Acta Crystallographica Section C
**Crystal Structure Communications**
ISSN 0108-2701

# (–)-Gibberic acid: hydrogen-bonding pattern of the monohydrate of a non-racemic tetracyclic δ-keto acid derivative of gibberellin $A_3$

**Hugh W. Thompson and Roger A. Lalancette***

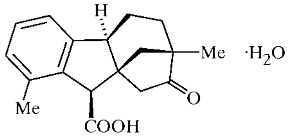
Carl A. Olson Memorial Laboratories, Department of Chemistry, Rutgers University, Newark, NJ 07102, USA
Correspondence e-mail: rogerlal@andromeda.rutgers.edu

Received 13 February 2001
Accepted 9 April 2001

In the the title compound, 1,7-dimethyl-8-oxo-4b$\alpha$,7$\alpha$-gibba-1,3,4a(10a)-triene-10$\beta$-carboxylic acid monohydrate, $C_{18}H_{20}O_3 \cdot H_2O$, the water of hydration accepts a hydrogen bond from the carboxyl and donates hydrogen bonds to the carboxyl carbonyl and the ketone in two different screw-related neighbors, which are mutually translational, yielding a complex three-dimensional hydrogen-bonding array.

## Comment

Our interest in the crystal structures of keto carboxylic acids concerns their five known hydrogen-bonding modes (Coté *et al.*, 1996; Lalancette *et al.*, 1999; Thompson *et al.*, 2001). The dimeric arrangement typical of functionally unelaborated acids is also dominant among keto acids overall. However, intermolecular acid-to-ketone patterns provide a sizable minority of cases and actually predominate when centrosymmetric arrangements are precluded. We report here the structure and hydrogen-bonding pattern of the monohydrate of gibberic acid, (I), a δ-keto acid derived from gibberellic acid (gibberellin $A_3$). The gibberellins are an important family of diterpenoid plant-growth factors first isolated from cultures of the fungus *Gibberella fujikuroi* in the late 1930s (Mander, 1992). The degradation leading to (I) involves separate acid-catalyzed processes which aromatize the *A*-ring by hydrolysis, decarboxylation and dehydration and which rearrange the bridged *C*/*D* ring system (Stork *et al.*, 1965).



(I)

Both the structure (Cross *et al.*, 1961) and stereochemistry (Hartsuck & Lipscomb, 1963; McCapra *et al.*, 1966) of gibberellic acid and of (I) have long been firmly established. Nevertheless, at least two major reference sources provide structures for (I) in which the stereochemistry assigned to C4b is incorrect, showing instead the stereochemistry for epigibberic acid (Buckingham, 1982; Connolly & Hill, 1991).

Fig. 1 shows the asymmetric unit for (I), with its Chemical Abstracts 'gibbane' numbering (Budavari, 1989), which differs from the alternative 'gibberellin' numbering often used (Mander, 1992). The H atoms at C4b and C10, as well as the ketone bridge, all lie on the 'lower' α face of the molecule. The molecule has no conformational flexibility and the only available rotations involve the methyl groups and the carboxyl, which is turned with its C═O in the β direction. The carboxyl is hydrogen bonded to a water of hydration, which in turn donates hydrogen bonds to two different C═O groups in separate neighboring molecules (see below). Fig. 1 shows this water molecule, arbitrarily, in its hydrogen-bonding relationship to the carboxyl OH.

Because the carboxyl is not dimerized but hydrogen bonded to another species, it shows no disorder. Averaging of C—O bond lengths and C—C—O angles by disorder is common in carboxyl dimers (Leiserowitz, 1976), but is not seen in catemers and other hydrogen-bonding arrangements whose geometry cannot support the mechanisms responsible for such averaging. In (I), these carboxyl C—O bond lengths are 1.213 (5) and 1.323 (4) Å, with carboxyl C—C—O angles of 124.7 (4) and 111.1 (4)°. Our own survey of 56 keto acid structures which are not acid dimers gives average values of 1.20 (1) and 1.32 (2) Å, and 124.5 (14) and 112.7 (17)°, for these lengths and angles, in accord with typical values of 1.21 and 1.31 Å, and 123 and 112°, cited for highly ordered dimeric carboxyls (Borthwick, 1980). No rotational disorder was observed for either methyl group.

