The Stereochemistry of Some Reactions at C-16 in Gibberellins; An *X*-Ray Crystallographic Study of the Methyl Esters of Gibberellin A_2 and Gibberellin A_9 Hydrochloride

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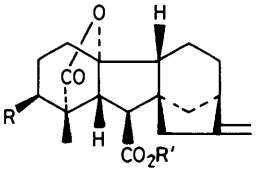
Hydration of the 16-ene in the gibberellins is shown, by a combination of spectroscopic and *X*-ray crystallographic means, to lead to (16*R*)-alcohols. The hydrochloride of gibberellin A_9 methyl ester possesses the same (16*R*)-stereochemistry.

The formation of 16-alcohols by hydration of the 16-ene of the kaurenoid and gibberellin metabolites of the fungus *Gibberella fujikuroi* is a common biotransformation.[1] The resultant 16-alcohols appear to be terminal metabolites and indeed it is possible that this represents a 'dumping' or 'salvage' mechanism.[2] Thus gibberellin A_9 (**1**) is converted into gibberellin A_{10} (**5**),[3] and gibberellin A_2 (**6**) is formed from gibberellin A_4 (**2**).[4] Gibberellins A_{41} (**8**) and A_{42} (**9**) are the hydrates of gibberellins A_{13} and A_{14} respectively.[5] Both gibberellins A_2 (**6**)[6] and A_{10} (**5**)[7] are also formed by the acid-catalysed hydration of the corresponding 16-enes. It is generally assumed by analogy with other tetracyclic diterpenoids[8] that these alcohols possess the (16*R*)-stereochemistry based on hydration from the less hindered face of the molecule. It is the object of the present work to provide a formal proof of this by spectroscopic and crystallographic means.

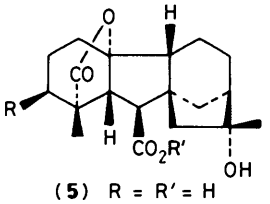
Treatment of the gibberellin A_4–A_7 mixture (3:7) with methanolic dil. hydrochloric acid[9] gave three compounds (**12**), (**13**), and (**6**) which were separated chromatographically. The first aromatic product (δ 6.88, 6.93, and 7.06) lacked the ^1H n.m.r. signals characteristic of the 16-ene, possessing instead additional signals for a C–Me (δ 1.19) and a methyl ether (δ 3.03). On methylation with diazomethane the compound gave a methyl ester (**14**). The (16*R*)-stereochemistry was assigned to this compound by a combination of ^1H n.m.r. spin decoupling studies to identify the C- and D-ring proton resonances, followed by nuclear Overhauser enhancement (n.O.e.) difference spectra.

In the gibberellins there is a long-range ^1H:^1H 'W' coupling between 15β-H and 14α-H which has been identified on a number of occasions.[10] In the present case a double doublet at δ 1.16 (*J* 2 and 15 Hz) was assigned to 15β-H. Irradiation of this signal caused the collapse of a doublet (δ 1.65, *J* 15 Hz) which was assigned to (15α-H) and also removed a small coupling (2 Hz) from a multiplet at δ 1.50 (14α-H). Irradiation of an eight-line system at δ 2.48 (*J* 1.2, 5, and 10.5 Hz) removed a 10.5 Hz coupling from the signal at δ 1.50 and a 5 Hz coupling from a multiplet at δ 2.12. Consequently the signal at δ 2.48 was assigned to 14β-H and that at δ 2.12 to 13-H. The decoupling experiment also showed that the small long-range coupling (1.2 Hz) was to a signal at δ 1.7 which was therefore assigned to 12β-H. Irradiation of the methoxy signal at δ 3.03 produced n.O.e. effects at δ 1.65 (15α-H), 2.12 (13-H), and 2.48 (14β-H), whilst irradiation of the *C*-methyl signal at δ 1.19 produced n.O.e. effects at δ 1.14 (15β-H), 1.7 (12β-H), 1.55 (11β-H?), and 2.12 (13-H). Hence the compound was assigned the (16*R*) stereochemistry (**12**).

