Transannular Participation of Some C-19 Esters in Reactions at C-20 of Gibberellin A_{13}

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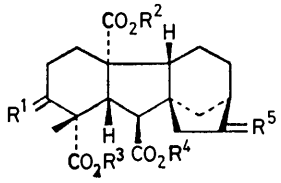
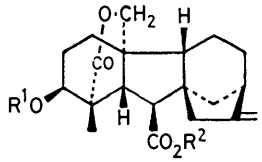
Methanolysis or sodium borohydride reduction of the 3-acetoxy-7,19-dimethyl ester of gibberellin A_{13} 20-toluene-*p*-sulphonyl anhydride afforded, respectively, the unusual 19-orthoester or epimeric 19-acetals as the major products rather than the products of simple displacement of the 20-toluene-*p*-sulphonoxy-group. The structure of the 19-orthoester was proven by *X*-ray analysis.

THE C_{20} gibberellins fall into a number of groups in which the oxidation level of C-20 differs from one member to the other (*e.g.* gibberellins A_{14}, A_{37}, A_{36}, and A_{13}).[1] In this group, gibberellin A_{13} (1) [2] appears to be a terminal metabolite in the fungus *Gibberella fujikuroi* and is more readily available than the other metabolites. Consequently we have explored methods of differentiating between the reactivity of the three carboxy-groups of gibberellin A_{13} with a view to altering the oxidation level of C-20. Previously the selective reduction of C-20 was achieved through the formation and reduction of a 20→3-lactone affording a partial synthesis of gibberellin A_{37} (2).[3,4] In the course of our work, we have examined the selective esterification and reduction of some derivatives of gibberellin A_{13}.[5] The results, which form the subject of this paper, reveal an unusual transannular participation between C-19 and C-20 which leads to the formation of ' orthoester ' derivatives.

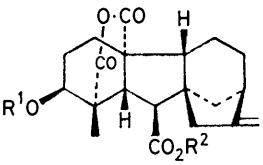
The ^1H n.m.r. methoxy-resonances of gibberellin A_{13} trimethyl ester (3) appear as three distinct singlets which could act as useful markers for selective reactions. Since gibberellins can occur as glucoside esters, the assignment of these methoxy-resonances could also have structural utility. The resonances were assigned in the following sequence of deuteriation reactions. Methanolysis of the gibberellin A_{13} 19,20-anhydride has been



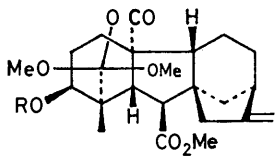


(1) R^1 = α-H, β-OH, $R^2=R^3=R^4$ = H, $R^5=CH_2$
(3) R^1 = α-H, β-OH, $R^2=R^3=R^4$ = Me, $R^5=CH_2$
(6) R^1 = α-H, β-OAc, R^2 = H, $R^3=C^2H_3$, R^4 = Me, $R^5=CH_2$
(7) R^1 = α-H, β-OAc, $R^2=R^4$ = Me, $R^3=C^2H_3$, $R^5=CH_2$
(9) R^1 = α-H, β-OAc, R^2 = Me, $R^3=R^4=C^2H_3$, $R^5=CH_2$
(10) R^1 = α-H, β-OAc, R^2 = H, $R^3=R^4$ = Me, $R^5=CH_2$
(11) R^1 = α-H, β-OAc, R^2 = Ts, $R^3=R^4$ = Me, $R^5=CH_2$
(13) R^1 = α-H, β-OAc, $R^2=R^3=R^4$ = Me, $R^5=CH_2$
(15) R^1 = O, $R^2=R^3=R^4$ = Me, $R^5=CH_2$
(17) R^1 = α-H, β-OH, $R^2=R^3=R^4$ = Me, R^5 = O
(18) R^1 = H, $\Delta^{2,3}$, $R^2=R^3=R^4$ = Me, R^5 = O
(19) R^1 = H, $\Delta^{2,3}$ $R^2=R^3=R^4$ = Me, R^5 = O
(29) R^1 = α-H, β-OH, R^2 = H, $R^3=R^4$ = Me, $R^5=CH_2$

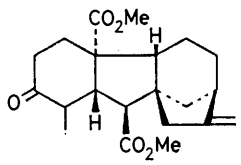
(2) $R^1=R^2$ = H
(24) R^1 = Ac, R^2 = Me
(27) R^1 = H, R^2 = Me



(4) R^1 = Ac, R^2 = H
(5) R^1 = Ac, R^2 = Me
(8) R^1 = Ac, R^2 = Ts



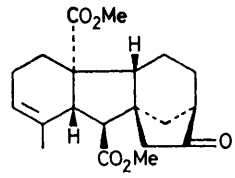
(12) R = Ac
(14) R = H



(16)

shown to lead [5] to the 19-monomethyl esters. Hence methylation of the 3-acetoxy-anhydride (4) with diazomethane followed by methanolysis of the ester anhydride (5) with [$^2H_4$]methanol gave the 3-acetoxy-7-methyl-19-([$^2H_3$]methyl) ester (6). Further methylation with diazomethane gave the 3-acetoxy-7,20-dimethyl-19-([$^2H_3$]methyl) ester (7). Conversion of the acetoxy-anhydride (4) into the mixed anhydride (8) with toluene-*p*-sulphonyl chloride and triethylamine followed by methanolysis with [$^2H_4$]methanol and methylation with diazomethane, gave the 3-acetoxy-7,19-di([$^2H_3$]methyl)-20-methyl ester (9). Comparison of the ^1H n.m.r. spectra of these compounds with the unlabelled ester led to the assignment of the resonances as δ 3.72 (7-OMe), 3.67 (19-OMe), and 3.60 (20-OMe).

