% EtOAc in petrol gave unchanged $PhCOCH_2Br$. Fractions eluted with 50–70% EtOAc in petrol were combined to give GA$_4$ norketone phenacyl ester (**17**) (2.4 g), mp 105–108° (from MeOH–H_2O) (Found: C, 69.1; H, 6.6. $C_{26}H_{28}O_7$ requires: C, 69.0; H, 6.25%); ν_{max} 3460, 1768, 1740, 1700, 1600, 745, 690 cm^{-1}; δ 1.25 (*s*, 18-H_3), 2.91 (*br*. removed by D_2O, OH), 2.89 and 3.25 (each *d*, J = 10 Hz, 6- and 5-H), 3.83 (*br*., $W_{1/2}$ = 7 Hz, 3-H), 5.27 and 5.47 (each *d*, J = 17 Hz, CO_2CH_2COPh), 6.50 (*m*, 3 × ArH) and 7.87 (*dd*, J = 2 and 8 Hz, 2 × ArH).

Benzoylmethyl ent-10β-*hydroxy*-17,20-*bisnor*-16-*oxo*-3α-*toluene*-p-*sulphonyloxygibberellan*-7-*oate*-19-*oic acid* 19,10-*lactone*. The foregoing phenacyl ester (**17**) (1.9 g) and 4-$MeC_6H_4SO_2Cl$ (5 g) in C_5H_5N (20 ml) were left for 3 days at room temp. The product, obtained by the usual work-up, was chromatographed on a column (38.0 × 3.5 cm) of Si gel (250 g). Fractions eluted with petrol (500 ml), 10% EtOAc (1 l.) and 15% EtOAc (500 ml) were discarded. The required toluene-*p*-sulphonate (2.3 g) was eluted with 50% EtOAc (1 l.), 60% EtOAc (500 ml) and Me_2CO (1.5 l.) and crystallized from Me_2CO–petrol, mp 209–221° (Found: C, 65.5; H, 5.9. $C_{33}H_{34}O_9S$ requires: C, 65.3; H, 5.65%); ν_{max} 1770, 1742, 1702, 1600, 1375, 1178, 818, 730, 690, 670 cm^{-1}; δ 0.98 (*s*, 18-H_3), 2.46 (*s*, ArMe), 2.85 and 3.17 (each *d*, J = 10 Hz, 6- and 5-H), 4.55 (*br*, $W_{1/2}$ = 7 Hz, 3-H), 5.29 and 5.54 (each *d*, J = 17 Hz, CO_2CH_2COPh), 7.50 (*m*, 5 × ArH) and 7.90 (*m*, 4 × ArH); *m/z* 578 ($M^+ - 28$, 1%), 434 (4), 271 (30), 225 (31), 120 (53), 105 (100), 91 (50), and 77 (37).

Benzoylmethyl ent-3α-*bromo*-2β-*fluoro*-17,20-*bisnor*-16-*oxogibberellan*-7-*oate*-19-*oic acid* 19,10-*lactone* (**40**). The foregoing toluene-*p*-sulphonate (2.25 g) and dry collidine (50 ml)

were refluxed for 9 hr and the reaction was worked up in the usual way. The product, in EtOAc, was washed with satd aq. $NaHCO_3$ and H_2O, and evapd to yield an oil which was chromatographed on a column (32.0 × 3.0 cm) of Si gel (150 g). Fractions eluted with 30–50% EtOAc in petrol yielded a mixture (1.1 g) shown by NMR to contain unreacted toluene-*p*-sulphonate (24%) and 2,3-didehydroGA$_9$ norketone phenacyl ester (**31**) (70%) with δ 1.35 (*s*, 18-H_3), 2.88 (*s*, 5- and 6-H), 5.30 and 5.52 (each *d*, J = 17 Hz, CO_2CH_2COPh), 5.76 (*m*, 2- and 3-H), 7.54 (*m*, 3 × ArH) and 7.91 (*dd*, J = 2 and 8 Hz, 2 × ArH). This inseparable mixture (1.0 g) in sulpholane (20 ml) was treated for 3 hr at room temp. with NBS (680 mg) and C_5H_3N–HF (17 ml) in a polythene flask. The reaction mixture was added carefully to ice–H_2O which was extracted with EtOAc to give an oil. Residual sulpholane was removed by prep. TLC on Si gel with EtOAc–petrol–HOAc (50:50:1). Recovery from the band at R_f 0.3–0.5 gave a gum (640 mg) which was rechromatographed in the same solvent system to give the unreacted toluene-*p*-sulphonate (108 mg) from R_f 0.35–0.45 and, from the band at R_f 0.45–0.55, the required bromofluoride (**40**) (323 mg) as a gum (Found: M^+ 534.087. $C_{26}H_{26}O_6{}^{81}BrF$ requires M^+ 534.088); $\nu_{max}^{CH_2Cl_2}$ 1781, 1740, 1707, 1600 cm^{-1}; δ (^{1}H NMR) 1.38 (*s*, 18-H_3), 3.01 and 3.56 (each *d*, J = 11 Hz, 6- and 5-H), 4.30 (*d*, J = 16 Hz, 3-H), 5.17 (*dd*, J = 47 and 4 Hz, 2-H), 5.30 and 5.53 (each *d*, J = 15 Hz, CO_2CH_2COPh), 7.54 (*m*, 3 × ArH), and 7.88 (*dd*, J = 2 and 8 Hz, 2 × ArH); Φ* (^{19}F NMR) 150.1 (14 lines, J = 47, 37, 21 and 16 Hz); *m/z* 534 and 532 (4%), 506 and 504 (2), 387 and 385 (3), 289 (10), 105 (100), 91 (16), and 77 (20).