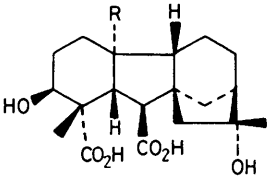
The second compound to be isolated was the known alcohol (**13**).[19] Comparison of the n.m.r. spectrum of this compound with that of the ether (**12**) facilitated the assignment of the ring-D proton resonances. In this compound the 14-H signal was shifted to lower field (δ 2.64) as would be anticipated for an interaction with a hydroxy group as opposed to a methoxy group. Hence this compound was assigned the same (16*R*)-stereochemistry.



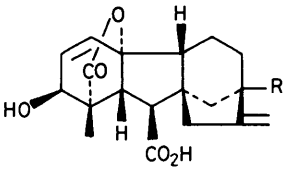
(**1**) R = R′ = H
(**2**) R = OH, R′ = H
(**3**) R = OH, R′ = Me
(**4**) R = H, R′ = Me



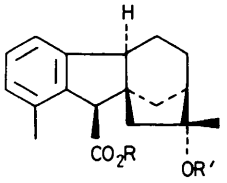
(**5**) R = R′ = H
(**6**) R = OH, R′ = H
(**7**) R = OH, R′ = Me



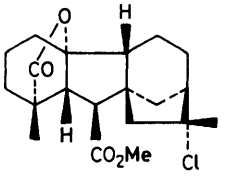
(**8**) R = CO_2H
(**9**) R = Me



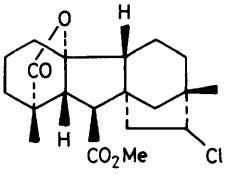
(**10**) R = H
(**11**) R = OH



(**12**) R = H, R′ = Me
(**13**) R = R′ = H
(**14**) R = R′ = Me



(**15**)



(**16**)

The third compound to be isolated was gibberellin A_2 (**6**). In this case the stereochemistry at C-16 was established by an *X*-ray crystallographic analysis of the methyl ester (**7**) (see Figure 1). This compound also possesses the (16*R*)-stereochemistry. Ring D adopts an envelope conformation with C-14 at the flap. The torsion angle C-8, C-15, C-16, C-13 is 3.7°. Gibberellin A_4

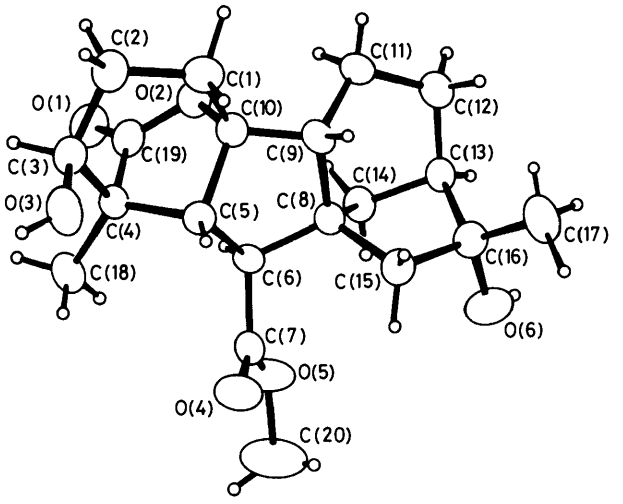


Figure 1. *X*-Ray molecular structure of gibberellin A_2 methyl ester (7)

methyl ester (**3**), with a 16-exocyclic methylene, possesses ring D as a twisted envelope with the C-8, C-15, C-16, C-13 torsion angle 16°.[11]

In the biosynthesis of gibberellic acid (**11**) ring A of gibberellin A_4 (**2**) is efficiently dehydrogenated to form gibberellin A_7 (**10**) prior to hydroxylation at C-13.[1,12,13] However, gibberellin A_2 (**6**) does not undergo dehydrogenation. In a study of the conformational distortions of ring A of the gibberellins we compared[11] the *X*-ray structures of gibberellins A_4 and A_{13}. Using our previous parameters for gibberellin A_4 methyl ester (**3**) we have made a computer graphics superposition of the structures of gibberellin A_2 and A_4 methyl esters (see Figure 2).

