Molecular and Crystal Structure of the Phytohormone Gibberellin A₃

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The structure of gibberellin A₃ has been determined by X-ray analysis. The compound crystallizes in the tetragonal space group $P4_32_12$ with the lattice parameters $a = b = 10.921$ Å and $c = 28.757$ Å. The final R value was 0.084.

Although the crystal structures of several derivatives of the gibberellins have been determined,[1-10] no X-ray analysis of any of these phytohormones has been published. In the case of the highly bioactive gibberellin A₃, structure data is only available for the di-p-bromobenzoate methyl ester.[1] The accuracy of this structure determination is limited by the derivatization with bulky heavy atoms containing substituents as well as the use of the film technique. For that reason an X-ray analysis of the free hormone gibberellin A₃ was performed.

For data collection a single crystal of the title compound ($C_{19}H_{27}O_6$) crystallized from acetone–hexane has been used.

Crystal Data.—Tetragonal, $a = b = 10.921$ (4), $c = 28.757$ (7) Å, $Z = 8$, $D_x = 1.386$ g cm⁻³, space group $P4_32_12$, m.p. 235—238 °C. The intensities of 1 550 independent reflections were measured on a Hilger–Watts four-circle diffractometer within a 2θ sphere of 48°, using graphite-monochromated Mo-K_α radiation and a ω/2θ scan mode. The intensity data were corrected for Lorentz and polarisation effects. No absorption and extinction corrections were applied.

The structure has been solved by direct methods using 200 normalized structure factors (E-values with $|E| > 1.48$) with the computer program MULTAN 78.[11] The E-map computed from the set with the best combined figure of merit produced the model of the molecule, which fitted the geometry of the title compound and revealed the positions of all non-hydrogen atoms. A few cycles of full-matrix least-squares refinement of the non-hydrogen atoms with at first isotropic and later anisotropic temperature factors reduced the discrepancy factor R to 0.104. The refinement was carried out with SHELX 76[12] using the weighting scheme $w = 1.75/\{[\sigma(F_0)]^2 + 0.0008\ F_0^2\}$. A subsequent difference Fourier map revealed the positions of H(03), H(013), H(071), H(171), and H(172) while the rest of the hydrogen atoms were generated geometrically. The anisotropic refinement of the non-hydrogen atoms led to the final value of $R = 0.084$ for all 1 150 reflections including the unobserved ones. The final atomic positional parameters are listed in Table 1. The molecular structure including bond lengths, bond angles, and torsion angles is shown in Figure 1. The estimated standard deviations for the bond lengths lie between 0.007 and 0.009 Å, for the bond angles between 0.4 and 0.7°, and for the torsion angles between 0.6 and 0.9°. Structure factor tables are available as a Supplementary Publication † (SUP No. 23582, 11 pages).

