The Stereochemistry and Hydrolysis of Gibberellin 16,17-Epoxides. *X*-Ray Molecular Structures of *ent*-17-Acetoxy-1α,10α-epoxy-2β,3α,13,16β-tetrahydroxy-20-norgibberella-7,19-dioic Acid 19,2-Lactone 7-Methyl Ester and of ent-17-Chloro-1α,10α-epoxy-2β,3α,13,16β-tetrahydroxy-20-norgibberella-7,19-dioic Acid 19,2-Lactone 7-Methyl Ester

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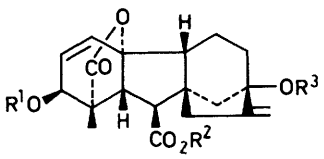
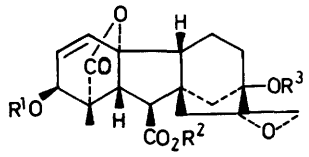
The 16*S* stereochemistry of the major 16,17-epoxides obtained from methyl gibberellate, its 13-acetate, and the 19,2α-isolactone, has been established by n.O.e. measurements. The structures of the hydrolysis products of the 16-epimeric epoxides were established by *X*-ray crystallography. Neighbouring group participation by the 13-acetoxy group may play a role in some of the hydrolyses. Unlike the Δ^1-3-hydroxy-19,10-lactones, the ring A double bond of the isomeric $\Delta^{1(10)}$-3-hydroxy-19,2α-lactones was readily epoxidized by *m*-chloroperbenzoic acid.

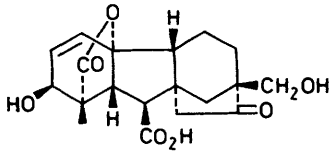
The epoxidation of gibberellic acid (**1**) and its relatives by peracids has been reported on a number of occasions.[1–8] Reaction occurs selectively at the 16,17-double bond,[1] although with excess of *m*-chloroperbenzoic acid (MCPBA) gibberellin A_7 has been reported[5] to give an inseparable mixture of mono- and di-epoxides. The 16*S* configuration (**5**) was assigned[3] to the epoxide obtained from gibberellic acid in the light of its readily rearrangement to an 8:13-isogibberellin (**9**). The same stereochemistry (**6**) has been assigned[6] to the major product of epoxidation of methyl 13-*O*-acetylgibberellate (**2**). However, the latter epoxide was surprisingly stable and could be reductively deoxygenated with zinc and sodium iodide in acetic acid without rearrangement.[6] In some previous work we have noted[9] the differing influence of the 13-hydroxy and -acetoxy groups on the stereochemistry of bromination of the 16,17-alkene and the contrasting reactivity of the resultant epimeric 16-bromo compounds.[10] Consequently we have examined the stereochemistry of epoxidation of the 3-mono- and 3,13-di-acetates of methyl gibberellate and the isomeric 19,2α-lactones[11] and the course of some of their reactions.



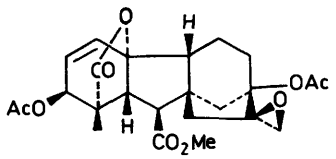
(**1**) $R^1 = R^2 = R^3 = H$
(**2**) $R^1 = H$, $R^3 = Me$, $R^3 = Ac$
(**3**) $R^1 = Ac$, $R^2 = Me$, $R^3 = H$
(**4**) $R^1 = R^3 = Ac$, $R^2 = Me$



(**5**) $R^1 = R^2 = R^3 = H$
(**6**) $R^1 = H$, $R^2 = Me$, $R^3 = Ac$
(**7**) $R^1 = Ac$, $R^2 = Me$, $R^3 = H$
(**8**) $R^1 = R^3 = Ac$, $R^2 = Me$



(**9**)



(**10**)

We have recently developed[12,13] a strategy for determining the stereochemistry of reactions at C-16 in the gibberellins. This is based on the assignment of the 14-H and 15-H proton resonances followed by decoupling or n.O.e. measurements from 17-H. The 14-H and 15-H resonances each show large geminal coupling constants (typically $J_{14,14'}$ 12 Hz; $J_{15,15'}$ 14 Hz) and may be distinguished from each other by an n.O.e. effect between the 6-H_α resonance and 14-H or, in the case of the 16-carbonyl compounds, by selective deuteriation. Furthermore the 14-H_α and 15-H_β signals show a 'W' long-range coupling (2—3 Hz) which permits a distinction to be made between both the 14-H_α and 14-H_β and the 15-H_α and 15-H_β signals. An n.O.e. enhancement between 17-H and either of the 15-H resonances may then serve to establish the stereochemistry at C-16. Molecular models show that the 15-H proton which experiences such an enhancement on irradiation of 17-H depends upon the stereochemistry at C-16.

