Novel Gibberellin Ring A Epoxy Alcohols: Synthesis and X-Ray Molecular Structure

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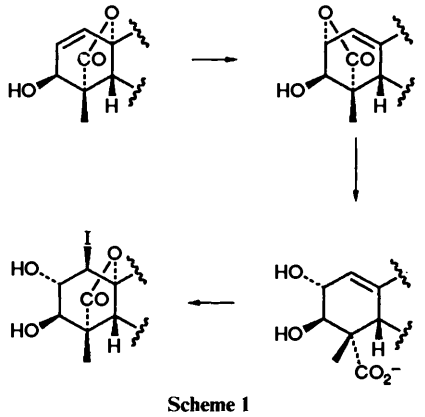
The syntheses of four new gibberellin vicinal epoxy alcohols are described. The 1α-hydroxy 2β,3β-epoxides **3** and **9** were prepared in good yield from the corresponding ring A iodo diol **2** or **8** *via* dehydrohalogenation followed by a Payne-type rearrangement. The structure of compound **3** was confirmed by X-ray crystallography. Although the 2β,3β-epoxide GA_6 **11** is a natural product, neither of the 1α-hydroxy derivatives was found to be naturally occurring.

Epoxide migration in which interconversion of vicinal hydroxy epoxides occurs by intramolecular nucleophilic attack of an oxy-anion upon an adjacent epoxide have long been known in carbohydrate chemistry.[1] More recently, Payne[2] published the first detailed observations on epoxide migration in simple acyclic 2,3-epoxy alcohols, the utility of which has been greatly extended by the asymmetric epoxidation developed by Sharpless.[3] These migrations are of particular value since methods are now available for the regio- and stereo-controlled nucleophilic ring opening of vicinal hydroxy epoxides.[4] During recent studies on the gibberellin plant hormones, we discovered a novel Payne-type rearrangement which led to formation of the remarkably stable 1α-hydroxy 2β,3β-epoxide moiety. This paper describes the synthesis and X-ray molecular structure of the epoxy alcohol **3** and outlines routes to other ring A vicinal hydroxy epoxides.

Results and Discussion

Gibberellin A_3 **7** and GA_7 **1** are available in reasonable quantities from commercial fermentation of the fungus *Gibberella fujikuroi*. Each may be readily converted into the corresponding ring A iodo diol derivative **8** or **2**—the immediate precursors of the target vicinal hydroxy epoxides (Schemes 2 and 3), by the hydrolysis–iodolactonisation procedure developed by Corey *et al.*[5] As shown in Scheme 1 the sequence proceeds *via* base-catalysed rearrangement of the allylic lactone moiety to the isomeric 19,2-lactone,[6] followed by hydrolysis of the lactone, then regeneration of the 19,10γ-lactone by iodolactonisation. The transformations **7** ⟶ **8** and **1** ⟶ **2** were each performed in one pot, giving good yields of the required ring A iodo diols **8** and **2**.



Scheme 1

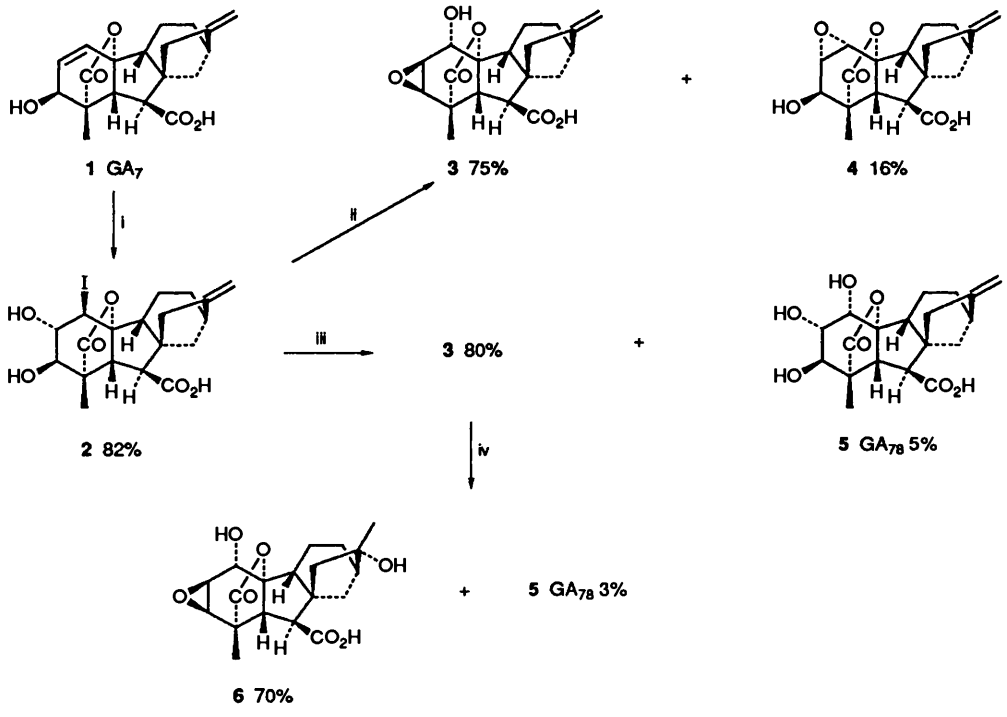
Treatment of the 13-deoxy iodo diol **2** with anhydrous potassium carbonate gave a mixture of two epoxy alcohols as shown in Scheme 2. The major product was separated by flash chromatography from the more polar minor component and it was apparent from their ^1H NMR and mass spectra that each compound was a vicinal hydroxy epoxide. However, their structures could not be unequivocally assigned using these techniques. Table 1 shows the assignments of the signals in the ^1H NMR spectra of each compound. The major, less polar product was crystallised from acetone and light petroleum, and X-ray crystallography confirmed it to be the 1α-hydroxy 2β,3β-epoxide **3** as shown in Fig. 1. The molecular structure of **3** is described later. This compound may be envisaged as being formed by a Payne-type rearrangement of the 3β-hydroxy 1α,2α-epoxide **4**, the predicted initial product from the dehydrohalogenation of the iodo diol **2**. Indeed, the more polar product from the reaction was the 1α,2α-epoxy 3β-alcohol **4** which, on further treatment with potassium carbonate in methanol, gave a 4:1 mixture of the rearranged product **3**: starting material **4**.