During the course of this work the 3-acetoxy-7,19-dimethyl ester (10) [3] was converted into the 20-toluene-*p*-sulphonyl anhydride (11) and immediately subjected to methanolysis. The product, subsequently assigned the structure (12), differed from the acetate (13) of gibberellin A_{13} trimethyl ester both in the position of the methoxy-resonances (δ 3.50, 3.52, and 3.69) and in the 5-H : 6-H proton signals [δ 2.65 and 3.11 (*J* 10 Hz)]. When the toluene-*p*-sulphonyl anhydride (11) was treated with methanolic sodium methoxide over a longer period of time, gibberellin A_{13} trimethyl ester (3) and the orthoester alcohol (14) were obtained. The gibberellin A_{13} trimethyl ester may be formed by the direct displacement of the toluene-*p*-sulphonyl group or by attack on the lactone of the orthoester (14) by the methoxide ion. The orthoester structure of the compounds (12) and (14) followed from the carbon-13 n.m.r. spectrum of (14) which showed a singlet at δ 116.9 (*cf.* ethyl orthoformate, δ 112.5) [6] and only two ester-carbonyl signals (δ 173.1 and 175.8). The full assignment of the spectrum was made by comparison with a series of gibberellin A_{13} derivatives



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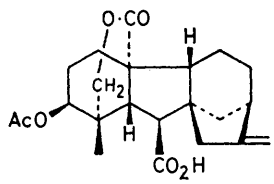

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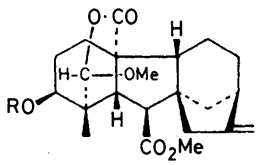
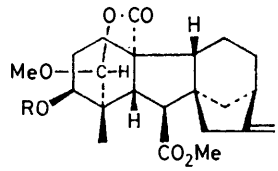
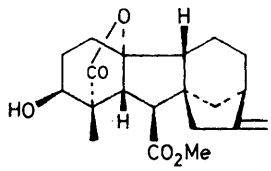


(22) R = Ac
(25) R = H



(23) R = Ac
(26) R = H



(28)

(see Table 1). The structure of this unusual orthoester was then confirmed by *X*-ray analysis (see later).

The reduction of mixed toluene-*p*-sulphonyl anhydrides with sodium borohydride has been described as a method of generating alcohols. However reduction of the mixed anhydride (11) with sodium borohydride gave a separable pair of acetals whose structure (22) and (23) again revealed the participation of C-19 in the reactions of C-20. The epimeric structures (22) and (23) followed from the

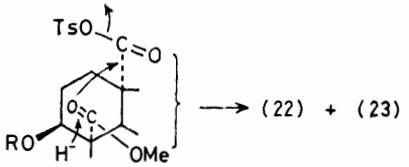
TABLE 1

^{13}C N.m.r. spectra of gibberellin A_{13} derivatives

Carbon atom	(3)	(15)	(16)	(17)	(18)	(19)	(20)	(4)	(21)	(14)	(25)	(26)
1	30.2	34.0	34.2	30.0	36.6 [a]	36.3	33.0	30.5	32.5	33.0	31.0 [a]	31.0 [a]
2	28.9	38.3	38.7	29.2	125.3 [b]	125.2 [a]	24.7	26.8	26.9	28.9	29.3	29.1
3	70.3	206.8	210.6	70.7	132.5 [b]	132.5 [a]	121.3	71.5	75.8	70.4	73.2	68.9
4	49.3 [a]	58.5	46.3	48.9 [a]	46.8	46.8	134.7	51.4	36.8	46.6	42.0	41.1
5	50.1 [b]	55.7	54.7	51.1	53.7	53.7	50.1	48.4	48.5	48.7	47.2	48.2
6	50.8 [b]	50.7	51.6	51.1	51.4	52.8	51.6	51.0	50.3	50.0	50.1	49.8
7	175.3 [c]	174.6 [a]	174.7	175.1	175.2	174.6	174.7	178.3	179.6	175.8	175.7	174.8
8	50.1 [a]	51.6	52.4	50.1 [a]	49.9	48.5	49.6	48.7	50.8	51.3	51.0	51.4
9	56.4	56.7	55.3	56.5	55.6	55.9	55.8	54.3	54.4	54.5	54.7	54.4
10	57.0	56.7	57.7	57.3	55.9	56.0	58.5	52.4	51.1	51.5	51.5	51.5
11	18.6	18.6	19.0	19.5	19.3	20.0	20.4	16.8	17.1	17.1	17.3	17.0
12	31.6	31.4	31.7	24.9	31.7	24.9	25.1	31.1	30.8	31.0	32.8 [a]	31.9 [a]
13	39.5	39.3	39.4	45.0	39.2	44.8	44.7	41.1	41.6	42.0	42.0	41.6
14	36.3	36.4	37.7	33.1	35.6 [a]	33.0	33.0	43.0	43.0	42.7	42.5 [b]	43.0 [b]
15	46.1	46.2	45.6	52.4	46.0	52.1	51.1	43.0	43.0	42.7	42.8 [b]	43.2 [b]
16	156.6	155.9	155.5	220.8	157.2	220.7	220.8	151.8	153.0	153.6	153.7	153.4
17	105.9	106.4	106.5		106.4			107.1	106.3	105.8	105.7	106.2
18	22.5	21.1	12.2	22.6	28.9	28.7	20.1	18.4	19.0	17.1	17.6	19.7
19	175.1 [c]	172.5 [a]		174.7	174.8	174.6		168.7	73.0	116.9	108.4	107.7
20	174.6 [c]	173.8 [a]	174.7	174.1	174.3	174.1	174.7	169.5	174.6	173.1	173.8	174.6
Esters	50.8	51.6	52.4	51.6	51.1	51.3	51.8	Ac	Ac	50.3	51.5	51.7
	51.1	51.6	52.4	51.6	51.6	51.7	51.8	21.0	21.1	51.6	57.4	58.1
	51.3	51.6		51.6	51.7	51.7		171.1	170.1	527		

