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Methyl 2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-nitrobenzoate

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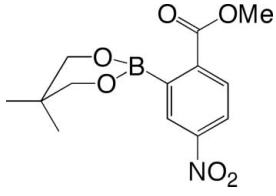
Key indicators: single-crystal X-ray study; T = 150 K; mean σ(C–C) = 0.002 Å; R factor = 0.044; wR factor = 0.114; data-to-parameter ratio = 17.3.

The six-membered boronate ester ring of the title compound, $C_{13}H_{16}BNO_6$, adopts an envelope conformation with the C atom bearing the dimethyl substituents at the flap. The O—B—C—C torsion angles between the boronate group and the benzene ring are 72.5 (2) and 81.0 (2)°. The 4-nitrobenzoate unit adopts a slightly twisted conformation, with dihedral angles between the benzene ring and the nitrate and methyl ester groups of 17.5 (2) and 14.4 (3)°, respectively. In the crystal, inversion-related pairs of molecules show weak π–π stacking interactions [centroid–centroid distance = 4.0585 (9) Å and interplanar spacing = 3.6254 (7) Å].

Related literature

For use of boronic acids as synthetic intermediates, see: Hall (2005); for their use as sensors in the alcoholic beverage industry, see: Wiskur & Anslyn (2001) and as saccharide sensors, see: Baxter *et al.* (1990); Fedorak *et al.* (1989); Yamamoto *et al.* (1990); Yasuda *et al.* (1990). For a review on borolectins, see: Yang *et al.* (2002, 2004). For the utilization of boronic acids as enzyme inhibitors, see: Adams *et al.* (1998); Fevig *et al.* (1996); Johnson & Houston (2002); Kettner *et al.* (1990); Prusoff *et al.* (1993). For the synthesis of aromatic *ortho*-substituted boronate esters, see: Baudoin *et al.* (2000); Fang *et al.* (2005); Ishiyama *et al.* (2010); Wang *et al.* (2006).



Experimental

Crystal data

$C_{13}H_{16}BNO_6$
M_r = 293.08
Monoclinic, $P2_1/n$
a = 12.1774 (3) Å
b = 9.7928 (3) Å
c = 13.4921 (4) Å
β = 115.4764 (12)°
V = 1452.49 (7) Å^3
Z = 4
Mo $K\alpha$ radiation
μ = 0.11 mm^{-1}
T = 150 K
0.25 × 0.20 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
Absorption correction: multi-scan (*DENZO/SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.92, T_{max} = 0.98
16148 measured reflections
3286 independent reflections
2229 reflections with $I > 2\sigma(I)$
R_{int} = 0.043

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.114
S = 0.92
3286 reflections
190 parameters
H-atom parameters constrained
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.39 e Å^{-3}

Data collection: *COLLECT* (Nonius, 2001); cell refinement: *DENZO/SCALEPACK* (Otwinowski & Minor, 1997); data reduction: *DENZO/SCALEPACK*; program(s) used to solve structure: *SIR92* (Altomare *et al.*, 1994); program(s) used to refine structure: *CRYSTALS* (Betteridge *et al.*, 2003); molecular graphics: *CAMERON* (Watkin *et al.*, 1996); software used to prepare material for publication: *CRYSTALS* and *PLATON* (Spek, 2009).

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Supplementary data and figures for this paper are available from the IUCr electronic archives (Reference: PK2392).

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Methyl 2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-nitrobenzoate

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S1. Comment

Boronic acids constitute an important class of synthetic intermediates (Hall, 2005). However, they have found wider applications more recently as sensors of 'gallate-like′ compounds in the alcoholic beverage industry (Wiskur & Anslyn, 2001), in the development of saccharide sensors (*in vivo* at neutral pH in aqueous environment) (Baxter *et al.*, 1990; Fedorak *et al.*, 1989; Yamamoto *et al.*, 1990; Yasuda *et al.*, 1990), boronolectins (Yang *et al.*, 2002, 2004), as protease (Fevig *et al.*, 1996; Kettner *et al.*, 1990; Prusoff *et al.*, 1993), glycosidase (Johnson & Houston, 2002) and proteasome inhibitors (Adams *et al.*, 1998).