Although potassium carbonate has previously been used to induce Payne rearrangements,[7] the reaction is most usually carried out with aq. sodium or potassium hydroxide. Treatment of the iodo diol **2** with 0.1 mol dm^{-3} aq. potassium hydroxide gave the 1α-hydroxy 2β,3β-epoxide **3** in 80% yield; none of the 1α,2α-epoxy 3β-alcohol **4** was detected. A trace amount of a trihydroxygibberellin was isolated from the reaction mixture. From comparison of its ^1H NMR spectrum and GC-mass spectrum of its methyl ester, trimethylsilyl ether derivative with those of an authentic sample of the fungal gibberellin 1α,2α,3β-trihydroxy GA_9 (GA_{78}, **5**),[8] it was indeed found to be GA_{78} **5**, arising from the *trans* diaxial opening of the 2β,3β-epoxide. The 1α-hydroxy 2β,3β-epoxide moiety has proved to be remarkably stable. For example, treatment of compound **3** with aqueous acid returned mainly unchanged substrate **3** and the diol **6** from hydration of the exocyclic double bond. Only a minor amount of GA_{78} **5** was isolated (Scheme 2). Further studies on the opening of the epoxide will be described elsewhere.

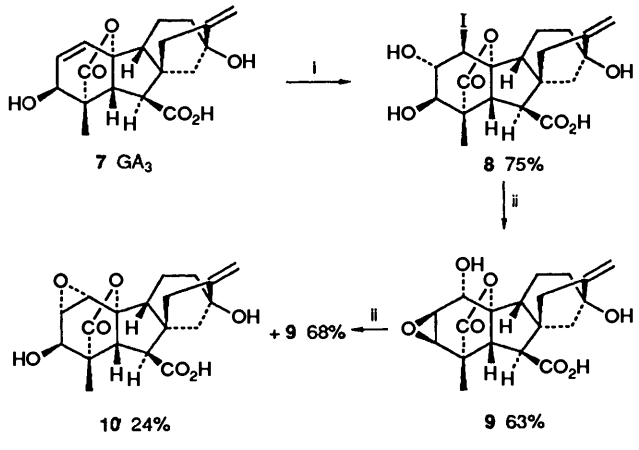
Only one of the 90 known naturally occurring gibberellins, GA_6 **11**, has the 2β,3β-epoxide function.[9] Since hydroxylation at C-1 occurs in plant and fungal systems,[8] we were interested in preparing 1α-hydroxy GA_6 **9** to determine if it is a natural product. Gibberellin A_3 **7** was subjected to the hydrolysis–iodolactonisation procedure described earlier to give the 1β-iodo triol **8** (Scheme 3). Treatment of iodide **8** with aq.

