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(1*R*,3*R*,4*S*)-1-Benzyl-3-(*tert*-butyldimethylsilyloxy)-4-(hydroxymethyl)pyrrolidine–borane: novel B—H···H—O hydrogen bonding

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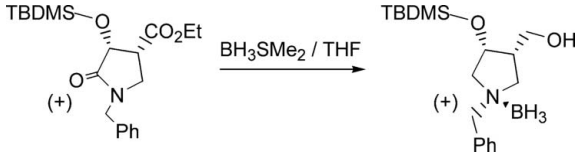
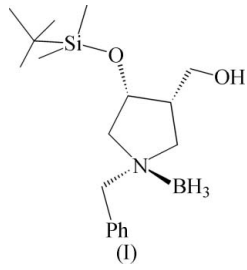
The absolute configuration of the title *cis*-(1*R*,3*R*,4*S*)-pyrrolidine–borane complex, $C_{18}H_{34}BNO_2Si$, was confirmed. Together with the related *trans* isomers (3*S*,4*S*) and (3*R*,4*R*), it was obtained unexpectedly from the $BH_3{\cdot}SMe_2$ reduction of the corresponding chiral (3*R*,4*R*)-lactam precursor. The phenyl ring is disordered over two conformations in the ratio 0.65:0.35. The crystallographic packing is dominated by the rarely found donor–acceptor hydroxy–borane O—H···H—B hydrogen bonds.

Comment

During the course of our efforts to synthesize the two pairs of enantiomeric 3-*O*-TBDMS-protected (TBDMS is *tert*-butyldimethylsilyl) 1-benzyl-3-hydroxy-4-(hydroxymethyl)pyrrolidine scaffolds by reduction of the corresponding enantiomeric pairs of lactam esters (Clinch *et al.*, 2007) with $BH_3{\cdot}SMe_2$, we recovered, unexpectedly, only the borane-complexed pyrrolidine derivatives as stable low-melting waxy solids. From the reduction of the (+)-*cis* lactam ester (see reaction scheme below), we were able to isolate the corresponding borane-complexed pyrrolidine title compound, (I), as large colourless



crystals. As a result of this particular reaction, only a single compound was isolated as was evinced from the appearance of a single resonance in the ^{11}B NMR spectrum and the appearance of a single peak in the chiral-phase HPLC chromatogram. In contrast, the borane complexes isolated from the reductions of the *trans*-lactams were also isolated as chromatographically homogeneous compounds but were shown to be diastereoisomeric, presumably as a result of the capture of each of the pyrrolidino 'invertomers'. In the ^1H and ^{11}B NMR spectra and in chiral-phase HPLC chromatograms, the ratios of the diastereoisomers were essentially consistent (at ∼2:1).



(I)

The crystal structure of the title (−)-*cis* borane complex is interesting in that, in binding the borane residue from the less-hindered face, the *N*-benzyl group is forced into a configuration *syn* to the substituents at C3 and C4. A similar phenomenon has been observed in the formation of the borane complex (adduct) with (*S*)-*N*-benzylproline methyl ester (Ferey *et al.*, 1996). Here, the *N*-boronato group and the carboxylate functionality at C2 are *cis* to each other, a configuration that relieves any potentially unfavourable interaction with the benzyl group.

The asymmetric unit of the title compound, (I), contains one independent (1*R*,3*R*,4*S*)-1-benzyl-3-(*tert*-butyldimethylsilyloxy)-4-(hydroxymethyl)pyrrolidine–borane molecule (Fig. 1). As shown in Fig. 1, the phenyl ring (C6–C11) is conformationally disordered in two orientations [in the ratio *a*:*b* of 0.65 (2):0.35 (2)]; the rings were refined as rigid bodies (C—C = 1.390 Å). The data would not support refinement of two independent sites for atom C1. The pyrrolidine ring adopts a twist ring conformation on C3—C4, with $Q(2)$ =

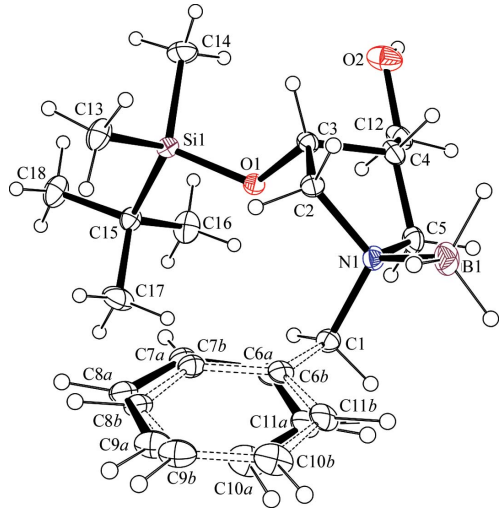


Figure 1
The contents of the asymmetric unit of (I), showing all atoms with displacement ellipsoids at the 30% probability level. The two phenyl-group orientations [labelled as *a* and *b* sets with occupancies of 0.65 (2) and 0.35 (2), respectively] are distinguished by full and dashed bonds. For the sake of clarity, only one set of H atoms on atom C1 is shown (see *Comment*).