The ^{1}H n.m.r. signals (determined at 360 MHz) for the major product (**7**) of epoxidation of methyl 3-*O*-acetylgibberellate (**3**) with MCPBA are given in Table 1. Irradiation at δ 1.79 produced an n.O.e. enhancement (7%) at the 6-H_α resonances (δ 2.82), leading to the assignment of the former as being due 14-H_β. A 2% enhancement at δ 1.67 (15-H_α), and a 24% enhancement at δ 2.15 (14-H_α) were also observed. The coupling pattern then led to the assignment for the ring D proton resonances (see Table 1). Irradiation at the epoxide signal (17-H, δ 2.93) produced an n.O.e. enhancement (26%) at the other epoxide signal (δ 2.86) and a 2% enhancement at δ 1.96 (15-H_β). On the other hand irradiation at δ 2.86 produced a 29% enhancement at δ 2.93 and a 6% enhancement of the 13-hydroxy proton resonance. This establishes the geometry shown in Figure 1. This stereochemistry is consistent with the ready

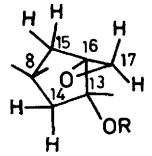


Figure 1.

Table 1. ^{1}H N.m.r. data (δ_H) for gibberellin epoxides and derivatives

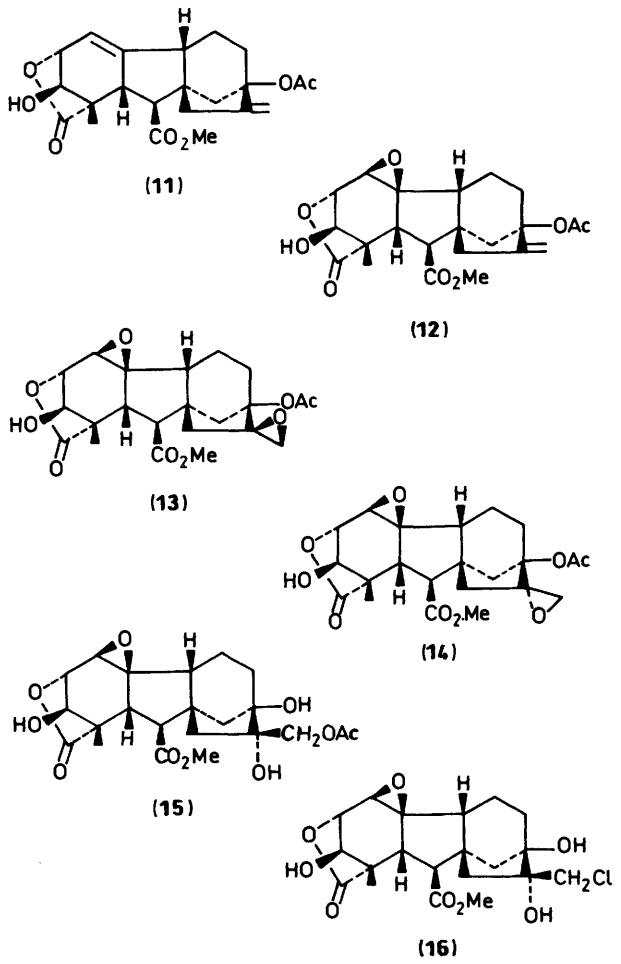
	Compound						
				(14)			
Atom	(7) $CDCl_3$	(10) $CDCl_3$	(8) $CDCl_3$	$CDCl_3$	C_5D_5N	(15) $CDCl_3$	(16) C_5D_5N
1-H	6.40	6.41	6.40	3.71	3.92	3.69	3.91
2-H	5.90	5.88	5.90	4.97	5.17	4.95	5.12
3-H	5.34	5.34	5.34	4.05	4.31	4.03	4.27
5-H	3.33	3.32	3.33	3.03	3.42	2.93	3.36
6-H	2.82	2.77	2.82	2.99	3.20	2.93	3.21
14-H_α	2.15,	2.56,	2.47,	1.93,	2.27,	1.40,	2.05,
14-H_β	1.79	2.30	2.20	2.29	2.69	1.95	1.96
15-H_α	1.67,	2.00,	1.70,	2.33	2.46,	2.05,	2.53,
15-H_β	1.96	1.46	1.83		1.82	1.69	2.11
17-H_2	2.86,	2.81,	2.75,	2.77,	2.77,	4.12,	3.94,
	2.93	3.04	3.12	3.09	3.09	4.18	3.99
18-H_3	1.15	1.14	1.15	1.21	1.29	1.20	1.28
OMe	3.76	3.76	3.75	3.73	3.60	3.75	3.54
OAc	2.12	1.99,	2.01,	1.98	1.82	2.10	
		2.12	2.12				
Selected coupling constants (Hz)							
1,2	9.3	9.3	9.3	3.3		3.4	3.3
2,3	3.8	3.8	3.8	5.5		5.6	5.5
5,6	10.9	10.9	10.9	4.2			
14,14′	11.2	11.6	11.2	11.5		11.5	11.3
14α,15β	2.4	3.3	2.4	2.3		2.2	2.2
15,15′	14.2	13.3	13.7	13.5		14.5	14.4
17,17′	4.4	5.0	5.3	5.7		12.8	10.1

rearrangement of the corresponding 7-carboxylic acid in boiling water to form the 8:13-isogibberellin (**9**).[2,3]

The presence of a 13-acetate has been shown to modify the course of halogenation.[9] When a 16,17-epoxide was used to protect the 16,17-double bond a 13-acetate was also employed to avoid the formation of unidentified isomers of gibberellin A_1 during the regeneration of the double bond.[5,6] Epoxidation of the 3,13-diacetate (**4**) of methyl gibberellate gave a separable mixture of two epoxides. The minor, less stable product was assigned the stereochemistry (**10**) whilst the major product was assigned the stereochemistry (**8**) on the basis of its ^{1}H n.m.r. spectrum. The proton resonances were readily assigned by comparison with the assignment for (**7**) (see Table 1). Irradiation of the 17-H signal, δ 2.75, produced an n.O.e. enhancement (32%) of the other epoxide signal (δ 3.12) and a 2.5% enhancement at δ 1.83 (15-H_β). Hence the major epoxide in both the 13-acetoxy and 13-hydroxy series has the same C-16 stereochemistry.

