Acta Crystallographica Section E
Structure Reports Online
ISSN 1600-5368

Butyl gallate dihydrate

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Received 1 March 2002
Accepted 13 March 2002
Online 22 March 2002

Key indicators

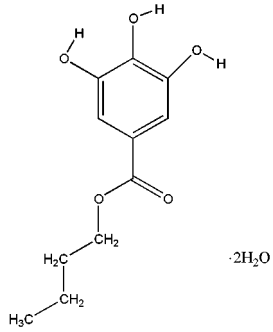
Single-crystal X-ray study
T = 296 K
Mean σ(C–C) = 0.005 Å
R factor = 0.048
wR factor = 0.185
Data-to-parameter ratio = 19.1

For details of how these key indicators were automatically derived from the article, see http://journals.iucr.org/e.

In the crystal structure of the title compound, 3,4,5-trihydroxybenzoic acid *n*-butyl ester dihydrate, $C_{11}H_{14}O_5\cdot 2H_2O$, the molecule is essentially in a planar conformation with a fully extended *trans* zigzag butyl ester group. There are two intramolecular hydrogen bonds between hydroxyl groups. The crystal structure is stabilized by the stacking interactions between gallate head groups, *i.e.* the 3,4,5-trihydroxybenzene part of butyl gallate, the hydrophobic interactions between alkyl groups, and all available intermolecular hydrogen bonds.

Comment

Gallic acid (3,4,5-trihydroxybenzoic acid) is a naturally occurring plant phenol. It shows selective cytotoxicity against tumor cells such as HL-60RG, HeLa, dRLh-84, PLC/PRF/5, and KB cells with higher sensitivity (Sakaguchi *et al.*, 1999; Satoh & Sakagami, 1997; Isuzugawa *et al.*, 2001). Gallic acid and its methyl, propyl, octyl and lauryl esters also act as excellent inhibitors of human spleen protein tyrosine kinases (PTK) (Lázaro *et al.*, 1995; Roy *et al.*, 2000). The more hydrophobic gallic acid esters (octyl and lauryl gallates) showed the highest inhibitory activity, compared to the methyl and propyl gallates. Lázaro *et al.* (1995) have examined the inhibitory activity for mono-, di- and triphenolic compounds and found that it is highest when a third hydroxyl group is introduced into the benzene ring. These results suggest the importance of the amphiphilic character of the gallate esters for their inhibitory action. We intend to investigate the structural features of gallic acid derivatives with amphiphilic characteristics by the introduction of a variety of alkyl groups. To this end we have now determined the structure of the *n*-butyl ester of gallic acid (butyl gallate) as its dihydrate, (I).



(I)

The structures of propyl gallate (Okabe & Kyoyama, 2002), and octyl gallate (Jeffrey & Yeon, 1990) have already been determined. The molecular structure of (I) is essentially