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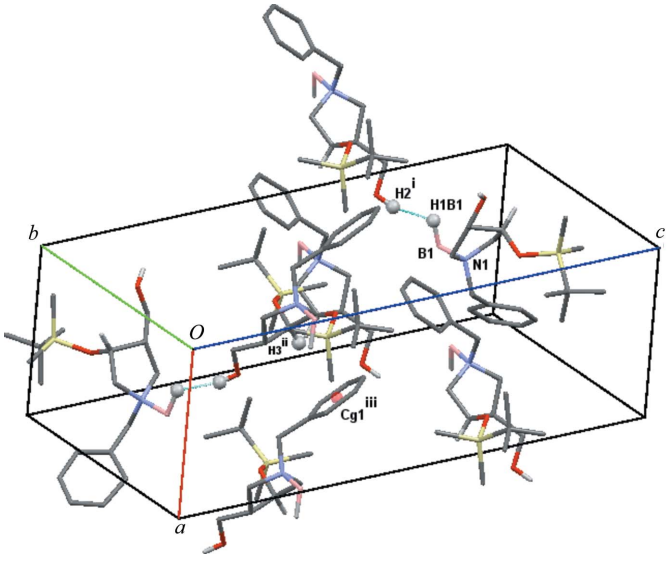

Figure 2
A *Mercury* packing view (Macrae *et al.*, 2008) of the cell highlighting the unusual B—H···H—O major hydrogen bond (dotted). Only selected H atoms involved in packing are shown in ball mode (see Table 1). [Symmetry codes: (i) $-x, \frac{1}{2}+y, \frac{3}{2}-z$; (ii) $\frac{1}{2}-x, 1-y, z-\frac{1}{2}$; (iii) $\frac{3}{2}-x, 1-y, z-\frac{1}{2}$.]

0.414 (2) Å and φ = 271.5 (3)° (Cremer & Pople, 1975). The absolute configurations are confirmed to be N1(*R*), C3(*R*) and C4(*S*), as expected from the synthesis, with a Hooft *y* parameter of 0.11 (6) (Hooft *et al.*, 2008).

Lattice binding is provided by unusual B—H···H—O hydrogen bonds (Table 1 and Fig. 2), in which the borane H atoms act as acceptors, generating what would be a *C*(8) binding motif (Bernstein *et al.*, 1995). This combination of hydroxy H-atom donors and borane H-atom acceptors is rarely observed; the one example located has two bifurcated O—H (weaker) interactions to both borane H atoms in (1*R*,2*S*,7*S*,7a*S*)-1,2-dihydroxy-7-(4-methoxybenzoyloxy)hexahydro-1*H*-pyrrolizine–borane [Cambridge Structural Database (CSD; Allen, 2002) refcode ABUKAJ (Blakemore *et al.*, 2001)], generating two *C*(7) motifs. This interaction does not appear to have affected the molecular bonding significantly, with a B—N bond length of 1.625 (3) Å compared with 1.637 (3) and 1.633 Å, respectively, in the related compounds (1*R*,2*S*)-1-(boryldiphenylphosphanylethyl)-1-boryl-2-(boryldiphenylphosphanylmethyl)pyrrolidine (TUSSOP; Lam *et al.*, 2002) and *N*-benzyl-*N*-boranylproline methyl ester (TUHJEL; Ferey *et al.*, 1996). We have previously noted the related (nitrogen equivalent) B—H···H—N strong lattice binding in amine–boranes [*e.g.* propylamine–borane; CSD refcode SOYTOQ (Gainsford & Bowden, 2009)]. A weak C—H···π interaction is also present (see Table 1), which has not prevented the observed conformational disorder in the ring.

Experimental

To an argon-blanketed solution of the (+)-silylated lactam ester (19.1 g, 50.7 mmol) in dry tetrahydrofuran (230 ml), cooled in an ice bath, was added BH_3·SMe_2 (25 ml, 253.5 mmol) dropwise over a period of about 10 min. The solution was warmed to 341 K and maintained as such for 16 h before being cooled (in ice) and quenched with excess methanol. The solution was concentrated and then fractionated by flash column chromatography on silica (10–20% ethyl acetate/hexane) to give the (+)-pyrrolidine (yield 9.38 g, 57%) as a colourless solid [m.p. 353 K (uncorrected), $[\alpha]_D^{23}$ +29.4 (*c* 0.895, MeOH)]. FT–IR (neat): υ_{max} 3505 (OH), 2953, 2931, 2883, 2857, 2406, 2322 (BH_3), 2267 (BH_3), 1464, 1252, 1163 (N—B), 1083, 1063, 1049, 1025, 1010, 978, 933, 903, 868, 837, 821, 803, 774, 701, 669 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.43–7.36 (*m*, 5H), 4.82 (*q*, 6.5 Hz, 1H), 4.06 (ABq, 12.9 Hz, 2H), 3.83 (*dt*, 12.0, 2.9 Hz, 1H), 3.53–3.48 (*m*, 1H), 3.39 (*dd*, 10.6, 6.5 Hz, 1H), 3.25 (*t*, 10.5 Hz, 1H), 3.15 (*m*, 1H) 2.91–2.84 (*m*, 1H), 2.66 (*dd*, 10.6, 6.5 Hz, 1H), 2.32 (*dd*, 9.8, 3.3 Hz, 1H), 0.88 (*s*, 9H), 0.11 (*s*, 3H), 0.07 (*s*, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 132.58, 131.35, 129.03, 128.20, 72.92, 67.46, 67.14, 60.23, 59.39, 41.78, 25.70, 17.85, −4.76, −5.18. ^{11}B NMR (160 MHz, $CDCl_3$): δ −10.3. HR ESMS: *M*H$^+$ *m*/*z* = 322.2197, $C_{18}H_{22}NO_2Si$ requires 322.2202, Δ 1.6 p.p.m.; *M*Na$^+$ *m*/*z* = 344.2021, $C_{18}H_{31}NO_2SiNa$ requires 344.2022, Δ 0.3 p.p.m.; *M*BH_3Na$^+$ = 358 a.m.u. Microanalysis (%) found: C 64.69, H 10.76, N 4.17; $C_{18}H_{34}BNO_2Si$ requires: C 64.48, H 10.15, N 4.18.