Epoxidation of the 13-acetate (**11**) of the isomeric 19,2α-lactone revealed some interesting differences. A monoepoxide and two diepoxides were obtained. The monoepoxide (**12**) retained the 17-alkene proton resonances. The 1β,10β-epoxide stereochemistry for these epoxides was assigned on the basis of the ring A coupling constants. Furthermore this epoxide is retained in the hydrolysis products (**15**) and (**16**) (*vide infra*), the structures of which were determined by *X*-ray crystallography. Hence in contrast to the ring A of gibberellic acid, the $\Delta^{1(10)}$-double bond of the 19,2α-isogibberellin reacts more rapidly than the Δ^{16}-double bond towards epoxidation by peracid. The two diepoxides were separated chromatographically. The first to be isolated, which was formulated as the 1β,10:16β,17-diepoxide (**13**), was unstable in solution and decomposed to give the 16α-hydroxy-17-acetate (**15**).

A series of n.O.e. studies was performed on the more stable



1β,10:16α,17-diepoxide (**14**) to establish its stereochemistry. As the spectra were better resolved in pyridine solution, the studies were done in that solvent. Irradiation of the 6-H resonance (δ 3.20) produced an n.O.e. enhancement (7%) of the signal at δ 2.69 (14-H_β). Further studies based on the irradiation of 14-H and 15-H led to the identification of the other ring D proton resonances (see Figure 2). There was a long-range coupling (*J*

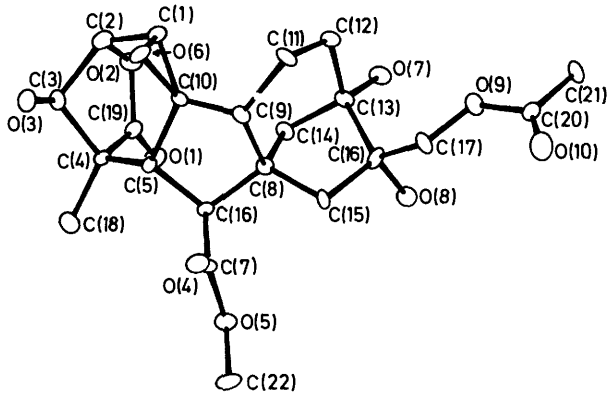


Figure 2. *X*-Ray molecular structure of compound (**15**). H-atoms are omitted for clarity

2.7 Hz) from 15-H_β (δ 1.82) to 14-H_α (δ 2.27). An n.O.e. enhancement (4%) was observed at δ 1.82 (15-H_β) on irradiation of the 17-H_2 signal (δ 2.77), leading to the 16*S* stereochemistry for this compound. Further decoupling and

Table 2. ^{13}C N.m.r. data for gibberellin epoxides (in $CDCl_3$)

	Compounds			
Atom	(7)	(14)	(15)	(16)
C-1	129.48	57.20	57.50	57.35
C-2	133.96	72.86	70.92	72.68
C-3	70.40	76.35	76.60	76.72
C-4	52.20	46.12	45.64	46.21
C-5	53.74	43.72	43.54	44.08
C-6	51.64	49.12	48.87	50.04
C-7	172.30	174.58	174.56	174.94
C-8	49.35	48.21	47.11	47.52
C-9	52.70	43.88	43.85	45.08
C-10	89.94	65.70	66.32	66.26
C-11	17.14	16.43	15.65	16.24
C-12	33.54	33.04	31.70	32.61
C-13	73.13	82.18	76.89	79.26
C-14	43.50	45.25	45.39	45.38
C-15	42.66	40.08	43.59	47.44
C-16	67.76	62.32	78.59	78.07
C-17	49.70	50.11	67.38	51.26
C-18	14.26	17.71	17.37	17.78
C-19	176.70	176.94	175.99	176.76
OMe	52.20	52.06	52.19	51.87
OAc	20.69, 169.83	21.69, 169.73	20.80, 171.24	

n.O.e. studies, based on the 2-H and 5-H resonances, led to the assignment of the remaining proton n.m.r. signals. A 2D-heteronuclear chemical-shift correlation spectrum then led to the assignment of the ^{13}C resonances. This was of particular use in differentiating between C-5 and C-9 and between C-2 and C-3. The assignments are given in Table 2.

Although the ^{1}H and ^{13}C n.m.r. spectra of the decomposition product of the epoxide (**13**) were compatible with the structure (**15**), there was a possibility of ambiguity particularly in the location of the acetoxy group and hence the structure was determined by *X*-ray crystallography (Figure 2). Mild hydrolysis of the more stable epoxide (**14**) with dil. methanolic hydrochloric acid at room temperature gave a chloro compound (**16**). Again, in order to avoid structural ambiguity particularly concerning the location of the chlorine atom, the structure was established by *X*-ray crystallography (Figure 3).

