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# 2-Bromo-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine, a new unexpected bifunctional building block for combinatorial chemistry

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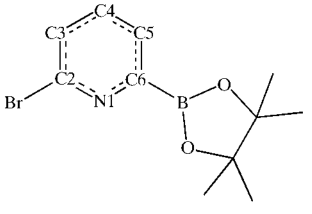
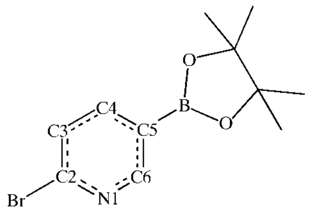
The first reported structure of a pyridin-2-ylboron derivative, *viz.* the title compound, $C_{11}H_{15}BBrNO_2$, (I), is compared with its regioisomer 2-bromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine, (II) [Sopková-de Oliveira Santos, Lancelot, Bouillon & Rault (2003). *Acta Cryst.* C**59**, o111–o113]. Structural differences are observed, firstly in the orientation of the dioxaborolane ring with respect to the pyridine ring and secondly in the bond angles of the $BO_2$ group. These differences do not explain the experimentally observed differences in chemical reactivity between (I) and (II) but do confirm the relatively lower stability of (I). However, *ab initio* calculations of the HOMO (highest occupied molecular orbital) and LUMO (lowest unoccupied molecular orbital), based on the known crystal structures of the two compounds, show different distributions, which correspond to the differences observed during chemical reactions.

## Comment

In continuation of our work concerning the synthesis of new pyridinylboronic acids and esters, we are now focusing on new and unexpected pyridin-2-ylboron derivatives. In comparison with the synthesis and isolation of pyridin-3-yl- (Bouillon *et al.*, 2002*a*) and pyridin-4-ylboronic acids (Bouillon *et al.*, 2002*b*) and esters, the situation for pyridin-2-ylboronic acids and esters is quite different, since the instability of non-substituted pyridin-2-ylboronic acid has been demonstrated (Fischer & Havinga, 1974). Moreover, a brominated pyridine ring has been shown to be weakened by the introduction of an alkylborane moiety (Utimoto *et al.*, 1976) so that it can be cleaved to give unsaturated nitriles. In this paper, the crystal structure of 2-bromo-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine, (I), is described and compared with its regioisomer 2-bromo-5-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine, (II), which was solved earlier (Sopková-de Oliveira Santos *et al.*, 2003), in order to try to find structural elements able to explain the differences in their stability and chemical reactivity.



(I)



(II)

Fig. 1 shows the asymmetric unit of (I). The dioxaborolane ring is in a half-chair conformation with an O1—C7—C8—O2 torsion angle of 28.0 (5)°; a similar numerical value was also found in (II) [O1—C7—C8—O2 = −20.9 (6)°]. The C6—$BO_2$ moiety is planar and the $BO_2$ group is rotated away from the plane of the pyridine ring by 13.0 (7)°. This deviation is higher than the value of 6.5 (6)° observed in the regioisomer, (II), and may be larger either because of crystal-packing effects or because of repulsion between adjacent N and O atoms [N1···O2 = 3.011 (6) Å]. No such repulsion is possible in (II). The existence of repulsion between adjacent N and O atoms in (I) is also the origin of the greater observed asymmetry between the C—B—O bond angles in the $BO_2$ group (Table 1) than is observed in aryl tetramethyl-1,3,2-dioxaborolane moieties deposited in the Cambridge Structural Database (CSD, Version 5.24; Allen, 2002). The average difference calculated for the 13 independent hits from the CSD is 3°, compared with 8° in (I).

The crystal packing of ester (I) is similar to that of ester (II) and so it is probably not the origin of the higher deviation of the $BO_2$ group plane from the pyridine ring plane.

