Reaction of Hydantoin with Boronic Acids

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We have examined the reaction of hydantoin (= imidazolidine-2,4-dione) with (formylphenyl)boronic acids, where the addition of a boronic acid group is hoped to increase bioactivities. Addition of (2-formylphenyl)boronic acid to hydantoin gave an unexpected azaborine compound, which presumably arises by initial formation of the (phenylmethylidene)hydantoin, with subsequent loss of H_2O to give the cyclized product. Reactions of (3-formylphenyl)- and (4-formylphenyl)boronic acids with hydantoin gave the corresponding [(*Z*)-phenylmethylidene]hydantoins in good-to-excellent yields. Attempts to use (3-formylthiophen-2-yl)boronic acid gave a product where the boronic acid group has been cleaved.

Introduction. – There has been recent considerable interest in compounds containing boronic acids, $HB(OH)_2$, or boronate esters, $HB(OR)_2$, as synthons in the *Suzuki–Miyaura* cross-coupling reaction [1] and as molecular sensors [2]. These remarkable compounds are also being examined for their potential biological activities [3]. For instance, α-aminoboronic acid derivatives are well-known for their ability to act as serine protease inhibitors. Indeed, bortezomib (aka PS-341 and Velcade; *Fig. 1*) is a boronic acid dipeptide that potently, selectively, and reversibly inhibits 26S proteasome and was developed specifically for the therapy of human tumors [4]. Studies at the *National Cancer Institute* have shown that bortezomib inhibited proliferation at a mean IC_{50} value of 7 nM in 60 cell lines. B-Containing amino acid derivatives have also been investigated for their use in boron neutron capture therapy for the treatment of cancer [5]. Unfortunately, the preparation of amino acids containing boron is somewhat limited due to the sensitive nature and incompatibility of the *Lewis*-acidic boronic acid group with many synthetic methods. In an elegant study, *Kabalka* and co-workers reported the hydroboration of hydantoin derivatives as a precursor to amino acids (*Scheme 1*) [6].

Hydantoins (= imidazolidine-2,4-diones), a class of cyclic imides, are an interesting family of compounds with potent pharmacological properties, including antitumor,

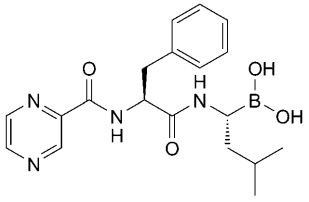
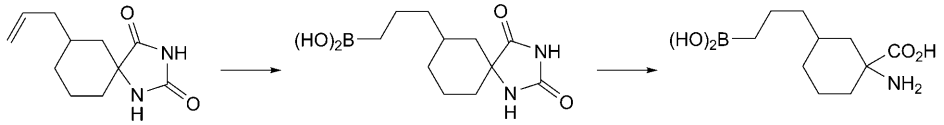


Fig. 1. *Bortezomib*

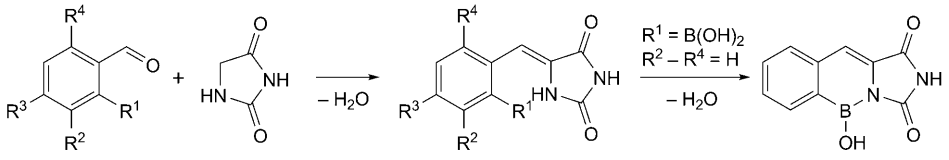
Scheme 1



fungicidal, herbicidal, anti-inflammatory, anti-HIV, and antihypertensive activities [7][8]. A number of (phenylmethylidene)hydantoins, prepared by the base-catalyzed condensation of hydantoins with substituted benzaldehydes, possess good anticonvulsant activity and are being examined as a potential treatment for epilepsy [8] as well as prostate cancer [9]. As part of our ongoing investigation into preparing novel antifungal boron compounds [10], and considering the bioactivities found in hydantoins, we decided to examine the reactions of hydantoin with B-containing (formylphenyl)boronic acids, where the addition of a boronic acid group is expected to increase bioactivities.