Benzoylmethyl ent-2*β*-*fluoro*-10*β*-*hydroxy*-17,20-*bisnor*-16-*oxogibberellan*-7-*oate*-19-*oic acid* 19,10-*lactone* (**41**). The bromofluoride (**40**) (269 mg) in dry C_6H_6 (25 ml) was refluxed for 35 min in an atmosphere of N_2 with *n*-Bu_3SnH (530 *μ*l) and 2,2-azo-bis(2-methylpropionitrile) (5 mg). The residue, obtained by evapn of the solvent was purified by prep. TLC on Si gel with EtOAc–petrol–HOAc (50:50:1) to give, from the band at R_f 0.3, the required 2*α*-fluoro-compound (**41**) (120 mg) (Found: M^+ 454.179. $C_{26}H_{27}O_6F$ requires M^+ 454.179); δ (^{1}H NMR) 1.26 (*s*, 18-H_3), 2.69 and 3.00 (each *d*, J = 10 Hz, 6- and 5-H), 5.06 (*br. d*. J = 47 Hz, 2-H), 5.30 and 5.54 (each *d*, J = 16 Hz, CO_2CH_2COPh), 7.53 (*m*, 3 × ArH), and 7.90 (*dd*, J = 2 and 8 Hz, 2 × ArH); Φ* (^{19}F NMR) 164.8 (17 lines, J = 47, 38, 41, 21, 21 Hz); *m/z* 454 (M^+, 23%), 105 (100), 91 (26) and 77 (29).

ent-2*β*-*Fluoro*-10*β*-*hydroxy*-17,20-*bisnor*-16-*oxogibberellane*-7,19-*dioic acid* 19,10-*lactone*. The phenacyl ester (**41**) (100 mg) in HOAc (7.5 ml) was treated for 45 min at room temp. with freshly activated Zn dust (1.0 g). After filtration of the reaction mixture, the filtrate was evaporated, adding toluene to facilitate removal of the HOAc. The residue was partitioned between satd aq. $NaHCO_3$ and EtOAc. Acidification and extraction of the alkaline layer gave the required 2*α*-fluoro-norketone (33 mg) (Found: M^+ 336.137. $C_{18}H_{21}O_5F$ requires M^+ 336.137); δ 1.20 (*s*, 18-H_3), 2.59 (*d*, J = 10 Hz, 5-H), 2.59 and 2.86 (each *d*, J = 10 Hz, 6- and 5-H), and 5.06 (*br. d*, J = 47 Hz, 2-H).

ent-2*β*-*Fluoro*-10*β*-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**35**). The foregoing 2*α*-fluoro-norketone (30 mg), in pyridine (600 *μ*l) containing HMDS (110 *μ*l) and TMCS (100 *μ*l), was left for 45 min at room temp. The residue, obtained by evapn in a stream of N_2, was dissolved in dry Me_2CO and filtered through Celite. Evapn of the filtrate yielded the TMSi ester which was treated with an aliquot (2.0 ml) of a soln, prepared from methyltriphenylphosphonium bromide (1.5 g), NaH (330 mg of a 60% dispersion in oil, washed with petrol) and THF (12 ml). After being stirred at room temp. for 1 hr, Me_2CO (1 ml) was added and the mixture was evapd in a stream of N_2. H_2O (3 ml) and HOAc (150 *μ*l) were added and the mixture was stirred at room temp. for 30 min. The aq. soln was diluted with satd aq. $NaHCO_3$ (40 ml) and washed twice with EtOAc. Acidification of the alkaline soln with 10 M HCl and extraction with EtOAc yielded an oil (30 mg) which was subjected to prep. TLC on Si gel with EtOAc–petrol–HOAc (50:50:1). Extraction of the band at R_f 0.7 yielded the required 2*α*-fluoroGA$_9$ (**35**) as an oil (12 mg) (Found: M^+ 334.158. $C_{19}H_{23}FO_4$ requires M^+ 334,158); *m/z* 334 (M^+, 3%), 316 (12), 290 (68), 247 (100), 245 (36), 222 (26), 221 (27), 177 (31), 129 (276), 105 (28) and 91 (58).