The geometry of the molecule is similar to that in the corresponding parts of the di-p-bromobenzoate of the methyl ester of gibberellic acid.[1] However the conformations of some rings are significantly different in the two structures. The conformations of the rings of the title compound are described by the
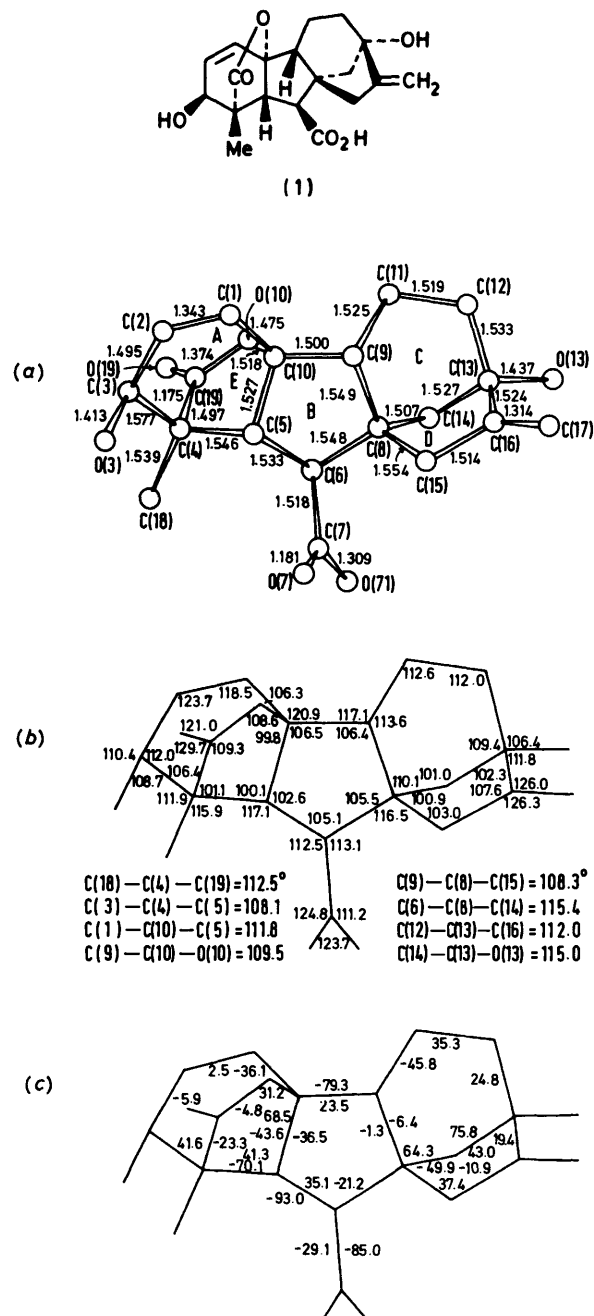
Figure 1. (a) Bond lengths in Å (e.s.d.s <0.009 Å); (b) bond angles in ° (e.s.d.s <0.7°); and (c) torsion angles in ° (e.s.d.s <0.9°)
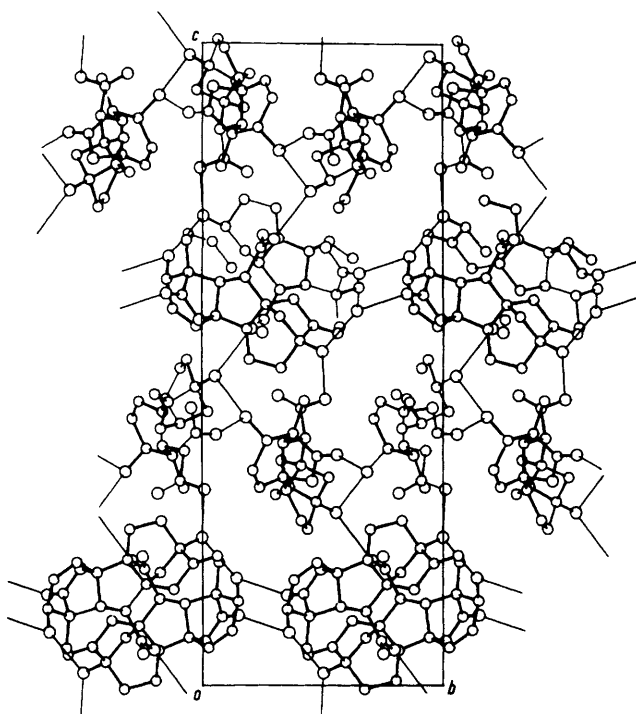
Figure 2. Molecular packing viewed along *a*. The hydrogen bonds are indicated

Table 1. Fractional atomic co-ordinates (e.s.d.s in parentheses)

Atom	x/a	y/b	z/c
C(1)	1.262 2(6)	1.025 0(6)	0.058 7(2)
C(2)	1.290 3(6)	1.121 9(6)	0.085 4(2)
C(3)	1.231 5(6)	1.147 8(5)	0.131 4(2)
C(4)	1.123 7(5)	1.056 0(5)	0.142 2(2)
C(5)	1.164 8(5)	0.926 4(5)	0.127 3(2)
C(6)	1.073 4(4)	0.821 7(5)	0.134 8(2)
C(7)	1.091 4(5)	0.757 5(5)	0.181 1(2)
C(8)	1.091 3(5)	0.735 7(5)	0.092 5(1)
C(9)	1.152 0(5)	0.815 4(5)	0.054 4(2)
C(10)	1.164 4(5)	0.941 5(5)	0.074 5(2)
C(11)	1.090 3(7)	0.804 7(6)	0.007 0(2)
C(12)	1.063 6(6)	0.672 7(6)	−0.006 3(2)
C(13)	1.028 3(5)	0.594 8(5)	0.035 9(2)
C(14)	0.976 1(4)	0.677 4(5)	0.073 9(2)
C(15)	1.172 5(5)	0.620 7(5)	0.100 5(2)
C(16)	1.140 2(5)	0.539 5(5)	0.059 7(2)
C(17)	1.196 1(7)	0.437 9(6)	0.047 6(2)
C(18)	1.077 6(6)	1.068 6(6)	0.192 5(2)
C(19)	1.025 6(6)	1.081 7(6)	0.107 1(2)
O(3)	1.318 9(4)	1.140 0(4)	0.167 5(2)
O(7)	1.185 8(4)	0.749 2(5)	0.200 8(1)
O(71)	0.990 7(4)	0.703 3(4)	0.194 7(1)
O(10)	1.044 9(4)	1.010 6(4)	0.068 4(1)
O(13)	0.946 1(4)	0.502 1(4)	0.019 2(1)
O(19)	0.942 1(5)	1.149 3(5)	0.109 2(2)
H(1)	1.312(5)	1.009(5)	0.027(2)
H(2)	1.358(5)	1.186(5)	0.072(2)
H(3)	1.195(5)	1.240(5)	0.129(2)
H(5)	1.246(5)	0.904(5)	0.146(2)
H(6)	0.981(5)	0.855(5)	0.137(2)
H(9)	1.243(5)	0.781(5)	0.044(2)
H(111)	1.143(5)	0.850(5)	−0.019(2)
H(112)	1.001(5)	0.851(5)	0.010(2)
H(121)	1.149(5)	0.637(5)	−0.022(2)
H(122)	0.993(5)	0.670(5)	−0.032(2)
H(141)	0.913(5)	0.744(5)	0.060(2)
H(142)	0.930(5)	0.624(5)	0.101(2)
H(151)	1.151(5)	0.577(5)	0.134(2)
H(152)	1.270(5)	0.643(5)	0.101(2)
H(171)	1.177(5)	0.394(5)	0.016(2)
H(172)	1.258(5)	0.402(5)	0.070(2)
H(181)	1.149(5)	1.054(5)	0.217(2)
H(182)	1.041(5)	1.161(5)	0.197(2)
H(183)	1.003(5)	1.004(5)	0.198(2)
H(03)	1.352(5)	1.219(5)	0.168(2)
H(071)	0.998(5)	0.685(5)	0.228(2)
H(013)	0.903(5)	0.481(5)	0.046(2)

