Acta Crystallographica Section E
**Structure Reports**
**Online**

ISSN 1600-5368

# Phenylboronate of an *N*-hydroxy-*N*-(2-hydroxyalkyl)pyridoxamine

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**Key indicators**

Single-crystal X-ray study
*T* = 133 K
Mean $\sigma$(C–C) = 0.002 Å
*R* factor = 0.041
*wR* factor = 0.122
Data-to-parameter ratio = 22.4

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

Received 16 August 2004
Accepted 17 August 2004
Online 21 August 2004

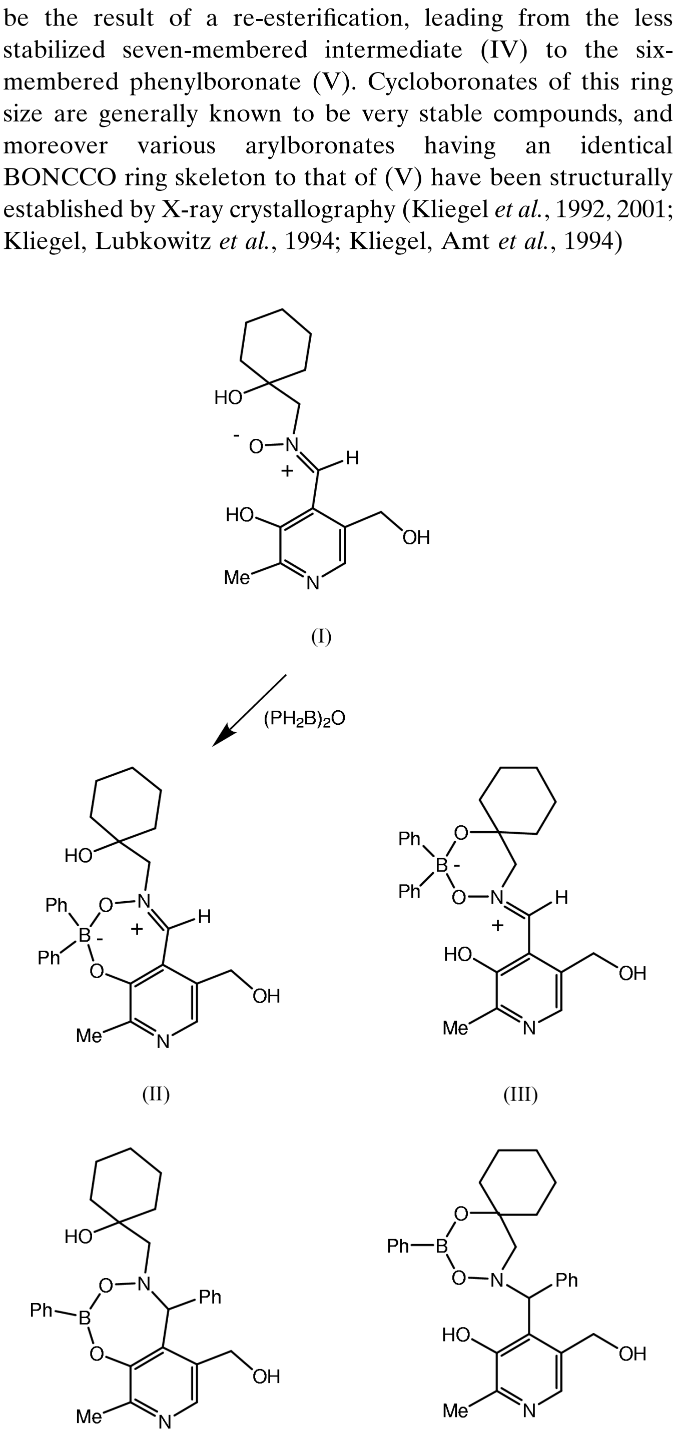
The title compound, 4-{[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridyl]phenylmethyl}-6,6-pentamethylene-2-phenyl-1,3-dioxa-4-aza-2-boracyclohexane, $C_{27}H_{31}BN_2O_4$, is formed by thermally induced rearrangement of the diphenylboron chelate of a pyridoxal nitrone derivative and contains a six-membered BONCCO heterocycle in which all atoms except for one carbon are approximately coplanar. The B—O bonds are short, consistent with a degree of O—B $p\pi$ back donation. An intramolecular hydrogen bond is formed between the phenolic OH of the pyridoxyl residue and the nitrogen of the BONCCO ring. Three intermolecular hydrogen bonds (one O—H$\cdots$N and two C—H$\cdots$O), all involving the hydroxymethyl O atom, link the molecules into chains parallel to the *c* axis.