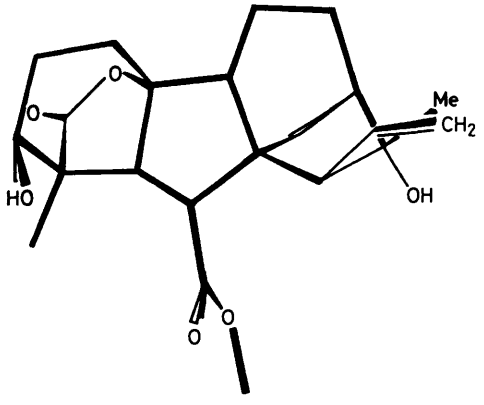


Figure 2. Superposition of gibberellin A_2 and A_4 methyl esters

This did not reveal any differences in the shape of ring A, the major difference being in ring D. Hence we conclude that it is the nature of ring D, either the additional hydroxy group or the different shape, which may affect binding to the ring A dehydrogenase.

Treatment of gibberellin A_9 methyl ester (**4**) with hydrogen chloride gas in chloroform gave a hydrochloride (**15**), the C-16 stereochemistry of which was not assigned.[14] Furthermore strongly acidic conditions are known to produce isomerization at C-9 in gibberellins.[15] The stereochemistry of this product was therefore established by *X*-ray crystallographic analysis (see Figure 3). The compound also possesses the (16*R*)-stereochemistry. It is isomeric with the chloro compound (**16**) obtained by the action of phosphorus pentachloride on an 8:13-isogibberellin 16β-alcohol.[10]

Table 1. Fractional atomic co-ordinates (× 10^4) with estimated standard deviations in parentheses for compound (7)·H_2O

	x	*y*	*z*
O(1)	6 595(3)	3 407(2)	5 230(1)
O(2)	4 915(2)	2 287(2)	5 715(1)
O(3)	7 772(3)	−688(2)	5 532(1)
O(4)	7 829(3)	762(3)	7 738(1)
O(5)	7 315(3)	2 739(3)	8 006(1)
O(6)	3 577(3)	2 238(3)	8 961(1)
O(7)	5 343(3)	5 765(3)	4 966(1)
C(1)	4 589(4)	58(4)	5 561(2)
C(2)	5 699(4)	138(4)	4 981(2)
C(3)	7 147(4)	417(3)	5 250(2)
C(4)	7 159(4)	1 449(3)	5 830(2)
C(5)	6 245(4)	1 005(3)	6 437(2)
C(6)	6 128(4)	1 883(3)	7 060(2)
C(7)	7 188(4)	1 698(4)	7 620(2)
C(8)	4 595(3)	1 778(3)	7 324(2)
C(9)	3 796(4)	1 181(3)	6 699(2)
C(10)	4 812(4)	1 066(3)	6 100(2)
C(11)	2 442(4)	1 874(4)	6 543(2)
C(12)	1 632(4)	2 177(4)	7 215(2)
C(13)	2 566(4)	2 627(3)	7 819(2)
C(14)	3 956(4)	3 048(3)	7 516(2)
C(15)	4 335(4)	1 034(3)	7 999(2)
C(16)	3 053(4)	1 616(4)	8 343(2)
C(17)	1 969(5)	684(5)	8 566(2)
C(18)	8 615(4)	1 872(4)	6 008(2)
C(19)	6 248(4)	2 504(3)	5 549(2)
C(20)	8 272(6)	2 727(6)	8 593(3)

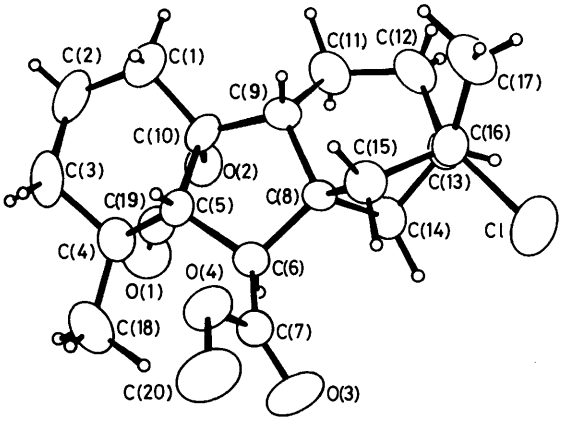


Figure 3. *X*-Ray molecular structure of gibberellin A_9 methyl ester hydrochloride (**15**)