Methylation of ent-10*β*-*hydroxy*-20-*nor*-3-*oxogibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**11**). (a) *With excess* MeI. K metal (135 mg) was dissolved in *t*-BuOH (12 ml, distilled from K) and C_6H_6 (12 ml, distilled from Na) by heating under reflux in N_2. The ketone [6] (**11**) (600 mg) and MeI (500 *μ*l, freshly distilled from P_2O_5) were added and the reaction was completed by refluxing for 40 min. The cooled soln was poured into dil HCl from which a gum was recovered by extraction with EtOAc. Prep. TLC of the product on Si gel with EtOAc–petrol (1:1) gave, at R_f 0.65–0.75, methyl *ent*-2,2-dimethyl-10*β*-hydroxy-20-nor-3-oxogibberell-16-en-7-oate-19-oic acid 19,10-lactone (**43**) (362 mg), mp 204–205° (from Me_2CO–petrol) (Found: C, 70.0; H, 7.6; M^+ 372.194. $C_{22}H_{28}O_5$ requires: C, 70.9; H, 7.6%; M^+ 372.194); ν_{max} 1865, 1735, 1713, 1658 and 888 cm^{-1}; δ 1.13 (*s*, 3 H), 1.17 (*s*, 6 H), 2.73 and 2.36 (AB, J = 14.5 Hz, 1-H_2), 2.77 and 3.01 (AB, J = 11 Hz, 5-and 6-H), 3.66 (*s*, CO_2Me), 4.81 and 4.94 (each *br*., 17-H_2); *m/z* 372 (M^+, 24) and 288 (100).

The prep. TLC band at 0.10 yielded *ent*-10*β*-hydroxy-20-nor-3,4-secogibberell-16-en-3,7,19-trioic acid 19,10-lactone (**56**) as a gum (97 mg) (Found: M^+ 362.172; $C_{20}H_{26}O_6$ requires M^+ 362.173); $\nu_{max}^{CH_2Cl_2}$ 3200–2500, 1765, 1725, 1660 and 886 cm^{-1}; *m/z* 362 (M^+, 0.7%), 302 (100), 274 (94), and 229 (67). Methylation (CH_2N_2) gave the Me ester (**57**) as a gum (Found: M^+ 376.187. $C_{21}H_{28}O_6$ requires M^+ 376.189); $\nu_{max}^{CH_2Cl_2}$ 1765, 1728, 1660, and 885 cm^{-1}; δ 1.21 [*d*, J = 7 Hz (*s* by irradiation at δ 3.05), 18-H_3], 3.05 [1 H, *m* (simplified to a *d*, J = 5 Hz on irradiation at δ 1.21)], 3.70 (*s*, 2 × CO_2Me), and 4.94 (*br*., $W_{1/2}$ = 5 Hz, 17-H_2); *m/z* 376 (9), 330 (100), 316 (58), 302 (48), 270 (61) and 243 (44).

(b) *With* 1 *equivalent of* MeI. As in (a) K metal (454 mg, 11.6 mmol) was dissolved in refluxing *t*-BuOH (30 ml) and C_6H_6 (30 ml) in N_2. The soln was cooled to 0° and the ketone (**11**) (4.0 g, 11.63 mmol) and MeI (750 *μ*l, 12 mmol) were added. The reaction soln was kept at 0° and monitored by GLC on a 2% QF-1 column. After 2.5 hr the reaction soln was poured into dil HCl. The product, extracted with EtOAc, was chromatographed on a Si gel column (32 × 3.5 cm) which was eluted with increasing amounts of EtOAc in petrol.

Fractions eluted with 9–12.5% EtOAc gave a mixture (593 mg) of a monomethyl derivative; *m/z* 358 (M^+, 43), 330 (36), 326 (100), 314 (41), 312 (35), 298 (42), 253 (39), 189 (38), 160 (40), and the dimethylketone (**43**) in the ratio 9:11 by GLC and GC/MS. Fractions, eluted with 13–27.5% EtOAc, were subjected to prep. TLC on Si gel with EtOAc–petrol (2:3). The band at R_f 0.65–0.75 gave a mixture (484 mg) of a monomethylketone and the dimethylketone (**43**) in the ratio 13:7. A band at R_f 0.55–0.65 gave the starting ketone (395 mg). Fractions eluted with 52.5–85% EtOAc gave the seco-acid (**56**) (564 mg) identified by the MS of the Me ester.