Results and Discussion. – Reactions were conducted in H_2O using a catalytic amount of Et_3N [11], and all new compounds have been prepared in good-to-excellent yields and characterized by a number of physical methods including multinuclear NMR spectroscopy. Interestingly, we have found that addition of (2-formylphenyl)boronic acid to hydantoin gave the unexpected fused azaborine **1**. Compound **1** presumably arises by initial formation of the (phenylmethylidene)hydantoin, with subsequent loss of H_2O to give the cyclized product (*Scheme 2*). Related diazaborines are remarkable compounds that display potent activity against a number of *Gram*-negative bacteria as well as malaria [12]. A broad peak at around 30 ppm in the ^{11}B-NMR spectra for **1** suggests that the B-atom lies in a three-coordinate environment in solution [13]. These results were confirmed by a single-crystal X-ray diffraction study (*Fig. 2* and *Table 1*). The bond distances of B(4)–N(3A) 1.435(4) Å, B(4)–O(3) 1.366(4) Å, and B(4)–C(4A) 1.546(4) Å are typical for those observed in related structures where the B-atom is three-coordinate [14] (*Table 2*).

Scheme 2



	R^1	R^2	R^3	R^4
2	H	$B(OH)_2$	H	H
3	H	$B(OH)_2$	H	MeO
4	H	H	$B(OH)_2$	H
5	H	H	$B(OH)_2$	F

1

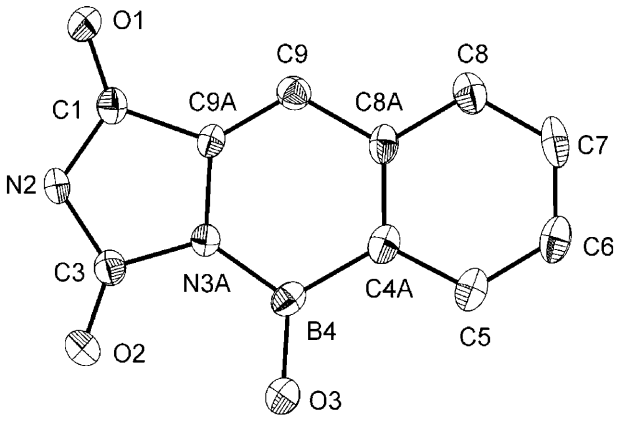


Fig. 2. *ORTEP Plot of* **1** *with H-atoms omitted for clarity* (50% probability ellipsoids)

Table 1. *Crystallographic Data-Collection Parameters*

Complex	**1**	**2**
Formula	$C_{10}H_7BN_2O_3$	$C_{10}H_9BN_2O_4 \cdot Me_2SO$
Molecular weight	213.99	310.13
Crystal system	monoclinic	triclinic
Space group	$P2(1)/c$	$P\bar{1}$
a [Å]	7.218(6)	8.7386(12)
b [Å]	19.423(15)	8.9309(12)
c [Å]	6.787(5)	9.3512(13)
α [°]	90	83.920(2)
β [°]	106.098(11)	79.177(2)
γ [°]	90	83.418(2)
V [Å^3]	914.1(12)	709.43(17)
Z	4	2
$\rho_{calc.}$ [mg m^{-3}]	1.555	1.452
Crystal size [mm^3]	$0.40 \times 0.10 \times 0.025$	$0.40 \times 0.20 \times 0.13$
Temp. [K]	173(1)	173(1)
Radiation	MoK_α ($\lambda = 0.71073$)	MoK_α ($\lambda = 0.71073$)
μ [mm^{-1}]	0.115	0.250
Total reflections	3512	4831
Total unique reflections	3512	3072
No. of variables	147	250
θ Range [°]	2.10 to 27.50	2.23 to 27.49
Largest difference peak/hole [e Å^{-3}]	0.315/ − 0.305	0.403/ − 0.227
S (GoF) on F^2	1.026	1.068
$R1$[a]) ($I > 2\sigma(I)$)	0.0633	0.0326
$wR2$[b]) (all data)	0.1844	0.0928

[a]) $R1 = \Sigma \,||F_o| - |F_c||\,/\Sigma\,|F_o|$. [b]) $wR2 = (\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[wF_o^4])^{1/2}$, where $w = 1/[\sigma^2(F_o^2) + (0.0912 \cdot P)^2]$ (**1**) and $1/[\sigma^2(F_o^2) + (0.0459 \cdot P)^2 + (0.2821 \cdot P)]$ (**2**), where $P = (\max(F_o^2, 0) + 2 \cdot F_c^2)/3$.