Table 1 Assignments of the signals in the ^1H NMR spectra of compounds **3** and **4** (in $[^2H_6]$acetone)

	Major product **3**	Minor product **4**
18-H_3	δ 1.24 (s)	δ 1.11 (s)
5-H	δ 2.91 (d, *J* 11 Hz)	δ 3.10 (d, *J* 11 Hz)
6-H	δ 2.63 (d, *J* 11 Hz)	δ 2.65 (d, *J* 11 Hz)
C*H*-OH	δ 4.04 (br s)	δ 3.90 (br s)
CH-CHO	δ 3.00 and 3.20 (each d, *J* 4 Hz)	δ 3.14 and 3.49 (each d, *J* 3 Hz)



Scheme 2 *Reagents and conditions:* i, aq. KOH (0.8 mol dm^{-3}), THF, 14 h, room temp. then adjust to pH 9, I_2, CH_2Cl_2, 2 h; ii, K_2CO_3, MeOH; iii, aq. KOH (0.1 mol dm^{-3}); iv, TsOH, aq. THF



Scheme 3 *Reagents and conditions:* i, aq. KOH (1.5 mol dm^{-3}), THF, 20 h, room temp. then adjust to pH 9, I_2, CH_2Cl_2, 6 h; ii, aq. KOH (0.8 mol dm^{-3})

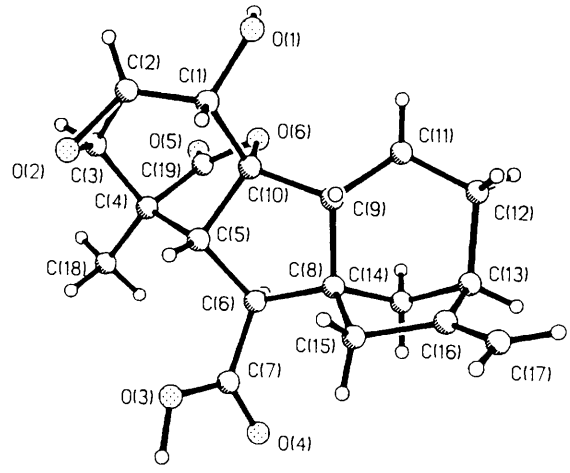
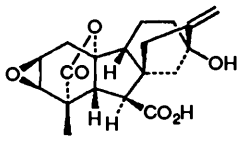


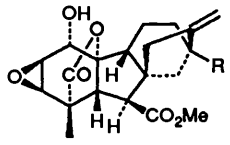
Fig. 1 X-Ray molecular structure of compound **3**

potassium hydroxide gave the required 1α-hydroxy GA_6 **9** as the sole product. None of the expected 1α,2α,3β,13-tetrol **14** was isolated from the reaction mixture. This may be due to the polar nature of tetrahydroxygibberellins[10] which renders them extremely water soluble. Interestingly, on one occasion treatment of the 1α-hydroxyGA_6 **9** with further potassium hydroxide gave ~3:1 mixture of starting material and a more polar vicinal hydroxy epoxide, presumed to be compound **10**. However, usually the reaction returned only starting material **9**.

1α-HydroxyGA_6 **9** and 1α-hydroxy-2β,3β-epoxyGA_9 **3** were separately methylated with ethereal diazomethane to give the corresponding 7-methyl esters **12** and **13**, which were in turn derivatised as their trimethylsilyl ethers. Comparison of their GC-mass spectra with detected but uncharacterised gibberellins[11] revealed that neither compound is a known natural product.



11 GA_6



12 R = OH
13 R = H

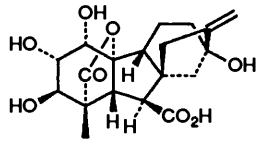


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Table 2 Bond lengths (Å) in structure **3** with e.s.d.s in parentheses

O(1)–C(1)	1.428(10)	O(2)–C(2)	1.466(14)
O(2)–C(3)	1.417(15)	O(3)–C(7)	1.312(13)
O(4)–C(7)	1.206(10)	O(5)–C(19)	1.167(14)
O(6)–C(10)	1.493(13)	O(6)–C(19)	1.351(12)
C(1)–C(2)	1.475(12)	C(1)–C(10)	1.531(12)
C(2)–C(3)	1.462(15)	C(3)–C(4)	1.527(11)
C(4)–C(5)	1.532(12)	C(4)–C(18)	1.544(13)
C(4)–C(19)	1.527(15)	C(5)–C(6)	1.562(10)
C(5)–C(10)	1.538(13)	C(6)–C(7)	1.507(12)
C(6)–C(8)	1.551(12)	C(8)–C(9)	1.564(11)
C(8)–C(14)	1.521(12)	C(8)–C(15)	1.538(13)
C(9)–C(10)	1.564(10)	C(9)–C(11)	1.552(14)
C(11)–C(12)	1.505(10)	C(12)–C(13)	1.559(12)
C(13)–C(14)	1.536(13)	C(13)–C(16)	1.535(16)
C(15)–C(16)	1.542(12)	C(16)–C(17)	1.321(14)