Experimental

Treatment of a Mixture of Gibberellins A_4 *and* A_7 *with Acid.*—A mixture of gibberellins A_4 (**2**) and A_7 (**10**) (1:3) (1.5 g) in methanol (35 ml) was treated with dil. hydrochloric acid (1 part conc. acid: 5 parts water) (35 ml) at room temperature for 5 days. The mixture was filtered to remove starting material (160 mg). The filtrate was diluted with water and the methanol was removed under reduced pressure. The organic products were recovered in ethyl acetate and chromatographed on silica. Elution with 40% ethyl acetate–light petroleum gave the *acid* (**12**) (60 mg), which was crystallized from ethyl acetate–light petroleum as needles, m.p. 157—159 °C (Found: C, 75.7; H, 7.9. $C_{19}H_{24}O_3$ requires C, 76.0; H, 8.05%); $\nu_{max.}$ 3 490br, 1 730, 1 620, and 1 595 cm^{-1}; δ_H(360 MHz; [$^2H_6$]acetone) 1.19 (3 H, s, 17-H_3), 2.19 (3 H, s, Ar*Me*), 2.56 (1 H, m, 14-H), 2.77 (1 H, m, 9-H), 3.03 (3 H, s, OMe), 3.88 (1 H, s, 6-H), 6.88 (1 H, d, *J* 7.5 Hz),

Table 2. Intramolecular distances (Å) and angles (°) with estimated standard deviations in parentheses for compound (7)·H_2O

(a) Bonds

O(1)–C(19)	1.191(4)	O(2)–C(10)	1.503(4)
O(2)–C(19)	1.347(5)	O(3)–C(3)	1.435(4)
O(4)–C(7)	1.200(5)	O(5)–C(7)	1.342(5)
O(5)–C(20)	1.452(6)	O(6)–C(6)	1.445(4)
C(1)–C(2)	1.542(5)	C(1)–C(10)	1.507(5)
C(2)–C(3)	1.520(6)	C(3)–C(4)	1.564(5)
C(4)–C(5)	1.532(5)	C(4)–C(18)	1.517(5)
C(4)–C(19)	1.530(5)	C(5)–C(6)	1.519(5)
C(5)–C(10)	1.528(5)	C(6)–C(7)	1.493(5)
C(6)–C(8)	1.568(5)	C(8)–C(9)	1.558(5)
C(8)–C(14)	1.539(5)	C(8)–C(15)	1.536(5)
C(9)–C(10)	1.511(5)	C(9)–C(11)	1.533(5)
C(11)–C(12)	1.536(5)	C(12)–C(13)	1.541(5)
C(13)–C(14)	1.529(5)	C(13)–C(16)	1.548(5)
C(15)–C(17)	1.534(5)	C(16)–C(17)	1.507(6)