Reactions of (3-formylphenyl)- and (4-formylphenyl)boronic acids with hydantoin gave the corresponding (phenylmethylidene)hydantoins **2**–**5** in good-to-excellent

Table 2. *Intramolecular Bond Distances and Bond Angles in Molecule* **1**

Bond distance [Å]		Bond angle [°]	
C(1)–O(1)	1.218(3)	O(1)–C(1)–N(2)	126.8(2)
C(1)–N(2)	1.372(3)	O(1)–C(1)–C(9A)	128.4(2)
C(1)–C(9A)	1.484(4)	N(2)–C(1)–C(9A)	104.7(2)
N(2)–C(3)	1.384(3)	C(1)–N(2)–C(3)	112.7(2)
C(3)–O(2)	1.213(3)	O(2)–C(3)–N(2)	128.6(2)
C(3)–N(3A)	1.404(3)	O(2)–C(3)–N(3A)	124.9(2)
N(3A)–C(9A)	1.400(3)	N(2)–C(3)–N(3A)	106.5(2)
N(3A)–B(4)	1.435(4)	C(9A)–N(3A)–C(3)	109.5(2)
B(4)–O(3)	1.366(4)	C(9A)–N(3A)–B(4)	122.2(2)
B(4)–C(4A)	1.546(4)	C(3)–N(3A)–B(4)	128.3(2)
C(8A)–C(9)	1.465(4)	O(3)–B(4)–N(3A)	121.9(3)
C(9)–C(9A)	1.349(3)	O(3)–B(4)–C(4A)	122.8(2)
		N(3A)–B(4)–C(4A)	115.3(3)
		C(5)–C(4A)–C(8A)	118.2(2)
		C(5)–C(4A)–B(4)	122.8(3)
		C(8A)–C(4A)–B(4)	119.1(2)

yields (*Scheme 2*). Although geometric isomers ((*E*)- and (*Z*)-isomers) are possible due to restricted rotation about the exocyclic C=C bond, the ^{1}H-NMR spectra for **2**–**5** showed the diagnostic alkene peak at δ 6.39–6.66 ppm, suggesting that these complexes are in the (*Z*)-form [15]. The H-atoms in the (*Z*)-form are deshielded with respect to their (*E*)-isomers (observed at δ 6.20–6.30 ppm) owing to the anisotropic effect exerted by the nearby C=O group. Of interest is the observation that the IR spectra for **2**–**5** shows the stretching of the C=C bond appearing between 1666–1637 cm^{-1}, compared to those expected for the (*E*)-isomers, which appear at somewhat lower frequencies (1640–1630 cm^{-1}). To confirm the formation of (*Z*)-derivatives of hydantoin in these reactions, we carried out an X-ray study on **2** (*Table 1*), and the molecular diagram of the expected (*Z*)-isomer is shown in *Fig. 3*.

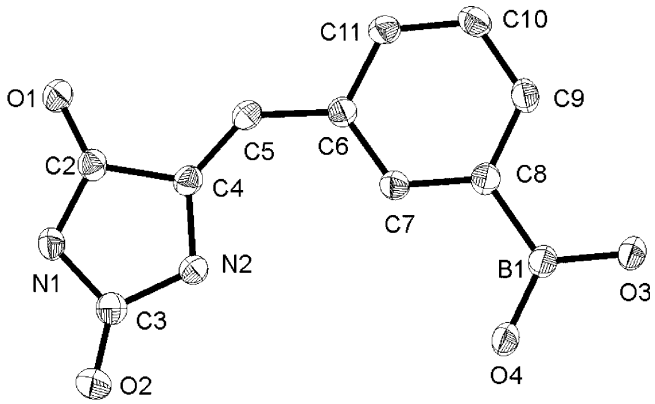


Fig. 3. *ORTEP Plot of* **2** *with H-atoms and the molecule of DMSO omitted for clarity* (50% probability ellipsoids)

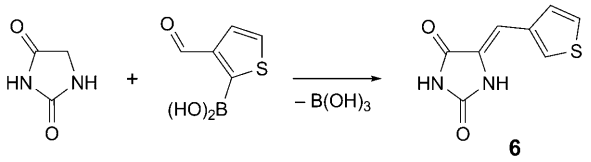
Bond distances and angles are consistent with those in related systems [16] (*Table 3*). The molecules form chains *via* H-bonding between adjacent boronic acid groups [17], and the OH and NH bonds of the hydantoin groups. These chains are further linked by H-bonding with the DMSO solvent molecules.

