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(*R**)-Methyl 3-carboxy-2-hydroxypropanoate

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Key indicators

Single-crystal X-ray study
T = 173 K
Mean σ(C–C) = 0.001 Å
R factor = 0.031
wR factor = 0.084
Data-to-parameter ratio = 11.6

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

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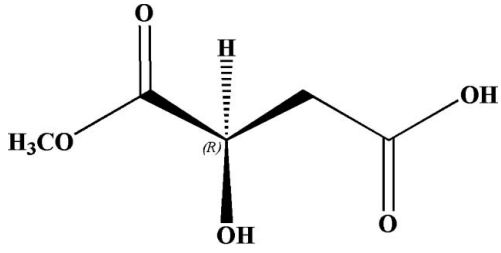
The crystal structure of the title compound, $C_5H_8O_5$, was determined at 173 K. The compound is a monomethyl ester of butanedioic acid and was isolated from fresh cranberries (*Vaccinium macrocarpon*). The crystal structure is stabilized by intermolecular O—H···O hydrogen bonds.

Comment

In continuing our efforts to seek bioactive components from fruits, vegetables and other natural products, bioactivity-guided fractionation of cranberries was used to determine the identity of bioactive compounds from cranberries with anti-cancer activity. The title compound, (I), a 2-hydroxybutanedioic acid 1-methyl ester, was isolated from the active fraction of cranberry extract. The scheme arbitrarily shows the (*R*) absolute configuration, but this could not be determined in this experiment.



(I)

The cranberry (*Vaccinium macrocarpon*), a native fruit in North America, has attracted public attention due to its potential health benefits. In previous studies, we have reported that cranberries contain an abundance of phenolic compounds and possess the highest level of antioxidant activity among the commonly consumed fruits and vegetables tested (Sun *et al.*, 2002; Chu *et al.*, 2002). In addition, cranberries have been reported to prevent both stomach ulcers and bacterial adhesion of *E. coli* in the urinary tract (Howell *et al.*, 1998; Foo *et al.*, 2000; Burger *et al.*, 2000), to exhibit *in vitro* anticancer activity (Sun *et al.*, 2002; Bomser *et al.*, 1996), and to protect against lipoprotein oxidation (Chu & Liu, 2005; Wilson *et al.*, 1998). Cranberries contain a diverse range of phytochemicals. With an attractive bright-red appearance and a distinctive flavour, cranberries are recognized as a concentrated source of dietary flavonoids, including anthocyanins (Zapsalis & Francis, 1965), proanthocyanidins (Foo & Porter, 1980; Hale *et al.*, 1986) and flavonol glycosides (Puski & Francis, 1967), as well as various phenolic acids (Schmid, 1977). Although the fraction of proanthocyanidins in cranberries was reported to be responsible for the prevention of urinary tract infection

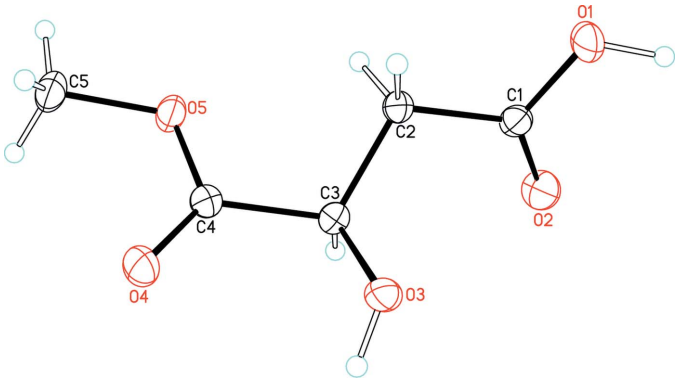


Figure 1
The structure of (I), showing 40% probability displacement ellipsoids. H atoms are shown as spheres of arbitrary size.

(Howell & Betsy, 2002), there is little available research on the bioactive compounds with anticancer activity.

In the structure of the title compound (Fig. 1), there are two pairwise hydrogen-bonding motifs (Table 1) with twofold symmetry. These propagate the structure in the *ac* plane (Fig. 2).

