# Reactions of 2-Chloro-*NN*-diethyl-1,1,2-trifluoroethylamine with Alcohols. Part 3.[1] In the Presence of Lithium Chloride; Preparation of Chlorogibberellins

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The reactions of gibberellin derivatives with 2-chloro-*NN*-diethyl-1,1,2-trifluoroethylamine in the presence of lithium chloride have been investigated in several different solvents. In all cases the bridgehead hydroxy-group was smoothly replaced by chlorine; in gibberellic acid and its esters a 4β-chloro-substituent was also introduced, but if ring A was saturated the 2β-hydroxy-group was eliminated. When the reaction was carried out in tetrahydrofuran or 1,2-dimethoxyethane as solvent, nucleophilic attack at the bridgehead by the oxygen of the ether also took place to give 7-alkoxygibberellins in 10—30% yield. 4β,7-Dichloro- and 7-chloro-4aα-hydroxy-1β,8-dimethylgibbane-1α,10β-dicarboxylic acid 1,4a-lactones (19) and (20), respectively, and 7-chloro-4aα-hydroxy-1β,8β-dimethylgibb-2-ene-1α,10β-dicarboxylic acid 1,4a-lactone (38) have been prepared and preliminary bioassay results are discussed.



THE interesting biological activities [2-6] of a number of fluorogibberellins prompted the preparation of some chloro-analogues.

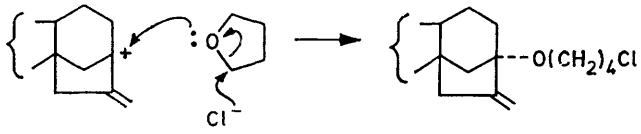
2-Chloro-*NN*-diethyl-1,1,2-trifluoroethylamine (fluoroamine) has been used successfully in the preparation [1,4] of a number of fluorogibberellins from the corresponding hydroxy-compounds. A brief report has described the use of fluoroamine–lithium chloride for the conversion of alcohols into chlorides.[7] This paper describes the preparation of chlorogibberellins with this reagent.†

In a model experiment treatment of methyl gibberellate (1) with an excess of fluoroamine and lithium chloride in tetrahydrofuran afforded two major products. The first was shown to be the 4β,7-dichlorogibberellin (7), (a) by analogy with the corresponding fluorination,[1] and (b) because its n.m.r., δ 5.85 (m, 2- and 3-H), and u.v. spectra, $\lambda_{max.}$ 227 nm (ε 1 150), were characteristic of gibb-2-enes.[5,8,9] The β-configuration of the ring A chlorine atom, which was expected from mechanistic considerations,[5] was confirmed by the deshielding of 10a-H in (7) by 0.46 p.p.m. relative to its position in the methyl ester of gibberellin $A_5$ (8); a similar deshielding is found in the n.m.r. spectrum of the 4β-fluoro-ester (9).[5] The position of the 7-chlorine atom was revealed by the increased difference in chemical shift of the two terminal methylene protons [δ 5.13 and 5.41 in (7); δ 5.09 and 5.28 in (10)] [1] (*cf.* ref. 10).

The other product from the chlorination of methyl gibberellate was shown by mass spectroscopy to have the formula $C_{24}H_{30}Cl_2O_5$. It was assigned structure (11) because its n.m.r. spectrum was almost identical with that of the dichloro-ester (7), except that it showed signals due to $OCH_2CH_2$ and $CH_2CH_2Cl$ groupings In agreement with the placement of the alkoxy-group at C-7, the two 8-methylene protons only differed in chemical shift by 0.05 p.p.m.[10] A minor product from the chlorination was shown to be the 4β-chloro-7-hydroxy-ester (12) by spectroscopy (see Experimental section).

Hydrogenation of the dichloro-ester (7) over rhodium on alumina resulted in partial hydrogenolysis of the 4β-chlorine atom, and gave mixtures of the 8-epimers of the methyl esters of the dichloro- and monochloro-acids (19) and (20), respectively.

Fluorination of the gibberellins at the bridgehead position, C-7, may take place *via* a carbocation type of intermediate.[1] Chlorination presumably occurs in a similar manner, and the absence of fluorination in the presence of chloride ions, reflects the poor nucleophilicity of fluoride relative to chloride. The ether (11) is believed to be formed by nucleophilic attack by the oxygen atom of tetrahydrofuran as shown in the Scheme.



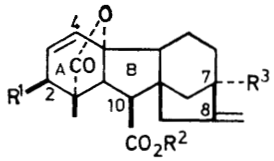

SCHEME

Carboxylic acids react with fluoroamine to give the relatively stable acyl fluorides,[11-13] and with fluoroamine–lithium chloride to give acyl chlorides. Consequently in the preparation of fluorogibberellins the carboxy-group was protected,[1,5,6] and it seemed likely that, despite the greater ease of hydrolysis of acyl chlorides, similar protection would be necessary in the preparation of some chlorogibberellins.

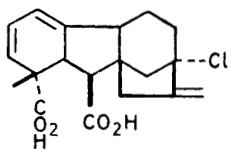
The *p*-bromophenacyl ester (3), used successfully in fluorinations,[1,5] was unsuitable. It gave the required 4β,7-dichloro-derivative (13), but, in contrast to fluorination,[1] none of the 2β-chloro-compound (4) was isolated. De-esterification of the 4β-chloro-ester with zinc dust led to dechlorination and opening of the lactone ring by neighbouring group participation (*cf.* ref. 14) to give a gum believed to contain the diene (18) and double bond isomers. Under similar conditions de-esterification of the 2β-chloro-isomer might have been successful.

Chlorination of benzyl gibberellate (5) [15] with fluoroamine and lithium chloride gave the 4β,7-dichloro-ester (14) and the 7-(4-chloro-n-butoxy)-ester (15); their structures were determined spectroscopically. Hydrogenation of the former over rhodium on alumina [16]

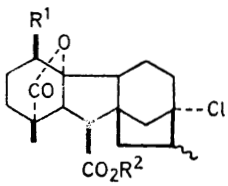
† Preliminary account, B. E. Cross and I. C. Simpson, *Tetrahedron Letters*, 1980, 215.