The synthesis of *ortho*-substituted aromatic esters becomes increasingly difficult as the aromatic ring becomes more substituted (Baudoin *et al.*, 2000; Fang *et al.*, 2005; Ishiyama *et al.*, 2010; Wang *et al.*, 2006). New strategies have recently been developed to circumvent the synthetic obstacles preventing these borylations (Baudoin *et al.*, 2000; Fang *et al.*, 2005; Ishiyama *et al.*, 2010; Wang *et al.*, 2006). Here we report the first successful synthesis and X-ray crystallographic analysis of boronate ester intermediate **2**, which is substituted at the *ortho* and *meta* positions by a methyl ester and a nitro group with respect to the boronate ester moiety (Fig. 1).

X-ray crystallography confirmed the structure of the title compound. The six-membered boronate ester ring adopts an envelope type conformation with C3 out of the plane (Fig. 1, 2). The torsion angles between the boronate and the aromatic ring system are 72.5 (2)° and 81.0 (2)°. The 4-nitrobenzoate moiety adopts a slightly twisted conformation with dihedral angles between the benzene ring and the nitrate and methyl ester groups of 17.5 (2)° and 14.4 (3)° respectively. Inversion-related pairs of molecules show π-stacking interactions: Centroid-centroid distance: 4.0585 (9) Å, interplanar spacing: 3.6254 (7) Å. There are no classical hydrogen bonds.

S2. Experimental

The bromo-nitroester starting material **1** undergoes borylation by stirring with bis(neopentyl glycolato)diboron (1.2 eq.) in the presence of [1,1-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (10 mol%), DMSO and potassium acetate (2.5 eq.) for 22 h at 60°C to afford the corresponding boronate ester **2** in 51% yield (Fig. 3). This reaction worked up to a half gram scale. The purification of the boronate ester **2** was difficult because the bis(neopentyl glycolato)diboron reagent, which was used in excess, proved difficult to completely remove *via* a variety of purification techniques (crystallizations using a range of solvent mixtures and temperatures, flash column chromatography using a range of neutral, acidic and basic solvent mixtures). Methyl 2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-nitrobenzoate **2** was isolated as a pale yellow oil which crystallized on standing: m.p. 345–353 K (DCM; it underwent a phase transition over the range 345–351 K, then melted at 351–353 K).

S3. Refinement

The H atoms were all located in a difference map, but those attached to carbon atoms were repositioned geometrically. The H atoms were initially refined with soft restraints on the bond lengths and angles to regularize their geometry (C—H in the range 0.93–0.98) and U_{iso}(H) (in the range 1.2–1.5 times U_{eq} of the parent atom), after which the positions were refined with riding constraints.