Table 3 Bond angles (°) in structure **3**, with e.s.d.s in parentheses

C(2)–O(2)–C(3)	60.9(7)	C(10)–O(6)–C(19)	109.3(8)
O(1)–C(1)–C(2)	111.7(6)	O(1)–C(1)–C(10)	111.5(8)
C(2)–C(1)–C(10)	109.9(8)	O(2)–C(2)–C(1)	115.3(8)
O(2)–C(2)–C(3)	57.9(7)	C(1)–C(2)–C(3)	122.8(7)
O(2)–C(3)–C(2)	61.2(7)	O(2)–C(3)–C(4)	118.4(7)
C(2)–C(3)–C(4)	117.5(7)	C(3)–C(4)–C(5)	108.0(8)
C(3)–C(4)–C(18)	113.0(7)	C(5)–C(4)–C(18)	117.0(7)
C(3)–C(4)–C(19)	103.7(7)	C(5)–C(4)–C(19)	101.4(7)
C(18)–C(4)–C(19)	112.4(9)	C(4)–C(5)–C(6)	117.6(8)
C(4)–C(5)–C(10)	99.3(7)	C(6)–C(5)–C(10)	103.6(7)
C(5)–C(6)–C(7)	115.3(8)	C(5)–C(6)–C(8)	106.4(7)
C(7)–C(6)–C(8)	112.0(6)	O(3)–C(7)–O(4)	121.6(9)
O(3)–C(7)–C(6)	115.8(7)	O(4)–C(7)–C(6)	122.4(9)
C(6)–C(8)–C(9)	105.9(5)	C(6)–C(8)–C(14)	115.1(8)
C(9)–C(8)–C(14)	110.1(7)	C(6)–C(8)–C(15)	116.9(8)
C(9)–C(8)–C(15)	107.0(7)	C(14)–C(8)–C(15)	101.6(6)
C(8)–C(9)–C(10)	106.6(7)	C(8)–C(9)–C(11)	112.1(7)
C(10)–C(9)–C(11)	115.7(7)	O(6)–C(10)–C(1)	108.8(6)
O(6)–C(10)–C(5)	103.2(8)	C(1)–C(10)–C(5)	110.8(8)
O(6)–C(10)–C(9)	108.4(7)	C(1)–C(10)–C(9)	118.1(8)
C(5)–C(10)–C(9)	106.5(6)	C(9)–C(11)–C(12)	110.1(8)
C(11)–C(12)–C(13)	111.4(7)	C(12)–C(13)–C(14)	108.9(7)
C(12)–C(13)–C(16)	111.3(8)	C(14)–C(13)–C(16)	102.5(8)
C(8)–C(14)–C(13)	100.5(8)	C(8)–C(15)–C(16)	101.9(8)
C(13)–C(16)–C(15)	107.5(8)	C(13)–C(16)–C(17)	125.5(9)
C(15)–C(16)–C(17)	127.0(10)	O(5)–C(19)–O(6)	122.3(10)
O(5)–C(19)–C(4)	128.8(9)	O(6)–C(19)–C(4)	108.8(9)

Molecular Structure of Compound **3**.—The molecular structure of compound **3** is shown in Fig. 1; bond distances and angles are listed in Tables 2 and 3.

The ring [C(1)–C(5),C(10)] adopts a chair conformation with the C(5) atom tilted by 0.87 Å out of the mean plane of the other five atoms (the ring folded by 63°). The epoxy ring plane is inclined to the latter plane by 72° in the same direction. The C(4)C(5)C(10)C(6)C(19) and C(5)C(6)C(8)C(9)C(10) rings both adopt envelope conformations with the C(5) atom tilted out of the plane of the four other atoms by 0.65 and 0.51 Å (ring folding of 41° and 32°), respectively. The C(8)C(14)C(13)C(16)C(15) ring has a half-chair conformation with C(8) and C(14) atoms tilted out of the C(13)C(16)C(15) plane by 0.37 and −0.43 Å, respectively, in the opposite directions.

The C(8)C(9)C(11)C(12)C(13)C(14) ring has a distorted boat conformation. The C(8), C(9), C(11) and C(14) atoms are co-planar within experimental error, and C(12) and C(13) deviate from this plane by 1.14 and 1.33 Å respectively.

Both hydroxy and carboxy group hydrogens are involved in strong intermolecular hydrogen bonds, *viz.* O(1)–H(01)···O(4) ($1-x, x-y, z-\frac{1}{3}$) (O···O 2.68, 0.80, H···O 1.90 Å, O–H–O 165°) and O(3)–H(03)···O(1) ($1-x, 1-y, z+\frac{1}{2}$), O···O 2.68, O–H 1.02, H–O 1.70 Å, O–H–O 160°). The former bonds link the molecules symmetrically dependent *via* 3_2 axes and the latter ones by 2_1 axes. Thus each molecule participates in four helical chains running in the *z* direction around two 3_2 and two 2_1 axes and forming a 3-dimensional network.