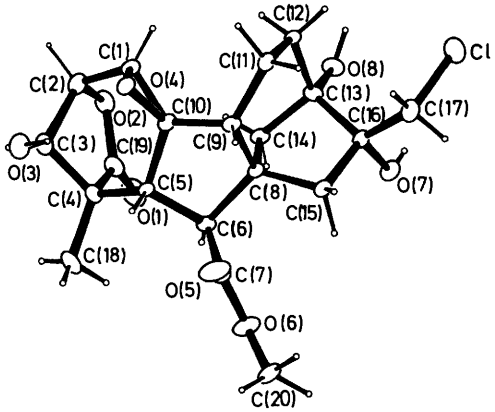
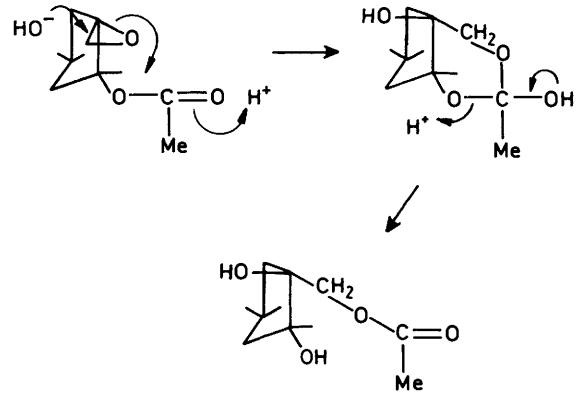


Figure 3. *X*-Ray molecular structure of compound (**16**)

The structures of these hydrolysis products are interesting. The product (**15**) not only represents the migration of an acetoxy group from C-13 to C-17 but also an inversion of configuration at C-16. A plausible mechanism for its formation is given in the Scheme. The chloro compound (**16**) is unusual in that the epoxide has opened in an abnormal manner with the anionic component entering at the less substituted carbon atom. This represents another example of an acid-catalysed hydrolysis of an epoxide in which conformational features have taken precedence over electronic ones.[14] Although the acetoxy group has been hydrolysed, the expected readily occurring Wagner–Meerwein rearrangement of ring D has not taken place. In both cases C-16 has achieved an identical configuration in which the hydroxy group is *trans* to the bond which migrates in the Wagner–Meerwein rearrangement.



Scheme.

Experimental

General Experimental Details.—Silica for flash chromatography was Merck 9385. Light petroleum refers to the fraction boiling in the range 60—80 °C. ^{1}H and ^{13}C n.m.r. spectra were determined on a Bruker WM 360 spectrometer. I.r. spectra are for Nujol mulls.

Epoxidation Reactions.—(*a*) A solution of methyl 3-*O*-acetylgibberellate (**3**) (1.65 g) in chloroform (40 ml) was treated with 85% MCPBA (0.8 g) at 0 °C overnight. The solution was washed successively with 10% aqueous sodium sulphite, aqueous sodium hydrogen carbonate, and water, and dried over magnesium sulphate. The solvent was evaporated off and the residue was crystallized from ethyl acetate–light petroleum to give the epoxide (**7**) (1.5 g), m.p. 177—179 °C (lit.,[3] 176—177 °C).

(*b*) Methyl 3,13-di-*O*-acetylgibberellate (**4**) (2.59 g) was dissolved in chloroform (150 ml) and treated with a solution of 85% MCPBA (2.5 g) in chloroform (50 ml) at room temperature for 24 h. Saturated aqueous sodium sulphite (20 ml) was added, and the organic phase was separated, extracted (×3) with saturated aqueous sodium hydrogen carbonate, and then dried. The solvent was evaporated off and the residue was then chromatographed on silica. Elution with ethyl acetate–light petroleum (2:3) gave the 16β,17-*epoxide* (**10**) (652 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 198—200 °C (Found: C, 61.5; H, 6.1. $C_{24}H_{28}O_9 \cdot 0.5H_2O$ requires C, 61.4; H, 6.0%); $\nu_{max.}$ 3 440 (H_2O), 1 776, 1 740, and 1 730 cm^{-1}. The ^{1}H n.m.r. data are given in Table 1.

Further elution gave the 16α,17-*epoxide* (**8**) (1.86 g), which was crystallized from ethyl acetate–light petroleum as prisms, m.p. 166—168 °C (Found: C, 62.1; H, 6.2. $C_{24}H_{28}O_9$ requires C, 62.6; H, 6.1%); $\nu_{max.}$ 1 780, 1 740, and 1 730 cm^{-1}. The ^{1}H n.m.r. data are given in Table 1.