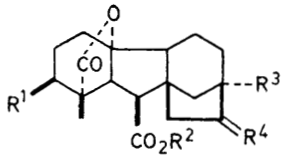
| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (1) | OH | Me | OH |
| (2) | Cl | H | Cl |
| (3) | OH | $p-BrC_6H_4COCH_2$ | OH |
| (4) | Cl | $p-BrC_6H_4COCH_2$ | Cl |
| (5) | HO | $PhCH_2$ | OH |
| (6) | Cl | H | Cl |



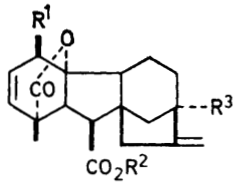
(18)



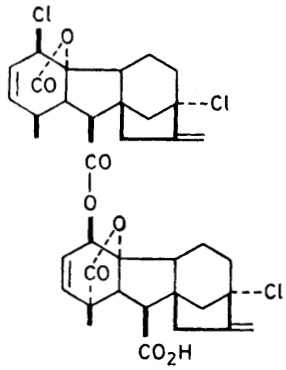
| | $R^1$ | $R^2$ |
|---|---|---|
| (19) | Cl | H |
| (20) | H | H |
| (21) | H | $C_6H_{11}.CH_2$ |
| (22) | Cl | $C_6H_{11}.CH_2$ |



| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| (24) | OH | Me | OH | α-H, β-Me |
| (25) | OH | Me | OH | α-Me, β-H |
| (26) | OH | H | OH | α-H, β-Me |
| (27) | OH | Me | F | α-H, β-Me |
| (28) | OH | Me | F | $CH_2$ |
| (29) | H | H | H | $CH_2$ |



| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (7) | Cl | Me | Cl |
| (8) | H | Me | OH |
| (9) | F | Me | OH |
| (10) | F | $p-BrC_6H_4COCH_2$ | F |
| (11) | Cl | Me | $O(CH_2)_4Cl$ |
| (12) | Cl | Me | OH |
| (13) | Cl | $p-BrC_6H_4COCH_2$ | Cl |
| (14) | Cl | $PhCH_2$ | Cl |
| (15) | Cl | $PhCH_2$ | $O(CH_2)_4Cl$ |
| (16) | Cl | H | $O(CH_2)_2OMe$ |
| (17) | Cl | H | Cl |



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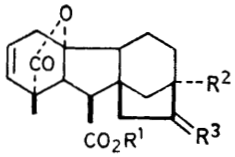

| | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|
| (30) | Me | Cl | α-H, β-Me |
| (31) | Me | Cl | α-Me, β-H |
| (32) | Me | $O(CH_2)_4Cl$ | α-H, β-Me |
| (33) | Me | $O(CH_2)_4Cl$ | α-Me, β-H |
| (34) | Me | F | α-H, β-Me |
| (35) | Me | F | α-Me, β-H |
| (36) | H | $O(CH_2)_4OMe$ | α-H, β-Me |
| (37) | H | $O(CH_2)_4OMe$ | α-Me, β-H |
| (38) | H | Cl | α-H, β-Me |
| (39) | H | OCO.CHClF | α-H, β-Me |
| (40) | H | OH | α-H, β-Me |
| (41) | H | OH | α-Me, β-H |
| (42) | H | $O(CH_2)_2OMe$ | α-H, β-Me |

yielded four products which were separated by p.l.c. Two bands afforded mixtures of the 8-epimers of (a) the dichlorogibberellin (19), and (b) the 7-chlorogibberellin (20), respectively. Another band gave a mixture of the 8-epimers of the cyclohexylmethyl ester (21) which was identified by n.m.r. and mass spectroscopy. The material from the fourth band was not obtained pure, but was believed to consist mainly of the cyclohexylmethyl ester (22).

The direct chlorination of gibberellic acid in 1,2-dimethoxyethane as solvent, followed by hydrolysis of the acid chloride group afforded the 7-alkoxy-derivative (16), identified spectroscopically (see Experimental section). This product is presumably formed by nucleophilic attack by an oxygen atom of the solvent (*cf.* Scheme). The second product from the chlorination gave analytical figures consistent with the formula $C_{38}H_{39}Cl_3O_6$ and has been provisionally assigned structure (23). It is presumably formed by nucleophilic attack by the carboxy-group of one molecule of gibberellic acid on the ring A allylic carbonium ion [5] (generated by attack by fluoroamine on the 2-hydroxy-group) of a second gibberellic acid molecule. The large size of the nucleophile should ensure attack at the least hindered 4β-position and the n.m.r. signals of the ester are only consistent with a gibb-2-ene structure in both units [δ 5.84 (m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H)].

Chlorination of gibberellic acid in acetone eliminated nucleophilic attack by the solvent and gave a better yield of the ester (23), together with a gum of lower $R_F$, believed to be mainly the 2β,7-dichloro-acid (6) from its n.m.r. spectrum, δ 4.64br (1 H, s, 2α-H), 5.89 (1 H, dd, *J* 10 and 3 Hz, 3-H), and 6.25 (1 H, dd, *J* 10 and 1.5 Hz, 4-H). However the spectrum showed a weak multiplet at 5.9, indicating the presence of some of the isomeric acid (17) which was not readily removed by p.l.c.

To extend the range of available chlorogibberellins, a mixture of 8-epimers of methyl tetrahydrogibberellate [(24) and (25)] was chlorinated with fluoroamine and lithium chloride in tetrahydrofuran. As expected the 2β-hydroxy-group was eliminated,[1] but substitution at position 7 gave the 7-chloro-esters (30) and (31) and the 7-(4-chloro-n-butoxy)-esters (32) and (33). Their structures were readily determined from their n.m.r. spectra (see Experimental section); the 7α-chlorine atom shifted both 8-methyl groups downfield with respect to the corresponding fluoro-esters (34) and (35).[1]

Hydrolysis of the epimeric esters (32) and (33) with sodium hydroxide in methanol led to displacement of the chlorine atom in the alkoxy-chain and gave the 7-(4-methoxy-n-butoxy)-acids (36) and (37).

To avoid the complications of working with mixtures of 8-epimers, gibberellic acid was reduced with di-imide to give the pure 8β-methyltetrahydro-acid (26) [4,17,18] in high yield. Methylation of the acid, or reduction of methyl gibberellate with di-imide, gave the tetrahydro-ester (24). Chlorination of the latter in tetrahydrofuran in the usual way gave, as expected, the 7-chloro-ester (30) and the 7-alkoxy-compound (32). Both were readily identified by their n.m.r. spectra. Alkaline hydrolysis of the 7-chloro-ester afforded the required 7-chlorogibberellin (38) which was more easily prepared from the acid (26) (see below).

An attempt to improve the yield of the ester (38) by carrying out the chlorination of the ester (24) with fluoroamine and potassium chloride in the presence of dicyclohexyl-18-crown-6 in dichloromethane was unsuccessful. The main product (38%) had the formula $C_{20}H_{27}FO_5$, and was assigned structure (27). The fluorine atom was located at C-7 by $^{19}F$ n.m.r. (φ* 147.05br) [1,4] and the structures of rings A and B were deduced by comparison of its n.m.r. spectrum with that of the ester of gibberellin $A_1$; [10] the survival of the 2β-hydroxy-group in the presence of an excess of fluoroamine is unusual.

The 7-chlorogibberellin (38) was readily prepared by reacting the tetrahydrogibberellic acid (26) with fluoroamine in the presence of lithium chloride and then decomposing the resultant acid chloride with sodium hydrogencarbonate solution. This chlorination was performed in two solvents. In dichloromethane the chloro-acid (38) (28%) and the 7-chlorofluoroacetoxy-derivative (39) (24%) (*cf.* ref. 5) were formed. The latter was characterised by mass spectrometry and by its n.m.r. spectrum which showed a doublet at δ 6.20 (*J* 51 Hz) due to the CHFCl group. Mild hydrolysis of the acetate (39) afforded the dihydrogibberellin $A_5$ (40).[15] When the reaction was carried out in 1,2-dimethoxyethane, the products were the 7-chloro-acid (38) (35%) and the 7-alkoxy-acid (42) (27%). The latter was characterised spectroscopically (see Experimental section). Further work on the effect of solvents on the chlorination reaction is obviously needed.