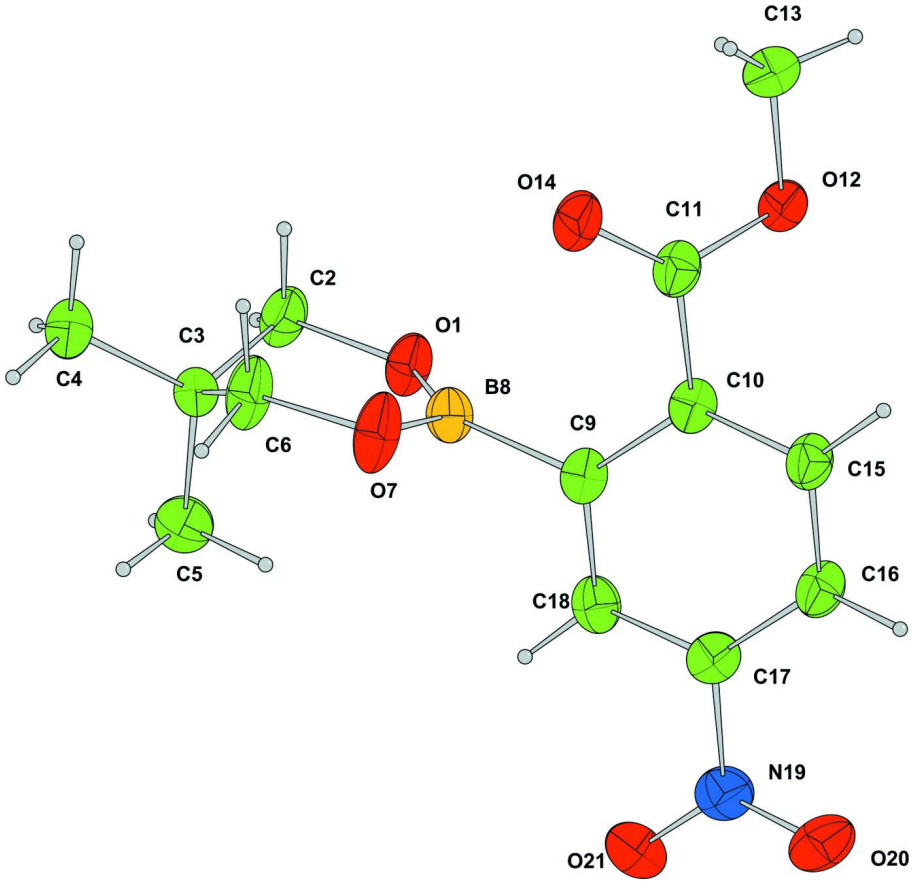

Figure 1

The title compound with displacement ellipsoids drawn at the 50% probability level. Hydrogen atoms are shown as spheres of arbitary radius.

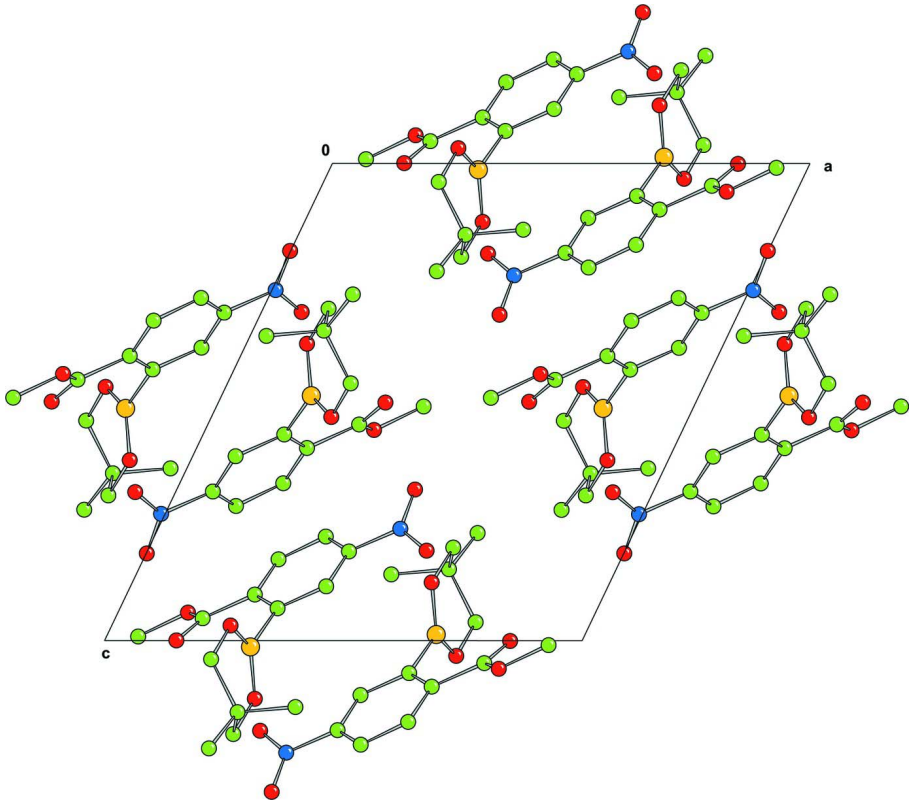

Figure 2

Packing diagram of the title compound projected along the *b*-axis.

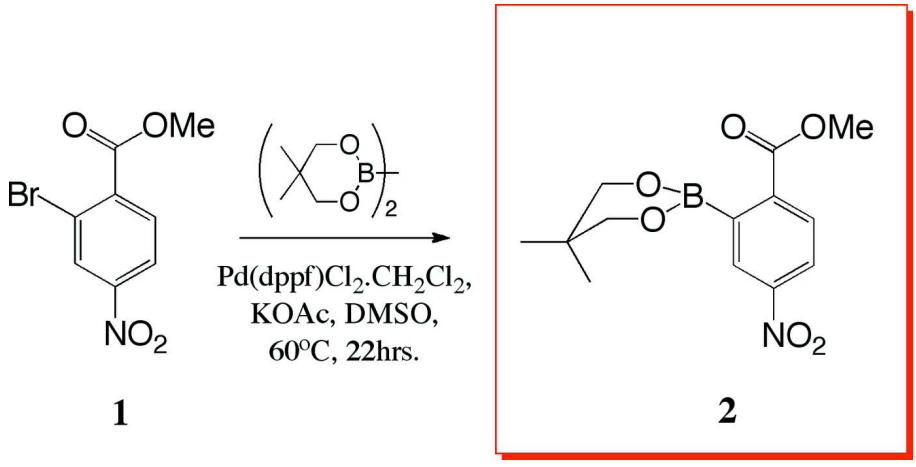

Figure 3

Synthesis of sterically hindered boronate ester **2** from the aryl bromide **1**.

