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3-(4-Dihydroxyborylphenyl)cyclobutanone

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Key indicators

Single-crystal X-ray study
T = 294 K
Mean σ(C–C) = 0.002 Å
R factor = 0.034
wR factor = 0.102
Data-to-parameter ratio = 11.2

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

The title compound, $C_{10}H_{11}BO_3$, may be developed as a potent boron neutron capture therapy (BNCT) drug for hepatoma treatment. The compound was obtained as transparent rectangular plate crystals. Intermolecular hydrogen bonds and π–π interactions help stabilize the crystal structure.

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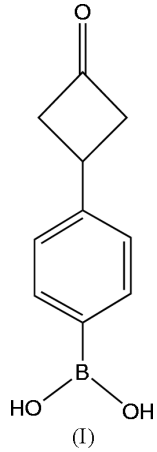
Comment

Hepatoma is one of the most prevalent malignant tumors occurring in Taiwan. Because the symptoms of hepatoma are not obvious and most patients would incur cirrhosis at the same time, it is difficult to treat hepatoma by surgical resection. Hepatoma treatment is also not very effective by means of chemical therapy or radiation therapy; boron neutron capture therapy (BNCT) has been recently considered as an alternative useful method for treating hepatoma (Aris *et al.*, 2004). The title compound, (I), has recently been developed in our laboratory as a potent BNCT agent for hepatoma treatment (Lo *et al.*, 2003). The compound has been successfully synthesized and grown as crystals. The crystal structure is reported here.



(I)

There exist two strong [O1—H1O···O2($2-x, -y, -z$) and O2—H2O···O1($2-x, \frac{1}{2}+y, \frac{1}{2}-z$)] hydrogen bonds and one weak [C10—H10*B*···O3($x, -\frac{1}{2}-y, z-\frac{1}{2}$)] hydrogen bond, with bond lengths (and angles) of 2.834 (3) Å [166 (2)°], 3.039 (4) Å [160 (3)°] and 3.447 (4) Å [166 (3)°], respectively. In addition to the intermolecular hydrogen bonds, the crystal packing involves intermolecular π–π interactions, mainly between cyclobutanone rings, ($1-x, -y, -z$), with a distance of 4.267 (4) Å, between benzene rings, ($-x, -y, 1-z$), with a distance of 4.770 (4) Å, and between the benzene ring and the cyclobutanone ring at ($1-x, -y, 1-z$), with a distance of 4.874 (4) Å. The benzene ring has a maximum deviation of

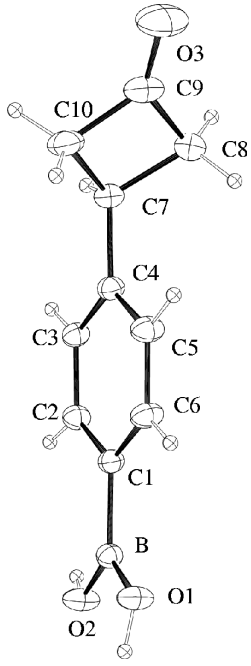


Figure 1
The molecular structure of the title compound, showing 30% probability displacement ellipsoids.

0.0047 (10) Å from its least-squares plane. The maximum deviation from the mean plane of the four-membered cyclobutanone ring is 0.0423 (9) Å. The benzene ring is almost perpendicular [86.71 (7)°] to the cyclobutanone ring and is coplanar [7.43 (9)°] with the plane formed by atoms C1, O1 and O2.

The B—C1 distance of 1.558 (2) Å is in good agreement with comparable phenylboronic acids where values range from 1.526 Å in *p*-bromophenylboronic acid (Zvonkova & Gluskova, 1958) to 1.597 Å in 6-bis(trifluoromethyl)phenyldihydroxyborane (Cornet *et al.*, 2003). B—O1 [1.364 (2) Å] and B—O2 [1.371 (2) Å] lie at the upper end of the corresponding range, viz. 1.323 Å in (*O,O′*)-[hydroxy[4-(dihydroxyboryl)phenyl]boron] bis(dimethylglyoximato)aquamethylcobalt trihydrate (Dreos *et al.*, 2003) to 1.376 Å in L-*p*-boronophenylalanine (Shull *et al.*, 2000). The situation is different in cyclo-tris[bis(pentafluorophenyl)borinic acid] (Beringhelli *et al.*, 2003), where steric crowding by the six pentafluorophenyl ligands results in much longer B—O distances, ranging from 1.519 to 1.535 Å.