(b) Angles

C(10)–O(2)–C(19)	109.2(3)	C(7)–O(5)–C(20)	118.2(4)
C(2)–C(1)–C(10)	110.5(3)	C(1)–C(2)–C(3)	114.2(3)
O(3)–C(3)–C(2)	110.6(3)	O(3)–C(3)–C(4)	108.4(3)
C(2)–C(3)–C(4)	112.6(3)	C(3)–C(4)–C(5)	108.1(3)
C(3)–C(4)–C(18)	112.1(3)	C(3)–C(4)–C(19)	105.7(3)
C(5)–C(4)–C(18)	117.2(3)	C(5)–C(4)–C(19)	99.4(3)
C(18)–C(4)–C(19)	113.0(3)	C(4)–C(5)–C(6)	116.2(3)
C(4)–C(5)–C(10)	101.0(3)	C(6)–C(5)–C(10)	103.6(3)
C(5)–C(6)–C(7)	115.2(3)	C(5)–C(6)–C(8)	106.1(3)
C(7)–C(6)–C(8)	114.1(3)	O(4)–C(7)–O(5)	123.1(3)
O(4)–C(7)–C(6)	126.8(3)	O(5)–C(7)–C(6)	110.1(3)
C(6)–C(8)–C(9)	104.6(3)	C(6)–C(8)–C(14)	113.1(3)
C(6)–C(8)–C(15)	117.5(3)	C(9)–C(8)–C(14)	110.3(3)
C(9)–C(8)–C(15)	110.3(3)	C(14)–C(8)–C(15)	101.1(3)
C(8)–C(9)–C(10)	106.8(3)	C(8)–C(9)–C(11)	111.9(3)
C(10)–C(9)–C(11)	116.5(3)	O(2)–C(10)–C(1)	107.5(3)
O(2)–C(10)–C(5)	100.6(3)	O(2)–C(10)–C(9)	109.9(3)
C(1)–C(10)–C(5)	112.7(3)	C(1)–C(10)–C(9)	118.8(3)
C(5)–C(10)–C(9)	105.9(3)	C(9)–C(11)–C(12)	112.0(3)
C(11)–C(12)–C(13)	113.0(3)	C(12)–C(13)–C(14)	109.0(3)
C(12)–C(13)–C(16)	116.2(3)	C(14)–C(13)–C(16)	100.6(3)
C(8)–C(14)–C(13)	100.5(3)	C(8)–C(15)–C(16)	106.3(3)
O(6)–C(16)–C(13)	108.1(3)	O(6)–C(16)–C(15)	104.7(3)
O(6)–C(16)–C(17)	108.6(3)	C(13)–C(16)–C(15)	104.7(3)
C(13)–C(16)–C(17)	115.8(3)	C(15)–C(16)–C(17)	114.3(3)
O(1)–C(19)–O(2)	122.0(3)	O(1)–C(19)–C(4)	128.2(4)
O(2)–C(19)–C(4)	109.8(3)		

(c) Hydrogen bonding

	O–H	O···H	O···O	O–Ĥ···O
O(6)–H(06)···O(3)′	0.84(4)	1.92(4)	2.75	168(3)
O(3)–H(03)···O(7)″	0.76(4)	1.91(4)	2.66	170(4)
O(7)–H(07A)···O(6)′	0.71(4)	2.12(4)	2.79	156(4)
O(7)–H(07B)···O(1)	0.70(4)	2.15(4)	2.85	169(4)

Symmetry elements ′ $1-x, \frac{1}{2}+y, 1\frac{1}{2}-z$
″ $\frac{1}{2}+x, \frac{1}{2}-y, 1-z$

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

	x	*y*	*z*
Cl	6 225(2)	9 619(2)	5 700(1)
O(1)	2 063(5)	6 382(4)	2 216(3)
O(2)	4 149(4)	7 296(3)	2 461(2)
O(3)	1 772(5)	9 634(4)	4 575(2)
O(4)	2 309(5)	11 004(4)	3 725(2)
C(1)	5 160(8)	8 975(6)	1 765(3)
C(2)	3 971(9)	8 740(7)	1 211(3)
C(3)	2 482(8)	9 059(6)	1 482(3)
C(4)	2 197(7)	8 634(6)	2 276(3)
C(5)	3 304(6)	9 240(5)	2 757(3)
C(6)	3 225(6)	8 982(5)	3 572(3)
C(7)	2 335(6)	9 868(5)	4 019(3)
C(8)	4 820(6)	8 891(5)	3 839(3)
C(9)	5 717(6)	8 699(5)	3 136(3)
C(10)	4 659(6)	8 584(5)	2 519(3)
C(11)	6 831(7)	7 669(7)	3 197(3)
C(12)	7 633(7)	7 708(7)	3 920(4)
C(13)	6 679(7)	8 069(5)	4 562(3)
C(14)	5 104(6)	7 847(5)	4 377(3)
C(15)	5 394(6)	9 997(5)	4 288(3)
C(16)	6 665(6)	9 482(6)	4 728(3)
C(17)	8 036(7)	10 161(6)	4 621(4)
C(18)	644(7)	8 771(7)	2 501(4)
C(19)	2 716(7)	7 308(6)	2 317(3)
C(20)	1 508(9)	11 915(6)	4 126(4)