[a, b, c] Resonances may be interchanged.

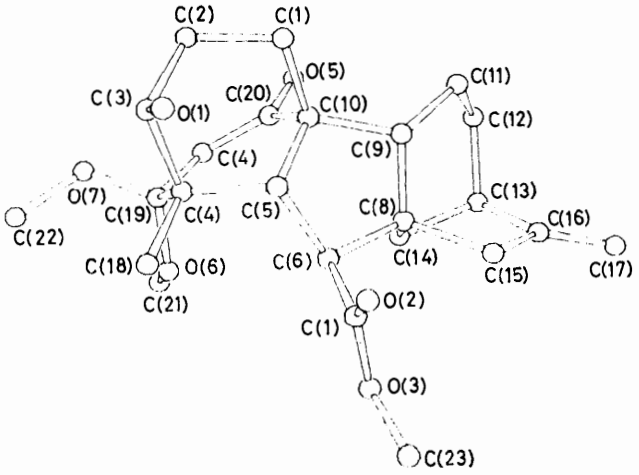
carbon-13 n.m.r. spectra. The C-19 signal appeared at δ 108.4 and 107.7 in the major and minor products, (22) and (23). The anomeric carbon atom of sugar methyl ethers resonates in the range δ 100—105.[7] A change in the position of the C-4 resonance and the similarity of the C-10 resonance between the anhydride (4), the lactone (21), the orthoester (14), and the acetals (22) and (23) indicated that the acetal was at C-19 and the carbonyl group at C-20. The stereochemistry of the acetals at C-19 was readily assigned. The *R*-epimer (22) showed a W long-range coupling, *J* 1.5 Hz, between the 19-H (δ 4.72) and the 5-H signal (δ 2.61) which was absent in the *S*-epimer (23).[5] This long-range coupling, which has previously been noted in compounds related to the lactone (21),[5] not only permits the assignment of the stereochemistry to the acetals but also serves to distinguish the 5- and 6-H proton resonances. Like other gibberellin A_{13} derivatives in which there is a C-19 or C-20 oxygen substituent lying on the α-face of ring B, the 6-H proton resonance in the *R*-acetal (22) appears at lower field (δ 3.24) compared to the *S*-epimer (δ 2.64). The *R*-epimer which is the major product, would correspond to attack of the hydride on the less hindered face of the C-19 ester (see Scheme).



SCHEME Transannular participation of the C-19 ester

When sodium borodeuteride was used as the reductant, the corresponding deuteriated acetals were obtained. If the reduction of the acetoxytoluene-*p*-sulphonyl anhydride was repeated on a larger scale and for a longer period of time, small amounts of the 3-acetate of gibberellin A_{37} methyl ester (24), together with the 3-hydroxy-acetals (25) and (26), were also obtained. The acetate of gibberellin A_{37} methyl ester was hydrolysed to the parent alcohol (27). It showed identical n.m.r. signals to those described in the literature [3,8] and differed from the isomeric 20,19-lactone particularly in the position of the H-18 and H-19/H-20 proton resonances.

In view of the unusual nature of the orthoester, it was subjected to an *X*-ray structure determination (see Figure). The juxtaposition of the C-19 carbonyl group and C-20, implicit in the participation of these centres in the formation of the orthoester and the acetals, can be seen in the *X*-ray structure of gibberellin A_{13} trimethyl ester.[9] It is informative to compare the structure of the orthoester with those of gibberellin A_{13} trimethyl ester (3) and the γ-lactone, gibberellin A_4 methyl ester (28).[9] Whilst ring A of the orthoester has a similar conformation to that of gibberellin A_{13} trimethyl ester, ring C has changed from a boat to a chair conformation. This is presumably to relieve the potentially unfavourable intramolecular contact between the C(20)–O(5) carbonyl group and the C(11)-methylene group. This chair conformation of ring C has, in turn, affected the conformation of the B and D rings. In gibberellin A_{13} and A_4, the ring B C(8)–C(9) torsion angles are −4.4° and −1.0° respectively and thus their B rings have the envelope conformation with C(5) as the flap. In contrast the chair conformation of ring C in the orthoester alters the endocyclic ring torsion angles at C(8)–C(9) for both rings B and C to −33.2° and −46.6° respectively. Thus ring B has



Molecular structure of the orthoester (14) showing the crystallographic numbering scheme

undergone a pseudo-rotation to a conformation which is intermediate between the C_5 envelope and the C_2 twist conformation. The ester group at C(7) of the orthoester has the same orientation as in gibberellin A_4 rather than that of gibberellin A_{13}.