Table 2. Intermolecular hydrogen bond lengths (Å) and angles (°) (e.s.d.s in parentheses)

	Bond lengths			Bond angles
X–H $\cdots$ Y	X–H	H $\cdots$ Y	X $\cdots$ Y	X–H $\cdots$ Y
O(3)–H(03) $\cdots$ O(19')	0.93(7)	1.92(7)	2.774(6)	152(6)
O(13)–H(013) $\cdots$ O(3')	0.94(7)	1.92(7)	2.767(6)	150(6)
O(71)–H(071) $\cdots$ O(13')	0.98(7)	1.86(7)	2.696(6)	142(6)

endocyclic torsion angles. Ring A containing a double bond between C(1) and C(2) has a sofa conformation. The mean torsion angle $\langle|\phi|\rangle = 37.5°$ deviates from the value of 30.3° predicted for free cyclohexene [13] while the asymmetry parameter [14] ΔC_s^2 is 3.8° characterizing the distortion of the ring from ideal symmetry. Ring B adopts a C(5)-envelope conformation, as shown by the parameters $\Delta = 31.3°$ and $\phi_m = 37.8°$.[15] This conformation agrees with that of 3-dehydrogibberellin A₃.[5]

For the di-*p*-bromobenzoate of the methyl ester of gibberellic acid [1] the corresponding values are $\Delta = 15.5°$ and $\phi_m = 39.6°$ indicating that the conformation of ring B is midway between that of a half-chair and an envelope ($\Delta = 0°$ corresponds to half-chair and $\Delta = 36°$ corresponds to envelope conformation, while ϕ_m is the maximum torsion angle attainable for the conformation described by Δ). Ring C has a distorted boat conformation, while the ring conformation of D is intermediate between a half-chair and a C(14)-envelope. The phase angle parameters are $\Delta = 10.5°$ and $\phi_m = 50.0°$. For the di-*p*-bromobenzoate of the methyl ester of gibberellic acid [1] these values are $\Delta = 25.5°$ and $\phi_m = 48.3°$. The lactone ring has a C(5)-envelope conformation, as shown by the torsion angle C(10)–O(10)–C(19)–C(4) = −4.8°. The conformation of the carboxy group is close to synplanar. The torsion angle C(5)–C(6)–C(7)–O(7) is −29.1°. This appears to be a preferred conformation for such a group,[16] as it has been observed in a number of other gibberellins.[6,9]

The bond lengths and angles are normal and correspond to the expected values. Of special interest is the significant shortening of the bond length C(9)–C(10) to 1.500(8) Å compared with the other C(sp³)–C(sp³) bond lengths in the molecule. A similar effect has been observed in the structures of 3-dehydrogibberellin A₃[5], 3-dehydrogibberellin A₃ methyl ester,[9] and in other gibberellin structures. The bond length C(3)–C(4) is lengthened significantly to 1.577(8) Å. It is common in gibberellin structures for C(3) and C(4) to lead to

an sp³ hybridized state. The increase of the angle C(5)–C(4)–C(18) to 115.9° may be caused by the close approach of C(18) to C(7).

The molecular packing arrangement is determined by hydrogen bonds and van der Waals forces. The structure is stabilized by a three-dimensional network of strong hydrogen bonds of the 0–H $\cdots$ O type (Table 2 and Figure 2).

Acknowledgements

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