## Comment

In the course of our investigations of seven-membered boron chelates of pyridoxal nitrones (Barakat, 2002; Barakat & Kliegel, unpublished results), we synthesized the diphenylboron chelate (II) by reaction of the *N*-(2-hydroxyalkyl)-nitrone of pyridoxal, (I), and diphenylborinic acid (anhydride). Similar seven-membered boron chelate rings had been previously obtained from various salicylaldehyde nitrones as bidentate ligands with *N*-oxide and phenolate functions, and are structurally established by X-ray crystallographic analyses of various examples (Kliegel *et al.*, 1987, 1998).

Though (II) could be recrystallized from ethanol, it isomerized during 4 h refluxing in THF. The resulting crystalline substance has the same elemental composition as (II), but does not show the $^1$H NMR signal of the cyclohexanol OH group; instead, a low field phenol OH resonance appears in the spectrum. An alternative chelate structure (III), incorporating the hydroxyalkyl group as a ligand, could be excluded because of the absence of signals for a nitrone N═C—H group in the IR and $^1$H NMR spectra. Furthermore, the reaction of the substance with diphenylcarbazone in methanol (Neu, 1960; Friese & Umland, 1978) did not give the characteristic blue colour indicating the diphenylboron moiety [as in (I)], but led instead to a pink–violet tint of the solution. This indicated the loss of one of the B-phenyl groups as a consequence of a thermolytic 1,4-phenyl migration that had taken place during reflux, as is known for other diarylboron complexes of nitrone ligands (Kliegel *et al.*, 2001, and references therein). The expected initial rearrangement product (IV), however, seemed unlikely because of the distinct phenol OH signal in the $^1$H NMR spectrum.

To characterize the product unambiguously, an X-ray crystallographic analysis, reported here, was undertaken, thereby establishing the molecular structure (V), which could be the result of a re-esterification, leading from the less stabilized seven-membered intermediate (IV) to the six-membered phenylboronate (V). Cycloboronates of this ring size are generally known to be very stable compounds, and moreover various arylboronates having an identical BONCCO ring skeleton to that of (V) have been structurally established by X-ray crystallography (Kliegel *et al.*, 1992, 2001; Kliegel, Lubkowitz *et al.*, 1994; Kliegel, Amt *et al.*, 1994)



(I)

(II)

(III)

(IV)

(V)

.

As is typical for six-membered cycloboronates, the BONCCO ring system in (V) contains a trigonally substituted $sp^2$-hybridized B atom (angle sum = 360°) with approximately planar OBON and OBOC groupings (for dihedral angles, see Table 1), resulting in a somewhat distorted sofa configuration (Bucourt & Hainaut, 1965), whereby C21 lies 0.710 (1) Å out of the plane of the other five ring atoms (r.m.s. deviation = 0.055 Å). The O—B bonds are relatively short (Table 1), which indicates some partial double-bond character resulting from O—B $p\pi$ back donation. As in the other above-mentioned arylboronates with a BONCCO ring system, the (C)O—B bond is distinctly shorter (by 0.023 Å) than the (N)O—B bond, implying a better $p(\pi)$ donor quality of the alcohol ligand compared to the hydroxylamine ligand. The increased double-bond character of the (C)O—B bond is also reflected by a comparison of the angles at the ring O atoms; the interior angle at O17 is somewhat compressed and is the smaller by almost 5° (Table 1), as a consequence of the reduced (N)O—B double-bond character. The short B—C(phenyl) distance in (V) lies in the typical range for ($sp^2$)B—C(aryl) bond distances in arylboronates (Kliegel *et al.*, 1991; Kliegel, Lubkowitz *et al.*, 1994; Kliegel, Amt *et al.*, 1994). The phenyl ring is rotated with respect to the $CBO_2$ grouping by an interplanar angle of 15.66 (6)°. Any $\pi$ interaction between the aromatic system and the unoccupied boron $p_z$ orbital seems therefore to play a minor role.