The striking difference [4] in the ease of reduction of the C-20 carbonyl between gibberellin A_{13} trimethyl ester and the 20,3-lactone can also be rationalized in terms of this participation. Examination of the *X*-ray structure of gibberellin A_{13} trimethyl ester suggests that approach of a nucleophile along the favoured trajectory at an angle of 105° to the C=O vector in the vertical plane containing the bisector of the angle between the substituents at C-20 will be impeded by C(11) on one face and by C(2) and the C(19) carbonyl on the other face. The latter interaction favours attack at C(19) and the observed formation of the 20,19 lactones by transannular participation. On the other hand the formation of the 20,3 lactone exposes one face of the 20-carbonyl group and the selective reduction of C-20 is then observed with participation of C-19 only when the free C-20 alkoxide is available for lactonization.

EXPERIMENTAL

General experimental details have been described previously.[10] ^{1}H N.m.r. spectra were determined for solutions in $CDCl_3$ at 60 MHz (Perkin-Elmer R12) or at 90 MHz (Perkin-Elmer R32). ^{13}C N.m.r. spectra were determined for solutions in $CDCl_3$ on a JEOL PFT 100 spectrometer at 25 MHz.

Preparation of the Mixed Anhydride (11).—The monocarboxylic acid (10) [11] (1 g) in dry tetrahydrofuran (50 ml)

and triethylamine (7 ml) was treated with toluene-*p*-sulphonyl chloride (750 mg) and stirred at room temperature for 7 h. The solution was used directly for the sodium borohydride reductions or for the methanolysis experiments.

Methanolysis Experiments.—(*a*) The mixed anhydride (11) [from the mono-carboxylic acid (90 mg)] was treated with methanol (0.5 ml) for 12 h. The solvent was evaporated off and the product was chromatographed on silica in 20% (v/v) ethyl acetate–light petroleum to afford the acetoxy-orthoester (12) (30 mg) as a gum, δ (60 MHz), 0.98 (3 H, s, 18-H_3), 2.07 (3 H, s, OAc), 2.65 and 3.11 (each 1 H, d, *J* 10 Hz, 5-H and 6-H respectively), 3.50, 3.52, and 3.69 (each 3 H, s, OMe), 4.90br (2 H, s, 17-H_2), and 5.28 (1 H, m, 3-H); *m/e* 462 (M^+), 430, 370, 342, and 310. Further elution gave the starting material (10).

(*b*) The mixed anhydride (11) [from the monocarboxylic acid (10) (1 g)] was treated with sodium methoxide (170 mg) in methanol (16 ml) for 65 h. A further portion of sodium methoxide (300 mg) was then added and the solution was then stirred for a further 98 h. The solvent was evaporated off, water was added, and the product was recovered in ethyl acetate to afford a gum which was chromatographed on silica. Elution with ethyl acetate–light petroleum (30% v/v) gave gibberellin A_{13} trimethyl ester (3) (55 mg) followed by the *hydroxy-orthoester* (14) (280 mg) which crystallized from light petroleum–ethyl acetate as prisms, m.p. 176.5—177.5 °C (Found: C, 66.0; H, 8.05. $C_{23}H_{32}O_7$ requires C, 65.7; H, 7.8%), δ (60 MHz) 1.11 (3 H, s, 18-H_3), 2.68 and 3.14 (each 1 H, d, *J* 10 Hz, 5-H and 6-H respectively), 3.50 3.52, and 3.69 (each 3 H, s, OMe), 4.04 (1 H, m, 3-H), and 4.90br (2 H, s, 17-H_2); *m/e* 420 (M^+), 389, 388, 360, 357, 356, 345, 343, 329, and 328. Further elution gave the *hydroxy-acid* (29) (550 mg) as a gum, δ (90 MHz), 1.24 (3 H, s, 18-H_3), 2.58 and 3.78 (each 1 H, d, *J* 10 Hz, 5-H and 6-H respectively), 3.65 and 3.73 (each 3 H, s, OMe), 4.10 (1 H, m, 3-H), and 4.83 (2 H, m, 17-H_2); *m/e* 406 (M^+), 374, 346, 328, 314, 286, 284, 283, and 282.