Table 3. *Intramolecular Bond Distances and Bond Angles in Molecule* **2**

Bond distance [Å]		Bond angle [°]	
B(1)–O(3)	1.356(2)	O(3)–B(1)–O(4)	119.29(14)
B(1)–O(4)	1.366(2)	O(3)–B(1)–C(8)	118.22(13)
B(1)–C(8)	1.577(2)	O(4)–B(1)–C(8)	122.45(13)
N(1)–C(2)	1.3620(19)	C(2)–N(1)–C(3)	111.65(12)
N(1)–C(3)	1.3933(19)	C(3)–N(2)–C(4)	111.12(12)
N(2)–C(3)	1.3745(19)	O(1)–C(2)–N(1)	127.05(14)
N(2)–C(4)	1.3951(18)	O(1)–C(2)–C(4)	127.20(13)
O(1)–C(2)	1.2249(18)	N(1)–C(2)–C(4)	105.75(12)
O(2)–C(3)	1.2120(18)	O(2)–C(3)–N(2)	127.28(14)
C(4)–C(5)	1.341(2)	O(2)–C(3)–N(1)	126.24(14)
C(5)–C(6)	1.459(2)	N(2)–C(3)–N(1)	106.49(12)
		C(5)–C(4)–N(2)	134.22(14)
		C(5)–C(4)–C(2)	120.83(13)
		N(2)–C(4)–C(2)	104.94(12)
		C(4)–C(5)–C(6)	132.15(13)

Attempts to use (3-formylthiophen-2-yl)boronic acid did not lead to the expected B-containing hydantoin, but to compound **6**, where the boronic acid group has been cleaved during the course of the reaction (*Scheme 3*). Although it is unclear at this time what causes this unusual reactivity, thiophene analogues of diazaborinines are known to decompose rapidly in air [14]. Reactions of other (formylthiophenyl)boronic acid also lead to deboronated products.

Scheme 3



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In conclusion, we have presented a convenient route to B(OH)-containing hydantoin derivatives which are valuable precursors to phenylalanines, amino acids that are well-known as interesting compounds in cancer research. Further work from our group will examine the biological activity of these unusual compounds, and the results will be published in due course.

Thanks are gratefully extended to the *Canada Research Chairs Program*, *Canadian Foundation for Innovation-Atlantic Innovation Fund*, *Merck Frosst Canada & Co.*, and Mount Allison University for financial support. We also thank *Roger Smith* and *Dan Durant* for expert technical assistance and anonymous reviewers for very helpful comments.

Experimental Part

General. Reagents and solvents used were obtained from *Aldrich Chemicals.* M.p.: *Mel-Temp* apparatus; uncorrected. IR Spectra: *Mattson Genesis II* FT-IR spectrometer; reported in cm^{-1}. NMR Spectra: *JEOL JNM-GSX270 FT* spectrometer; ^{1}H-NMR chemical shifts are reported in ppm and referenced to residual solvent H-atoms in deuterated solvent at 270 MHz; ^{11}B-NMR chemical shifts are reported in ppm and are referenced to $BF_3 \cdot OEt_2$ as an external standard at 87 MHz; ^{13}C-NMR chemical shifts are reported in ppm and referenced to solvent C-atom resonances as internal standards at 68 MHz; and ^{19}F-NMR chemical shifts are reported in ppm and are referenced to CF_3CO_2H as an external standard at 254 MHz; ov. = overlapping. Microanalyses for C, H, and N: *Vario EL III*.

General Procedure. Hydantoin (= imidazolidine-2,4-dione) was dissolved in hot H_2O, and the pH was adjusted to 7 by the addition of $NaHCO_3$. An EtOH soln. of the appropriate boronic acid (1:1 molar ratio) and a catalytic amount of Et_3N (1 mol-%) were added, and the soln. was heated at reflux for 72 h. Upon cooling to r.t., a white precipitate formed and was collected by suction filtration to afford the desired product.