The methylketones from the above and similar preparations were later shown by the following reductions to contain varying amounts of the Me enol ether (**58**) which was inseparable from the 2,2-dimethylketone (**43**) by GLC and TLC.

Sodium borohydride reduction of methyl ent-2,2-*dimethyl*-10*β*-*hydroxy*-3-*oxo*-20-*norgibberell*-16-*ene*-7-*oate*-19-*oic acid* 19,10-*lactone* (**43**). (a) *In* THF–MeOH. The ketone (460 mg) in THF (10 ml) and MeOH (10 ml), was treated with $NaBH_4$ (70 mg) for 2 hr at room temp. then for 0.5 hr under reflux. The mixture was poured into H_2O which was adjusted to pH 3.0 with 10 M HCl

and extracted with EtOAc. The product, recovered from the EtOAc, was separated by prep. TLC with EtOAc–petrol–HOAc (50:50:1) into three products: (i) from R_f 0.75–0.85, methyl *ent*-2-methyl-3-methoxy-10β-hydroxy-20-norgibberell-2,16-diene-7-oate-19-oic acid 19,10-lactone (**58**) (41 mg), mp 181–183° (from Me_2CO–petrol) (Found: C, 70.6; H, 7.4. $C_{22}H_{28}O$ requires: C, 70.9; H, 7.6%); ν_{max} 1764, 1770, 1661 and 885 cm^{-1}; δ 1.20 (*s*, 18-H_3), 1.66 (*s*, 2-Me), 2.63 and 2.87 (each *d*, *J* = 11 Hz, 5- and 6-H), 3.52 (*s*, OMe), 3.69 (*s*, CO_2Me), 4.83 and 4.94 (each *br.*, 17-H_2); *m/z* 372 (M^+, 9%), 328 (100), 253 (82) and 237 (67); (ii) from R_f 0.55–0.65 methyl *ent*-2,2-dimethyl-3α, 10β-dihydroxy-20-norgibberell-16-en-7-oate-19-oic acid 19,10-lactone (**45**) (41 mg), mp 243–245° (from Me_2CO–petrol) (Found: C, 69.6; H, 8.1; M^+ 374.208. $C_{22}H_{30}O_5$ requires: C, 70.6; H, 8.1%; M^+ 374.209); ν_{max} 3493, 1760, 1735 and 1662 cm^{-1}; δ 1.03 (*s*, 2 × Me), 1.12 (*s*, 1 × Me), 1.49 and 1.74 (each *d*, *J* = 14.5 Hz, 1-H_2), 2.66 and 3.12 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.45 (*s*, 3-H), 3.76 (*s*, CO_2Me), 4.81 and 4.94 (each *br.*, 17-H_2); *m/z* 374 (M^+, 3%), 356 (5), 328 (16), 312 (100), 252 (63), 237 (53) and 91 (52); and (iii) from R_f 0.35–0.55 methyl *ent*-2,2-dimethyl-3β,10β-dihydroxy-20-norgibberell-16-en-7-oate-19-oic acid 19,10-lactone (**44**) (203 mg), mp 211–212° (from Me_2CO–petrol) (Found: C, 70.3; H, 8.3. $C_{22}H_{30}O_5$ requires C, 70.6; H, 8.1%); ν_{max} 3497, 1763, 1735, 1655 and 877 cm^{-1}; δ 1.06 (*s*, 1 × Me), 1.17 (*s*, 2 × Me), 1.52 and 2.17 (each *d*, *J* = 14.5 Hz, 1-H_2), 2.59 and 2.79 (each *d*, *J* = 11 Hz, 5- and 6-H), 3.54 (*s*, 3-H), 3.72 (*s*, CO_2Me), 4.86 and 4.98 (each *br.*, 17-H_2); *m/z* 374 (M^+, 9%), 356 (55), 328 (100), 314 (66), 300 (75) and 91 (44).

(b) *In* 1,2-*dimethoxyethane*. The ketone (**43**) (140 mg) in 1,2-dimethoxyethane (10 ml) was treated with $NaBH_4$ (15 mg) and the reaction mixture was refluxed for 1 hr. Work-up and prep. TLC as in (a) gave (i) from R_f 0.75–0.85, the Me enol ether (**58**) (16 mg); (ii) from R_f 0.55–0.65, the 3β-alcohol (**45**) (40 mg), and (iii) from R_f 0.35–0.55, the 3α-alcohol (**44**) (38 mg).