Reductions with Sodium Borohydride.—A solution of the toluene-*p*-sulphonyl anhydride (11) (from the monocarboxylic acid, 400 mg) in dry tetrahydrofuran (20 ml) was treated with sodium borohydride (500 mg) and stirred for 16 h. The solvent was evaporated off and the product was recovered in ethyl acetate, washed with water, and dried. The solvent was evaporated off and the product was chromatographed on silica in 5% (v/v) ethyl acetate–chloroform to afford the 3-acetoxy-acetal (23) (95 mg) as a gum, δ (60 MHz), 0.92 (3 H, s, 18-H_3), 2.07 (3 H, s, OAc), 2.62 (2 H, s, 5- and 6-H), 3.59 and 3.71 (each 3 H, s, OMe), 4.92br (2 H, s, 17-H_2), 5.15 (1 H, s, 19-H), and 5.30 (1 H, m, 3-H); *m/e* 432 (M^+), 400, 372, 340, 312, and 294. Further elution gave the epimeric 3-acetoxy-acetal, (22) (125 mg) as a gum, δ (60 MHz), 0.89 (3 H, s, 18-H_3), 2.10 (3 H, s, OAc), 2.58 (1 H, dd, *J* 1.5 and 10 Hz, 5-H), 3.28 (1 H, d, *J* 10 Hz, 6-H), 3.57 and 3.69 (each 3 H, s, OMe), and 4.90 (4 H, m, 17-H_2, 3-H and 19-H); *m/e* 432 (M^+), 400, 372, 340, 312, and 284. Further elution gave the monocarboxylic acid (10) (120 mg). When the reduction was repeated using sodium borohydride (1 g) and a solution of the toluene-*p*-sulphonyl anhydride (11) [from the monocarboxylic acid (10) (1 g)] and stirred for 90 h, the following products were obtained: (i) the 3-acetoxy-acetal (23) (140 mg); (ii) the 3-acetoxy-acetal (22) (130 mg); (iii) 3-acetoxygibberellin A_{37} methyl ester (24) (20 mg) as a gum, δ (90 MHz), 1.12 (3 H, s, 18-H_3), 2.14 (3 H, s, OAc), 2.73 and 2.77 (2 H, overlapping AB doublets, 5-H and 6-H), 3.71 (3 H, s, OMe), 4.14 and 4.52 (each 1 H, d, *J* 12 Hz, 20-H_2, the lower-field doublet showed a long-range coupling, *ca.* 1 Hz), 4.95 (1 H, s, 3-H), and 4.98br (2 H, s, 17-H_2), *m/e* 402 (M^+), 371, 360, 342, 310, and 284; (iv) the *hydroxy-acetal* (26) (120 mg) which crystallized from ethyl acetate–light petroleum as prisms, m.p. 252—253 °C (Found: C, 67.55; H, 7.3. $C_{22}H_{30}O_6$ requires C, 67.7; H, 7.7%), δ (360 MHz) 1.03 (3 H, s, 18-H_3), 2.59 and 2.65 (each 1 H, d, *J* 10.1 Hz, 5-H and 6-H), 3.57 and 3.71 (each 3 H, s, OMe), 4.06 (1 H, q, *J* 2.5 and 7 Hz, 3-H), 4.90 (2 H, m, 17-H_2), and 5.15 (1 H, s, 19-H), *m/e* 390 (M^+), 372, 358, 330, 312, 302, 301, 298, and 296; (v) the monocarboxylic acid (10) (60 mg); (vi) the *hydroxy-acetal* (25) (155 mg) which crystallized from ethyl acetate–light petroleum as prisms, m.p. 227—228 °C (Found: C, 67.6; H, 8.1. $C_{22}H_{30}O_6$ requires C, 67.7; H, 7.7%), δ (360 MHz) 1.00 (3 H, s, 18-H_3), 2.61 (1 H, q, *J* 1.5 and 10.5 Hz, 5-H), 3.24 (1 H, d, *J* 10.5 Hz), 3.54 (3 H, s, OMe), 3.64 (1 H, m, 3-H), 3.69 (3 H, s, OMe), 4.72 (1 H, d, *J* 1.5 Hz, 19-H), and 4.9 (2 H, m, 17-H_2), *m/e* 358 (M^+ — 32), 330, 312, 302, and 298; and (vii) the hydroxy-acid (29) (120 mg).

Repetition of the reduction using sodium [^{2}H]borohydride (500 mg) and the toluene-*p*-sulphonyl anhydride obtained from the monocarboxylic acid (10) (380 mg) gave the [19-^{2}H]acetoxy-acetal (23) (100 mg), *m/e* 433 (M^+), 401, 400, 373, 347, 341, 314, 298, and 274, and the [19-^{2}H]acetoxy-acetal (22) (110 mg), *m/e* 433 (M^+), 402, 401, 400, 373, 347, 341, 314, 298, and 274.

Hydrolysis of the 3-Acetate of Gibberellin A_{37} Methyl Ester (24).—The 3-acetate of gibberellin A_{37} methyl ester (18 mg) was dissolved in methanol (3 ml) and treated with potassium hydroxide (30 mg) for 2 h. The solution was treated with dilute hydrochloric acid (1 drop) and the product was recovered in ethyl acetate. The extract was washed with water and dried, and the solvent was evaporated off. The