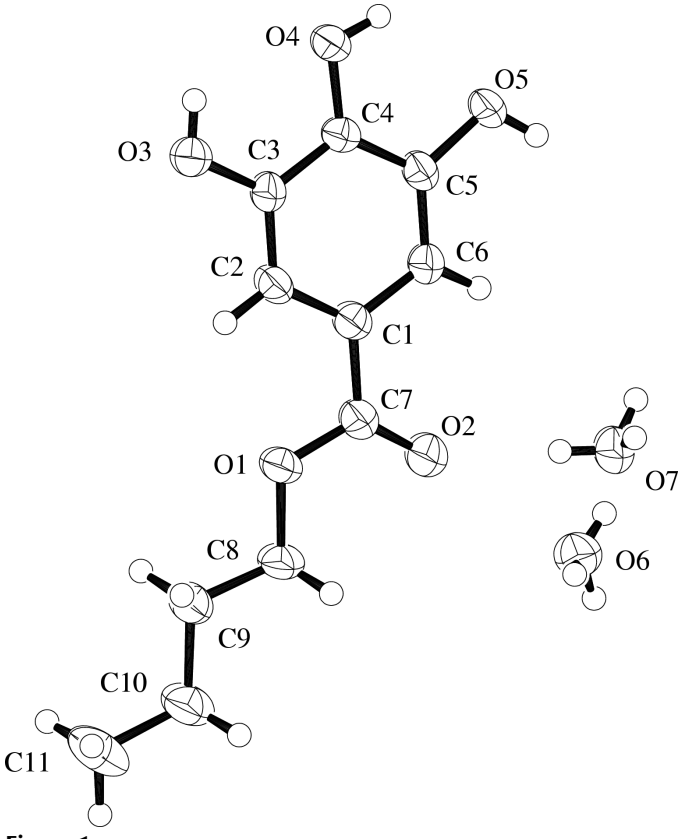


Figure 1
*ORTEP*II (Johnson, 1976) drawing of the title compound, with the atomic numbering scheme. Ellipsoids for non-H atoms are drawn at the 50% probability level.

planar, with a fully extended *trans* zigzag butyl ester group, as shown in Fig. 1. This fully extended planar conformation is also present in the crystal structures of propyl gallate and octyl gallate. Two intramolecular hydrogen bonds exist between a pair of hydroxyl groups at positions 3 and 4, and at positions 4 and 5. Similar intramolecular hydrogen bonds are also present in gallic acid monohydrate (Okabe *et al.*, 2001), propyl gallate (Okabe & Kyoyama, 2002), and octyl gallate (Jeffrey & Yeon, 1990). In the crystal packing, stacking interactions between the gallate head groups, *i.e.* the 3,4,5-trihydroxybenzene part of butyl gallate, and hydrophobic interactions between the alkyl chains are observed (Fig. 2). These modes of interaction resemble those in octyl gallate but are somewhat different from those in propyl gallate. In the case of propyl gallate, the hydrophobic interactions between terminal methyl groups are present, but stacking interactions between the gallate head groups are not. All of the available intra- and intermolecular hydrogen bonds are present, as listed in Table 2. The structural features of gallate esters determined in this and other studies (Jeffrey & Yeon, 1990; Okabe & Kyoyama, 2002) may have an important role in the investigation of their biological activity.

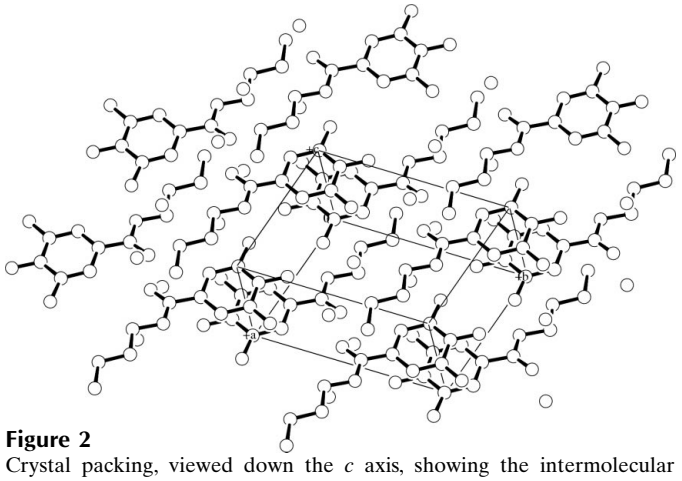


Figure 2
Crystal packing, viewed down the *c* axis, showing the intermolecular interactions.

Experimental

A colorless pillar-like crystal was obtained by slow evaporation from a 10% methanol–water solution.

Crystal data

$C_{11}H_{14}O_5\cdot 2H_2O$
$M_r = 262.25$
Triclinic, $P\overline{1}$
$a = 6.556\ (8)$ Å
$b = 10.02\ (2)$ Å
$c = 11.37\ (2)$ Å
$\alpha = 76.5\ (1)^\circ$
$\beta = 104.1\ (1)^\circ$
$\gamma = 108.2\ (1)^\circ$
$V = 678\ (2)$ Å^3
$Z = 2$
$D_x = 1.285$ Mg m^{-3}
Mo Kα radiation
Cell parameters from 25 reflections
$\theta = 13.9$–15.0°
$\mu = 0.11$ mm^{-1}
$T = 296.2$ K
Pillar, colorless
0.50 × 0.20 × 0.10 mm