Sodium borohydride reduction of methyl ent-2α-*methyl- and* ent-2,2-*dimethyl*-10β-*hydroxy*-3-*oxo*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactones* (**49** *and* **43**). The mixture (240 mg) of the monomethyl- (65%) and dimethyl- (35%) ketones in THF (7.5 ml) and MeOH (7.5 ml) was treated with $NaBH_4$ (17 mg) for 1 hr at 0°. The usual work-up and prep. TLC of the product as in the previous experiment gave: (i) from R_f 0.75–0.85 the Me enol ether (**58**) (30 mg); (ii) from R_f 0.75–0.85, a mixture (90 mg), separated by prep. TLC after development (×3) with EtOAc–petrol–HOAc (30:70:1) to give, at R_f 0.45, *ent*-2α-methyl-3α,10β-dihydroxy-20-norgibberell-16-en-7-oate-19-oic acid 19,10-lactone (**51**) (45 mg), mp 154–155° (from Me_2CO–petrol) (Found: C, 70.6; H, 8.3. $C_{21}H_{28}O_5$ requires: C, 70.1; H, 7.8%); ν_{max} 3505, 1763, 1735, and 1660 cm^{-1}; δ 1.03 (*d*, *J* = 6.5 Hz, 2-Me), 1.16 (*s*, 18-H_3), 2.68 and 3.17 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.61 (*d*, *J* = 3 Hz, 3-H), 3.71 (*s*, CO_2Me), 4.87 and 4.98 (each *br.*, 17-H_2); *m/z* 360 (M^+, 5%), 328 (65), 298 (70), 238 (100), 91 (50), and 58 (51).

From R_f 0.35 the 2,2-dimethyl 3α-alcohol (**44**) (38 mg) was obtained. (iii) From R_f 0.4–0.5 of the original prep. TLC methyl *ent*-2α-methyl-3β,10β-dihydroxy-20-norgibberell-16-en-7-oate-19-oic acid 19,10-lactone (**50**) (88 mg), mp 173–175° (from Me_2CO–petrol) (Found: M^+ 360.194. $C_{21}H_{28}O_5$ requires M^+ 360.194); ν_{max} 3498, 1753, 1655, and 878 cm^{-1}; δ 1.03 (*d*, *J* = 6.5 Hz), 1.07 (*s*, 18-H_3), 2.53 and 2.75 (each *d*, *J* = 11 Hz, 5- and 6-H), 3.23 (*d*, *J* = 10, 3-H), 3.71 (*s*, CO_2Me), 4.85 and 4.98 (each *br.*, 17-H_2); *m/z* 360 (M^+, 6%), 342 (68), 328 (84), 314 (79), 300 (100), 286 (56), 282 (50) and 199 (59).

ent-2α-*Methyl*-3α,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**52**). To the 2β-methyl-3β-alcohol Me ester (**51**) (53 mg), in CH_2Cl_2 (8 ml), dihydropyran (50 μl) and 4-$MeC_6H_4SO_3H$ acid (1 crystal) were added and the mixture was stirred at room temp. for 4 hr. H_2O (10 ml) was added and the organic layer was collected. The H_2O layer was re-extracted with EtOAc. The combined organic extracts were washed with H_2O and then evapd to yield a gum. Prep. TLC on Si gel (EtOAc–petrol, 2:3) yielded, at R_f 0.55, the 3β-THP-ether (**53**) (65 mg) as a gummy mixture of diastereoisomers as shown by its NMR spectrum. (Found: M^+ 444.251. $C_{26}H_{36}O_6$ requires M^+ 444.251); δ 0.94–1.19 (2 × *d* and 1 × *s*, 2-Me and 18-H_3), 2.67 and 3.20 (each *d*, *J* = 11 Hz, 6- and 5-H), 4.05–3.70 (*m*, 6′-H_2), 4.55 (*br.*, 2′-H), 4.97 (*d*, *J* = 3 Hz, 3-H), 4.84 and 4.97 (each *br.*, 17-H_2); *m/z* 444 (M^+, 90.7), 360 (24), 342 (32), 314 (30), 298 (30), 239 (30), 86 (65) and 35 (100).