The difference in the geometry of the $BO_2$ group cannot in itself explain the experimentally observed differences during chemical reactions. In an aromatic nucleophilic substitution with nucleophiles that are compatible with the boronic ester moiety (Matteson, 1999), ester (II) gave good to excellent results; only bromine was substituted, leaving the boronic

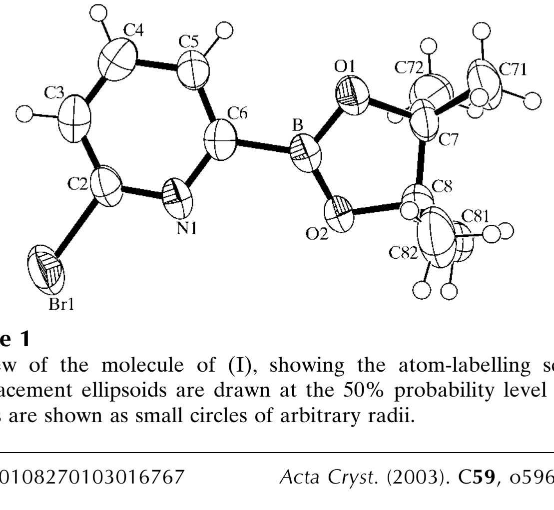


**Figure 1**
A view of the molecule of (I), showing the atom-labelling scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small circles of arbitrary radii.

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ester unchanged. The case of ester (I) was quite different, since every attempt led essentially to decomposition products.

The different reactivity of the two esters can be explained by our modelling results of the distribution of the LUMO (lowest unoccupied molecular orbital) in the structures. The *ab initio* calculation carried out on the crystal structures using the program *MOPAC* (method Austin Model 1 or AM1; Zerner *et al.*, 1980) showed that the LUMO is by far the most dense on atom C2 next to the Br atom in ester (II). In ester (I), on the other hand, the LUMO is equally dense on all three C atoms sensitive to nucleophilic attack, namely atoms C2 (next to Br), C4 and C6 (next to B). This explains why the reaction of (I) with a nucleophile does not provide a single product but several decomposition products, probably resulting from different simultaneous attacks.

## Experimental

The title ester, (I), was synthesized from 2,6-dibromopyridine using the method described by Bouillon *et al.* (2003). Suitable crystals of (I) were obtained by slow evaporation from acetonitrile at room temperature.

### *Crystal data*

$C_{11}H_{15}BBrNO_2$
$M_r = 283.96$
Orthorhombic, $P2_12_12_1$
$a = 6.4917$ (8) Å
$b = 12.3270$ (10) Å
$c = 15.8440$ (10) Å
$V = 1267.9$ (2) Å$^3$
$Z = 4$
$D_x = 1.488$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 25 reflections
$\theta = 18$–23°
$\mu = 3.23$ mm$^{-1}$
$T = 293$ (2) K
Prism, colourless
0.65 × 0.35 × 0.08 mm

### *Data collection*

Enraf–Nonius CAD-4 diffractometer
$\theta/2\theta$ scans
Absorption correction: Gaussian (*GAUSSIAN*98; Frisch *et al.*, 1998)
$T_{\min} = 0.140$, $T_{\max} = 0.660$
4581 measured reflections
3689 independent reflections
1857 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.038$
$\theta_{\max} = 30°$
$h = -9 \rightarrow 9$
$k = 0 \rightarrow 17$
$l = 0 \rightarrow 22$
3 standard reflections
frequency: 60 min
intensity decay: 3.8%

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.062$
$wR(F^2) = 0.166$
$S = 0.97$
3689 reflections
161 parameters
H-atom parameters constrained
$w = 1/[\sigma^2(F_o^2) + (0.0878P)^2]$
where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\max} = 0.003$
$\Delta\rho_{\max} = 0.57$ e Å$^{-3}$
$\Delta\rho_{\min} = -0.79$ e Å$^{-3}$
Absolute structure: Flack (1983), 1560 Friedel pairs
Flack parameter = −0.02 (2)

**Table 1**
Selected geometric parameters (Å, °).

| | | | |
|---|---|---|---|
| C6—B | 1.578 (8) | O1—C7 | 1.451 (6) |
| B—O2 | 1.328 (7) | O2—C8 | 1.483 (6) |
| B—O1 | 1.383 (7) | C7—C8 | 1.532 (9) |
| | | | |
| O2—B—O1 | 114.1 (5) | O1—B—C6 | 119.2 (5) |
| O2—B—C6 | 126.7 (5) | | |

H atoms were treated as riding, with C—H distances in the range 0.93–0.96 Å.

Data collection: *CAD*-4-*PC Software* (Enraf–Nonius, 1996); cell refinement: *CAD*-4-*PC Software*; data reduction: *JANA*98 (Petříček & Dušek, 1998); program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); 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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Supplementary data for this paper are available from the IUCr electronic archives (Reference: FG1698). Services for accessing these data are described at the back of the journal.

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