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N-[(Benzylcarbamoyl)(phenyl)methyl]-*N*-[3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl]benzamide

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Key indicators

Single-crystal X-ray study
T = 198 K
Mean σ(C–C) = 0.003 Å
R factor = 0.057
wR factor = 0.164
Data-to-parameter ratio = 12.6

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

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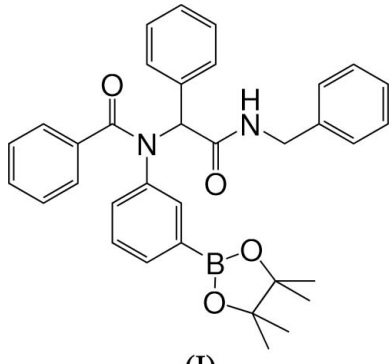
The title compound, $C_{34}H_{35}BN_2O_4$, was readily synthesized *via* an Ugi four-component reaction (U-4CR) by condensation of benzoic acid, benzaldehyde, benzyl isocyanide and an aniline derivative containing a boronate ester group. No significant intra- or intermolecular interactions are observed between the amide groups and the Lewis acidic B atom.

Comment

Velcade (also known as PS-341 and Bortezomib) is a dipeptide boron compound developed specifically for the treatment of human tumors (Adams, 2002; Kamat *et al.*, 2005). Preclinical studies have shown that Velcade inhibits proliferation at a mean IC_{50} of 7 n*M* in 60 cell lines included in the National Cancer Institute's panel. Velcade is the most potent compound tested in this screen to date. The maximum tolerated dose of this compound (1 mg kg^{-1}) inhibits the growth of several human xenografts in nude mice (Teicher *et al.*, 1999). As a result, much research effort has been focused on this boron-containing compound for its potential anticancer properties. We have begun a systematic study generating novel Velcade derivatives using the multicomponent Ugi reaction. The title compound, (I), was synthesized by the addition of 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine to benzoic acid, benzaldehyde and benzyl isocyanide.



(I)

The molecular structure of (I) confirms the formation of this novel velcade derivative and is shown in Fig. 1. The bond lengths and angles in (I) are comparable with those reported for related Ugi structures (Ebert *et al.*, 1998). Likewise, the B—O bond distances of (I) (Table 1) are typical for those observed in other Bpin structures (HBpin = pinacolborane), where the B is three-coordinate (Hawkeswood & Stephan, 2005).

No appreciable intra- or intermolecular interactions between the Lewis acidic B atom and the amide groups are

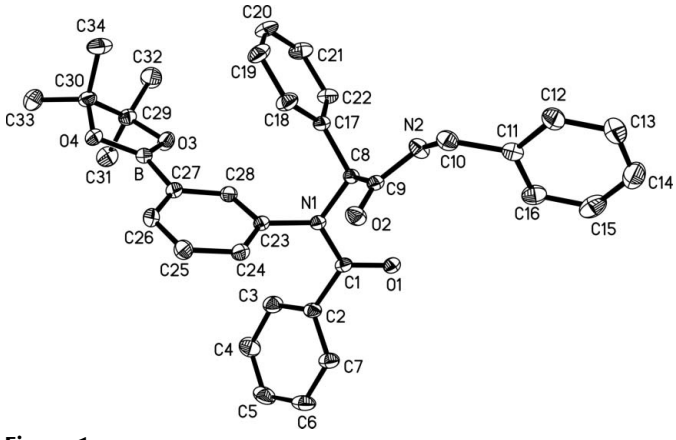


Figure 1
A view of the molecular structure, with displacement ellipsoids drawn at the 30% probability level. H atoms have been omitted for clarity.

observed in the solid-state structure of (I). Such interactions may be responsible for the observed antimicrobial properties of related diaminoboron compounds (Irving *et al.*, 2003). Centrosymmetric dimers are formed through N—H···O hydrogen bonds, with O···H distances of 2.22 (2) Å (Table 2). The 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl group is roughly coplanar with the adjacent aromatic ring [the angle between arene ring C23–C28 and the C27/B/O3/O4 plane is 15.16 (5)°] , as expected if dative bonding occurs between the π system of the arene ring and the empty *p*-orbital on the B atom.

Experimental

All chemicals were purchased from Aldrich and used without further purification. 3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)benzenamine (175 mg, 0.8 mmol), benzaldehyde (86 mg, 0.7 mmol) and benzoic acid (98 mg, 0.8 mmol) were added together in MeOH (3 ml) with a catalytic amount of LiBr (7 mg, 10 mol%). Benzyl isocyanide (80 mg, 0.7 mmol) was added after 20 min and the reaction mixture was stirred for 10 h. The solvent was removed under a vacuum and an oil was obtained. Diethyl ether (2 ml) was added to the mixture, whereupon a white precipitate was collected by suction filtration. Crystals of (I) suitable for X-ray diffraction analysis were obtained by recrystallization from a diethyl ether solution at 278 K (yield 207 mg, 54%; m.p. 485–487 K).

Crystal data

$C_{34}H_{35}BN_2O_4$
M_r = 546.45
Triclinic, $P\overline{1}$
a = 11.439 (2) Å
b = 11.648 (2) Å
c = 12.055 (2) Å
α = 74.377 (4)°
β = 82.844 (3)°
γ = 75.982 (3)°
V = 1497.8 (4) Å^3
Z = 2
D_x = 1.212 Mg m^{-3}
Mo $K\alpha$ radiation
μ = 0.08 mm^{-1}
T = 198 (1) K
Plate, colorless
0.50 × 0.23 × 0.08 mm

Data collection

Bruker AXS SMART1000/P4 CCD area-detector diffractometer
φ and ω scans
Absorption correction: none
10043 measured reflections
6445 independent reflections
4461 reflections with $I > 2\sigma(I)$
R_{int} = 0.029
θ_{max} = 27.5°

Refinement

Refinement on F^2
$R[F^2 > 2\sigma(F^2)]$ = 0.057
$wR(F^2)$ = 0.165
S = 0.99
6445 reflections
510 parameters
All H-atom parameters refined
$w = 1/[\sigma^2(F_o^2) + (0.1093P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{max} < 0.001$
$\Delta\rho_{max}$ = 0.41 e Å^{-3}
$\Delta\rho_{min}$ = −0.25 e Å^{-3}

Table 1
Selected geometric parameters (Å, °).

B—O3	1.360 (2)	B—C27	1.557 (3)
B—O4	1.373 (2)		
O3—B—O4	113.73 (16)	O4—B—C27	124.74 (17)
O3—B—C27	121.52 (16)		

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

D—H···A	D—H	H···A	D···A	D—H···A
N2—H2···O1^{i}	0.86 (2)	2.22 (2)	3.023 (2)	156 (2)

Symmetry code: (i) $-x+1, -y+2, -z+2$.

The crystal was a multiple twin and the orientation matrix of the major component was determined using *SMART* (Bruker, 1999). H atoms were found in Fourier difference maps and refined using isotropic U. N—H = 0.86 (2) Å and C—H bond distances range from 0.89 (3) to 1.05 (3) Å

Data collection: *SMART* (Bruker, 1999); cell refinement: *SAINT* (Bruker, 2003; data reduction: *SAINT*; program(s) used to solve structure: *SHELXS97* (Sheldrick, 1997); program(s) used to refine structure: *SHELXL97* (Sheldrick, 1997); molecular graphics: *SHELXTL* (Sheldrick, 2000); software used to prepare material for publication: *SHELXTL*.

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