(*c*) A solution of *ent*-13-acetoxy-2β,3α-dihydroxy-20-norgibberella-1(10),16-diene-7,19-dioic acid 19,2-lactone 7-methyl ester (11) (200 mg) in chloroform (10 ml) was treated with MCPBA (300 mg) at room temperature overnight. The solution

Table 3. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound (**15**)

	x	*y*	*z*
O(1)	9 981(9)	7 102(4)	797(3)
O(2)	6 792(9)	6 906(3)	610(3)
O(3)	4 651(9)	6 536(4)	2 441(3)
O(4)	8 078(10)	9 107(4)	3 251(3)
O(5)	11 139(9)	9 052(4)	2 837(3)
O(6)	3 470(8)	7 927(3)	1 868(3)
O(7)	8 119(8)	9 856(3)	−437(3)
O(8)	10 338(9)	10 584(3)	573(3)
O(9)	7 276(10)	11 550(3)	107(3)
O(10)	7 414(13)	12 762(4)	563(4)
C(1)	4 312(12)	7 724(5)	1 147(5)
C(2)	5 042(13)	6 887(5)	1 096(5)
C(3)	5 901(14)	6 544(5)	1 815(5)
C(4)	7 744(11)	7 062(4)	1 879(4)
C(5)	7 120(11)	7 908(4)	2 118(4)
C(6)	8 722(11)	8 556(4)	2 040(4)
C(7)	9 210(12)	8 924(4)	2 774(4)
C(8)	7 847(11)	9 199(4)	1 501(4)
C(9)	5 613(11)	9 105(5)	1 642(4)
C(10)	5 375(12)	8 251(5)	1 678(4)
C(11)	4 337(11)	9 608(5)	1 116(5)
C(12)	5 196(13)	9 753(5)	332(5)
C(13)	7 439(12)	9 784(5)	316(4)
C(14)	8 232(13)	9 040(4)	681(4)
C(15)	8 515(13)	10 059(4)	1 613(4)
C(16)	8 359(14)	10 440(4)	837(5)
C(17)	7 291(14)	11 232(4)	879(4)
C(18)	9 361(15)	6 730(6)	2 385(5)
C(19)	8 347(12)	7 043(4)	1 066(5)
C(20)	7 350(13)	12 324(5)	37(6)
C(21)	7 408(15)	12 571(5)	−771(5)
C(22)	11 819(16)	9 407(6)	3 548(5)

was washed successively with aqueous sodium sulphite, aqueous sodium hydrogen carbonate, and water, and dried. The solvent was evaporated off and the residue was chromatographed on silica. Elution with 40% ethyl acetate–light petroleum gave the unstable 1β,10:16β,17-diepoxide (**13**) (70 mg), m.p. 218—220 °C; $\nu_{max.}$ 3 460, 1 780, and 1 735 cm^{-1}; δ(60 MHz) 1.2 and 2.00 (each 3 H, s), 2.8—3.0 (5 H, 5-, 6-, and 9-H and 17-H_2), 3.7 (4 H, OMe and 1-H), 4.1 (3-H), and 4.9 (2-H). This compound was unstable in solution and rearranged to form ent-17-*acetoxy*-1α,10α-*epoxy*-2β,3α,13,16β-*tetrahydroxy*-20-*norgibberella*-7,19-*dioic acid* 19,2-*lactone* 7-*methyl ester* (**15**) which was purified by chromatography on silica in 60% ethyl acetate–light petroleum. It was crystallized from ethyl acetate as needles, m.p. 213—215 °C (Found: C, 58.5; H, 6.2. $C_{22}H_{28}O_{10}$ requires C, 58.4; H, 6.2%). The ^1H n.m.r. spectra are in Table 1.

Further elution gave ent-13-*acetoxy*-1α,10α:16β,17-*diepoxy*-2β,3α-*dihydroxy*-20-*norgibberella*-7,19-*dioic acid* 19,2-*lactone* 7-*methyl ester* (**14**) (90 mg), which was crystallized from ethyl acetate as needles, m.p. 265—266 °C (Found: C, 60.8; H, 5.9. $C_{22}H_{26}O_9$ requires C, 60.8; H, 6.0%); $\nu_{max.}$ 3 420, 1 760, 1 740, and 1 710 cm^{-1}. The n.m.r. spectra are in Table 1.

On one occasion ent-13-*acetoxy*-1α,10α-*epoxy*-2β,3α-*dihydroxy*-20-*norgibberell*-16-*ene*-7,19-*dioic acid* 19,2-*lactone* 7-*methyl ester* (**12**) was isolated. It was recrystallized from ethyl acetate–light petroleum as needles, m.p. 215—216 °C (Found: C, 63.1; H, 6.3. $C_{22}H_{26}O_8$ requires C, 63.1; H, 6.3%); $\nu_{max.}$ 3 400, 1 780, 1 730, 1 660, and 880 cm^{-1}; δ(60 MHz) 1.20 (3 H, s, 18-H_3), 2.00 (3 H, s, OAc), 2.73 (1 H, d, *J* 5.5 Hz, 6-H), 3.00 (1 H, m, 5-H), 3.74 (3 H, s, OMe), 4.12 (1 H, d, *J* 5 Hz, 1-H), 4.22 (1 H, br s, 3-H), 4.92 (1 H, m, 2-H), and 5.00 (2 H, br s, 17-H_2).