TABLE 2

Final atomic co-ordinates (× 10^4) with estimated standard deviations in parentheses

	x	*y*	*z*
O(1)	5 250(2)	6 419(4)	1 865(4)
O(2)	5 854(2)	10 093(3)	3 684(4)
O(3)	6 035(2)	10 369(3)	6 068(4)
O(4)	6 359(1)	5 068(3)	5 601(4)
O(5)	7 249(2)	4 880(3)	4 753(5)
O(6)	5 710(2)	6 273(3)	6 942(4)
O(7)	5 462(2)	4 368(3)	5 742(4)
C(1)	6 543(2)	5 795(6)	2 163(5)
C(2)	6 004(3)	4 894(5)	2 376(6)
C(3)	5 471(2)	5 578(5)	2 981(6)
C(4)	5 595(2)	6 426(5)	4 378(5)
C(5)	6 105(2)	7 328(4)	3 997(5)
C(6)	6 316(2)	8 373(4)	5 084(5)
C(7)	6 033(2)	9 686(4)	4 832(5)
C(8)	7 002(2)	8 453(4)	4 873(5)
C(9)	7 129(2)	7 617(5)	3 512(5)
C(10)	6 658(2)	6 528(4)	3 598(5)
C(11)	7 786(2)	7 319(5)	3 275(6)
C(12)	8 167(2)	7 257(6)	4 642(6)
C(13)	7 980(2)	8 252(6)	5 790(5)
C(14)	7 341(2)	7 949(5)	6 237(5)
C(15)	7 296(2)	9 808(5)	4 689(6)
C(16)	7 930(2)	9 599(6)	5 180(6)
C(17)	8 346(2)	10 489(7)	5 160(7)
C(18)	5 045(2)	7 243(5)	4 700(7)
C(19)	5 763(2)	5 564(5)	5 669(5)
C(20)	6 792(2)	5 475(4)	4 673(5)
C(21)	5 927(4)	5 677(7)	8 233(6)
C(22)	4 872(3)	4 376(6)	6 233(10)
C(23)	5 842(3)	11 715(5)	5 956(8)

TABLE 3

Intramolecular distances and angles and selected torsion angles with estimated standard deviations in parentheses

(*a*) Bonds (Å)

C(4)–C(19)	1.524(7)	O(1)–C(3)	1.429(7)
C(5)–C(6)	1.541(6)	O(2)–C(7)	1.202(6)
C(5)–C(10)	1.540(6)	O(3)–C(7)	1.332(6)
C(6)–C(7)	1.509(6)	O(3)–C(23)	1.451(7)
C(6)–C(8)	1.564(6)	O(4)–C(19)	1.443(6)
C(8)–C(9)	1.542(6)	O(4)–C(20)	1.362(6)
C(8)–C(14)	1.556(7)	O(5)–C(20)	1.203(6)
C(8)–C(15)	1.551(6)	O(6)–C(19)	1.381(6)
C(9)–C(10)	1.546(7)	O(6)–C(21)	1.420(7)
C(9)–C(11)	1.532(7)	O(7)–C(19)	1.404(6)
C(10)–C(20)	1.493(6)	O(7)–C(22)	1.410(8)
C(11)–C(12)	1.552(8)	C(1)–C(2)	1.544(8)
C(12)–C(13)	1.526(8)	C(1)–C(10)	1.538(7)
C(13)–C(14)	1.534(7)	C(2)–C(3)	1.500(8)
C(13)–C(16)	1.494(8)	C(3)–C(4)	1.574(7)
C(15)–C(16)	1.518(7)	C(4)–C(5)	1.518(6)
C(16)–C(17)	1.312(9)	C(4)–C(18)	1.531(7)

(*b*) Angles (°)

C(23)–O(3)–C(7)	116.1(4)	C(15)–C(8)–C(14)	100.0(4)
C(20)–O(4)–C(19)	126.2(4)	C(10)–C(9)–C(8)	103.4(4)
C(21)–O(6)–C(19)	116.6(4)	C(11)–C(9)–C(8)	114.0(4)
C(22)–O(7)–C(19)	118.0(4)	C(11)–C(9)–C(10)	122.1(4)
C(10)–C(1)–C(2)	108.5(4)	C(5)–C(10)–C(1)	109.1(4)
C(3)–C(2)–C(1)	113.7(4)	C(9)–C(10)–C(1)	115.2(4)
C(2)–C(3)–O(1)	107.3(4)	C(9)–C(10)–C(5)	100.8(4)
C(4)–C(3)–O(1)	108.2(4)	C(20)–C(10)–C(1)	104.2(4)
C(4)–C(3)–C(2)	114.6(4)	C(20)–C(10)–C(5)	113.2(4)
C(5)–C(4)–C(3)	106.5(4)	C(20)–C(10)–C(9)	114.6(4)
C(18)–C(4)–C(3)	108.3(4)	C(12)–C(11)–C(9)	116.2(4)
C(18)–C(4)–C(5)	109.2(4)	C(13)–C(12)–C(11)	112.5(4)
C(19)–C(4)–C(3)	110.8(4)	C(14)–C(13)–C(12)	108.0(4)
C(19)–C(4)–C(5)	110.1(4)	C(16)–C(13)–C(12)	112.4(4)
C(19)–C(4)–C(18)	111.7(4)	C(16)–C(13)–C(14)	102.5(4)
C(6)–C(5)–C(4)	120.7(4)	C(13)–C(14)–C(8)	100.5(4)
C(10)–C(5)–C(4)	110.3(3)	C(16)–C(15)–C(8)	104.3(4)
C(10)–C(5)–C(6)	105.8(4)	C(15)–C(16)–C(13)	108.2(4)
C(7)–C(6)–C(5)	113.0(4)	C(17)–C(16)–C(13)	126.5(5)
C(8)–C(6)–C(5)	105.3(3)	C(17)–C(16)–C(15)	125.1(5)
C(8)–C(6)–C(7)	110.8(3)	O(6)–C(19)–O(4)	107.6(4)
O(3)–C(7)–O(2)	124.3(4)	O(7)–C(19)–O(4)	98.4(4)
C(6)–C(7)–O(2)	125.9(4)	O(7)–C(19)–O(6)	112.2(4)
C(6)–C(7)–O(3)	109.7(4)	C(4)–C(19)–O(4)	113.8(4)
C(9)–C(8)–C(6)	104.8(4)	C(4)–C(19)–O(6)	109.2(4)
C(14)–C(8)–C(6)	111.8(4)	C(4)–C(19)–O(7)	115.1(4)
C(14)–C(8)–C(9)	112.0(4)	O(5)–C(20)–O(4)	115.1(4)
C(15)–C(8)–C(6)	119.1(4)	C(10)–C(20)–O(4)	119.2(4)
C(15)–C(8)–C(9)	109.3(4)	C(10)–C(20)–O(5)	125.5(4)