6.93 (1 H, d, *J* 7.5 Hz, 1- and 3-H), and 7.06 (1 H, t, *J* 7.5 Hz, 2-H). Methylation with ethereal diazomethane gave the *methyl ester* (**14**), which was crystallized from methanol as needles, m.p. 70—72 °C (Found: C, 73.5; H, 8.2. $C_{20}H_{26}O_3{\cdot}CH_3OH$ requires C, 72.8; H, 8.7%); $\nu_{max.}$ 1 735 and 1 590 cm^{-1}; δ_H(360 MHz; [$^2H_6$]acetone) 1.16 (1 H, dd, *J* 2 and 15 Hz, 15-H), 1.19 (3 H, s, 17-H), 2.12 (3 H, s, Ar*Me* and 1 H, m, 13-H), 2.48 (1 H, octet, *J* 1.2, 5, and 10.5 Hz, 14-H), 2.80 (1 H, t, *J* 6 Hz, 9-H), 3.03 and 3.74 (each 3 H, s, OMe), 3.92 (1 H, s, 6-H), 6.90 and 6.95 (each 1 H, d, *J* 7.5 Hz, together 1- and 3-H), and 7.08 (1 H, t, *J* 7.5 Hz, 2-H).

Elution with 50% ethyl acetate–light petroleum gave the acid (**13**) (67 mg), which was crystallized from ethyl acetate–light petroleum as plates, m.p. 221—222 °C (lit.,[9] 220—222 °C) (Found: C, 75.5; H, 7.9. Calc. for $C_{18}H_{22}O_3$: C, 75.5; H, 7.7%); $\nu_{max.}$ 3 420 and 1 680 cm^{-1}. The compound was not sufficiently soluble in $CDCl_3$ or [$^2H_6$]acetone to obtain an n.m.r. spectrum. Methylation with ethereal diazomethane gave the methyl ester, m.p. 144—146 °C (lit.,[9] 145—148 °C) (Found: C, 75.8; H, 8.2. Calc. for $C_{19}H_{24}O_3$: C, 76.0; H, 8.05%); $\nu_{max.}$ 3 480—3 360br, 1 715, and 1 600 cm^{-1}; δ_H(360 MHz; $CDCl_3$) 1.30 (3 H, s, 17-H_3), 2.16 (3 H, s, Ar*Me*), 2.64 (1 H, dd, *J* 4.8 and 10.8 Hz, 14-H), 2.80 (1 H, m, 9-H), 3.79 (3 H, s, OMe), 3.97 (1 H, s, 6-H), 6.90 and 6.99 (each 1 H, d, *J* 7.5 Hz, together 1- and 3-H), and 7.12 (1 H, t, *J* 7.5 Hz, 2-H).

Further elution with 60% ethyl acetate–light petroleum gave gibberellin A_7 (**10**) (650 mg), identified by its n.m.r. spectrum.

Elution with ethyl acetate–methanol (1:1) gave gibberellin A_2 (**6**) (85 mg), the methyl ester of which [(**7**)] was prepared with diazomethane. The ester was crystallized from acetone as plates, m.p. 134—136 °C (lit.,[6] 120 and 190 °C for hydrate and anhydrous forms) (Found: C, 62.55; H, 7.6. Calc. for $C_{20}H_{28}O_6{\cdot}H_2O$: C, 62.8; H, 7.9%); $\nu_{max.}$ 3 480, 3 340, 1 760, and 1 720 cm^{-1}. Gibberellin A_2 methyl ester (**7**) was identified by comparison of its ^1H n.m.r. spectrum with that described previously:[16] δ_H (360 MHz; [$^2H_6$]acetone) 1.04 (3 H, s, H-18$_3$), 1.31 (3 H, s, H-17$_3$), 2.60 and 3.15 (each 1 H, d, *J* 10.6 Hz, 6- and 5-H respectively), 3.67 (3 H, s, OMe), and 3.71 (1 H, m, 3-H). Signals at δ 3.4 and 4.5 disappeared on treatment with ^2H_2O. Decoupling experiments showed that the signal at δ 4.5 was coupled (*J* 4.3 Hz) to the 3α-H signal at δ 3.71.