Table 4. Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound (**15**)

(*a*) Bonds

O(1)–C(19)	1.217(10)	O(2)–C(2)	1.476(10)
O(2)–C(19)	1.357(10)	O(3)–C(3)	1.404(11)
O(4)–C(7)	1.189(10)	O(5)–C(7)	1.337(10)
O(5)–C(22)	1.477(11)	O(6)–C(1)	1.449(10)
O(6)–C(10)	1.449(10)	O(7)–C(13)	1.427(9)
O(8)–C(16)	1.450(11)	O(9)–C(17)	1.478(9)
O(9)–C(20)	1.313(10)	O(10)–C(20)	1.195(11)
C(1)–C(2)	1.501(12)	C(1)–C(10)	1.488(12)
C(2)–C(3)	1.524(12)	C(3)–C(4)	1.535(12)
C(4)–C(5)	1.549(10)	C(4)–C(18)	1.531(12)
C(4)–C(19)	1.508(11)	C(5)–C(6)	1.552(10)
C(5)–C(10)	1.538(11)	C(6)–C(7)	1.487(10)
C(6)–C(8)	1.569(10)	C(8)–C(9)	1.552(11)
C(8)–C(14)	1.510(10)	C(8)–C(15)	1.535(10)
C(9)–C(10)	1.452(11)	C(9)–C(11)	1.536(11)
C(11)–C(12)	1.536(12)	C(12)–C(13)	1.531(12)
C(13)–C(14)	1.515(11)	C(13)–C(16)	1.575(11)
C(15)–C(16)	1.529(11)	C(16)–C(17)	1.524(11)
C(20)–C(21)	1.502(13)		

(*b*) Angles

C(2)–O(2)–C(19)	106.4(6)	C(7)–O(5)–C(22)	116.5(7)
C(1)–O(6)–C(10)	61.8(5)	C(17)–O(9)–C(20)	116.7(6)
O(6)–C(1)–C(2)	114.0(7)	O(6)–C(1)–C(10)	59.1(5)
C(2)–C(1)–C(10)	116.0(7)	O(2)–C(2)–C(1)	106.4(7)
O(2)–C(2)–C(3)	101.1(7)	C(1)–C(2)–C(3)	115.8(7)
O(3)–C(3)–C(2)	116.0(7)	O(3)–C(3)–C(4)	116.3(7)
C(2)–C(3)–C(4)	99.2(7)	C(3)–C(4)–C(5)	108.7(6)
C(3)–C(4)–C(18)	115.1(7)	C(3)–C(4)–C(19)	98.0(6)
C(5)–C(4)–C(18)	111.9(6)	C(5)–C(4)–C(19)	111.0(6)
C(18)–C(4)–C(19)	111.3(7)	C(4)–C(5)–C(6)	115.6(6)
C(4)–C(5)–C(10)	114.8(6)	C(6)–C(5)–C(10)	103.5(6)
C(5)–C(6)–C(7)	111.9(6)	C(5)–C(6)–C(8)	106.0(6)
C(7)–C(6)–C(8)	109.5(6)	O(4)–C(7)–O(5)	122.5(7)
O(4)–C(7)–C(6)	126.4(7)	O(5)–C(7)–C(6)	111.1(6)
C(6)–C(8)–C(9)	101.7(6)	C(6)–C(8)–C(14)	113.8(6)
C(6)–C(8)–C(15)	117.6(6)	C(9)–C(8)–C(14)	108.0(6)
C(9)–C(8)–C(15)	111.6(6)	C(14)–C(8)–C(15)	104.0(6)
C(8)–C(9)–C(10)	102.6(6)	C(8)–C(9)–C(11)	113.6(6)
C(10)–C(9)–C(11)	120.9(7)	O(6)–C(10)–C(1)	59.1(5)
O(6)–C(10)–C(5)	115.6(6)	O(6)–C(10)–C(9)	119.0(7)
C(1)–C(10)–C(5)	118.5(7)	C(1)–C(10)–C(9)	128.3(7)
C(5)–C(10)–C(9)	108.0(6)	C(9)–C(11)–C(12)	115.4(6)
C(11)–C(12)–C(13)	113.7(7)	O(7)–C(13)–C(12)	110.1(6)
O(7)–C(13)–C(14)	111.0(6)	O(7)–C(13)–C(16)	111.6(6)
C(12)–C(13)–C(14)	108.7(7)	C(12)–C(13)–C(16)	114.3(7)
C(14)–C(13)–C(16)	100.8(6)	C(8)–C(14)–C(13)	101.9(6)
C(8)–C(15)–C(16)	105.1(6)	O(8)–C(16)–C(13)	107.2(6)
O(8)–C(16)–C(15)	107.4(7)	O(8)–C(16)–C(17)	108.3(6)
C(13)–C(16)–C(15)	105.4(6)	C(13)–C(16)–C(17)	117.1(7)
C(15)–C(16)–C(17)	111.0(7)	O(9)–C(17)–C(16)	106.1(6)
O(1)–C(19)–O(2)	119.5(7)	O(1)–C(19)–C(4)	128.8(8)
O(2)–C(19)–C(4)	111.6(7)	O(9)–C(20)–O(10)	122.8(9)
O(9)–C(20)–C(21)	111.6(8)	O(10)–C(20)–C(21)	125.5(8)

Hydrolysis of the Epoxide (**14**).—The epoxide (**14**) (100 mg) was dissolved in methanol (50 ml) and conc. hydrochloric acid (2 drops) was added. The reaction mixture was left at room temperature for 4 days. The crystals that formed were filtered off, washed with water, and dried to give ent-17-*chloro*-2β,3α,13,16β-*tetrahydroxy*-20-*norgibberella*-7,19-*dioic acid* 19,2-*lactone* 7-*methyl ester* (**16**) (69 mg), m.p. 247—248 °C (Found: C, 55.8; H, 6.3. $C_{20}H_{25}ClO_8$ requires C, 56.0; H, 5.9%); $\nu_{max.}$ 3 420, 1 770, 1 715, and 925 cm^{-1}.