Experimental

Fresh cranberries of Stevens cultivar (1000.0 g) were homogenized with chilled 80% acetone–water (1:2 *w*/*v*) for 5 min using a chilled Waring blender (Sun *et al.*, 2002). Samples were then homogenized further using a Polytron homogenizer for an additional 3 min. The homogenates were filtered and the filtrate was evaporated under vacuum at 318 K until approximately 90% of the filtrate had been evaporated. The residue was then recovered with 500 ml water and extracted with the same volume of ethyl acetate three times, and then with water-saturated *n*-butanol three times, respectively. The butanol fraction (16.06 g) was subjected to silica-gel column chromatography (230–400 mesh, 75 × 200 mm) and eluted with a dichloromethane–methanol–water system. The fraction eluted with dichloromethane–methanol–water in the ratio 80:20:1.5 was further isolated by silica-gel column chromatography (230–400 mesh, 25 × 300 mm) and eluted with dichloromethane–methanol with gradual increase of the ratio of methanol. The title compound (37.3 mg) was obtained from the dichloromethane–methanol elution in the ratio 20:1 (*v*/*v*). Colourless crystals of (I) were obtained from a solution in dichloromethane. Spectroscopic analysis: ^{1}H NMR (400 MHz, DMSO-d_6, δ, p.p.m.): 12.31 (H, *s*), 5.68 (H, *s*), 4.33 (H, *t*, *J* = 6.3 Hz), 3.62 (3H, *s*), 2.62 (H, *dd*, *J* = 15.9 and 5.1 Hz), 2.48 (H, *dd*, *J* = 16.2 and 7.2 Hz); ^{13}C NMR (400 MHz, DMSO-d_6, δ, p.p.m.): 173.4 (C), 171.6 (C), 67.0 (CH), 51.7 (CH_3), 39.1 (CH_2).

Crystal data

$C_5H_8O_5$
M_r = 148.11
Monoclinic, *C*2
a = 22.699 (5) Å
b = 4.1854 (9) Å
c = 6.9782 (15) Å
β = 100.415 (18)°
V = 652.0 (2) Å^3
Z = 4
D_x = 1.509 Mg m^{-3}
Mo *K*α radiation
Cell parameters from 4381 reflections
θ = 3.0–34.3°
μ = 0.14 mm^{-1}
T = 173 (2) K
Block, colourless
0.50 × 0.40 × 0.30 mm

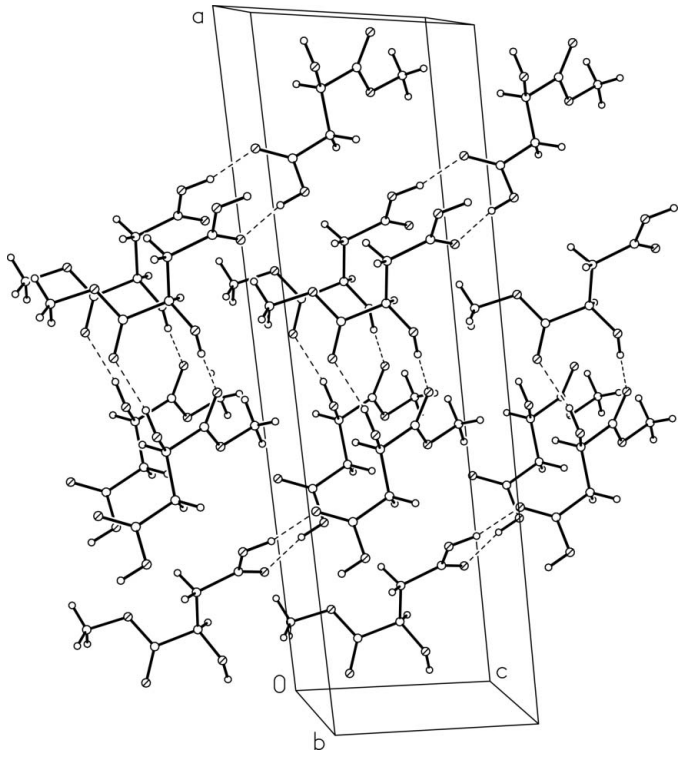


Figure 2
A view, down the *b* axis, of the packing of the structure of (I). Dashed lines indicate hydrogen bonds.

Data collection

Bruker X8 APEX II diffractometer
φ and ω scans
Absorption correction: multi-scan (*SADABS*; Sheldrick, 1996)
T_{min} = 0.934, T_{max} = 0.960
6931 measured reflections
1421 independent reflections
1323 reflections with $I > 2\sigma(I)$
R_{int} = 0.052
θ_{max} = 34.3°
h = −34 → 36
k = −6 → 5
l = −11 → 11

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.031
$wR(F^2)$ = 0.084
S = 1.09
1421 reflections
123 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.0589P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.013
$\Delta\rho_{max}$ = 0.24 e Å^{-3}
$\Delta\rho_{min}$ = −0.19 e Å^{-3}

Table 1
Hydrogen-bond geometry (Å, °).

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O1—H1···O2^{i}	0.94 (2)	1.73 (2)	2.6527 (11)	168 (2)
O3—H3···O4^{ii}	0.86 (2)	1.92 (2)	2.7663 (11)	167 (2)

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

In the absence of significant anomalous scattering, Friedel pairs have been merged and the absolute configuration has been assigned arbitrarily; it is unknown.

Data collection: *APEX2* (Bruker, 2004); cell refinement: *SAINT-Plus* (Bruker, 2003); data reduction: *SAINT-Plus*; program(s) used to solve structure: *SHELXTL* (Bruker, 1999); program(s) used to refine structure: *SHELXTL*; molecular graphics: *SHELXTL*; software used to prepare material for publication: *SHELXTL*.

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