(*c*) Torsion angles (°)

C(23)–O(3)–C(7)–O(2)	−4.3(7)
C(23)–O(3)–C(7)–C(6)	172.8(4)
C(20)–O(4)–C(19)–O(6)	−109.0(4)
C(20)–C(4)–C(19)–O(7)	134.4(4)
C(20)–O(4)–C(19)–C(4)	12.2(6)
C(19)–O(4)–C(20)–O(5)	−176.3(4)
C(19)–O(4)–C(20)–C(10)	−0.3(6)
C(21)–O(6)–C(19)–O(4)	−47.5(6)
C(21)–O(6)–C(19)–O(7)	59.7(6)
C(21)–O(6)–C(19)–C(4)	−171.5(5)
C(22)–O(7)–C(19)–O(4)	162.4(4)
C(22)–O(7)–C(19)–O(6)	49.4(6)
C(22)–O(7)–C(19)–C(4)	−76.3(6)
C(10)–C(1)–C(2)–C(3)	51.8(6)
C(2)–C(1)–C(10)–C(5)	−59.3(5)
C(2)–C(1)–C(10)–C(9)	−171.7(4)
C(2)–C(1)–C(10)–C(20)	61.8(5)
C(1)–C(2)–C(3)–O(1)	70.2(5)
C(1)–C(2)–C(3)–C(4)	−49.9(6)
O(1)–C(3)–C(4)–C(5)	−67.0(5)

TABLE 3 (*continued*)

(*c*) Torsion angles (°)

O(1)–C(3)–C(4)–C(18)	50.4(5)
O(1)–C(3)–C(4)–C(19)	173.3(4)
C(2)–C(3)–C(4)–C(5)	52.7(5)
C(2)–C(3)–C(4)–C(18)	170.1(4)
C(2)–C(3)–C(4)–C(19)	−67.1(5)
C(3)–C(4)–C(5)–C(6)	175.6(4)
C(3)–C(4)–C(5)–C(10)	−60.6(5)
C(18)–C(4)–C(5)–C(6)	58.8(5)
C(18)–C(4)–C(5)–C(10)	−177.4(4)
C(19)–C(4)–C(5)–C(6)	−64.2(5)
C(19)–C(4)–C(5)–C(10)	59.6(5)
C(3)–C(4)–C(19)–O(4)	76.1(5)
C(3)–C(4)–C(19)–O(6)	−163.7(4)
C(3)–C(4)–C(19)–O(7)	−36.5(5)
C(5)–C(4)–C(19)–O(4)	−41.6(5)
C(5)–C(4)–C(19)–O(6)	78.7(5)
C(5)–C(4)–C(19)–O(7)	−154.1(4)
C(18)–C(4)–C(19)–O(4)	−163.1(4)
C(18)–C(4)–C(19)–O(6)	−42.8(5)
C(18)–C(4)–C(19)–O(7)	84.4(5)
C(4)–C(5)–C(6)–C(7)	−94.2(5)
C(4)–C(5)–C(6)–C(8)	144.8(4)
C(10)–C(5)–C(6)–C(7)	139.9(4)
C(10)–C(5)–C(6)–C(8)	18.8(4)
C(4)–C(5)–C(10)–C(1)	67.3(5)
C(4)–C(5)–C(10)–C(9)	−171.0(4)
C(4)–C(5)–C(10)–C(20)	−48.2(5)
C(6)–C(5)–C(10)–C(1)	−160.6(4)
C(6)–C(5)–C(10)–C(9)	−39.0(4)
C(6)–C(5)–C(10)–C(20)	83.9(4)
C(5)–C(6)–C(7)–O(2)	−28.0(6)
C(5)–C(6)–C(7)–O(3)	155.0(4)
C(8)–C(6)–C(7)–O(2)	89.9(5)
C(8)–C(6)–C(7)–O(3)	−87.1(4)
C(5)–C(6)–C(8)–C(9)	8.9(4)
C(5)–C(6)–C(8)–C(14)	−112.6(4)
C(5)–C(6)–C(8)–C(15)	131.5(4)
C(7)–C(6)–C(8)–C(9)	−113.6(4)
C(7)–C(6)–C(8)–C(14)	124.9(4)
C(7)–C(6)–C(8)–C(15)	9.0(5)
C(6)–C(8)–C(9)–C(10)	−33.2(4)
C(6)–C(8)–C(9)–C(11)	−168.0(4)
C(14)–C(8)–C(9)–C(10)	88.2(4)
C(14)–C(8)–C(9)–C(11)	−46.6(5)
C(15)–C(8)–C(9)–C(10)	−162.0(4)
C(15)–C(8)–C(9)–C(11)	63.3(5)
C(6)–C(8)–C(14)–C(13)	−175.1(4)
C(9)–C(8)–C(14)–C(13)	67.6(4)
C(15)–C(8)–C(14)–C(13)	−48.1(4)
C(6)–C(8)–C(15)–C(16)	155.7(4)
C(9)–C(8)–C(15)–C(16)	−83.9(5)
C(14)–C(8)–C(15)–C(16)	33.7(4)
C(8)–C(9)–C(10)–C(1)	161.5(4)
C(8)–C(9)–C(10)–C(5)	44.3(4)
C(8)–C(9)–C(10)–C(20)	−77.6(4)
C(11)–C(9)–C(10)–C(1)	−68.5(6)
C(11)–C(9)–C(10)–C(5)	174.3(4)
C(11)–C(9)–C(10)–C(20)	52.5(6)
C(8)–C(9)–C(11)–C(12)	29.1(6)
C(10)–C(9)–C(11)–C(12)	−96.3(5)
C(1)–C(10)–C(20)–O(4)	−99.8(4)
C(1)–C(10)–C(20)–O(5)	75.8(6)
C(5)–C(10)–C(20)–O(4)	18.6(6)
C(5)–C(10)–C(20)–O(5)	−165.9(4)
C(9)–C(10)–C(20)–O(4)	133.4(4)
C(9)–C(10)–C(20)–O(5)	−51.1(6)
C(9)–C(11)–C(12)–C(13)	−36.3(6)
C(11)–C(12)–C(13)–C(14)	61.2(5)
C(11)–C(12)–C(13)–C(16)	−51.2(6)
C(12)–C(13)–C(14)–C(8)	−74.3(4)
C(16)–C(13)–C(14)–C(8)	44.5(4)
C(12)–C(13)–C(16)–C(15)	92.1(5)
C(12)–C(13)–C(16)–C(17)	−92.4(7)
C(14)–C(13)–C(16)–C(15)	−23.6(5)
C(14)–C(13)–C(16)–C(17)	151.9(6)
C(8)–C(15)–C(16)–C(13)	−6.8(5)
C(8)–C(15)–C(16)–C(17)	177.7(5)