In the lettuce hypocotyl bioassay the 7-chlorogibberellins (38) and (20) were comparable in activity to dihydrogibberellin $A_5$ [(40) and (41)] and $A_9$ (29). However the 4β,7-dichlorogibberellin (19) was much less active.[19] The three chlorogibberellins were all more active than dihydrogibberellin $A_5$, but less active than gibberellin $A_9$, in the Tanginbozu dwarf rice bioassay.[19] Comparison of the bioassay results of the above chlorogibberellins with those of the fluorogibberellins [3] shows that the 7-monohalogenogibberellins are the more active in both series.

The 7-alkoxygibberellins (16) and [(36) and (37)] showed very low activity in the Tanginbozu rice bioassay.[19]

## EXPERIMENTAL

Details of chromatographic materials and conditions for the determination of physical data, *etc.*, have been reported.[20] $^{19}F$ N.m.r. spectra were measured as described in ref. 21.

Unless otherwise stated the abundance of ions in mass spectra are relative.

*Reaction of Methyl Gibberellate* (1) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—Methyl gibberellate (1.42 g) and anhydrous

lithium chloride (4.0 g) were stirred together in tetrahydrofuran (75 ml) at 0 °C and treated dropwise with an excess of fluoroamine (9 ml) over 30 min. The resultant solution was stirred for 3 h at 0 °C and then for 1 h at room temperature. Removal of the solvent *in vacuo* gave an oil containing chloro-*NN*-diethylfluoroacetamide. The latter was partially removed by evaporation *in vacuo* (0.1 mmHg) at 65 °C, to give a solid which was chromatographed on silica gel (160 g). Elution with ethyl acetate–light petroleum (1 : 19) gave a fraction which on purification by p.l.c. (development with benzene) afforded a gum (267 mg) which sublimed at 90 °C (bath temperature) and $6.5 \times 10^{-6}$ mmHg to give 4β,7-*dichloro*-10β-*methoxycarbonyl*-1β-*methyl*-8-*methylene*-*gibb*-2-*ene*-1α,4aα-*carbolactone* (7) as a glass (Found: C, 60.45; H, 5.8; Cl, 17.3. $C_{20}H_{22}Cl_2O_4$ requires C, 60.45; H, 5.6; Cl, 17.9%), $\nu_{max.}$ 1 788, 1 737, and 912 cm$^{-1}$; $\lambda_{max.}$ 277 nm (ε 1 150); δ 1.24 (3 H, s, 1β-Me), 2.62 (1 H, d, *J* 10 Hz, 10-H), 3.10 (1 H, dd, *J* 10 and 3 Hz, 10a-H), 3.73 (3 H, s, OMe), 4.50 (1 H, d, *J* 3 Hz, 4α-H), 5.13br (1 H) and 5.41br (1 H) (8-$CH_2$), and 5.85 (2 H, m, $W_{\frac{1}{2}}$ 12.5 Hz, 2- and 3-H); *m/e* 398 ($M^+$, 2.3%), 396 ($M^+$, 9.7), and 257 (100).

Elution of the column with ethyl acetate–light petroleum (1 : 19), gave a semi-solid which on purification by p.l.c. (development with benzene) afforded two bands. Recovery of material from the band of higher $R_F$ gave 4β-*chloro*-7-(4-*chloro*-*n*-*butoxy*)-10β-*methoxycarbonyl*-1β-*methyl*-8-*methylene*-*gibb*-2-*ene*-1α,4aα-*carbolactone* (11) as a gum (121 mg) (Found: *m/e*, 470.1436. $C_{24}H_{30}{}^{35}Cl^{37}ClO_5$ requires *M*, 470.1441), $\nu_{max.}$ 1 780, 1 732, and 895 cm$^{-1}$; δ 1.24 (3 H, s, 1β-Me), 2.63 (1 H, d, *J* 10.5 Hz, 10-H), 3.10 (1 H, d, *J* 10.5 Hz, 10a-H), 3.34 (2 H, t, *J* 6 Hz, O$CH_2$), 3.56 (2 H, t, *J* 7 Hz, $CH_2$Cl), 3.74 (3 H, s, OMe), 4.52 (1 H, d, *J* 2.5 Hz, 4α-H), 5.08br (1 H) and 5.43br (1 H) (8-$CH_2$), and 5.86 (2 H, m, $W_{\frac{1}{2}}$ 12.5 Hz, 2- and 3-H); *m/e* 472 ($M^+$, 4.7%), 470 ($M^+$, 24.9), 468 ($M^+$, 35), 364 (13), 317 (17), and 257 (78). The band of lower $R_F$ gave further 4β,7-dichloro-ester (7) (40 mg).

Elution of the column with ethyl acetate–light petroleum (2 : 23) and (3 : 17) gave a gum, which after purification by p.l.c. [development with ethanol–benzene (3 : 47) and benzene], yielded 4β-*chloro*-7-*hydroxy*-10β-*methoxycarbonyl*-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,4aα-*carbolactone* (12) as a gum (44 mg) (Found: *m/e*, 378.1231 and 380.1209. $C_{20}H_{23}{}^{35}ClO_5$ and $C_{20}H_{23}{}^{37}ClO_5$ require *M*, 378.1234 and 380.1204, respectively), $\nu_{max.}$ 3 440, 1 787, 1 735, 920, 900, and 878 cm$^{-1}$; $\lambda_{max.}$ 224 nm (ε 2 144); δ 1.25 (3 H, s, 1β-Me), 2.63 (1 H, d, *J* 10 Hz, 10-H), 3.12 (1 H, d, *J* 10 Hz, 10a-H), 3.74 (3 H, s, OMe), 4.50 (1 H, d, *J* 3.5 Hz, 4α-H), 4.98br (1 H) and 5.25br (1 H) (8-$CH_2$), and 5.85 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 380 (33%), 378 (100), 346 (24), and 319 (62).