*5-Hydroxyimidazo[1,5-*b*][2,1]benzazaborine-1,3(2*H*,5*H*)-dione* (**1**). Yield: 93%. M.p. 344–347° (dec.). IR (nujol): 3744, 3459, 3201, 2928, 2854, 2724, 2359, 2335, 1828, 1771, 1708, 1645, 1542, 1449, 1340, 1226, 1180, 1088, 1052, 1027, 993, 959, 893, 830, 774, 703, 663, 564. ^{1}H-NMR ((D$_6$)DMSO): 11.70 (br. *s*, NH); 9.05 (br. *s*, BOH); 8.20 (*d*, *J* = 7.4, 1 arom. H); 7.78 (*d*, *J* = 7.4, 1 arom. H); 7.66 (ov. *dd*, *J* = 7.4, 1 arom. H); 7.51 (ov. *dd*, *J* = 7.4, 1 arom. H); 7.13 (*s*, C=CH). ^{11}B-NMR (THF): 29. ^{13}C{^{1}H}-NMR ((D$_6$)DMSO): 164.8; 156.7; 140.4; 133.8; 132.6; 130.6; 130.2; 130 (br., C–B); 128.7; 110.2. Anal. calc. for $C_{10}H_7BN_2O_3$ (214.00): C 56.12, H 3.30, N 13.09; found: C 56.43, H 3.42, N 12.91.

*3-[(*Z*)-(2,5-Dioxoimidazolidin-4-ylidene)methyl]phenylboronic Acid* (**2**). Yield: 85%. M.p. 302–305° (dec.). IR (nujol): 3334, 3246, 3180, 3062, 2929, 2913, 2858, 2359, 2335, 1764, 1724, 1660, 1597, 1423, 1396, 1352, 1265, 1205, 1066, 1024, 871, 790, 685, 651. ^{1}H-NMR ((D$_6$)DMSO): 11.30 (br. *s*, NH); 10.39 (br. *s*, NH); 8.19 (*s*, B(OH)$_2$); 7.86 (*s*, 1 arom. H); 7.70 (*d*, *J* = 7.7, 1 arom. H); 7.61 (*d*, *J* = 7.7, 1 arom. H); 7.36 (*t*-like, *J* = 7.7, 1 arom. H); 6.39 (*s*, C=CH). ^{11}B-NMR (THF): 26. ^{13}C{^{1}H}-NMR ((D$_6$)DMSO): 166.2, 156.4, 135.5 (br., C–B), 134.9, 134.5, 132.7, 132.2, 128.8, 128.3, 109.2. Anal. calc. for $C_{10}H_9BN_2O_4$ (232.02): C 51.76, H 3.92, N 12.08; found: C 51.43, H 4.15, N 12.22.

*4-Methoxy-3-[(*Z*)-(2,5-dioxoimidazolidin-4-ylidene)methyl]phenylboronic Acid* (**3**). Yield: 85%. M.p. 264–266° (dec.). IR (nujol): 3405, 3231, 3135, 3069, 2925, 2753, 2357, 2334, 1752, 1713, 1666, 1560, 1503, 1400, 1338, 1251, 1191, 1144, 1098, 1023, 875, 740, 711, 652, 597. ^{1}H-NMR ((D$_6$)DMSO): 10.23 (br. *s*, NH); 8.07 (br. *s*, B(OH)$_2$); 7.79 (*s*, 1 arom. H); 7.72 (*d*, *J* = 8.2, 1 arom. H); 7.03 (*d*, *J* = 8.2, 1 arom. H); 6.66 (*s*, C=CH); 3.85 (*s*, MeO). ^{11}B-NMR (THF): 27. ^{13}C{^{1}H}-NMR ((D$_6$)DMSO): 166.2; 159.5; 156.3; 137.3; 134.7; 128.2; 126 (br., C–B); 121.6; 111.2; 103.4; 56.3. Anal. calc. for $C_{11}H_{11}BN_2O_5$ (262.05): C 50.41, H 4.24, N 10.69; found: C 50.65, H 4.03, N 11.02.