Experimental

The precursor for synthesizing the title compound, 3-(4-boronophenyl)cyclobutanone ethylene ketal, was obtained by a previously reported process (Fu, 2002; Srivastava *et al.*, 1999). A 100 ml round-bottomed flask was charged with 3-(4-dihydroxyborylphenyl)cyclobutanone ethylene ketal (5.8 mmol, 1.36 g) in methanol (14 ml), along with concentrated hydrochloric acid (10 drops). The contents of the flask were stirred overnight at room temperature, and then the solvent was removed under reduced pressure by a rotary evaporator. The residue was dissolved in diethyl ether and washed with water and then brine. The organic layer was collected and dried over anhydrous magnesium sulfate and concentrated under reduced pressure. The product was purified using silica gel chromatography (20 × 2 cm, 20 and 40% ethyl acetate in hexane) to obtain the final product as a white solid (0.46 g, 33.8% yield): *Rf* = 0.46 (50% ethyl acetate in hexane, silica gel TLC). For recrystallization, the white solid was dissolved in diethyl ether to form a near saturated solution, which was filtered through a filter paper. The resulting clear filtrate was poured into a glass column bottle, covered with a filter paper and kept in a refrigerator at 268 K for 24 h, allowing the solvent to evaporate gradually. With the remaining 3 ml of solution, the bottle was moved from the refrigerator and kept at room temperature to expedite the evaporation. Rectangular crystals formed after some time and suitable crystals were harvested for X-ray structure analysis. M.p. 367–371 K. ^{1}H NMR ($CDCl_3$): δ 7.71 (*d*, *J* = 7.3 Hz, 2H), 7.32 (*d*, *J* = 7.3 Hz, 2H), 3.64 (*m*, 1H), 3.47 (*m*, 2H), 3.22 (*m*, 2H). ^{13}C NMR ($CDCl_3$): δ 206.38, 148.13, 135.64, 126.24, 54.43, 28.56.

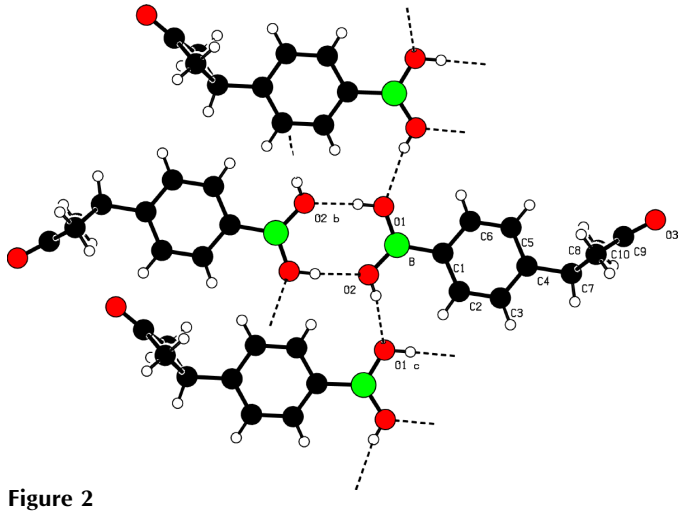


Figure 2
The two-dimensional hydrogen-bonding network (dashed lines) of the title compound.

Crystal data

$C_{10}H_{11}BO_3$	D_x = 1.353 Mg m^{-3}
M_r = 190.00	Mo $K\alpha$ radiation
Monoclinic, $P2_1/c$	Cell parameters from 5680 reflections
a = 11.4645 (11) Å	θ = 2.0–28.0°
b = 9.8317 (9) Å	μ = 0.10 mm^{-1}
c = 8.3674 (8) Å	T = 294 (2) K
β = 98.551 (2)°	Rectangular plate, colourless
V = 932.65 (15) Å^3	0.15 × 0.10 × 0.05 mm
Z = 4	

Data collection

Bruker SMART CCD area-detector diffractometer	1915 independent reflections
φ and ω scans	1198 reflections with $I > 2\sigma(I)$
Absorption correction: multi-scan (*SHELXTL*; Bruker, 2000)	R_{int} = 0.076
T_{min} = 0.927, T_{max} = 0.993	θ_{max} = 26.4°
5481 measured reflections	$h = -14 \rightarrow 12$
	$k = -11 \rightarrow 12$
	$l = -10 \rightarrow 10$

Refinement

Refinement on F^2	All H-atom parameters refined
$R[F^2 > 2\sigma(F^2)]$ = 0.034	$w = 1/[\sigma^2(F_o^2)(0.1P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$wR(F^2)$ = 0.102	$(\Delta/\sigma)_{max} < 0.001$
S = 0.96	$\Delta\rho_{max}$ = 0.15 e Å^{-3}
1915 reflections	$\Delta\rho_{min}$ = −0.13 e Å^{-3}
171 parameters	

Table 1
Selected geometric parameters (Å, °).

O1—B	1.364 (2)	O3—C9	1.200 (2)
O2—B	1.371 (2)	C1—B	1.558 (2)
C2—C1—B	122.9 (1)	O1—B—O2	117.1 (1)
C6—C1—B	120.8 (1)	O1—B—C1	119.1 (1)
O3—C9—C10	134.0 (2)	O2—B—C1	123.8 (1)
O3—C9—C8	132.8 (2)		

H atoms were located in a difference Fourier synthesis and refined isotropically [C—H = 0.924 (17)–1.009 (19) Å].

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 2000); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1997); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *ORTEP*-3 *for Windows* (Farrugia, 1997); software used to prepare material for publication: *SHELXL*97.

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