Data collection

Rigaku AFC-5*R* diffractometer
ω–2θ scans
Absorption correction: none
3296 measured reflections
3117 independent reflections
1362 reflections with $I > 2\sigma(I)$
$R_{int} = 0.016$
$\theta_{max} = 27.5^\circ$
$h = -8 \rightarrow 8$
$k = 0 \rightarrow 13$
$l = -14 \rightarrow 14$
3 standard reflections
every 150 reflections
intensity decay: 0.2%

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)] = 0.048$
$wR(F^2) = 0.185$
$S = 0.93$
3117 reflections
163 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} = 0.001$
$\Delta\rho_{max} = 0.21$ e Å^{-3}
$\Delta\rho_{min} = -0.28$ e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

O1—C7	1.334 (3)	C1—C7	1.479 (4)
O1—C8	1.455 (4)	C2—C3	1.371 (4)
O2—C7	1.209 (4)	C3—C4	1.395 (4)
O3—C3	1.370 (3)	C4—C5	1.389 (4)
O4—C4	1.358 (4)	C5—C6	1.373 (4)
O5—C5	1.375 (3)	C8—C9	1.500 (4)
C1—C2	1.388 (4)	C9—C10	1.516 (5)
C1—C6	1.395 (4)	C10—C11	1.528 (5)
C7—O1—C8	115.8 (2)	O5—C5—C4	115.8 (3)
C2—C1—C6	120.2 (3)	O5—C5—C6	124.2 (3)
C2—C1—C7	121.6 (2)	C4—C5—C6	119.9 (2)
C6—C1—C7	118.1 (3)	C1—C6—C5	119.7 (3)
C1—C2—C3	120.2 (2)	O1—C7—O2	122.6 (3)
O3—C3—C2	119.8 (2)	O1—C7—C1	113.1 (3)
O3—C3—C4	120.7 (3)	O2—C7—C1	124.3 (2)
C2—C3—C4	119.6 (3)	O1—C8—C9	108.1 (2)
O4—C4—C3	116.9 (2)	C8—C9—C10	111.0 (3)
O4—C4—C5	122.7 (2)	C9—C10—C11	113.1 (3)
C3—C4—C5	120.4 (3)		

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

D—H···A	D—H	H···A	D···A	D—H···A
O3—H3···O4	0.82	2.27	2.707 (5)	114
O4—H4···O5	0.82	2.29	2.724 (5)	113
O3—H3···O7^{i}	0.82	1.97	2.734 (5)	156
O4—H4···O5^{ii}	0.82	2.05	2.736 (4)	142
O5—H5···O6^{iii}	0.82	1.92	2.715 (5)	164
O6—H6*A*···O7^{iv}	0.75	2.06	2.803 (4)	172
O6—H6*B*···O6^{v}	0.86	1.90	2.755 (4)	179
O6—H6*C*···O3^{vi}	0.86	1.95	2.803 (4)	180
O7—H7*A*···O2	0.78	1.96	2.739 (3)	174
O7—H7*B*···O7^{iv}	0.86	1.91	2.768 (5)	180
O7—H7C···O6^{iv}	0.85	1.98	2.803 (4)	163

Symmetry codes: (i) $x, 1+y, z$; (ii) $-1-x, 2-y, 1-z$; (iii) $x-1, y, z$; (iv) $-x, 1-y, 1-z$; (v) $1-x, 1-y, 1-z$; (vi) $1-x, 2-y, 1-z$.

All H atoms were located from difference Fourier maps. With the exception of those in the water molecules, the H atoms were included in the refinement in the riding model approximation. Each water molecule has one ordered and one disordered H atom. Thus O6 is bonded to H6*C* (ordered) and H6*A*, H6*B* (disordered); O7 is bonded to H7*A*(ordered) and H7*B*, H7*C* (disordered). The H atoms of the water molecules were not refined.

Data collection: *MSC/AFC Diffractometer Control Software* (Molecular Structure Corporation and Rigaku Corporation, 1999); cell refinement: *MSC/AFC Diffractometer Control Software*; data reduction: *TEXSAN* (*Molecular Structure Corporation and Rigaku Corporation*, 1999); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997) and *DIRDIF*94 (Beurskens *et al.*, 1994); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*II (Johnson, 1976); software used to prepare material for publication: *TEXSAN*.

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