Crystal-structure Determinations.—(a) *Gibberellin A_2 methyl ester* (**7**). $C_{20}H_{28}O_6{\cdot}H_2O$, *M* = 382.5, orthorhombic, space group $P2_12_12_1$, *a* = 9.660(1), *b* = 10.717(1), *c* = 19.067(2) Å, *V* = 1 973.8 Å^3 *Z* = 4, D_c = 1.29 g cm^{-3}, monochromated Mo-K_α radiation, λ = 0.710 69 Å, μ = 0.9 cm^{-1}.

A crystal of *ca.* 0.4 × 0.3 × 0.1 mm was mounted on an Enraf-Nonius CAD 4 diffractometer. Intensities for unique data $2 < \theta < 22°$ were measured by an ω–2θ scan with a maximum scan time of 1 min. No correction was made for absorption. Out

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

(a) Bonds

Cl–C(16)	1.841(6)	O(1)–C(19)	1.193(8)
O(2)–C(10)	1.487(7)	O(2)–C(19)	1.362(7)
O(3)–C(7)	1.178(7)	O(4)–C(7)	1.352(7)
O(4)–C(20)	1.444(8)	C(1)–C(2)	1.524(10)
C(1)–C(10)	1.519(8)	C(2)–C(3)	1.516(11)
C(3)–C(4)	1.555(8)	C(4)–C(5)	1.510(8)
C(4)–C(18)	1.512(9)	C(4)–C(19)	1.527(9)
C(5)–C(6)	1.528(7)	C(5)–C(10)	1.517(8)
C(6)–C(7)	1.516(8)	C(6)–C(8)	1.568(8)
C(8)–C(9)	1.553(8)	C(8)–C(14)	1.531(8)
C(8)–C(15)	1.557(8)	C(9)–C(10)	1.509(8)
C(9)–C(11)	1.534(9)	C(11)–C(12)	1.525(9)
C(12)–C(13)	1.529(9)	C(13)–C(14)	1.526(9)
C(13)–C(16)	1.571(8)	C(15)–C(16)	1.540(8)
C(16)–C(17)	1.489(9)		

(b) Angles

C(10)–O(2)–C(19)	108.6(4)	C(7)–O(4)–C(20)	115.9(4)
C(2)–C(1)–C(10)	110.2(6)	C(1)–C(2)–C(3)	114.2(5)
C(2)–C(3)–C(4)	113.4(5)	C(3)–C(4)–C(5)	107.6(5)
C(3)–C(4)–C(18)	113.0(5)	C(3)–C(4)–C(19)	105.9(5)
C(5)–C(4)–C(18)	116.8(5)	C(5)–C(4)–C(19)	99.8(5)
C(18)–C(4)–C(19)	112.5(5)	C(4)–C(5)–C(6)	117.4(5)
C(4)–C(5)–C(10)	101.1(4)	C(6)–C(5)–C(10)	103.7(4)
C(5)–C(6)–C(7)	116.1(4)	C(5)–C(6)–C(8)	105.8(4)
C(7)–C(6)–C(8)	112.9(4)	O(3)–C(7)–O(4)	122.5(5)
O(3)–C(7)–C(6)	125.2(5)	O(4)–C(7)–C(6)	112.2(4)
C(6)–C(8)–C(9)	105.0(4)	C(6)–C(8)–C(14)	114.4(4)
C(6)–C(8)–C(15)	116.3(4)	C(9)–C(8)–C(14)	110.1(4)
C(9)–C(8)–C(15)	111.1(4)	C(14)–C(8)–C(15)	100.1(4)
C(8)–C(9)–C(10)	106.6(4)	C(8)–C(9)–C(11)	113.7(5)
C(10)–C(9)–C(11)	115.9(5)	O(2)–C(10)–C(1)	106.7(4)
O(2)–C(10)–C(5)	101.6(4)	O(2)–C(10)–C(9)	109.9(4)
C(1)–C(10)–C(5)	113.1(5)	C(1)–C(10)–C(9)	117.7(5)
C(5)–C(10)–C(9)	106.7(4)	C(9)–C(11)–C(12)	112.0(5)
C(11)–C(12)–C(13)	113.3(5)	C(12)–C(13)–C(14)	110.3(5)
C(12)–C(13)–C(16)	114.0(5)	C(14)–C(13)–C(16)	101.0(5)
C(8)–C(14)–C(13)	101.1(4)	C(8)–C(15)–C(16)	105.1(4)
Cl–C(16)–C(13)	105.7(4)	Cl–C(16)–C(15)	108.0(4)
Cl–C(16)–C(17)	106.2(4)	C(13)–C(16)–C(15)	105.2(5)
C(13)–C(16)–C(17)	117.1(5)	C(15)–C(16)–C(17)	114.1(5)
O(1)–C(19)–O(2)	121.5(6)	O(1)–C(19)–C(4)	129.2(6)
O(2)–C(19)–C(4)	109.2(5)		