The THP ether (**53**) (65 mg), in MeOH (60 ml) and 2 M NaOH (60 ml), was refluxed overnight. The MeOH was removed *in vacuo* and the aq. concentrate was further diluted with H_2O before acidification to pH 3.0 with conc HCl. The product, recovered in EtOAc, was dissolved in Me_2CO (6 ml) and MeOH (0.5 ml). 4-$MeC_6H_4SO_3H$ (3 mg) was added and the soln stirred at room temp. until the hydrolysis was complete (2 hr, TLC monitoring). The solvents were removed *in vacuo* and the product was purified by prep. TLC with EtOAc–petrol–HOAc (50:50:1). Extraction of the band at R_f 0.3 gave 2β-methylGA$_4$ (**52**) (23 mg) as a gum, pure by GLC (as its TMSi derivative) (Found: M^+ 346.177. $C_{20}H_{26}O_5$ required M^+ 346.178); 1.03 (*d*, *J* = 6.5 Hz, 2-Me), 1.22 (*s*, 18-H_3), 2.72 and 3.10 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.66 (*d*, *J* = 3 Hz, 3-H), 4.86 and 5.00 (each *br.*, 17-H_2), *m/z* 346 (M^+, 7), 328 (18), 310 (17), 300 (25), 284 (100), 282 (41), 269 (21), 239 (36), 238 (30), 223 (23), 105 (26) and 91 (46).

Re-methylation with CH_2N_2 gave a single GLC peak with an MS identical to starting material (**51**).

ent-2,2-*Dimethyl*-3α,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**42**). To the 2,2-dimethyl-3β-alcohol (**45**) (40 mg), in CH_2Cl_2 (4 ml), dihydropyran (40 μl) and 4-$MeC_6H_4SO_3H$ (1 crystal) were added and the mixture was stirred at room temp. for 3 hr. Work-up as above and prep. TLC with EtOAc–petrol (2:3) gave, at R_f 0.65, the 3β-THP-ether (**46**) (52 mg) as a diastereoisotopic mixture (Found: M^+ 458.266. $C_{27}H_{38}O_6$ requires M^+ 458.267); δ 1.05 (*s*, 2 × Me), 1.15 (*s*, 1 × Me), 2.55 (*d*, *J* = 11 Hz, 6-H), 3.13 and 3.17 (each *d*, *J* = 11 Hz, 5-H), 3.72 (*s*, CO_2Me), 3.75–4.05 (*m*, 6′-H_2), 4.56 (*br.* 2′-H), 4.99 (*s*, 3-H), 4.85 and 4.99 (each *br.*, 17-H_2); *m/z* 458 (M^+, 0.3) and 85 (100).

The THP ether (**46**) (52 mg) in MeOH (50 ml) and 2 M NaOH (50 ml) was refluxed overnight. The reaction was worked up as in the previous experiment. Treatment of the product with 4-$MeC_6H_4SO_3H$ (2 mg) in Me_2CO (10 ml) and MeOH (1 ml) gave, after prep. TLC with EtOAc–petrol–HOAc (70:30:1), at R_f 0.6, 2,2-dimethylGA$_4$ (**42**) (20 mg) as a gum (Found: M^+ 360.193. $C_{21}H_{28}O_5$ requires M^+ 360.194); δ 1.88 (*s*, 2 × Me), 1.23 (*s*, 1 × Me), 2.71 and 3.11 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.39 (*s*, 3-H), 4.85 and 4.97 (each *br.*, 17-H_2); *m/z* 360 (M^+, 6), 342 (3), 314 (14), 298 (40), 237 (28), 101 (37) and 85 (100).

Methyl ent-2α-*methyl*-3α-*chloro*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**55**). The 2β-methyl-3α-alcohol (**50**) (127 mg) in dry pyridine (15 ml) was refluxed for 3 hr with $POCl_3$ (260 μl), and the soln was then poured into H_2O. Acidification to pH 3.0 with 10 M HCl and extraction with EtOAc yielded an oil. Purification by prep. TLC with EtOAc–petrol (2:3) gave, at R_f 0.65, the 3β-chloro-compound (**55**) (101 mg), mp 58–60° (from MeOH–H_2O) (Found: C, 66.5; H, 7.1. $C_{21}H_{27}O_4Cl$ requires C, 66.6; H, 7.2%); ν_{max} 1788, 1743, and 1658 cm^{-1}; δ 1.09 (*d*, *J* = 6.5 Hz, 2-Me), 1.22 (*s*, 18-H_3), 2.71 and 3.26 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.71 (*s*, CO_2Me), 3.98 (*d*, *J* = 4.5, 3-H), 4.88 and 4.95 (each *br.*, 17-H_2); *m/z* 380 (M^+ + 2), 378 (M^+, 4), 346 (73), 318 (100), 298 (55) and 239 (53).