*4-[(*Z*)-(2,5-Dioxoimidazolidin-4-ylidene)methyl]phenylboronic Acid* (**4**). Yield: 85%. M.p. 282–285° (dec.). IR (nujol): 3459, 3155, 2943, 2906, 2860, 2724, 2360, 2341, 1711, 1637, 1462, 1377, 1194, 1103, 1022, 877, 844, 764. ^{1}H-NMR ((D$_6$)DMSO): 11.29 (br. *s*, NH); 10.58 (br. *s*, NH); 8.15 (*s*, B(OH)$_2$); 7.80 (*d*, *J* = 7.4, 2 arom. H); 7.56 (*d*, *J* = 7.4, 2 arom. H); 6.39 (*s*, C=CH). ^{11}B-NMR (THF): 28. ^{13}C{^{1}H}-NMR ((D$_6$)DMSO): 166.2; 156.3; 135.2 (br., C–B); 135.1; 135.0; 129.0; 128.9; 109.0. Anal. calc. for $C_{10}H_9BN_2O_4$ (232.02): C 51.76, H 3.92, N 12.08; found: C 52.03, H 4.23, N 11.89.

*3-Fluoro-4-[(*Z*)-(2,5-dioxoimidazolidin-4-ylidene)methyl]phenylboronic Acid* (**5**). Yield: 92%. M.p. 300–302° (dec.). IR (nujol): 3732, 3563, 3461, 3275, 3173, 3056, 2978, 2930, 2854, 2728, 2360, 2342, 1765, 1714, 1657, 1633, 1556, 1508, 1429, 1370, 1305, 1249, 1154, 1105, 1054, 1019, 898, 819, 766, 676, 595. ^{1}H-NMR ((D$_6$)DMSO): 11.38 (br. *s*, NH); 10.64 (br. *s*, NH); 8.32 (*s*, B(OH)$_2$); 7.71–7.54 (ov. *m*, 3 arom. H); 6.42 (*s*, C=CH). ^{11}B-NMR (THF): 28. ^{13}C{^{1}H}-NMR ((D$_6$)DMSO): 165.8; 160.1 (*d*, *J*(C,F) = 246, C–F); 156.1; 137.9 (br., C–B); 130.8 (*d*, *J*(C,F) = 3, Ar); 130.5; 129.3; 122.8 (*d*, *J*(C,F) = 12, Ar); 120.7 (*d*, *J*(C,F) = 19, Ar); 99.4 (*d*, *J*(C,F) = 6, Ar). ^{19}F-NMR ((D$_6$)DMSO): –118.0. Anal. calc. for $C_{10}H_8BFN_2O_4$ (250.01): C 48.04, H 3.23, N 11.21; found: C 48.42, H 3.47, N 11.37.

*5-[(*Z*)-(Thiophen-3-yl)methylidene]imidazolidine-2,4-dione* (**6**). Yield: 64%. M.p. 260–263° (dec.). IR (nujol): 3732, 3524, 3455, 3280, 3108, 3014, 2750, 2358, 2050, 1737, 1711, 1658, 1519, 1395, 1351, 1246, 1220, 1172, 1101, 1025, 947, 894, 866, 830, 780, 695, 656, 633, 598. ^{1}H-NMR ((D$_6$)DMSO): 7.94 (*s*, 1 arom.

H); 7.58 (*d*, *J* = 5.2, 1 arom. H); 7.47 (*d*, *J* = 5.2, 1 arom. H); 6.46 (*s*, C=CH). $^{13}C\{^1H\}$-NMR ((D$_6$)DMSO): 166.4, 156.2, 134.9, 129.1, 127.5, 127.4, 127.3, 103.9. Anal. calc. for $C_8H_6N_2O_2S$ (194.23): C 49.47, H 3.12, N 14.43; found: C 50.13, H 3.36, N 14.22.