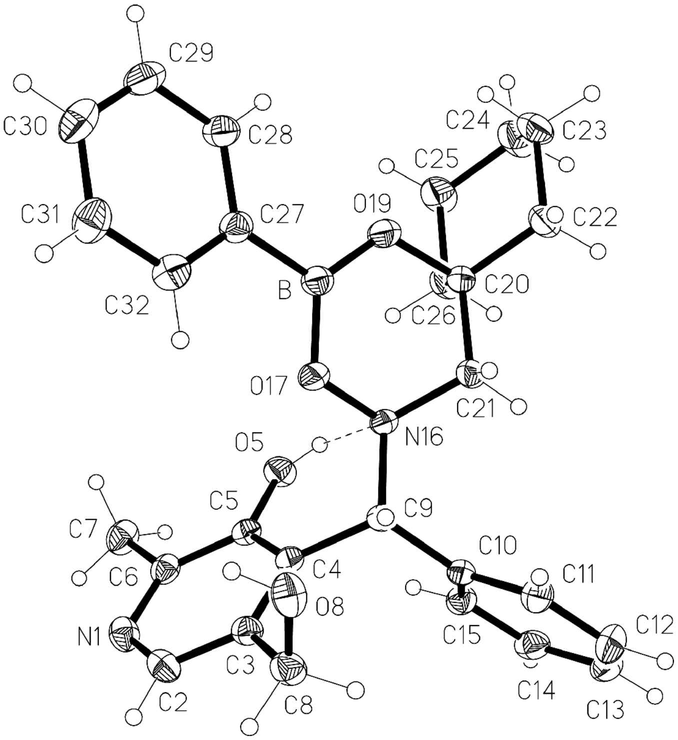


**Figure 1**
The structure of compound (V) in the crystal. Displacement ellipsoids are drawn at the 50% probability level. H-atom radii are arbitrary.

The cyclohexane ring in (V) displays an almost ideal chair form with an axial orientation of the oxygen substituent, O19, and equatorial position of the aminomethyl carbon C21, both part of the spiro-connected BONCCO ring. This conformation has also been found in other cyclohexane–BONCCO spiro compounds (Kliegel, Amt *et al.*, 1994).

An intramolecular O—H···N hydrogen bond is observed from the phenol group of the pyridoxal moiety to the hydroxylamine N atom of the BONCCO ring (Table 2). This interaction contributes to the pyramidality at the N atom, which lies 0.522 (1) Å out of the plane of its substituents in the direction of the phenolic H atom.

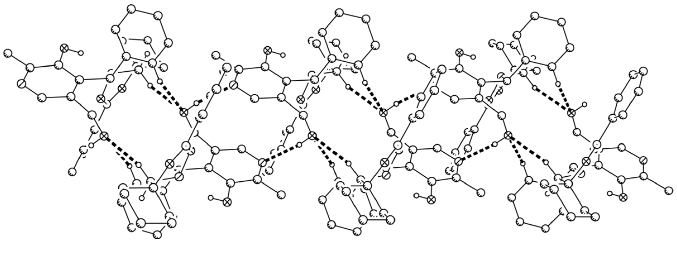


**Figure 2**
The packing of compound (V), showing hydrogen bonds as dashed lines. H atoms not involved in the hydrogen bonding have been omitted for clarity. The view direction is approximately perpendicular to the *bc* plane.

The hydroxymethyl OH group acts as donor in an intermolecular hydrogen bond to the pyridyl N atom. Additionally, there are two 'weak' C—H···O interactions, both to the hydroxymethyl O atom as acceptor. The net effect is to link the molecules to form chains parallel to the *c* axis (Table 2 and Fig. 2).

## Experimental

For the preparation of *C*-[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridyl]-*N*-(1-hydroxy)cyclohexylmethyl-nitrone, (I), pyridoxal hydrochloride (2.04 g, 10 mmol) and *N*-(1-hydroxy)-cyclohexylmethylhydroxylamine hydrochloride (1.82 g, 10 mmol) were dissolved by stirring in a sufficient quantity of methanol in the dark. After addition of triethylamine (2.02 g, 20 mmol) in a small amount of methanol, stirring was continued for about 6 h, the solvent evaporated *in vacuo*, and the oily residue dissolved in acetone. Upon cooling, $Et_3N.HCl$ precipitated and was filtered off. The solution was evaporated and the solid residue recrystallized from ethanol (yield: 2.47 g, 84%) as yellow crystals (m.p. 458 K, from 50% ethanol–water). IR (KBr): 3437, 3321, 3237 (O—H), 1599 $cm^{-1}$ (C═N/C═C); $^1H$ NMR (90 MHz, $d^6$-DMSO–TMS): $\delta$ 1.54 [*s*, $(CH_2)_5$], 2.40 (*s*, $CH_3$), 4.07 (*s*, N—$CH_2$), 4.55 (*m*, O—$CH_2$), 4.85 (*s*, exchangeable, OH), 5.34 (*t*, exchangeable, OH), 7.93 (*s*, 1 aromatic H), 8.33 (*s*, N═CH), 11.67 (*s*, exchangeable, phenolic OH). Analysis calculated for $C_{15}H_{22}N_2O_4$: C 61.21, H 7.53, N 9.52%; found: C 61.23, H 7.49, N 9.51%.