Methyl ent-2α-*methyl*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**39**). To the 2β-methyl-3β-chloro-compound (**55**) (90 mg) in dry C_6H_6 (22 ml) were added *n*-

Bu_3SnH (180 μl) and 2,2-azobis(2-methylpropionitrile) (2 mg). The soln was refluxed for 0.5 hr. After removal of the solvent *in vacuo* the product was separated from the tin-containing compounds by prep. TLC with EtOAc–petrol (3:7). The band at R_f 0.65 yielded 2β-methylGA$_9$ Me ester (**39**) (79 mg), mp 116–117° (from Me_2CO–petrol) (Found: C, 73.0; H, 8.3%. $C_{21}H_{28}O_4$ requires: C, 73.2; H, 8.2%); ν_{max} 1765, 1726, 1662, and 885 cm^{-1}; δ 0.98 (*d*, *J* = 6.5 Hz, 2-Me), 1.07 (*s*, 18-H_3), 2.48 and 2.68 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.67 (*s*, CO_2Me), 4.82 and 4.93 (each *br*., 17-H_2); *m/z* 344 (M^+, 16), 312 (100), 300 (28), 284 (77), 257 (52), 241 (48), 240 (59), 239 (29) and 231 (26).

Reaction of methyl ent-2,2-*dimethyl*-3β,10β-*dihydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**44**) *with phosphoryl chloride.* (a) *In* C_5H_5N. The alcohol (40 mg) in dry C_5H_5N (5 ml) was treated with $POCl_3$ (80 μl). The soln was refluxed for 3 hr and then poured into H_2O. Acidification with 10 M HCl and extraction with EtOAc yielded a brown oil (60 mg). Analytical TLC showed that the starting alcohol had been consumed and that the sole product was at R_f 0. This experiment was repeated twice with the same result.

(b) *In collidine.* The alcohol (65 mg) in dry collidine (12 ml) was treated with $POCl_3$ (120 μl) at reflux for 0.75 hr. Work-up as normal and prep. TLC of the product with EtOAc–petrol (7:11) gave at R_f 0.6 methyl *ent*-2,2-dimethyl-3α-chloro-10β-hydroxy-20-norgibberell-16-en-7-oate-19-oic acid 19,10-lactone (**48**) (10 mg), mp 162–163° (Me_2CO–petrol) (Found: M^+ 392.164. $C_{22}H_{29}O_4{}^{35}Cl$ requires M^+ 392.175); ν_{max} 1784, 1745, 1658, and 880 cm^{-1}; δ 1.22 (*s*, 2 × Me), 1.27 (*s*, 1 × Me), 1.43 and 1.98 (each *d*, *J* = 14.5 Hz, 1-H_2), 2.73 and 3.27 (each *d*, *J* = 11 Hz, 6- and 5-H), 3.72 (*s*, CO_2Me), 3.89 (*s*, 3-H), 4.89 and 4.98 (each *br*., 17-H_2); *m/z* 392 (M^+, 15), 360 (95), 346 (8), 332 (100), 312 (38), 253 (38), 237 (83), 169 (72) and 91 (70). This reaction was repeated twice with longer reflux times (1 hr and 1.5 hr) without any significant increase in yield.

Methyl ent-2,2-*dimethyl*-10β-*hydroxy*-20-*norgibberell*-16-*en*-7-*oate*-19-*oic acid* 19,10-*lactone* (**37**). To the 2,2-dimethyl-3β-chloro-compound (**48**) (35 mg) in C_6H_6 (5 ml) was added *n*-BuSnH (70 μl) and 2,2-azo-bis(2-methylpropionitrile) (1 mg). The soln was refluxed for 40 min. The solvent was removed *in vacuo* and the residue subjected to prep. TLC with EtOAc–petrol (1:3). The band at R_f 0.7 yielded 2,2-dimethylGA$_9$ Me ester (**37**) (28 mg), mp 169–171° (from Me_2CO) (Found: C, 73.5; H, 8.6. $C_{22}H_{30}O_4$ requires: C, 73.7; H, 8.4%); δ 1.03, 1.05 and 1.06 (each *s*, 3 × Me), 1.37 and 2.02 (each *d*, *J* = 14.5 Hz, 1-H_2), 2.53 and 2.73 (each *d*, *J* = 11 Hz, 5- and 6-H), 3.65 (*s*, CO_2Me), 4.84 and 4.96 (each *br*., 17-H_2); *m/z* 358 (M^+, 4), 326 (100), 314 (12), 312 (12), 298 (96), 271 (42), 255 (73), 254 (93), 245 (44) and 187 (27).