Crystallographic Data.—(a) *Compound* (**15**). $C_{22}H_{28}O_{10}$, *M* = 452.5, orthorhombic, space group $P2_12_12_1$, *a* = 6.818(2),

Table 5. Fractional atomic co-ordinates ($\times 10^4$) with estimated standard deviations in parentheses for compound (**16**)

	x	*y*	*z*
Cl	4 682(2)	2 900(1)	5 308(1)
O(1)	3 165(5)	8 279(2)	4 147(2)
O(2)	437(5)	7 811(2)	4 396(2)
O(3)	−1 880(5)	7 837(2)	2 577(2)
O(4)	−1 528(4)	6 087(2)	3 157(2)
O(5)	3 116(5)	5 659(3)	1 716(2)
O(6)	5 681(4)	6 224(3)	2 073(2)
O(7)	6 463(4)	4 675(3)	4 585(2)
O(8)	3 984(5)	5 152(2)	5 551(2)
C(1)	−979(6)	6 493(3)	3 880(3)
C(2)	−1 095(7)	7 543(3)	3 942(3)
C(3)	−759(7)	8 047(3)	3 186(3)
C(4)	1 208(6)	7 844(3)	3 082(2)
C(5)	1 451(6)	6 804(3)	2 870(2)
C(6)	3 346(6)	6 405(3)	2 940(2)
C(7)	3 989(6)	6 055(3)	2 172(2)
C(8)	3 217(6)	5 582(3)	3 523(2)
C(9)	1 329(6)	5 227(3)	3 400(2)
C(10)	333(6)	6 124(3)	3 339(2)
C(11)	744(6)	4 505(3)	3 983(3)
C(12)	1 516(6)	4 627(3)	4 781(2)
C(13)	3 401(6)	5 016(3)	4 783(2)
C(14)	3 416(6)	5 916(3)	4 354(2)
C(15)	4 561(6)	4 784(3)	3 486(2)
C(16)	4 736(6)	4 419(3)	4 318(3)
C(17)	4 581(7)	3 368-3)	4 360(3)
C(18)	2 157(8)	8 467(3)	2 522(3)
C(19)	1 783(8)	8 007(3)	3 909(3)
C(20)	6 485(8)	5 843(4)	1 395(3)

b = 16.882(2), c = 17.837(2) Å, V = 2 053.1 Å^3, Z = 4, $D_{calc.}$ = 1.46 g cm^{-3}, $F(000)$ = 960. Monochromated Mo-K_α radiation, λ = 0.710 69 Å, μ = 1.1 cm^{-1}. Data were collected using a crystal of *ca.* 0.4 × 0.2 × 0.05 mm on an Enraf-Nonius CAD 4 diffractometer, in the θ–2θ mode with $\Delta\theta = (0.8 + 0.35 \tan\theta)°$ and a maximum scan time of 1 min. A total of 2 107 unique reflections were measured for $2 < \theta < 25°$ and $+h, +k, +l$, and 1 208 reflections with $|F^2| > \sigma(F^2)$ were used in the refinement where $\sigma(F^2 = [\sigma^2(I) + (0.04I)^2]^{\frac{1}{2}}/L_p$. There was no crystal decay and no absorption correction was made. The structure was solved by direct methods using MULTAN and refined by full-matrix least-squares with non-hydrogen atoms anisotropic. Hydrogen atoms were held fixed at positions taken from a difference map and with B_{iso} = 4.0 Å^2, except for the methyl hydrogen atoms which appeared to be disordered and were omitted. The weighting scheme was $w = 1/\sigma^2(F)$ and the final residuals were R = 0.065, R' = 0.072. Programs from the Enraf-Nonius SDP-Plus package were run on a MicroVax computer. Final atom co-ordinates are given in Table 3, and bond lengths and angles in Table 4.*

(b) *Compound* (**16**). $C_{20}H_{25}ClO_8$, M = 428.9, orthorhombic, space group $P2_12_12_1$, a = 7.607(1), b = 14.314(1), c = 17.449(2) Å, V = 1 900.1 Å^3, Z = 4, D_c = 1.50 g cm^{-3}. Monochromated Mo-K_α radiation, λ = 0.710 69 Å, μ = 2.4 cm^{-1}. Data were collected using a crystal of *ca.* 0.75 × 0.5 × 0.2 mm on an Enraf-Nonius CADV diffractometer θ–2θ mode with $\Delta\theta = (0.8 + 0.35 \tan\theta)°$ and a maximum scan time of 1 min. A total of 1 943 unique reflections were measured for $2 < \theta < 25°$ and $+h, +k, +l$, and 1 446 reflections with $|F^2| > \sigma(F^2)$ were used in the refinement where $\sigma(F^2) = [\sigma^2(I) + (0.04I)^2]^{\frac{1}{2}}/L_p$.

* *Supplementary data* (see section 5.6.3 of Instructions for Authors, in the January issue). Torsion angles, anisotropic temperature factors, hydrogen atom co-ordinates, and H-bond data have been deposited at the Cambridge Crystallographic Data Centre.