Crystal data

$C_{18}H_{34}BNO_2Si$
M_r = 335.36
Orthorhombic, $P2_12_12_1$
a = 7.8078 (7) Å
b = 11.2328 (10) Å
c = 23.639 (2) Å
V = 2073.2 (3) Å^3
Z = 4
Mo *K*α radiation
μ = 0.12 mm^{-1}
T = 113 K
0.65 × 0.60 × 0.30 mm

Data collection

Bruker APEXII CCD diffractometer
Absorption correction: multi-scan (Blessing, 1995)
T_{min} = 0.418, T_{max} = 0.746
42018 measured reflections
4901 independent reflections
4409 reflections with $I > 2\sigma(I)$
R_{int} = 0.089

Refinement

$R[F^2 > 2\sigma(F^2)]$ = 0.049
$wR(F^2)$ = 0.134
S = 1.07
4901 reflections
225 parameters
1 restraint
H atoms treated by a mixture of independent and constrained refinement
$\Delta\rho_{max}$ = 0.63 e Å^{-3}
$\Delta\rho_{min}$ = −0.44 e Å^{-3}
Absolute structure: Flack (1983), 2102 Friedel pairs
Flack parameter: 0.07 (13)

Table 1
Hydrogen-bond geometry (Å, °).

*Cg*1 is the centre of the C6a–C10a phenyl ring.

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
O2—H2···H1*B*1^{i}	0.89 (3)	1.76 (4)	2.62 (2)	162 (3)
C3—H3···*Cg*1^{ii}	1.00	2.78	3.662 (3)	147

Symmetry codes: (i) $-x, y-\frac{1}{2}, -z+\frac{3}{2}$; (ii) $x-1, y, z$.

Two low-angle reflections affected by the backstop were removed from the refinement. Conformational disorder involving phenyl plane orientations was modelled *via* linked occupancies of two rigid hexagonal phenyl groups (C—C = 1.390 Å, atoms C6–C11; see Fig. 1): final occupancies for the *a*:*b* set were 0.65 (2):0.35 (2). Each *a*,*b* set of

phenyl-group C atoms was refined with the same anisotropic displacement parameters [using the EADP function in *SHELXL97* (Sheldrick, 2008)]. The data would not support two independent sites for atom C1; two sets of bound H atoms (H1*A*/H1*B* and H1*C*/H1*D*) were calculated, given *a*,*b* occupancies as appropriate and fixed positionally. The C1—C6*a* and C1—C6*b* distances were restrained to be equal (SADI function in *SHELXL97*, with an effective standard deviation of 0.005 Å). The borane and hydroxy H atoms were located in difference Fourier maps and refined with isotropic displacement parameters.

The methyl H atoms were constrained to an ideal geometry (C—H = 0.98 Å), with U_{iso}(H) = 1.5U_{eq}(C), but were allowed to rotate freely about the adjacent C—C bond. All other H atoms were placed in geometrically idealized positions and constrained to ride on their parent atoms, with C—H distances of 1.00 (primary), 0.99 (methylene) or 0.95 Å (phenyl). The phenyl H atoms were refined with U_{iso}(H) = 1.5U_{eq}(C) and the remainder with U_{iso}(H) = 1.2U_{eq}(C).

Data collection: *APEX2* (Bruker, 2005); cell refinement: *SAINT* (Bruker, 2005); data reduction: *SAINT* and *SADABS* (Bruker, 2005); program(s) used to solve structure: *SHELXS97* (Sheldrick, 2008); program(s) used to refine structure: *SHELXL97* (Sheldrick, 2008); molecular graphics: *ORTEP-3* (Farrugia, 1997) and *PLATON* (Spek, 2009); software used to prepare material for publication: *SHELXL97* and *PLATON*.

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Supplementary data for this paper are available from the IUCr electronic archives (Reference: GD3351). Services for accessing these data are described at the back of the journal.

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