*Hydrogenation of the* 4β,7-*Dichloro-ester* (7).—The ester (104 mg) in ethyl acetate–cyclohexane (3 : 97; 100 ml) was hydrogenated over 5% rhodium on alumina (318 mg) in a 'bomb' hydrogenator at 60 °C and 21 atm for 6.5 h. Recovery afforded a gum which was purified by p.l.c. (development with benzene) and gave two bands. Material from the band of lower $R_F$ yielded a mixture of the 8-epimers of 7-*chloro*-10β-*methoxycarbonyl*-1β,8-*dimethyl*-*gibbane*-1α,4aα-*carbolactone* as a gum (15 mg) (Found: *m/e*, 366.1596. $C_{20}H_{27}{}^{35}ClO_4$ requires *M*, 366.1598), $\nu_{max.}$ 1 770, 1 732, 977, and 880 cm$^{-1}$; δ 1.02 (d, *J* 5.5 Hz) and 1.05 (d, *J* 5.5 Hz) (8α- and 8β-Me), 1.25 (3 H, s, 1β-Me), 2.94 (1 H, d, *J* 10.5 Hz, 10-H), 2.67 (1 H, d, *J* 10.5 Hz, 10a-H), and 3.73 (3 H, s, OMe); *m/e* 366 ($M^+$, 0.3%), 324 (8.1), 322 (23), and 287 (100). Material from the band of higher $R_F$ yielded a mixture of the 8-epimers of 4β,7-*dichloro*-10β-*methoxycarbonyl*-1β,8-*dimethylgibbane*-1α,4aα-*carbolactone* (Found: *m/e*, 400.1211. $C_{20}H_{26}{}^{35}Cl_2O_4$ requires *M*, 400.1208), $\nu_{max.}$ 1 790, 1 738, and 888 cm$^{-1}$; δ 1.03 (d, *J* 5.5 Hz) and 1.07 (d, *J* 5.5 Hz) (8α- and 8β-Me), 1.27 (3 H, s, 1β-Me), 2.64 (1 H, d, *J* 10.5 Hz, 10-H), 3.28 (1 H, d, *J* 10.5 Hz, 10a-H), 3.75 (3 H, s, OMe), and 4.27br (1 H, s, 4α-H); *m/e* 404 ($M^+$, 2.2%), 402 ($M^+$, 7.1), 400 (11), 366 (18), and 322 (36).

*Reaction of* p-*Bromophenacyl Gibberellate with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—The ester (1.66 g) and anhydrous lithium chloride (5.0 g) in tetrahydrofuran (100 ml) were stirred at 0 °C and treated with an excess of fluoroamine (12.5 ml) added dropwise over 40 min. Removal of the solvent *in vacuo* followed by chromatography on silica gel (370 g) and elution with ethyl acetate–light petroleum (1 : 19) afforded the early fractions as an oil which was mainly chloro-*NN*-diethylfluoroacetamide (see below).

Continued elution with ethyl acetate–light petroleum (1 : 4) gave a fraction which on purification by p.l.c. (development with benzene × 3) yielded a gum. Precipitation of the latter from ether-light petroleum gave 10β-p-*bromophenacyloxycarbonyl*-4β-*chloro*-7-*hydroxy*-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,4aα-*carbolactone* as a solid (185 mg), m.p. 119—121 °C (Found: C, 57.55; H, 4.5; Cl, 6.3. $C_{27}H_{26}BrClO_6$ requires C, 57.7; H, 4.6; Cl, 6.3%); $\nu_{max.}$ 3 440, 1 787, 1 745, 1 706, 1 645, 900, and 877 cm$^{-1}$; δ 1.38 (3 H, s, 1β-Me), 2.82 (1 H, d, *J* 10.5 Hz, 10-H), 3.15 (1 H, d, *J* 10.5 Hz, 10a-H), 4.49 (1 H, d, *J* 3.5 Hz, 4α-H), 5.10br (1 H, ½ × 8-$CH_2$) and 5.32br (3 H, s, ½ × 8-$CH_2$ and O$CH_2$CO), 5.48 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H), and 7.61 (2 H, d, *J* 9 Hz) and 7.77 (2 H, d, *J* 9 Hz) (aromatic H); *m/e* 377 ($M^+$, 2.3%), 375 ($M^+$, 2.4), 373 ($M^+$, 2.9), 283 (7.4), 265 (6.3), and 239 (9.8).

The early chloro-*NN*-diethylfluoroacetamide fractions were evaporated *in vacuo* at 60 °C and 0.3 mmHg and the residual solid was rechromatographed on silica gel (44 g). Elution with ethyl acetate–light petroleum (1 : 19) and (1 : 9) gave a fraction which crystallised from ethyl acetate–light petroleum as needles, m.p. 181—184 °C, of 10β-p-*bromophenacyloxycarbonyl*-4β,7-*dichloro*-1β-*methyl*-8-*methylene*-*gibb*-2-*ene*-1α,4aα-*carbolactone* (13) (Found: C, 55.9; H, 4.1; Cl, 12.2. $C_{27}H_{25}BrCl_2O_5$ requires C, 55.9; H, 4.3; Cl, 12.2%); $\nu_{max.}$ 1 787, 1 743, 1 702, 1 662, 970, and 822 cm$^{-1}$; δ 1.38 (3 H, s, 1β-Me), 2.82 (1 H, d, *J* 10.5 Hz, 10-H), 3.15 (1 H, d, *J* 10.5 Hz, 10a-H), 4.51 (1 H, d, *J* 3 Hz, 4α-H), 5.14br (1 H) and 5.42br (1 H) (8-$CH_2$), 5.34 (2 H, s, O$CH_2$-CO), 5.86 (2 H, m, $W_{\frac{1}{2}}$ 12.5 Hz, 2- and 3-H), and 7.62 (2 H, d, *J* 9 Hz) and 7.79 (2 H, d, *J* 9 Hz) (aromatic H); *m/e* 582 ($M^+$, 1.7%), 580 ($M^+$, 4.3), 578 ($M^+$, 3.0), 337 (15), 301 (100), and 257 (100).

*De-esterification of the* 4β,7-*Dichloro-ester* (13).—Activated zinc (292 mg) was added to the ester (180 mg) in glacial acetic acid (20 ml) and the mixture was stirred at room temperature for 4.5 h. Filtration and evaporation of the solvent *in vacuo* afforded a gum which was separated into acidic and neutral fractions in the usual way. The acidic fraction was purified by p.l.c. [development with acetic acid–benzene (3 : 47)] and yielded a gum (47 mg) believed to be the diene (18) and isomers, $\lambda_{max.}$ 230 (ε 4 070) and 273 nm (4 025), $\nu_{max.}$ ($CHCl_3$) 1 702 and 1 697 cm$^{-1}$.

*Preparation of Benzyl Gibberellate* (5).—The ester, prepared by the literature method, had m.p. 162—165 °C (lit.,[15] 164—168 °C); δ 1.21 (3 H, s, 1β-Me), 2.84 (1 H, d, *J* 10.5 Hz, 10-H), 3.27 (1 H, d, *J* 10.5 Hz, 10a-H), 4.14 (1 H, d, *J* 3.5 Hz, 2α-H), 4.92 (1 H) and 5.26 (1 H) (8-$CH_2$), 5.19 (2 H, d,

*J* 2 Hz, $OCH_2Ar$), 5.92 (1 H, dd, *J* 9.5 and 4.5 Hz, 3-H), 6.34 (1 H, d, *J* 9.5 Hz, 4-H), and 7.37 (5 H, s, aromatic H); *m/e* 436 ($M^+$, 6.9%), 418 (7.2), 373 (14), 345 (28), and 327 (25).