residue was chromatographed on silica to afford gibberellin A_{37} methyl ester (27) [3,8] (10 mg) (Found: M^+, 360.189. Calc. for $C_{21}H_{28}O_5$: 360.194), δ (60 MHz), 1.20 (3 H, s, 18-H_3), 2.77 (2 H, s, 5- and 6-H), 3.67 (3 H, s, OMe), 4.09 and 4.48 (each, 1 H, d, J 12 Hz, 20-H_2), and 4.82 and 4.93 (each 1 H, s, 17-H_2), *m/e* 360, 342, 332, 329, 328, 312, 310, 300, 296, 284, 283, 282, 256, and 237. A second more polar product (4 mg) was obtained and was possibly the 3-epimer of gibberellin A_{37} methyl ester.

Crystallographic Data for the Orthoester (14).—$C_{23}H_{32}O_7$, M = 420.5, orthorhombic, a = 22.621(4), b = 10.257(2), c = 9.171(2) Å, U = 2 127.9 Å^3, Z = 4, D_c = 1.31 g cm^{-3}, $F(000)$ = 904. Mo-K_α radiation, λ = 0.710 69 Å, μ = 0.6 cm^{-1}. Space group $P2_12_12_1$ from systematic absences of $h00$ for h odd, $0k0$ for k odd, $00l$ for l odd.

Data were collected on a Hilger and Watts Y290 four-circle diffractometer using a single crystal of size *ca.* 0.3 × 0.3 × 0.2 mm. Accurate cell parameters were derived from the setting angles for 12 reflections. Intensities of unique reflections with $2 < \theta < 25°$ were measured by an ω–2θ step scan-with monochromated Mo-K_α radiation. Three standard reflections monitored every 100 reflections showed no significant variations during the data collection, After correction for Lorentz and polarisation effects but not for absorption, 1 527 reflections with $I > 3\sigma(I)$ were used in the structure analysis.

The positions of all non-hydrogen atoms were located by routine direct methods using the SHELX program system. The absolute configuration was chosen to be that known from chemical considerations. Full-matrix least-squares refinement with anisotropic temperature factors was done in two large blocks refined in alternate cycles, converging at R = 0.084. An angle-weighted difference map revealed the hydrogen atoms which were subsequently held fixed at positions from the map and with a common U_{iso} value of 0.06 Å^2. Continued refinement with a weighting scheme of $\omega = 1.0/[\sigma^2(F) + 0.009F^2]$ converged at R = 0.053, R' = 0.082 with a maximum shift to error ratio of 0.04. A final difference map was everywhere <0.2 eÅ^{-3}.

The structure solution and refinement was done with the SHELX program system and scattering factors and dispersion corrections were taken from ref. 12. Final atom coordinates are given in Table 2 with intramolecular distances and selected torsion angles in Table 3. Lists of temperature factors, hydrogen atom positions, and structure factors have been deposited as Supplementary Publication No. SUP 23124 (10 pp.).*

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* For details see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 1*, 1980, Index issue.

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