ent-2α-*Methyl*-10β-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**38**). 2β-MethylGA$_9$ Me ester (**39**) (20 mg) in MeOH (20 ml) and 2 M NaOH (20 ml) was refluxed for 19 hr. The MeOH was removed *in vacuo* and the aq. concentrate further diluted with H_2O. Acidification to pH 3.0 with 10 M HCl followed by extraction with EtOAc yielded a gum consisting of two compounds by TLC. The product was held at 80° under N_2 for 0.5 hr, after which time TLC showed the presence of one major component mixed with a trace of starting Me ester. The product was dissolved in EtOAc which was extracted with satd aq. $NaHCO_3$. Neutralization of the alkaline layer with 10 M HCl and extraction with EtOAc yielded pure 2β-methylGA$_9$ (**38**) (15 mg) as a gum. (Found: M^+ 330.183. $C_{20}H_{26}O_4$ requires M^+ 330.183); δ 0.99 (*d*, *J* = 6.5 Hz), 1.13 (*s*, 18-H_3), 2.46 and 2.75 (each *d*, *J* = 11 Hz, 6- and 5-H), 4.85 and 4.97 (each *br*., 17-H_2); *m/z* 330 (M^+, 2), 312 (10), 286 (31), 284 (18), 243 (51), 111 (43), 97 (60), 95 (46), 85 (59), 83 (59), 81 (47), 71 (98) and 69 (100).

ent-2,2-*Dimethyl*-10β-*hydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (**36**). 2,2-DimethylGA$_9$ Me ester (**37**) (23 mg) in MeOH (20 l) and 2 M NaOH (20 ml) was refluxed for 24 hr. Work-up as above yielded a gum which was heated at 80° under N_2 until it gave a single spot on TLC. Traces of Me ester were removed by extraction of an EtOAc soln of the product with satd aq. $NaHCO_3$. Acidification and extraction of the alkaline layer gave pure 2,2-dimethylGA$_9$ (**36**) (14.5 mg) as a gum. (Found: M^+ 344.198. $C_{21}H_{28}O_4$ requires M^+ 344.199); δ 1.07 and 1.04 (each *s*, 2 × Me), 1.26 (*s*, 1 × Me), 2.47 and 2.73 (each *d*, *J* = 11 Hz, 5- and 6-H), 4.84 and 4.97 (each *br*., 17-H_2); *m/z* 344 (M^+, 7), 326 (19), 300 (100), 298 (47), 285 (21), 257 (92), 255 (65), 231 (75), 187 (34), 105 (36), 91 (62), 83 (35), 79 (39), 77 (36), 69 (44) and 67 (29).

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REFERENCES

1. Crozier, A., Kuo, C. C., Durley, R. C. and Pharis, R. P. (1970) *Can. J. Botany* **48,** 867.
2. Reeve, D. R. and Crozier, A. (1974) *J. Exp. Botany* **25,** 431.
3. Reeve, D. R. and Crozier, A. (1975) in *Gibberellins and Plant Growth* (Krishnamoorthy, H. N., ed.) p. 35. Wiley Eastern Press, New Delhi.
4. Sponsel, V. M., Hoad, G. V. and Beeley, L. J. (1977) *Planta* **135,** 143.
5. Beale, M. H., Gaskin, P., Kirkwood, P. S. and MacMillan, J. (1980) *J. Chem. Soc. Perkin Trans.* 1, 885.
6. Grove, J. F., MacMillan, J., Mulholland, T. P. C. and Turner, W. D. (1960) *J. Chem. Soc.* 3049.
7. Beeley, L. J. and MacMillan, J. (1976) *J. Chem. Soc. Perkin Trans.* 1, 1322.
8. Yamaguchi, I., Miyamato, M., Yamane, H., Murofushi, N., Takahashi, N. and Fujita, K. (1975) *J. Chem. Soc. Perkin Trans.* 1, 996.
9. Yarovenko, N. N. and Raksha, M. A. (1959) *J. Gen. Chem. U.S.S.R.* **29,** 2125.
10. Gurvich, I. A., Milstein, I. M. and Kucherov, V. F. (1967) *Tetrahedron Letters* 4293.
11. Cross, B. E., Grove, J. F., MacMillan, J., Mulholland, T. P. C. and Sheppard, N. (1958) *Proc. Chem. Soc.*, 221.
12. Cross, B. E., Grove, J. F. and Morrison, A. (1961) *J. Chem. Soc.* 2498.
13. Zook, H. D., Russo, T. J., Ferrand, E. F. and Stotz, D. S. (1968) *J. Org. Chem.* 2222.
14. Hanson, J. R. (1965) *J. Chem. Soc.* 5036.
15. Beale, M. H. and MacMillan, J. (1980) *J. Chem. Soc. Perkin Trans.* 1, 877.