Methyl 2-(5,5-dimethyl-1,3,2-dioxaborinan-2-yl)-4-nitrobenzoate

Crystal data

$C_{13}H_{16}BNO_6$
$M_r = 293.08$
Monoclinic, $P2_1/n$
Hall symbol: -P 2yn
$a = 12.1774$ (3) Å
$b = 9.7928$ (3) Å

c = 13.4921 (4) Å
β = 115.4764 (12)°
V = 1452.49 (7) Å^3
Z = 4
F(000) = 616
D_x = 1.340 Mg m^{-3}
Mo $K\alpha$ radiation, λ = 0.71073 Å

Cell parameters from 3373 reflections
θ = 5–27°
μ = 0.11 mm^{-1}
T = 150 K
Plate, colourless
0.25 × 0.20 × 0.15 mm

Data collection

Nonius KappaCCD diffractometer
Graphite monochromator
ω scans
Absorption correction: multi-scan (*DENZO*/*SCALEPACK*; Otwinowski & Minor, 1997)
T_{min} = 0.92, T_{max} = 0.98

16148 measured reflections
3286 independent reflections
2229 reflections with $I > 2\sigma(I)$
R_{int} = 0.043
θ_{max} = 27.5°, θ_{min} = 5.1°
h = −15→15
k = −12→12
l = −17→17

Refinement

Refinement on F^2
Least-squares matrix: full
$R[F^2 > 2\sigma(F^2)]$ = 0.044
$wR(F^2)$ = 0.114
S = 0.92
3286 reflections
190 parameters
0 restraints
Primary atom site location: structure-invariant direct methods

Hydrogen site location: inferred from neighbouring sites
H-atom parameters constrained
Method = Modified Sheldrick $w = 1/[\sigma^2(F^2) + (0.05P)^2 + 0.66P]$, where $P = (\max(F_o^2,0) + 2F_c^2)/3$
$(\Delta/\sigma)_{max}$ = 0.0002
$\Delta\rho_{max}$ = 0.36 e Å^{-3}
$\Delta\rho_{min}$ = −0.39 e Å^{-3}

Fractional atomic coordinates and isotropic or equivalent isotropic displacement parameters (Å²)

	x	*y*	*z*	U_{iso}*/U_{eq}
O1	0.12715 (11)	0.67634 (11)	0.37794 (9)	0.0363
C2	0.13726 (17)	0.77688 (17)	0.30436 (13)	0.0384
C3	0.14982 (15)	0.91980 (17)	0.35044 (13)	0.0325
C4	0.17357 (18)	1.01872 (19)	0.27425 (15)	0.0443
C5	0.0341 (2)	0.9608 (2)	0.3611 (2)	0.0649
C6	0.25847 (18)	0.91925 (19)	0.46109 (14)	0.0457
O7	0.25147 (12)	0.81218 (13)	0.53161 (9)	0.0474
B8	0.18826 (16)	0.69741 (19)	0.48684 (14)	0.0305
C9	0.17022 (14)	0.59224 (16)	0.56803 (12)	0.0295
C10	0.23148 (13)	0.46714 (17)	0.59640 (12)	0.0301
C11	0.31710 (14)	0.43635 (17)	0.54680 (13)	0.0329
O12	0.35352 (10)	0.30678 (12)	0.55875 (10)	0.0380
C13	0.43385 (17)	0.2710 (2)	0.50882 (15)	0.0444
O14	0.34969 (12)	0.52155 (13)	0.50062 (11)	0.0502
C15	0.21684 (14)	0.37785 (18)	0.67027 (13)	0.0344
C16	0.14051 (14)	0.41192 (18)	0.71801 (13)	0.0345
C17	0.07746 (14)	0.53350 (17)	0.68739 (12)	0.0312
C18	0.09013 (14)	0.62350 (17)	0.61390 (13)	0.0325
N19	−0.00773 (13)	0.56838 (15)	0.73455 (12)	0.0385