Packing of the molecules of compound **3** in the crystal is rather loose, with wide channels along the 6_5 axis occupied by disordered molecules of crystallisation. It was impossible unequivocally to identify the solvent. The strongest peaks of electron density inside the channels were treated in the refinement as carbon atoms (C1S), C(2S) and C(S) with occupancy factors of 0.35, 0.25 and 0.40, respectively. They form, with their symmetrical equivalents, an infinite helical chain around the 6_5 axis, with C···C distances of 1.4(2) to 1.8(1) Å. The shortest contacts between these likely solvent atoms and any C, O and H atoms of compound **3** are equal to 3.96. 3.48 and 3.22 Å , respectively, *i.e.* they exceed the sums of Van der Waals radii.[12]

Experimental

General experimental details have been described in a previous paper.[13] NMR samples were run in [$^2H_6$]acetone unless otherwise stated. The X-ray diffraction study of compound **3** was carried out at room temperature using a computer-controlled four-circle Siemens R3m/v diffractometer (graphite-monochromated Mo-Kα radiation). All calculations were performed on a MicroVax II computer using SHELXTL PLUS programs.[14]

ent-2β,3α,10β-*Trihydroxy*-1α-*iodo*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* **2**.—A solution of gibberellin A_7 **1** (1 g) in tetrahydrofuran (THF) (10 cm^3) and aq. potassium hydroxide (0.8 mol dm^3; 15 cm^3) was stirred for 14 h at room temperature. The solution was adjusted to pH 9 with 2 mol dm^{-3} hydrochloric acid. Methylene dichloride (10 cm^3) and iodine (0.7 g) were added and stirred vigorously for 2 h at room temperature. The organic phase was decanted off. The aqueous layer was acidified to pH 2 with 2 mol dm^{-3} hydrochloric acid and extracted with ethyl acetate. The extract was washed successively with aq. sodium thiosulfate and water, dried (Na_2SO_4), and concentrated under reduced pressure. The iodo diol **2** was crystallised from ethyl acetate–light petroleum as needles (1.18 g), m.p. 146–148 °C (previously isolated as a non-crystalline solid[15]); δ 1.17 (s, 18-H_3), 2.62 (d, *J* 10.5, 6-H), 3.76 (br s, 3-H), 3.84 (d, *J* 10.5, 5-H), 4.44 (br s, 2-H), 4.64 (br s, 1-H) and 4.89 and 4.99 (2 br s, 17-H_2); *m/z* 474 (M^+, 31%), 456 (22), 347 (21), 329 (39), 284 (85), 239 (80), 128 (100) and 91 (65).

Treatment of 1β-*IodoGA*$_{47}$ **2** *with Potassium Carbonate in Methanol.*—A solution of 1β-iodogibberellin A_{47} **2** (150 mg) in methanol (4 cm^3) was stirred with anhydrous potassium carbonate (30 mg) for 14 h at room temperature. The reaction mixture was worked up as usual and purified by flash chromatography. Elution with 35% ethyl acetate in light petroleum (+1% acetic acid) gave ent-2α,3α-*epoxy*-1β,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* **3**, which was crystallised from acetone–light petroleum as needles (82 mg), m.p. 159–161 °C (Found: C, 65.7; H, 6.7. $C_{19}H_{22}O_6$ requires C, 65.89; H, 6.36%); δ 1.24 (s, 18-H_3), 2.63 (d, *J* 11, 6-H), 2.91 (d, *J* 11, 5-H), 3.00 and 3.20 (2 × d, each *J* 4, 2- and 3-H), 4.04 (br s, 3-H) and 4.85 and 4.97 (2 br s, 17-H_2); δ(^{13}C) [$(CD_3)_2CO$] 14.6 (C-18), 18.5 (C-11), 32.4 (C-12), 37.3 (C-14), 39.5 (C-13), 44.8 (C-15), 47.2 (C-5), 48.8 (C-8), 51.4 (C-4), 52.2 (C-6), 54.2 (C-9), 55.3 and 57.2 (C-2 and -3), 71.8 (C-1), 92.8 (C-10), 107.7 (C-17), 158.2 (C-16), 173.3 (C-7) and 176.5 (C-19); *m/z* 346 (M^+, 66%), 328 (90), 274 (100), 201 (38), 105 (30) and 91 (60). Further elution with 40% ethyl acetate in light petroleum (+1% acetic acid) gave ent-1β,2β-*epoxy*-3α,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* **4** as a gum (18 mg) (Found: M^+, 346.143. $C_{19}H_{22}O_6$ requires M, 346.142); δ 1.11 (s, 18-H_3), 2.65 (d, *J* 11, 6-H), 3.10 (d, *J* 11, 5-H), 3.14 and 3.49 (2 × d, each *J* 3, 1- and 2-H), 3.72 (s, OH), 3.90 (br s, 3-H) and 4.88 and 4.92 (2 br s, 17-H_2); *m/z* 346 (M^+, 4%), 328 (10), 300 (4), 284 (10), 239 (8), 99 (68) and 55 (100).