X-Ray Crystallography. Crystals of **1** and **2** were grown from sat. aq. and DMSO solns., resp., at r.t. Single crystals were coated with *Paratone-N* oil, mounted using a *Cryo*-loop (crystals of **1**) or a polyimide MicroMount (crystals of **2**), and frozen in the cold stream of the goniometer. A hemisphere of data were collected on a *Bruker AXS P4/SMART 1000* diffractometer using ω and θ scans with a scan width of 0.3° and 40-s exposure times. The detector distance was 5 cm. The data were reduced [18] and corrected for absorption. The structures were solved by direct methods and refined by full-matrix least squares on F^2. All non-H-atoms were refined anisotropically. The H-atoms were included in calculated positions and refined using a riding model. Crystallographic information has also been deposited with the *Cambridge Crystallographic Data Centre* (CCDC-747582 and -747610). Copies of the data can be obtained free of charge *via* www.ccdc.cam.ac.uk/conts/retrieving.html (or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB21EZ, UK; fax: +44 1223 336033; or deposit@ccdc.cam.ac.uk).

REFERENCES

[1] N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; S. Kotha, K. Lahiri, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633.

[2] S. Gamsey, A. Miller, M. M. Olmstead, C. M. Beavers, L. C. Hirayama, S. Pradhan, R. A. Wessling, B. Singaram, *J. Am. Chem. Soc.* **2007**, *129*, 1278; S. Goeb, R. Ziessel, *Org. Lett.* **2007**, *9*, 737; J. Yoshino, N. Kano, T. Kawashima, *Chem. Commun.* **2007**, 559; J. Ugolotti, S. Hellstrom, G. J. P. Britovsek, T. S. Jones, P. Hunt, A. J. P. White, *Dalton Trans.* **2007**, 1425; Y. Zhang, M. Li, S. Chandrasekaran, X. Gao, X. Fang, H.-W. Lee, K. Hardcastle, J. Yang, B. Wang, *Tetrahedron* **2007**, *63*, 3287; R. Ziessel, C. Goze, G. Ulrich, *Synthesis* **2007**, 936; M. J. D. Bosdet, C. A. Jaska, W. E. Piers, T. S. Sorensen, M. Parvez, *Org. Lett.* **2007**, *9*, 1395.

[3] W. Yang, X. Gao, B. Wang, *Med. Res. Rev.* **2003**, *23*, 346; S. A. Amin, F. C. Küpper, D. H. Green, W. R. Harris, C. J. Carrano, *J. Am. Chem. Soc.* **2007**, *129*, 478; S. J. Baker, Y.-K. Zhang, T. Akama, A. Lau, H. Zhou, V. Hernandez, W. Mao, M. R. K. Alley, V. Sanders, J. J. Plattner, *J. Med. Chem.* **2006**, *49*, 4447; T. Tran, C. Quan, C. Y. Edosada, M. Mayeda, C. Wiesmann, D. Sutherlin, B. B. Wolf, *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1438; V. J. Reddy, J. S. Chandra, M. V. R. Reddy, *Org. Biomol. Chem.* **2007**, *5*, 889; Y. Hattori, H. Yamamoto, H. Ando, H. Kondoh, T. Asano, M. Kirihata, Y. Yamaguchi, T. Wakamiya, *Bioorg. Med. Chem.* **2007**, *15*, 2198.

[4] J. Adams, *Cancer Treat. Rev.* **2003**, *29*, 3; J. Adams, *Trends Mol. Med.* **2002**, *8*, S49.

[5] A. H. Soloway, W. Tjarks, B. A. Barnum, F.-G. Rong, R. F. Barth, I. M. Codogni, J. G. Wilson, *Chem. Rev.* **1998**, *98*, 1515; M.-S. Koo, T. Ozawa, R. A. Santos, K. R. Lamborn, A. W. Bollen, D. F. Deen, S. B. Kahl, *J. Med. Chem.* **2007**, *50*, 820; H. Nakamura, M. Ueno, J.-D. Lee, H. S. Ban, E. Justus, P. Fan, D. Gabel, *Tetrahedron Lett.* **2007**, *48*, 3151; J.-D. Lee, M. Ueno, Y. Miyajima, H. Nakamura, *Org. Lett.* **2007**, *9*, 323.

[6] G. W. Kabalka, M.-L. Yao, Z. Wu, *Org. Process Res. Dev.* **2006**, *10*, 1059.

[7] O. Payen, S. Top, A. Vessières, E. Brulé, M.-A. Plamont, M. J. McGlinchey, H. Müller-Bunz, G. Jaouen, *J. Med. Chem.* **2008**, *51*, 1791; R. G. Murray, D. M. Whitehead, F. Le Strat, S. J. Conway, *Org. Biomol. Chem.* **2008**, *6*, 988.