*Reaction of Benzyl Gibberellate* (5) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—A stirred suspension of benzyl gibberellate (503 mg) and anhydrous lithium chloride (1.0 g) in tetrahydrofuran (20 ml) was treated with fluoroamine (3 ml) at 0 °C over 30 m. After stirring for a further 30 min at 0 °C and for 1 h at room temperature, removal of the solvent *in vacuo* afforded an oil from which chloro-*NN*-diethylfluoroacetamide was removed by evaporation at 60 °C (1.0 mmHg). The residue was chromatographed on silica gel (132 g). Elution with ethyl acetate–light petroleum (1 : 19) gave a fraction with on purification by p.l.c. (development with benzene × 2) yielded 10β-*benzyloxycarbonyl*-4β,7-*dichloro*-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,4aα-*carbolactone* (14) as a gum (123 mg) (Found: *m/e*, 472.1212 and 474.1184. $C_{26}H_{26}{}^{35}Cl_2O_4$ and $C_{26}H_{26}{}^{35}Cl^{37}ClO_4$ require *M*, 472.12 08 and 474.1179, respectively), $\nu_{max.}$ ($CHCl_3$ film) 1 784, 1 730, and 908 $cm^{-1}$; δ 1.22 (3 H, s, 1β-Me), 2.64 (1 H, d, *J* 9 Hz, 10-H), 3.10 (1 H, d, *J* 9 Hz, 10a-H), 4.51 (1 H, d, *J* 2.5 Hz, 4α-H), 5.06br (1 H) and 5.39br (1 H) (8-$CH_2$), 5.17 (2 H, d, *J* 2.5 Hz, $CH_2Ar$), 5.83 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H), and 7.35 (5 H, s, aromatic H); *m/e* 474 ($M^+$, 2.4), 472 ($M^+$, 2.7), 456 (2.3), 436 (2.9), 381 (5.3), 357 (5.8), 301 (17), and 285 (15).

Elution with ethyl acetate–light petroleum (2 : 23) afforded an oil which on purification by p.l.c. (development with benzene × 2) yielded 10β-*benzyloxycarbonyl*-4β-*chloro*-7α-(4-*chloro*-*n*-*butoxy*)-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,-4aα-*carbolactone* (15) as a gum (144 mg) (Found: *m/e*, 544.1789. $C_{30}H_{34}{}^{35}Cl_2O_5$ requires *M*, 544.1783), $\nu_{max.}$ ($CHCl_3$) 1 788, 1 734, 699, and 665 $cm^{-1}$; δ 1.21 (3 H, s, 1β-Me), 2.66 (1 H, d, *J* 10 Hz, 10-H), 3.13 (1 H, d, *J* 10 Hz, 10a-H), 3.25 (2 H, t, *J* 7 Hz, $OCH_2$), 3.56 (2 H, t, J 7 Hz, $CH_2Cl$), 4.51 (1 H, d, *J* 2.5 Hz, 4α-H), 4.97br (1 H) and 5.05 (1 H) (8-$CH_2$), 5.20 (2 H, d, *J* 2.5 Hz, $OCH_2Ar$), 5.84 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H), and 7.36 (5 H, s, aromatic H); *m/e* 548 ($M^+$, 0.9%), 546 ($M^+$, 5.0), 544 ($M^+$, 5.7), 453 (13), 363 (11), and 257 (15).

*Hydrogenation of the* 4β,7-*Dichloro-ester* (14).—The ester (110 mg) in ethyl acetate–cyclohexane (3 : 97; 100 ml) was hydrogenated over 5% rhodium on alumina at 30 °C and 21 atm. Recovery by filtration and evaporation *in vacuo* gave a gum which was purified by p.l.c. [development with benzene and formic acid–ethanol–benzene (1 : 4 : 95)] to give two sets of two bands. From the faster moving pair of bands, the band of lower $R_F$ yielded a mixture of the 8-epimers of 7-*chloro*-10β-*cyclohexylmethoxycarbonyl*-1β,8-*dimethylgibbane*-1α,4aα-*carbolactone* (21) as a gum (23 mg) (Found: *m/e* 448.2380. $C_{26}H_{37}{}^{35}ClO_4$ requires *M*, 488.2380), $\nu_{max.}$ ($CHCl_3$) 1 780, 1 737, 1 733, 993, and 880 $cm^{-1}$; δ 0.85 (d, *J* 7 Hz) and 1.00 (d, *J* 7 Hz) (8α- and 8β-Me), 1.08 (3 H, s, 1β-Me), 1.25br (11 H, s, cyclohexyl H), 2.49 (1 H, d, *J* 10 Hz, 10-H), 2.67 (1 H, d, *J* 10 Hz, 10a-H), and 3.93 (2 H, d, *J* 6 Hz, $OCH_2$); *m/e* 448 ($M^+$, 1.9%), 406 (7.3), 404 (22), 369 (87), 309 (43), and 273 (100). The material from the band of higher $R_F$ yielded a gum (26 mg) believed to be a mixture of the 7-chloro-ester (21) and the 8-epimers of 4β,7-dichloro-10β-cyclohexylmethoxycarbonyl-1β,8-dimethyl-gibbane-1α,4aα-carbolactone (22) (Found: *m/e* 484.1955. $C_{26}H_{36}{}^{35}Cl^{37}ClO_4$ requires $M^+$, 484.1961).

The slower moving pair of bands were recovered together to afford a solid which on further purification by p.l.c. [development with formic acid–benzene × 2 (1 : 99) and formic acid–ethanol–benzene (1 : 3 : 96)] gave two bands. The band of lower $R_F$ yielded a solid (14 mg) which crystallised from ethyl acetate–light petroleum as plates, m.p. 195—202 °C (decomp.), of a mixture of the 8-epimers of 7-*chloro*-4aα-*hydroxy*-1β,8-*dimethylgibbane*-1α,10β-*dicarboxylic acid*-1,4aα-*lactone* (20) (Found: *m/e* 352.1436. $C_{19}H_{25}{}^{35}ClO_4$ requires *M*, 352.1441), $\nu_{max.}$ 3 530, 3 460, 1 780, 1 745, and 850 $cm^{-1}$; δ 1.10 (d, *J* 7 Hz) and 1.11 (d, *J* 7 Hz) (8α- and 8β-Me), 1.27 (3 H, s, 1β-Me), 2.46 (1 H, d, *J* 10 Hz, 10-H), 2.70 (1 H, d, *J* 10 Hz, 10a-H); *m/e* 352 ($M^+$, 3.9), 308 (14), 306 (32), 274 (53), and 273 (100).