Fig. 2 illustrates the packing arrangement with its hydrogen bonding, which adheres to a recurrent pattern among hydrated keto acids. The carboxyl donates its hydrogen bond to the water molecule [O···O 2.603 (4) Å], which in turn

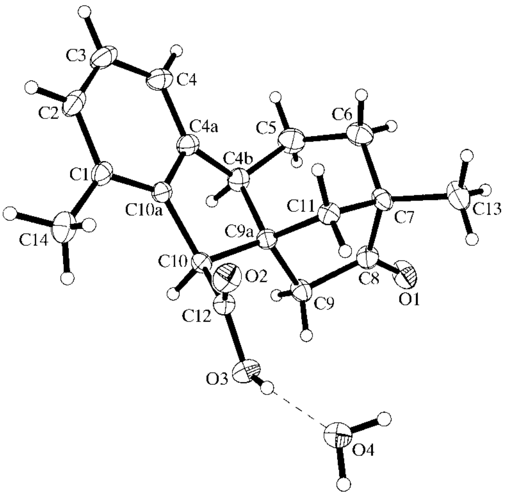


**Figure 1**
The molecular structure of the asymmetric unit of (I), with its gibbane numbering. The water of hydration is shown, arbitrarily, in its hydrogen-bonding relationship to the carboxyl OH group. Displacement ellipsoids are drawn at the 20% probability level and H atoms are shown as small spheres of arbitrary radii.

donates hydrogen bonds to the carbonyls of a ketone [O···O 2.903 (4) Å] and a carboxyl [O···O 2.831 (4) Å] in separate adjacent molecules, in this instance, both screw-related to the first but mutually translational. Thus, each water molecule participates in hydrogen bonds to three separate gibberic acid molecules, while each of the latter participates in hydrogen bonds to three separate water molecules, producing a complex three-dimensional network.

We characterize the geometry of hydrogen bonding to carbonyls using a combination of the H···O═C angle and the H···O═C—*X* torsion angle. These describe the approach of the H atom to the O atom in terms of its deviation from, respectively, C═O axiality (ideal = 120°) and planarity with the carbonyl (ideal = 0°). In (I), these criteria are applicable to two of the three hydrogen bonds present. Approach angles for the water-to-acid hydrogen bond are 135.0 (13) and −35.4 (18)°, and for the water-to-ketone hydrogen bond, 131.8 (13) and −9.3 (17)°. No C—H···O close contacts were found within the 2.7 Å range we usually employ for such non-bonded packing interactions (Steiner, 1997).

The solid-state (KBr) IR spectrum of (I) displays C═O absorptions at 1719 and 1701 cm$^{-1}$ for hydrogen-bonded ketone and carboxyl groups, respectively. In $CHCl_3$ solution, where the ketone is presumably not hydrogen bonded, these bands appear at 1737 and 1711 cm$^{-1}$.

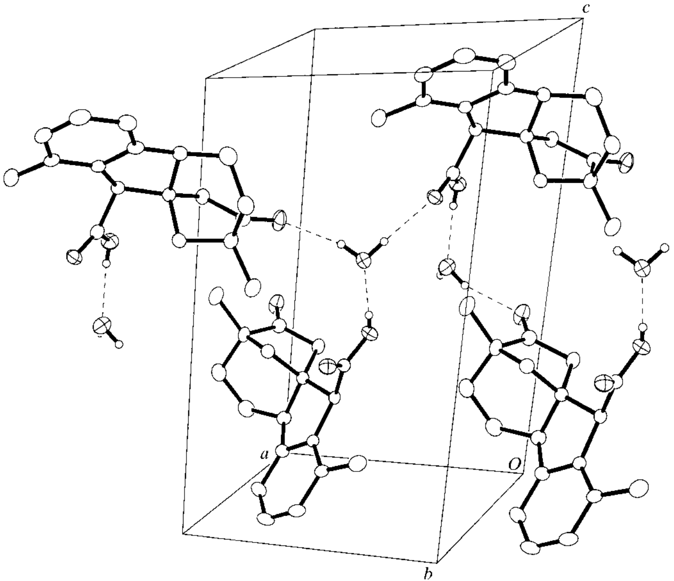


**Figure 2**
A partial packing diagram with extracellular molecules, illustrating the complex three-dimensional hydrogen-bonding arrangement for (I). All carbon-bound H atoms have been removed for clarity, but some peripheral water molecules are shown.

## Experimental

Commercial '90%+ pure' gibberellic acid, obtained from Acros Organics/Fisher Scientific, Springfield, NJ, USA, was treated with refluxing 1.75 *M* HCl as described by Cross (1954). Recrystallization of isolated (I) from formic acid yielded the material used, which loses water below its melting point of 427 K. The higher-melting (*ca* 545 K) anhydrous form gave only microneedles, which were unsuitable for X-ray analysis.