of 1 520 reflections measured, 1 177 with $|F^2| > \sigma(F^2)$ were used in the refinement where $(F^2) = [\sigma^2(I) + (0.04I)^2]^{\frac{1}{2}}/\text{Lp}$.

The structure was solved by direct methods using MULTAN and refined by full-matrix least-squares with anisotropic temperature factors for C and O. Hydrogen atoms were located on a difference map and refined isotropically. The final *R*-factors were $R = 0.033$ and $R' = 0.039$. The weighting scheme was $w = 1/\sigma^2(F)$. All calculations were done on a PDP 11/34 computer using the Enraf-Nonius SDP-Plus program package.

(b) *Gibberellin A_9 methyl ester hydrochloride* (**15**) (*with M. Cockett*). $C_{20}H_{27}ClO_4$, $M = 366.9$, orthorhombic, space group $P2_12_12_1$, $a = 9.320(1)$, $b = 10.906$ (2), $c = 18.388(2)$ Å, $V =$ 1 868.9 Å^3, $Z = 4$, $D_c = 1.30$ g cm^{-3}, graphite-monochromated Mo-K_α radiation, $\lambda = 0.710\,69$ Å, $\mu = 2.2$ cm^{-1}.

A crystal of *ca.* 1.4 × 0.9 × 0.6 mm was mounted on an Enraf-Nonius CAD 4 diffractometer. Intensities for unique data $2 < \theta < 25°$ were measured by a ω–2θ scan with a maximum scan time of 1 minute. No correction was made for absorption. Out of 1 907 reflections measured, 1 140 with $|F^2| > \sigma(F^2)$ were used in the refinement where $\sigma(F^2) = [\sigma^2(I) + (0.04I)^2]^{\frac{1}{2}}/\text{Lp}$.

The structure was solved by direct methods using MULTAN and refined by full-matrix least-squares with anisotropic temperature factors for Cl, C, and O. All hydrogen atoms except for those on C-20, which appears to be a disordered methyl group, were located on a difference map and refined isotropically. The final *R*-factors were $R = 0.039$ and $R' = 0.041$. The weighting scheme was $w = 1/\sigma^2(F)$. All calculations were done on a PDP11/34 computer using the Enraf-Nonius SDP-Plus program package.

Fractional atomic co-ordinates, and intramolecular distances and angles, are given in Tables 1 and 2 (gibberellin A_2 methyl ester) and Tables 3 and 4 (gibberellin A_9 methyl ester hydrochloride).*

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* *Supplementary data* (see section 5.6.3 of Instructions for Authors, in the January issue). Tables of hydrogen atom co-ordinates, torsion angles, and anisotropic thermal parameters have been deposited at the Cambridge Crystallographic Data Centre.

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