Material from the band of higher $R_F$ gave a mixture of the 8-epimers of 4β,7-*dichloro*-4aα-*hydroxy*-1β,8-*dimethylgibbane*-1α,10β-*dicarboxylic acid* 1,4a-*lactone* (19) (25 mg) which crystallised from ethyl acetate–light petroleum as plates, m.p. 218—223 °C (decomp.) (Found: *m/e*, 386.1055. $C_{19}H_{24}{}^{35}Cl_2O_4$ requires *M*, 386.1052), $\nu_{max.}$ 3 165br, 1 756, 1 738, 922, and 888 $cm^{-1}$; δ 1.09 (d, *J* 7 Hz) and 1.11 (d, *J* 7 Hz) (8α- and 8β-Me), 1.26 (3 H, s, 1β-Me), 2.66 (1 H, d, *J* 10 Hz, 10-H), 3.17 (1 H, d, *J* 10 Hz, 10a-H), 4.28br (1 H, m, $W_{\frac{1}{2}}$ 5 Hz, 4α-H); *m/e* 388 ($M^+$, 6.2%), 386 ($M^+$, 7.3), 323 (37), 306 (100), and 272 (54).

*Reaction of Methyl Tetrahydrogibberellate* [(24) and (25)] *with* 2-*Chloro*-NN-*dimethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—A stirred suspension of the tetrahydro-ester (520 mg) and anhydrous lithium chloride (2.54 g) in tetrahydrofuran (30 ml) was treated at 0 °C with an excess of fluoroamine (3 ml) during 80 min. Stirring was continued for a further 30 min at 0 °C and for 1 h at room temperature. Evaporation of the chloro-*NN*-diethyl-fluoroacetamide *in vacuo* (65 °C and 0.3 mmHg) during 8 h afforded a solid, which was chromatographed on silica gel (95 g). Elution with ethyl acetate–light petroleum (1 : 19) gave a mixture of the 8-epimers of 7-*chloro*-10β-*methoxycarbonyl*-1β,8-*dimethylgibb*-2-*ene*-1α,4aα-*carbolactone* [(30) and (31)] (212 mg) which crystallised from ethyl acetate–light petroleum as prisms, m.p. 153—158 °C (Found: C, 66.0; H, 6.95%; *m/e*, 364.1448. $C_{20}H_{25}{}^{35}ClO_4$ requires C, 65.8; H, 6.9%; *M*, 364.1441), $\nu_{max.}$ ($CHCl_3$ film) 1 776, 1 740, 912, and 893 $cm^{-1}$; δ 1.06 (d, *J* 7 Hz) and 1.07 (d, *J* 7 Hz) (8α- and 8β-Me), 1.24 (3 H, s, 1β-Me), 2.60 (1 H, d, *J* 10.5 Hz, 10-H), 2.77 (1 H, d, *J* 10.5 Hz, 10a-H), 3.74 (3 H, s, OMe), and 5.74 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 366 ($M^+$, 0.9%), 364 ($M^+$, 2.1), 322 (14), 320 (40), 285 (78), and 260 (100).

Elution with ethyl acetate–light petroleum (2 : 23) gave a fraction which, after further purification by pl.c. [development with ethanol–benzene (1 : 24)], yielded a mixture of the 8-epimers of 7α-(4-*chloro*-*n*-*butoxy*)-10β-*methoxycarbonyl*-1β,8-*dimethylgibb*-2-*ene*-1α,4aα-*carbolactone* [(32) and (33)] which crystallised from ethyl acetate–light petroleum as needles (61 mg), m.p. 146—149 °C (Found: C, 66.3; H, 7.65; Cl, 7.8%; *m/e*, 436.2019. $C_{24}H_{33}{}^{35}ClO_5$ requires C, 66.0; H, 7.6; Cl, 8.0%; *M*, 436.2017), $\nu_{max.}$ 1 772, 1 730, 939, and 756 $cm^{-1}$; δ 0.93 (d, *J* 7 Hz) and 0.96 (d, *J* 7 Hz) (8α- and 8β-Me), 1.22 (3 H, s, 1β-Me), 2.74 (2 H, m, 10- and 10a-H), 3.40 (2 H, t, *J* 6 Hz, $OCH_2$), 3.57 (2 H, t, *J* 6 Hz, $CH_2Cl$), 3.74 (3 H, s, OMe), and 5.72 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 438 ($M^+$, 8.4%), 436 ($M^+$, 22), 393 (27), and 321 (14).

*Di-imide Reduction of Gibberellic Acid*.—Gibberellic acid (1.03 g) and hydrazine hydrate (90%; 6 ml) in ethanol (25 ml) were stirred at 0 °C and treated with hydrogen peroxide (30%; 6 ml) added dropwise during 1 h. After 3 h at 0 °C, additional hydrogen peroxide (6 ml) was added. The solu-

tion was stirred for 1 h at 0 °C and then allowed to come to room temperature and left overnight. Removal of the ethanol *in vacuo*, followed by acidification of the aqueous residue with 2N-hydrochloric acid at 0 °C, and recovery in ethyl acetate afforded the 8β-epimer of tetrahydrogibberellic acid (26) as a solid (997 mg), which crystallised from ethanol-water as prisms, m.p. 298—300 °C (decomp.) [lit.,[18] 300—301 °C (decomp.)], δ ([$^2H_5$]pyridine) 1.12 (3 H, d, *J* 6.5 Hz, 8β-Me), 1.63 (3 H, s, 1β-Me), 3.16 (1 H, d, *J* 10 Hz, 10-H), 3.90 (1 H, d, *J* 10 Hz, 10a-H), and 4.12br (1 H, s, 2α-H).

Methylation gave the 8β-epimer of methyl tetrahydrogibberellate, which crystallised from aqueous methanol as prisms, m.p. 269—270 °C (decomp.) [lit.,[18] 271—272 °C (decomp.)], δ ([$^2H_5$]pyridine) 1.08 (3 H, d, *J* 7 Hz, 8β-Me), 1.46 (3 H, s, 1β-Me), 2.97 (1 H, d, *J* 10.5 Hz, 10-H), 3.71 (3 H, s, OMe), 3.73 (1 H, d, *J* 10.5 Hz, 10a-H), and 4.06br (1 H, s, 2α-H).

*Reaction of Methyl Tetrahydrogibberellate* (24) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—A stirred suspension of the ester (530 mg) and anhydrous lithium chloride (2.5 g) in tetrahydrofuran (20 ml) was treated with an excess of fluoroamine (4 ml) as before. The solution was stirred for 1 h at 0 °C and for 4 h at room temperature, after which the usual work-up afforded a gum which was chromatographed on silica gel (46 g). Elution with ethyl acetate–light petroleum (1 : 19) gave 7-*chloro*-10β-*methoxycarbonyl*-1β,8β-*dimethylgibb*-2-*ene*-1α,-4aα-*carbolactone* (30) as a gum (196 mg) (Found: *m/e*, 364.1437. $C_{20}H_{25}{}^{35}ClO_4$ requires *M*, 364.1441), δ 1.07 (3 H, d, *J* 7 Hz, 8β-Me), 1.23 (3 H, s, 1β-Me), 2.60 (1 H, d, *J* 10.5 Hz, 10-H), 2.77 (1 H, d, *J* 10.5 Hz, 10a-H), 3.74 (3 H, s, OMe), and 5.74 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 322 (15%), 320 (42), 285 (62), and 260 (100).