Treatment of 1β-*IodoGA*$_{47}$ **2** *with Aqueous Potassium Hydroxide.*—A solution of 1β-iodoGA_{47} **2** (300 mg) in aq. potassium hydroxide (0.1 mol dm^{-3}; 50 cm^3) was stirred for 2 h at room temperature. The usual work-up followed by purification by flash chromatography gave, on elution with 35% ethyl acetate in light petroleum (+1% acetic acid), the 1α-hydroxy2β,3β-epoxide **3** (175 mg) whose spectroscopic data were identical with those previously obtained. Elution with 38% ethyl acetate in light petroleum gave a mixture of unchanged starting material and the 1α-hydroxy2β,3β-epoxide **3** (28 mg). Finally elution with 70% ethyl acetate in light petroleum gave ent-1β,2β,3α,10β-*tetrahydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* (*GA*$_{78}$) **5** as a gum (10 mg) (Found: M^+, 364.153. $C_{23}H_{30}O_7$ requires M, 364.152); δ 1.12 (s, 18-H_3), 2.67 (d, *J* 11, 6-H), 3.23 (d, *J* 11, 5-H), 3.73 (d, *J* 2, 3-H), 3.94 (d, *J* 5.5, 1-H), 4.00 (dd, *J* 2 and 5.5, 2-H) and 4.85 and 4.98 (2 br s, 17-H_2); *m/z* 364 (M^+, 40%), 346 (23), 328 (22), 318 (13), 300 (20), 284 (27), 274 (100) and 91 (33). The Me, TMSi derivative gave KRI 2735; *m/z* 594 (M^+, 65%), 579 (20), 547 (30), 418 (8), 401 (12), 319 (26), 217 (83), 204 (43), 147 (33), 75 (50) and 73 (100).[8]

ent-2α,3α-*Epoxy*-1β,10β-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,10-*Lactone* **13**.—A solution of the epoxy acid **3** (20 mg) in methanol (0.5 cm^3) was treated dropwise with ethereal diazomethane at 0 °C until the yellow colour persisted. The solvent was blown off under a stream of nitrogen to give the 1α-*hydroxy*-2β,3β-*epoxide methyl ester* **13** as a gum (Found: M^+, 360.159. $C_{20}H_{22}O_6$ requires M, 360.157); δ ($CDCl_3$) 1.29 (s, 18-H_3), 2.69 (d, *J* 11, 6-H), 3.02 (d, *J* 11, 5-H), 3.05 and 3.18 (2 d, each *J* 3, 2- and 3-H), 3.71 (s, OMe), 3.99 (br s, 1-H) and 4.86 and 4.98 (2 br s, 17-H_2); *m/z* 360 (M^+, 30%), 328 (100), 240 (45), 238 (26) and 91 (34); *m/z* (Me, TMSi) 432 (M^+, 2%), 417 (3), 385 (100), 288 (30), 201 (59), 145 (88) and 73 (90).

Treatment of the 1α-*Hydroxy* 2β,3β-*Epoxide* **3** *with Aqueous Toluene*-p-*sulfonic Acid.*—A solution of the epoxide **3** (60 mg) in THF (4 cm^3)–water (250 mm^3) was stirred with toluene-*p*-sulfonic acid (20 mg) for 24 h. No reaction was apparent by TLC. The mixture was heated to reflux for 2 days and then worked up as usual. The products were purified by flash chromatography. Elution with 35% ethyl acetate in light petroleum (+1% acetic acid) gave unchanged starting material **3** (23 mg). Further elution with 45% ethyl acetate in light petroleum (+1% acetic acid) gave ent-2α,3α-*epoxy*-1β,10β,16β-*trihydroxy*-20-*norgibberellane*-7,19-*dioic acid* 19,10-*lactone* **6** as a gum (34 mg) (Found: M^+, 364.153. $C_{19}H_{24}O_7$ requires M, 364.152); δ 1.28 (s, 18-H_3), 1.33 (s, 17-H_3), 2.60 (d, *J* 10.5, 6-H), 2.82 (d, *J* 10.5, 5-H), 3.00 and 3.19 (2 d, each *J* 3.5, 2- and 3-H) and 4.03 (br s, 1-H); *m/z* 364 (M^+, 8%), 346 (66), 328 (22), 307 (36), 289 (66), 91 (38) and 43 (100). Elution with 70% ethyl acetate in light petroleum (+1% acetic acid) gave GA_{78} **5** (3 mg) whose spectral data were identical with those previously obtained.