For the preparation of 8-[(1-hydroxy)-cyclohexylmethyl]-1-(hydroxymethyl)-4-methyl-6,6-diphenyl-5,7-dioxa-3-aza-8-azonia-6-borata-6,7-dihydro-5*H*-benzocycloheptene, (II), (I) (0.29 g, 1 mmol) and oxybis(diphenylborane) (0.17 g, 0.5 mmol) were dissolved, each in 1 ml of ethanol, and mixed, with brief heating to boiling point. Cooling of the solution yielded 0.46 g (100%) of yellow crystals (m.p. 400 K, from ethanol). IR (KBr): 3425–3391 (O—H), 1636 $cm^{-1}$ (C═N/C═C); $^1H$ NMR (90 MHz, $d^6$-DMSO–TMS): $\delta$ 1.58 [*s*, $(CH_2)_5$], 2.68 (*s*, $CH_3$), 4.19 (*s*, N—$CH_2$), 4.50 (*s*, O—$CH_2$), 4.94 (*s*, exchangeable, OH), 5.39 (*s*, broad, exchangeable, OH), 7.02–7.50 (*m*, 10 aromatic H), 7.90 (*s*, 1 aromatic H), 8.48 (*s*, N═CH); $^{11}B$ NMR (64 MHz, DMSO–$Et_2OBF_3$): $\delta$ 1.2. Analysis calculated for $C_{27}H_{31}BN_2O_4$: C 70.75, H 6.82, B 2.36, N 6.11%; found: C 70.37, H 6.92, B 2.41, N 6.06%. The compound gives a blue coloured reaction with diphenylcarbazone in methanolic solution, indicating the presence of a diphenylboron moiety (Neu, 1960; Friese & Umland, 1978).

For the preparation of 4-{[3-hydroxy-5-(hydroxymethyl)-2-methyl-4-pyridyl]phenylmethyl}-6,6-pentamethylene-2-phenyl-1,3-dioxa-4-aza-2-boracyclohexane, (V), compound (II) (0.92 g, 2 mmol) is refluxed for 4 h in 20–3–0 ml of THF, whereby the refluxing solution was periodically checked with diphenylcarbazone to register the progress of the isomerization. As soon as the blue colour was no longer observed, the solution was partially evaporated, and yielded, upon cooling, 0.57 g (62%) of colourless crystals (m.p. 484 K, from 50% ethanol–water). Single crystals suitable for X-ray crystallography were obtained by slow crystallization from ethanol. IR (KBr): 3240 (O—H), 1603 $cm^{-1}$ (C═C); $^1H$ NMR (90 MHz, $d^6$-DMSO–TMS): $\delta$ 1.19–1.88 [*m*, $(CH_2)_5$], 2.42 (*s*, $CH_3$), 2.97 (*s*, N—$CH_2$), 4.57 (*m*, O—$CH_2$), 5.24 (*t*, *J* = 9 Hz, exchangeable, alkanol–OH), 5.65 (*s*, O—N—CH), 7.30–7.78 (*m*, 10 aromatic H), 8.00 (*s*, 1 aromatic H), 10.68 (*s*, broad, exchangeable, phenol–OH). Analysis calculated for $C_{27}H_{31}BN_2O_4$: C 70.75, H 6.82, B 2.36, N 6.11%; found: C 70.77, H 7.09, B 2.43, N 5.74%. The compound gives a pink–violet colour with diphenylcarbazone in methanolic solution, indicating a monophenylboron moiety (Neu, 1960).