Elution with ethyl acetate–light petroleum (1 : 9) gave a gum (202 mg) believed to be mainly 7α-(4-chloro-n-butoxy)-10β-methoxycarbonyl-1β,8β-dimethylgibb-2-ene-1α,4aα-carbolactone (32), δ 0.96 (3 H, d, *J* 7 Hz, 8β-Me), 1.22 (3 H, s, 1β-Me), 2.73 (2 H, m, 10- and 10a-H),3.37 (2 H, dt, *J* 6 and 2 Hz, $OCH_2$), 3.57 (2 H, t, *J* 6 Hz, $CH_2Cl$), 3.74 (3 H, OMe), and 5.74 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H).

*Reaction of Methyl Tetrahydrogibberellate* (24) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Potassium Chloride and a Crown Ether*.—A stirred suspension of the ester (430 mg), anhydrous potassium chloride (1.76 g), and dicyclohexyl-18-crown-6 (4 drops) in dichloromethane (20 ml), was treated with fluoroamine (3 ml) dropwise over 40 min at 0 °C. After stirring for 1 h at 0 °C and for 3 h at room temperature, evaporation, followed by removal of the chloro-*NN*-diethylfluoroacetamide *in vacuo* (60 °C and 0.5 mmHg) gave a solid which was chromatographed on silica gel (58 g). Elution with ethyl acetate–light petroleum (1 : 9) afforded a gum (251 mg) which on purification by p.l.c. [development with ethanol–benzene (3 : 47) × 2] gave 2β-*hydroxy*-7-*fluoro*-10β-*methoxycarbonyl*-1β,8β-*dimethylgibbane*-1α,4aα-*carbolactone* (27) which crystallised from ethyl acetate–light petroleum as plates, m.p. 171—174 °C (decomp.) (Found: C, 65.5; H, 7.5; F, 5.4%; *m/e*, 366.1834. $C_{20}H_{27}FO_5$ requires C, 65.6; H, 7.4; F, 5.2%; *M*, 366.1842), $\nu_{max.}$ 3 510, 1 750, 1 730, 892, and 753 $cm^{-1}$; δ 1.02 (3 H, d, *J* 7 Hz, 8β-Me), 1.12 (3 H, s, 1β-Me), 2.65 (1 H, d, *J* 10.5 Hz, 10-H), 3.19 (1 H, d, *J* 10.5 Hz, 10a-H), 3.74 (3 H, s, OMe), and 3.82 (1 H, m, $W_{\frac{1}{2}}$ 6 Hz, 2α-H); $\phi$* 147.05br (m, $W_{\frac{1}{2}}$ 45 Hz, 7α-F); *m/e* 366 ($M^+$, 1.3%), 348 (25), 304 (53), 261 (100), and 244 (45).

Elution of the column with ethyl acetate–light petroleum (1 : 1) afforded the starting ester (59 mg).

*Hydrolysis of the Mixture of* 8-*Epimers of the* 7α-(4-*Chloro-n-butoxy*)-*esters* [(32) *and* (33)].—The esters (62 mg) in methanol (10 ml) and 2N-sodium hydroxide (10 ml) were refluxed for 8 h under nitrogen. Acidification of the solution with 2N-hydrochloric acid at 0 °C and recovery in ethyl acetate gave a mixture of the 8-epimers of 7α-(4-*methoxy-n-butoxy*)-4aα-*hydroxy*-1β,8-*dimethylgibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1,4a-*lactone* [(36) and (37)] which crystallised from ethyl acetate–light petroleum as needles, m.p. 178—180 °C (decomp.) (Found: C, 68.6; H, 8.35%; *m/e*, 418.2349. $C_{24}H_{34}O_6$ requires C, 68.8; H, 8.2%; *M*, 418.2355), δ 0.92 (3 H, d, *J* 7 Hz, 8α- and 8β-Me), 1.24 (3 H, s, 1β-Me), 2.68 (2 H, m, 10- and 10a-H), 3.33 (3 H, s, OMe), 3.38br (4 H, s, $OCH_2$), and 5.70 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 418 ($M^+$, 2.4%), 374 (1.3), and 307 (9.8).

*Hydrolysis of the* 7-*Chloro-ester* (30).—A stirred suspension of the ester (196 mg) and powdered potassium hydroxide (1.8 g) in t-butyl alcohol (20 ml) was refluxed for 3 h under nitrogen. Water (30 ml) was added, the alcohol was removed *in vacuo*, and the aqueous residue was acidified at 0 °C with 2N-hydrochloric acid. Recovery in ethyl acetate followed by purification by p.l.c. [development with ethanol–benzene (3 : 2 : 95), (3 : 3 : 94), and (3 : 4 : 93) × 2] yielded a foam (120 mg) which crystallised from ethyl acetate–light petroleum as prisms, m.p. 215—219 °C (decomp.), of 7-*chloro*-4aα-*hydroxy*-1β,8β-*dimethylgibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1,4a-*lactone* (38) (Found: C, 65.2; H, 6.7; Cl, 9.8%; *m/e*, 350.1293. $C_{19}H_{23}{}^{35}ClO_4$ requires C, 65.1; H, 6.6; Cl, 10.1%; *M*, 350.1285), $\nu_{max.}$ 3 420br, 1 740, 940, and 700 $cm^{-1}$; δ 1.09 (3 H, d, *J* 6.5 Hz, 8β-Me), 1.28 (3 H, s, 1β-Me), 2.71 (2 H, m, 10- and 10a-H), 5.77 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); δ ([$^2H_4$]methanol) 2.52 (1 H, d, *J* 9 Hz, 10-H) and 2.75 (1 H, d, *J* 9 Hz, 10a-H); *m/e* 350 ($M^+$, 0.9%), 308 (18), 306 (44), 271 (73), and 261 (18).

*Reaction of Tetrahydrogibberellic Acid* (26) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—(a) *In Dichloromethane*. A stirred suspension of tetrahydrogibberellic acid (300 mg) and anhydrous lithium chloride (1.5 g) in dichloromethane (12 ml) was treated dropwise with fluoroamine (2.5 ml) at 0 °C over 30 min and stirring was continued for 30 min at 0 °C and for 4 h at room temperature. Evaporation *in vacuo* afforded a gum which was taken up in ethyl acetate and the solution was washed with sodium hydrogencarbonate solution. The combined sodium hydrogencarbonate extracts were acidified at 0 °C with 2N-hydrochloric acid. Recovery in ethyl acetate followed by purification by p.l.c. [development with formic acid–ethanol–benzene (2 : 3 : 45)] gave two bands. The band of higher $R_F$ afforded the chloro-lactone (38) (84 mg) identical (n.m.r. spectrum) with the sample prepared above.

The band of lower $R_F$ yielded 7α-*chlorofluoroacetoxy*-4aα-*hydroxy*-1β,8β-*dimethylgibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1,4a-*lactone* (39) as a gum (70 mg) (Found: *m/e*, 426.1257. $C_{21}H_{24}{}^{35}ClFO_6$ requires *M*, 426.1245), $\nu_{max.}$ ($CHCl_3$ film) 3 500br, 3 300, 1 774, 1 749, 1 715, 920, and 810 $cm^{-1}$; δ 1.10 (3 H, d, *J* 6.5 Hz, 8β-Me), 1.27 (3 H, s, 1β-Me), 2.73 (2 H, m, 10- and 10a-H), 5.74 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H), and 6.20 (1 H, d, *J* 51 Hz, OCOCHClF); *m/e* 384 (6.9%), 382 (16), 308 (6.4), 306 (13), and 271 (34).