ent-1α-*Iodo*-2β,3α,10β,13-*tetrahydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* **8**.—A solution of gibberellin A_3 **7** (2 g) in THF (10 cm^3)–aq. potassium hydroxide (1.5 mol dm^{-3}; 15 cm^3) was stirred for 20 h at room temperature. The solution was adjusted to pH 9 with 2 mol dm^{-3} hydrochloric acid. Methylene dichloride (20 cm^3) and iodine (1.78 g) were added and the mixture was stirred vigorously for 6 h. The reaction mixture was worked up as previously described for the synthesis of 1β-iodoGA_{47} **2**. Purification of the product by flash chromatography, and elution with 75% ethyl acetate in light petroleum (+1% acetic acid), gave 1β-iodoGA_{56} **8** (2.11 g), which was crystallised from acetone–light petroleum, m.p. 162–163 °C (previously obtained as an amorphous solid[15]); δ 1.18 (s, 18-H_3), 2.62 (d, *J* 10, 6-H), 3.77 (br s, 3-H), 3.85 (d, *J* 10, 5-H), 4.43 (br s, 2-H), 4.63 (br s, 1-H) and 4.92 and 5.22 (2 br s, 17-H_2); *m/z* (methyl ester) 504 (M^+, 22%) 445 (43), 376 (11), 359 (12), 345 (15), 297 (39), 254 (93) and 237 (41).

ent-2α,3α-*Epoxy*-1β,10β,13-*trihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 19,10-*Lactone* **9**.—A solution of 1β-iodoGA_{56} **8** (500 mg) in aq. potassium hydroxide (0.8 mol dm^{-3}; 20 cm^3) was stirred for 6 h at room temperature. The usual work-up, followed by flash chromatography gave, on elution with 90% acetone in light petroleum (+2% acetic acid) the 1α,13-*dihydroxy* 2β,3β-*epoxide* **9** (150 mg), which was recrystallised from methanol, m.p. 253–254 °C (Found: M^+ 362.135. $C_{19}H_{22}O_7$ requires M, 362.136); δ(C_5D_5N) 1.57 (s, 18-H_3), 3.24 (d, *J* 10, 6-H), 3.45 and 3.47 (2 d, each *J* 3, 2- and 3-H), 3.56 (d, *J* 10, 5-H), 4.51 (br s, 1-H) and 5.04 and 5.61 (2 br s, 17-H_2); *m/z* 362 (M^+, 18%), 344 (15), 326 (47), 231 (100) and 163 (49).

Owing to the polar nature of product (it was only sparingly soluble in ethyl acetate), further 1α,13-dihydroxy 2β,3β-epoxide **9** (84 mg) crystallised out from the aqueous layer after seven days.

ent-2α,3α-*Epoxy*-1β,10β.13-*trihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic Acid* 7-*Methyl Ester* 19,10-*Lactone* **12**.—A solution of the 1α,13-dihydroxy 2β,3β-epoxide **9** (20 mg) in methanol (0.5 cm^3) was treated dropwise with ethereal diazomethane at 0 °C until the yellow colour persisted. The solvent was blown off under nitrogen to give the 1α,13-*dihydroxy* 2β,3β-*epoxide methyl ester* **12** as a gum (Found: M^+ 376.150. $C_{20}H_{24}O_7$ requires M, 376.152); δ 1.21 (s, 18-H_3), 2.64 (d, *J* 10, 6-H), 2.94 and 2.98 (2 d, each *J* 3.5, 2- and 3-H), 3.21 (d, *J* 10, 5-H), 3.71 (s, OMe), 4.06 (br s, 1-H) and 4.86 and 5.19 (2 br s, 17-H_2); *m/z* 376 (M^+, 8%), 362 (9), 344 (18), 326 (49), 231 (89) and 163 (49); *m/z* (Me, TMSi) 520 (41), 473 (11), 376 (41), 303 (100), 235 (77), 207 (49) and 73 (87).