[8] J. C. Thenmozhiyal, P. T.-H. Wong, W.-K. Chui, *J. Med. Chem.* **2004**, *47*, 1527.

[9] M. Mudit, M. Khanfar, A. Muralidharan, S. Thomas, G. V. Shah, R. W. M. van Soest, K. A. El Sayed, *Bioorg. Med. Chem.* **2009**, *17*, 1731.

[10] C. M. Vogels, L. G. Nikolcheva, D. W. Norman, H. A. Spinney, A. Decken, M. O. Baerlocher, F. J. Baerlocher, S. A. Westcott, *Can. J. Chem.* **2001**, *79*, 1115; A. M. Irving, C. M. Vogels, L. G. Nikolcheva, J. P. Edwards, X.-F. He, M. G. Hamilton, M. O. Baerlocher, F. J. Baerlocher, A. Decken, S. A. Westcott, *New J. Chem.* **2003**, *27*, 1419.

[11] J. M. Sayer, W. P. Jencks, *J. Am. Chem. Soc.* **1973**, *95*, 5637.

[12] M. P. Groziak, L. Chen, L. Yi, P. D. Robinson, *J. Am. Chem. Soc.* **1997**, *119*, 7817; M. C. Davis, S. G. Franzblau, A. R. Martin, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 843; I.-H. Lee, E.-J. Kim, Y.-H. Cho, J. K. Lee, *Biochem. Biophys. Res. Commun.* **2002**, *299*, 621; B. Johnson-Restrepo, L. Pacheco-Londoño, J. Olivero-Verbel, *J. Chem. Inf. Comput. Sci.* **2003**, *43*, 1513; A. Jabbour, D. Steinberg, V. M. Dembitsky, A. Moussaieff, B. Zaks, M. Srebnik, *J. Med. Chem.* **2004**, *47*, 2409; M. Svobodová, J. Bárta, P. Šimůnek, V. Bertolasi, V. Macháček, *J. Organomet. Chem.* **2009**, *694*, 63; G. T. Lee, K. Prasad, O. Repič, *Tetrahedron Lett.* **2002**, *43*, 3255; C. Baldock, J. B. Rafferty, S. E. Sedelnikova, P. J. Baker, A. J. Stuitje, A. R. Slabas, T. R. Hawkes, D. W. Rice, *Science* **1996**, *274*, 2107; A. Roujeinikova, S. Sedelnikova, G.-J. de Boer, A. J. Stuitje, A. R. Slabas, J. B. Rafferty, D. W. Rice, *J. Biol. Chem.* **1999**, *274*, 30811.

[13] H. Nöth, B. Wrackmeyer, 'Nuclear magnetic resonance spectroscopy of boron compounds', Springer-Verlag, Berlin, 1978.

[14] P. D. Robinson, M. P. Groziak, *Acta Crystallogr., Sect. C* **1999**, *55*, 1701; P. D. Robinson, M. P. Groziak, L. Chen, *Acta Crystallogr., Sect. C* **1998**, *54*, 71; P. D. Robinson, M. P. Groziak, L. Yi, *Acta Crystallogr., Sect. C* **1996**, *52*, 2826.

[15] K. Kleinpeter, *Struct. Chem.* **1997**, *8*, 161.

[16] P. Molina, A. Tárraga, D. Curiel, C. Ramirez de Arellano, *Tetrahedron* **1997**, *53*, 15895; X.-H. Chang, *Acta Crystallogr., Sect. E* **2006**, *62*, o5184.

[17] V. Barba, R. Hernández, H. Höpfl, R. Santillan, N. Farfán, *J. Organomet. Chem.* **2009**, *694*, 2127; L. Ren, Z. Liu, M. Dong, M. Ye, H. Zou, *J. Chromatogr., A* **2009**, *1216*, 4768.

[18] SAINT 6.02, *Bruker AXS, Inc.*, Madison (1997–1999); G. M. Sheldrick, SADABS, *Bruker AXS, Inc.*, Madison (1999); G. M. Sheldrick, SHELXTL 5.1, *Bruker AXS, Inc.*, Madison (1997).

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