*Hydrolysis of the* 7α-*Chlorofluoroacetoxy-acid* (39).—Treatment of the 7α-chlorofluoroacetoxy-acid in methanol

with potassium carbonate under reflux and work-up in the usual way gave the dihydrogibberellin $A_5$ (40).[15]

*Reaction of Tetrahydrogibberellic Acid* (26) *with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—(b) *In* 1,2-*dimethoxyethane*. The reaction of tetrahydrogibberellic acid (300 mg) and lithium chloride (1.5 g) in 1,2-dimethoxyethane (12 ml) with fluoroamine (2.5 ml) was performed as in (a). The usual work-up afforded a gum (298 mg), which was purified by p.l.c. [development with formic acid–ethanol–benzene (3 : 2 : 45)] and gave two main bands. The band of higher $R_F$ yielded the 7-chloro-lactone (38), m.p. 210—215 °C (decomp.), identical (n.m.r. spectrum) with the sample prepared above. The band of lower $R_F$ yielded 7α-(2-*methoxyethoxy*)-4aα-*hydroxy*-1β,8β-*dimethylgibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1,4a-*lactone* (42) as a gum (82 mg) (Found: *m/e*, 390.2040. $C_{22}H_{30}O_6$ requires *M*, 390.2042), $\nu_{max.}$ ($CHCl_3$ film) 3 140br, 1 770, 1 730, 1 709, 910, 863, and 804 $cm^{-1}$; δ 0.92 (3 H, d, *J* 6 Hz, 8β-Me), 1.17 (3 H, s, 1β-Me), 2.52 (1 H, d, *J* 10.5 Hz, 10-H), 2.67 (1 H, d, *J* 10.5 Hz, 10a-H), 3.28 (3 H, s, OMe), 3.44 (4 H, s, 2 × $OCH_2$), and 5.73 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 390 ($M^+$, 21%), 347 (31), and 287 (6.9).

*Reaction of Gibberellic Acid with* 2-*Chloro*-NN-*diethyl*-1,1,2-*trifluoroethylamine in the Presence of Lithium Chloride*.—(a) *In* 1,2-*dimethoxyethane*. A stirred suspension of gibberellic acid (1.0 g) and lithium chloride (2.5 g) in 1,2-dimethoxyethane (50 ml) was treated with fluoroamine (6 ml) at 0 °C for 2 h and then at room temperature for 2 h. Work-up, as above, gave an acidic foam (422 mg) which on purification by p.l.c. [development with formic acid–ethanol–benzene (1 : 1 : 23) × 3, (2 : 3 : 45) × 2, and (1 : 2 : 22)] gave two major bands. Material from the band of higher $R_F$ yielded 4β-*chloro*-7α-(2-*methoxyethoxy*)-4aα-*hydroxy*-1β-*methyl*-8-*methylenegibb*-2-*ene*-1α,10β-*dicarboxylic acid* 1,4α-*lactone* (16) which crystallised from ethyl acetate–light petroleum as plates (32 mg), m.p. 183—187 °C (Found: C, 62.55; H, 6.6%; *m/e*, 422.1482. $C_{22}H_{27}{}^{35}ClO_6$ requires C, 62.5; H, 6.4%; *M*, 422.1496), $\nu_{max.}$ 3 200br, 1 788, 1 727, 901, 840, and 783 $cm^{-1}$; δ 1.24 (3 H, s, 1β-Me), 2.63 (1 H, d, *J* 10 Hz, 10-H), 3.04 (1 H, d, *J* 10 Hz, 10a-H), 3.34 (3 H, s, OMe), 3.46 (4 H, s, 2 × $OCH_2$), 4.47 (1 H, d, *J* 3.5 Hz, 4α-H), 5.05br (1 H) and 5.13br (1 H) (8-$CH_2$), and 5.81 (2 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2- and 3-H); *m/e* 424 ($M^+$, 3.9%), 422 ($M^+$, 9.0), 221 (4.8), and 194 (5.1).

Material from the band of lower $R_F$ was further purified by p.l.c. [development with formic acid–ethanol–benzene (1 : 1 : 23), (1 : 2 : 22), and (2 : 5 : 43)] to afford the trichloro-ester (23) as a gum (12 mg) which was identical (i.r. and n.m.r. spectrum) with the specimen prepared in (b) below.

(b) *In acetone*. The reaction was repeated as in (a), but using acetone (50 ml) as the solvent. The usual work-up afforded a gum which was purified by p.l.c. [development with formic acid–ethanol–benzene (1 : 1 : 23), (4 : 7 : 89), and (2 : 5 : 43)] to give two major bands. Material from the band of higher $R_F$ crystallised from ethyl acetate–light petroleum as prisms, m.p. 159—162 °C (decomp.), of the *trichloro-ester* (23) (Found: C, 62.5; H, 6.0; Cl, 14.2. $C_{38}H_{39}Cl_3O_8$ requires C, 62.5; H, 5.4; Cl, 14.6%), $\nu_{max.}$ 3 400br, 1 781, 1 707, 900, and 873 $cm^{-1}$; δ 1.28 (6 H, s, 2 × 1β-Me), 2.64 (2 H, d, *J* 10 Hz, 2 × 10-H), 3.06 (2 H, d, *J* 10 Hz, 2 × 10a-H), 4.51 (2 H, d, *J* 3 Hz, 2 × 4α-H), 4.98br (2 H) and 5.27br (2 H) (2 × 8-$CH_2$), and 5.48 [4 H, m, $W_{\frac{1}{2}}$ 12 Hz, 2 × (2- and 3-H)]; *m/e* 364 (3.1%), 348 (17), 346 (48), 329 (21), 319 (44), 285 (44), and 239 (100).

The band of lower $R_F$ yielded a gum (76 mg) believed to be 2β,7-dichloro-4aα-hydroxy-1β-methyl-8-methylenegibb-3-ene-1α,10β-dicarboxylic acid 1,4a-lactone (6) δ 1.25 (3 H, s, 1β-Me), 2.75 (1 H, d, *J* 10.5 Hz, 10-H), 3.03 (1 H, d, *J* 10.5 Hz, 10a-H), 4.64br, (1 H, 2α-H), 4.97br (1 H) and 5.28br (1 H) (8-$CH_2$), 5.89 (1 H, dd, *J* 10 and 3 Hz, 3-H), and 6.25 (1 H, dd, *J* 10 and 1.5 Hz, 4-H); its n.m.r. spectrum showed that it contained traces of the 4β,7-dichloro-acid (17); *m/e* 348 (13%), 346 (33), 329 (59), 311 (24), 285 (49), 283 (83), and 239 (100).

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