O20	0.00100 (11)	0.50649 (14)	0.81687 (10)	0.0451
O21	−0.08423 (13)	0.65719 (14)	0.68873 (13)	0.0569
H22	0.2125	0.7563	0.2935	0.0495*
H21	0.0629	0.7702	0.2345	0.0499*
H42	0.1825	1.1106	0.3051	0.0710*
H41	0.2498	0.9921	0.2680	0.0704*
H43	0.1034	1.0155	0.2010	0.0710*
H52	0.0436	1.0553	0.3874	0.1049*
H53	0.0229	0.8990	0.4128	0.1046*
H51	−0.0345	0.9535	0.2899	0.1051*
H62	0.2630	1.0067	0.4988	0.0527*
H61	0.3341	0.9062	0.4495	0.0531*
H132	0.4574	0.1757	0.5267	0.0723*
H131	0.5044	0.3321	0.5356	0.0723*
H133	0.3879	0.2814	0.4298	0.0724*
H151	0.2617	0.2923	0.6890	0.0415*
H161	0.1301	0.3524	0.7695	0.0400*
H181	0.0457	0.7074	0.5971	0.0378*

Atomic displacement parameters (Å²)

	U^{11}	U^{22}	U^{33}	U^{12}	U^{13}	U^{23}
O1	0.0496 (7)	0.0290 (6)	0.0286 (6)	−0.0096 (5)	0.0151 (5)	0.0004 (5)
C2	0.0548 (10)	0.0329 (9)	0.0298 (8)	−0.0059 (8)	0.0204 (8)	0.0027 (7)
C3	0.0400 (9)	0.0271 (8)	0.0358 (8)	0.0050 (7)	0.0212 (7)	0.0057 (7)
C4	0.0591 (11)	0.0335 (10)	0.0478 (10)	0.0048 (9)	0.0300 (9)	0.0102 (8)
C5	0.0695 (14)	0.0599 (14)	0.0888 (16)	0.0288 (12)	0.0564 (13)	0.0306 (12)
C6	0.0613 (12)	0.0318 (10)	0.0396 (10)	−0.0140 (9)	0.0175 (9)	0.0046 (8)
O7	0.0626 (8)	0.0362 (7)	0.0305 (6)	−0.0196 (6)	0.0078 (6)	0.0041 (5)
B8	0.0313 (9)	0.0274 (10)	0.0290 (9)	−0.0022 (7)	0.0093 (7)	0.0010 (7)
C9	0.0295 (8)	0.0292 (9)	0.0251 (7)	−0.0046 (7)	0.0072 (6)	0.0005 (6)
C10	0.0266 (7)	0.0323 (9)	0.0272 (8)	−0.0035 (7)	0.0077 (6)	0.0025 (7)
C11	0.0292 (8)	0.0347 (10)	0.0317 (8)	−0.0009 (7)	0.0103 (7)	0.0068 (7)
O12	0.0403 (6)	0.0366 (7)	0.0451 (7)	0.0044 (5)	0.0260 (5)	0.0098 (5)
C13	0.0498 (10)	0.0436 (11)	0.0531 (11)	0.0030 (9)	0.0348 (9)	0.0049 (9)
O14	0.0525 (8)	0.0402 (8)	0.0727 (9)	0.0043 (6)	0.0408 (7)	0.0197 (7)
C15	0.0308 (8)	0.0362 (10)	0.0345 (9)	0.0029 (7)	0.0124 (7)	0.0107 (7)
C16	0.0341 (8)	0.0385 (10)	0.0293 (8)	−0.0012 (7)	0.0120 (7)	0.0070 (7)
C17	0.0310 (8)	0.0345 (9)	0.0262 (8)	−0.0051 (7)	0.0104 (6)	−0.0046 (7)
C18	0.0345 (8)	0.0268 (9)	0.0308 (8)	−0.0030 (7)	0.0091 (7)	−0.0018 (7)
N19	0.0441 (8)	0.0347 (8)	0.0399 (8)	−0.0064 (7)	0.0211 (7)	−0.0089 (7)
O20	0.0517 (7)	0.0552 (8)	0.0336 (6)	−0.0089 (6)	0.0233 (6)	−0.0066 (6)
O21	0.0658 (9)	0.0415 (8)	0.0790 (10)	0.0151 (7)	0.0459 (8)	0.0069 (7)