Table 6. Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound (**16**)

(*a*) Bonds

Cl–C(17)	1.785(5)	O(1)–C(19)	1.196(6)
O(2)–C(2)	1.461(6)	O(2)–C(19)	1.359(6)
O(3)–C(3)	1.395(6)	O(4)–C(1)	1.450(6)
O(4)–C(10)	1.452(5)	O(5)–C(7)	1.181(6)
O(6)–C(7)	1.321(6)	O(6)–C(20)	1.440(6)
O(7)–C(16)	1.442(6)	O(8)–C(13)	1.425(5)
C(1)–C(2)	1.509(7)	C(1)–C(10)	1.472(6)
C(2)–C(3)	1.525(7)	C(3)–C(4)	1.535(7)
C(4)–C(5)	1.545(6)	C(4)–C(18)	1.507(7)
C(4)–C(19)	1.526(7)	C(5)–C(6)	1.556(6)
C(5)–C(10)	1.530(6)	C(6)–C(7)	1.513(6)
C(6)–C(8)	1.560(6)	C(8)–C(9)	1.539(6)
C(8)–C(14)	1.534(6)	C(8)–C(15)	1.535(6)
C(9)–C(10)	1.495(6)	C(9)–C(11)	1.517(6)
C(11)–C(12)	1.521(6)	C(12)–C(13)	1.538(6)
C(13)–C(14)	1.489(6)	C(13)–C(16)	1.556(6)
C(15)–C(16)	1.548(6)	C(16)–C(17)	1.510(7)

(*b*) Angles

C(2)–O(2)–C(19)	108.4(4)	C(1)–O(4)–C(10)	61.0(3)
C(7)–O(6)–C(20)	116.9(4)	O(4)–C(1)–C(2)	116.4(4)
O(4)–C(1)–C(10)	59.6(3)	C(2)–C(1)–C(10)	116.4(4)
O(2)–C(2)–C(1)	104.7(4)	O(2)–C(2)–C(3)	102.2(4)
C(1)–C(2)–C(3)	113.5(4)	O(3)–C(3)–C(2)	117.0(4)
O(3)–C(3)–C(4)	117.7(4)	C(2)–C(3)–C(4)	100.2(4)
C(3)–C(4)–C(5)	109.0(4)	C(3)–C(4)–C(18)	115.6(4)
C(3)–C(4)–C(19)	98.0(4)	C(5)–C(4)–C(18)	110.9(4)
C(5)–C(4)–C(19)	109.8(4)	C(18)–C(4)–C(19)	112.7(4)
C(4)–C(5)–C(6)	116.5(4)	C(4)–C(5)–C(10)	114.7(4)
C(6)–C(5)–C(10)	103.8(3)	C(5)–C(6)–C(7)	110.6(3)
C(5)–C(6)–C(8)	105.7(3)	C(7)–C(6)–C(8)	110.4(3)
O(5)–C(7)–O(6)	123.2(4)	O(5)–C(7)–C(6)	125.1(4)
O(6)–C(7)–C(6)	111.8(4)	C(6)–C(8)–C(9)	102.5(3)
C(6)–C(8)–C(14)	112.0(3)	C(6)–C(8)–C(15)	119.6(3)
C(9)–C(8)–C(14)	109.1(3)	C(9)–C(8)–C(15)	111.7(3)
C(14)–C(8)–C(15)	101.9(3)	C(8)–C(9)–C(10)	101.5(3)
C(8)–C(9)–C(11)	113.9(3)	C(10)–C(9)–C(11)	118.9(4)
O(4)–C(10)–C(1)	59.4(3)	O(4)–C(10)–C(5)	116.6(3)
O(4)–C(10)–C(9)	118.6(3)	C(1)–C(10)–C(5)	119.4(4)
C(1)–C(10)–C(9)	127.3(4)	C(5)–C(10)–C(9)	107.7(4)
C(9)–C(11)–C(12)	115.0(4)	C(11)–C(12)–C(13)	113.8(3)
O(8)–C(13)–C(12)	110.0(3)	O(8)–C(13)–C(14)	110.6(3)
O(8)–C(13)–C(16)	111.2(4)	C(12)–C(13)–C(14)	108.6(4)
C(12)–C(13)–C(16)	114.1(3)	C(14)–C(13)–C(16)	102.0(3)
C(8)–C(14)–C(13)	101.8(3)	C(8)–C(15)–C(16)	105.6(3)
O(7)–C(16)–C(13)	106.6(4)	O(7)–C(16)–C(15)	107.2(4)
O(7)–C(16)–C(17)	108.0(4)	C(13)–C(16)–C(15)	104.3(3)
C(13)–C(16)–C(17)	118.1(4)	C(15)–C(16)–C(17)	112.1(4)
Cl–C(17)–C(16)	114.6(3)	O(1)–C(19)–O(2)	120.9(4)
O(1)–C(19)–C(4)	129.0(5)	O(2)–C(19)–C(4)	110.1(4)

There was no crystal decay and no absorption corrections were made. The structure was solved by routine direct methods (MULTAN) and refined by full-matrix least-squares with non-hydrogen atoms anisotropic. Hydrogen atoms were located on a difference map and refined isotropically. The weighting scheme was $w = 1/\sigma^2(F)$ and the final residuals were R = 0.038, R' = 0.038. A final difference map was featureless. Programs from the Enraf-Nonius SDP-Plus package were run on a PDP 11/34 computer. Final atom co-ordinates are given in Table 5, and bond distances and angles are in Table 6.*

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