*Crystal data*

$C_{18}H_{20}O_3{\cdot}H_2O$
$M_r = 302.36$
Monoclinic, $P2_1$
$a = 8.841$ (3) Å
$b = 6.283$ (3) Å
$c = 14.646$ (4) Å
$\beta = 103.45$ (2)°
$V = 791.2$ (5) Å$^3$
$Z = 2$
$D_x = 1.269$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 35 reflections
$\theta = 2.3$–14.5°
$\mu = 0.09$ mm$^{-1}$
$T = 293$ (2) K
Parallelepiped, colorless
0.28 × 0.10 × 0.08 mm

*Data collection*

Siemens *P*4 diffractometer
$2\theta/\theta$ scans
Absorption correction: numerical (*SHELXTL*; Sheldrick, 1997)
$T_{\min} = 0.98$, $T_{\max} = 0.99$
3208 measured reflections
1517 independent reflections
1021 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.071$
$\theta_{\max} = 25°$
$h = -10 \rightarrow 10$
$k = -7 \rightarrow 7$
$l = -17 \rightarrow 17$
3 standard reflections every 97 reflections intensity variation: <1.5%

*Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.041$
$wR(F^2) = 0.084$
$S = 1.00$
1517 reflections
208 parameters
H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.0247P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} < 0.001$
$\Delta\rho_{\max} = 0.19$ e Å$^{-3}$
$\Delta\rho_{\min} = -0.13$ e Å$^{-3}$
Extinction correction: *SHELXTL*
Extinction coefficient: 0.041 (4)

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| O2—C12 | 1.213 (5) | O3—C12 | 1.323 (4) |
| O2—C12—C10 | 124.7 (4) | O3—C12—C10 | 111.1 (4) |

**Table 2**
Hydrogen-bonding geometry (Å, °).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O3—H3···O4 | 0.82 | 1.79 | 2.603 (4) | 174 |
| O4—H4*AA*···O2$^{\rm i}$ | 0.84 (5) | 1.99 (5) | 2.831 (4) | 173 (4) |
| O4—H4*BB*···O1$^{\rm ii}$ | 0.85 (4) | 2.08 (4) | 2.903 (4) | 162 (4) |

Symmetry codes: (i) $1 - x, y - \frac{1}{2}, 1 - z$; (ii) $2 - x, \frac{1}{2} + y, 1 - z$.

All H atoms for (I) were found in electron-density difference maps but were placed in calculated positions and allowed to refine as riding models, except for the two H atoms of the water molecule, the positional parameters of which were allowed to refine, but with their isotropic displacement parameters fixed at 0.08 Å$^2$. C—H distances were fixed at 0.93 (phenyl), 0.98 (methine), 0.97 (methylene) or 0.96 Å (methyl), and O—H distances were fixed at 0.82 Å.

Data collection: *XSCANS* (Siemens, 1996); cell refinement: *XSCANS*; data reduction: *XSCANS*; program(s) used to solve structure: *SHELXTL* (Sheldrick, 1997); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FR1327). Services for accessing these data are described at the back of the journal.

## References

Borthwick, P. W. (1980). *Acta Cryst.* B**36**, 628–632.

Buckingham, J. (1982). Editor. *Dictionary of Organic Compounds*, 5th ed., Vol. 3, p. 2746. London: Chapman & Hall.

Budavari, S. (1989). Editor. *The Merck Index*, 11th ed., p. 4313. Rahway, New Jersey: Merck & Co.

Connolly, J. D. & Hill, R. A. (1991). Editors. *Dictionary of Terpenoids*, Vol. 2, p. 977. London: Chapman & Hall.

Coté, M. L., Lalancette, R. A. & Thompson, H. W. (1996). *Acta Cryst.* C**52**, 1535–1537.

Cross, B. E. (1954). *J. Chem. Soc.* pp. 4670–4676.

Cross, B. E., Grove, J. F., McCloskey, P., MacMillan, J., Moffatt, J. S. & Mulholland, T. P. C. (1961). *The Structure of the Fungal Gibberellins*, in *Gibberellins*. ACS Advances in Chemistry Series (No. 28), edited by R. F. Gould. Washington: American Chemical Society.

Hartsuck, J. A. & Lipscomb, W. N. (1963). *J. Am. Chem. Soc.* **85**, 3414–3419.

Lalancette, R. A., Brunskill, A. P. J. & Thompson, H. W. (1999). *Acta Cryst.* C**55**, 568–572.

Leiserowitz, L. (1976). *Acta Cryst.* B**32**, 775–802.

McCapra, F., McPhail, A. T., Scott, A. I., Sim, G. A. & Young, D. W. (1966). *J. Chem. Soc. C*, pp. 1577–1585.

Mander, L. N. (1992). *Chem. Rev.* **92**, 573–612.

Sheldrick, G. M. (1997). *SHELXTL*. Version 5.10. Bruker AXS Inc., Madison, Wisconsin, USA.

Siemens (1996). *XSCANS*. Version 2.2. Siemens Analytical X-ray Instruments Inc., Madison, Wisconsin, USA.

Steiner, T. (1997). *J. Chem. Soc. Chem. Commun.* pp. 727–734.

Stork, G., Malhotra, S., Thompson, H. & Uchibayashi, M. (1965). *J. Am. Chem. Soc.* **87**, 1148–1149.

Thompson, H. W., Lalancette, R. A. & Brunskill, A. P. J. (2001). *Acta Cryst.* C**57**, 632–633.