Geometric parameters (Å, º)

O1—C2	1.4406 (18)	C9—C10	1.399 (2)
O1—B8	1.347 (2)	C9—C18	1.395 (2)

C2—C3	1.512 (2)	C10—C11	1.492 (2)
C2—H22	1.009	C10—C15	1.394 (2)
C2—H21	0.989	C11—O12	1.331 (2)
C3—C4	1.528 (2)	C11—O14	1.2061 (19)
C3—C5	1.531 (2)	O12—C13	1.4492 (19)
C3—C6	1.510 (2)	C13—H132	0.976
C4—H42	0.977	C13—H131	0.979
C4—H41	1.002	C13—H133	0.974
C4—H43	0.990	C15—C16	1.380 (2)
C5—H52	0.980	C15—H151	0.972
C5—H53	0.977	C16—C17	1.380 (2)
C5—H51	0.967	C16—H161	0.956
C6—O7	1.443 (2)	C17—C18	1.384 (2)
C6—H62	0.986	C17—N19	1.471 (2)
C6—H61	1.006	C18—H181	0.955
O7—B8	1.349 (2)	N19—O20	1.2291 (18)
B8—C9	1.586 (2)	N19—O21	1.2292 (19)

C2—O1—B8	118.43 (13)	O7—B8—C9	116.97 (14)
O1—C2—C3	111.88 (13)	O1—B8—C9	118.56 (14)
O1—C2—H22	108.4	B8—C9—C10	122.79 (14)
C3—C2—H22	107.9	B8—C9—C18	119.65 (14)
O1—C2—H21	107.3	C10—C9—C18	117.56 (14)
C3—C2—H21	110.0	C9—C10—C11	116.57 (14)
H22—C2—H21	111.4	C9—C10—C15	121.85 (15)
C2—C3—C4	108.97 (13)	C11—C10—C15	121.53 (15)
C2—C3—C5	110.29 (16)	C10—C11—O12	113.52 (13)
C4—C3—C5	110.20 (15)	C10—C11—O14	122.73 (16)
C2—C3—C6	107.08 (14)	O12—C11—O14	123.75 (15)
C4—C3—C6	109.18 (14)	C11—O12—C13	115.50 (13)
C5—C3—C6	111.04 (16)	O12—C13—H132	107.6
C3—C4—H42	108.4	O12—C13—H131	110.0
C3—C4—H41	110.0	H132—C13—H131	112.0
H42—C4—H41	109.7	O12—C13—H133	107.4
C3—C4—H43	108.6	H132—C13—H133	109.9
H42—C4—H43	110.1	H131—C13—H133	109.8
H41—C4—H43	110.0	C10—C15—C16	120.07 (15)
C3—C5—H52	108.1	C10—C15—H151	119.8
C3—C5—H53	108.7	C16—C15—H151	120.2
H52—C5—H53	110.9	C15—C16—C17	117.93 (15)
C3—C5—H51	108.9	C15—C16—H161	121.2
H52—C5—H51	110.2	C17—C16—H161	120.9
H53—C5—H51	109.8	C16—C17—C18	123.00 (15)
C3—C6—O7	112.30 (14)	C16—C17—N19	118.41 (14)
C3—C6—H62	109.8	C18—C17—N19	118.59 (15)
O7—C6—H62	107.3	C9—C18—C17	119.52 (15)
C3—C6—H61	108.5	C9—C18—H181	121.0
O7—C6—H61	109.1	C17—C18—H181	119.4

H62—C6—H61	109.8	C17—N19—O20	118.24 (14)
C6—O7—B8	119.62 (13)	C17—N19—O21	118.01 (14)
O7—B8—O1	123.85 (15)	O20—N19—O21	123.75 (15)

Hydrogen-bond geometry (Å, º)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C4—H42···O21^{i}	0.98	2.59	3.460 (3)	149
C13—H132···O20^{ii}	0.98	2.56	3.356 (3)	139
C13—H131···O14^{iii}	0.98	2.49	3.373 (3)	150
C16—H161···O7^{ii}	0.96	2.47	3.205 (3)	134

Symmetry codes: (i) −*x*, −*y*+2, −*z*+1; (ii) −*x*+1/2, *y*−1/2, −*z*+3/2; (iii) −*x*+1, −*y*+1, −*z*+1.