Treatment of the 1α,13-*Dihydroxy* 2β,3β-*Epoxide* **9** *with Aqueous Potassium Hydroxide.*—A solution of the 1α,13-dihydroxy 2β,3β-epoxide **9** (100 mg) in aq. potassium hydroxide (0.8 mol dm^{-3}; 5 cm^3) was stirred for 20 h at room temperature. The reaction mixture was worked up as usual and the products

Table 4 Atomic co-ordinates ($\times 10^4$) for compound **3**, with e.s.d.s in parentheses

	x	*y*	*z*
O(1)	3808(4)	2928(4)	0
O(2)	3012(4)	2986(5)	2459(6)
O(3)	5770(4)	5782(4)	3558(6)
O(4)	7368(4)	6179(4)	3536(6)
O(5)	5369(5)	2013(4)	2364(6)
O(6)	5326(4)	3040(4)	1287(5)
C(1)	3926(6)	3347(6)	926(7)
C(2)	3246(6)	2582(7)	1614(7)
C(3)	3578(7)	2485(7)	2559(7)
C(4)	4706(6)	3119(5)	2782(7)
C(5)	5111(6)	4154(6)	2309(7)
C(6)	6261(6)	4940(6)	2430(6)
C(7)	6517(6)	5671(6)	3240(7)
C(8)	6627(6)	5494(6)	1467(6)
C(9)	5852(6)	4770(6)	715(7)
C(10)	5024(6)	3831(5)	1267(6)
C(11)	6377(7)	4533(6)	−106(7)
C(12)	7196(6)	5502(6)	−534(7)
C(13)	7798(6)	6309(6)	241(7)
C(14)	7696(6)	5767(6)	1185(6)
C(15)	6672(6)	6521(6)	1372(7)
C(16)	7304(6)	6950(6)	462(7)
C(17)	7416(7)	7730(7)	−38(7)
C(18)	4945(7)	3115(7)	3842(6)
C(19)	5184(7)	2646(6)	2168(7)
C(1S)	−57(70)	8751(63)	1684(84)
C(2S)	531(45)	9961(60)	1975(50)
C(3S)	−501(57)	8805(44)	2527(69)

were purified by flash chromatography. Elution with 90% ethyl acetate in light petroleum (+1% acetic acid) gave unchanged starting material **9** (68 mg recovery). Further elution with 90% acetone in light petroleum (+1% acetic acid) gave ent-1β,2β-*epoxy*-3α,10β,13-*trihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,10-*lactone* **10** as a gum (24 mg) (Found: M^+, 362.135. $C_{19}H_{22}O_7$ requires M, 362.136); δ(C_5D_5N) 1.54 (s, 18-H_3), 3.17 (d, *J* 10, 6-H), 3.42 (br s, 1- and 2-H), 3.57 (d, *J* 10, 5-H), 4.47 (br s, 3-H) and 5.01 and 5.58 (2 br s, 17-H_2); *m*/*z* 362 (M^+, 12%), 344 (10), 326 (53) and 231 (100).

Crystal-Structure Determination.—Crystal data for compound **3**: $C_{19}H_{22}O_6$, M = 346.4, hexagonal, space group $P6_5$ (no. 170), *a* = 15.253(2), *c* = 14.137(3) Å, V = 2848(1) Å^3, *Z* = 6, μ(Mo-Kα) = 0.09 mm^{-1}, D_c = 1.21 g cm^{-3}, *F*(000) = 1104 (not including solvent).

From a crystal of compound **3** (hexagonal needle of 0.1 × 0.1 × 0.5 mm), using a $\theta/2\theta$ scan technique the intensities of 2150 reflections (representing 1505 independent ones and partially their Friedel equivalents) with $2\theta \leqslant 54°$ were measured, of which 1368 reflections with $I \geqslant 2\sigma(I)$ (including 1006 independent) were used in subsequent calculations. The structure was solved by direct methods. All ordered non-hydrogen atoms were refined by full-matrix least-squares techniques with anisotropic atomic displacement parameters. The hydroxy and carboxy hydrogen atoms were located by a difference Fourier synthesis and included in the refinement as fixed contributions; other hydrogens were treated as riding in idealized positions on the corresponding carbons. The refinement converged at $R = 0.059$ ($R_w = 0.065$). No absorption correction was applied. It was impossible to determine absolute configuration of the structure from X-ray anomalous scattering (refinement of both enantiomeric structures gave no significant difference in *R*-values), thus the known configuration of the parent compound was attributed to compound **3**. The solvent of crystallisation was not identified and was treated in the refinement as carbon atoms C(1S), C(2S) and C(3S) with occupancy factors of 0.25, 0.35 and 0.40, respectively (giving the best fit) in an isotropic approximation. On this assumption D_c = 1.25 g cm^{-3}, *F*(000) = 1140 for $C_{20}H_{22}O_6$ (M = 358.4). Atomic co-ordinates are given in Table 4.*

* *Supplementary material:* Additional material available from the Cambridge Crystallographic Data Centre comprises H-atom co-ordinates and thermal parameters of all atoms. See Instructions for authors, in the January issue.

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