### *Crystal data*

$C_{27}H_{31}BN_2O_4$
$M_r = 458.35$
Monoclinic, $P2_1/c$
$a = 11.3840\ (12)$ Å
$b = 21.504\ (2)$ Å
$c = 10.1728\ (11)$ Å
$\beta = 103.437\ (3)^\circ$
$V = 2422.2\ (4)$ Å$^3$
$Z = 4$

$D_x = 1.257$ Mg m$^{-3}$
Mo $K\alpha$ radiation
Cell parameters from 5414 reflections
$\theta = 2.3$–$30.5^\circ$
$\mu = 0.08$ mm$^{-1}$
$T = 133\ (2)$ K
Tablet, colourless
0.50 × 0.28 × 0.11 mm

### *Data collection*

Bruker SMART 1000 CCD diffractometer
$\omega$ scans
Absorption correction: none
33115 measured reflections
7074 independent reflections

5325 reflections with $I > 2\sigma(I)$
$R_{\rm int} = 0.038$
$\theta_{\rm max} = 30.0^\circ$
$h = -15 \rightarrow 16$
$k = -29 \rightarrow 30$
$l = -14 \rightarrow 14$

### *Refinement*

Refinement on $F^2$
$R[F^2 > 2\sigma(F^2)] = 0.042$
$wR(F^2) = 0.122$
$S = 1.09$
7074 reflections
316 parameters

H atoms treated by a mixture of independent and constrained refinement
$w = 1/[\sigma^2(F_o^2) + (0.071P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$
$(\Delta/\sigma)_{\rm max} = 0.001$
$\Delta\rho_{\rm max} = 0.43$ e Å$^{-3}$
$\Delta\rho_{\rm min} = -0.26$ e Å$^{-3}$

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

| | | | |
|---|---|---|---|
| B—O19 | 1.3540 (14) | B—C27 | 1.5600 (16) |
| B—O17 | 1.3769 (13) | | |
| O19—B—O17 | 123.29 (10) | B—O17—N16 | 116.58 (8) |
| O19—B—C27 | 120.11 (9) | B—O19—C20 | 121.13 (8) |
| O17—B—C27 | 116.59 (9) | | |
| O19—B—O17—N16 | −3.47 (15) | B—O19—C20—C21 | −17.88 (13) |
| C21—N16—O17—B | 39.61 (11) | O17—N16—C21—C20 | −65.11 (10) |
| O17—B—O19—C20 | −7.70 (16) | O19—C20—C21—N16 | 54.15 (10) |

**Table 2**
Hydrogen-bonding geometry (Å, °).

| *D*—H···*A* | *D*—H | H···*A* | *D*···*A* | *D*—H···*A* |
|---|---|---|---|---|
| O5—H05···N16 | 0.876 (17) | 1.802 (17) | 2.6142 (12) | 153.3 (16) |
| O8—H08···N1$^{\rm i}$ | 0.834 (17) | 2.052 (17) | 2.8646 (13) | 164.8 (16) |
| C11—H11···O8$^{\rm ii}$ | 0.95 | 2.58 | 3.3794 (14) | 143 |
| C21—H21*B*···O8$^{\rm ii}$ | 0.99 | 2.47 | 3.3979 (13) | 155 |

Symmetry codes: (i) $-x, 1-y, 2-z$; (ii) $-x, 1-y, 1-z$.

*Acta Cryst.* (2004). E**60**, o1589–o1592 Wolfgang Kliegel *et al.* • $C_{27}H_{31}BN_2O_4$ **o1591**

The OH H atoms were refined freely. Methyl H atoms were identified in difference syntheses, idealized and then refined using rigid methyl groups (C—H = 0.98 Å and H—C—H = 109.5°). Other H atoms were included using a riding model with fixed C—H bond lengths (Å) of 0.95 ($sp^2$ CH), 0.99 ($sp^3$ CH) or 1.00 ($CH_2$). $U(_{iso}H)$ values were fixed at 1.2 times the $U_{eq}$ values of the parent C atoms.

Data collection: *SMART* (Bruker, 1998); cell refinement: *SAINT* (Bruker, 1998); data reduction: *SAINT*; program(s) used to solve structure: *SHELXS*97 (Sheldrick, 1990); program(s) used to refine structure: *SHELXL*97 (Sheldrick, 1997); molecular graphics: *XP* (Siemens, 1994); software used to prepare material for publication: *SHELXL*97.

We thank Mr A. Weinkauf for technical assistance.

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