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Synthesis of glycosyl boranes and glycosyl borinates†

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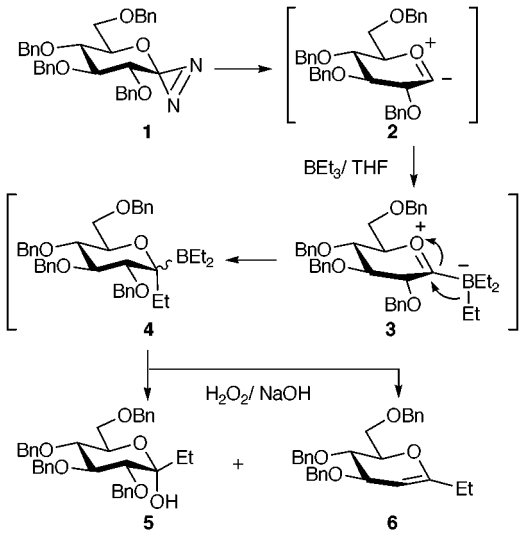
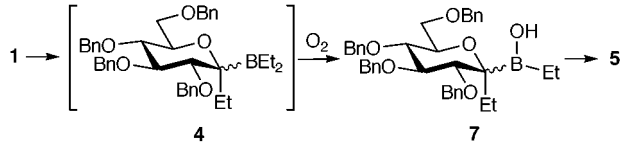
Insertion of glycosylidene carbenes into a B–C bond of BEt_3 leads to unstable glycosyl boranes, while insertion into a B–C bond of borinic esters yields stable anomeric glycosyl borinates.

Insertion of glycosylidene carbenes, generated by thermolysis or photolysis of glycosylidene diazirines, into HX bonds leads to *O*-, *C*- and *N*-glycosides,[1] glycosyl phosphines[2] and glycosyl stannanes.[3] We speculated that reaction of a borane with the carbene **2** would lead to a zwitterion such as **3**; migration of a B-substituent—as proposed for the reaction of methoxycarbene with trialkylboranes[4]—should lead to the as yet unknown glycosyl boranes (Scheme 1).



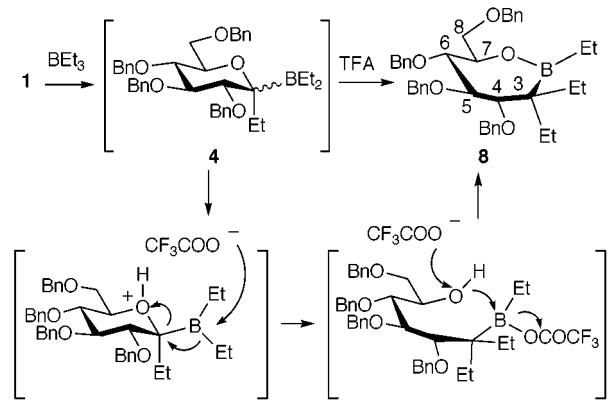
Scheme 1

Thermolysis of the diazirine **1**[5] in degassed THF in the presence of 1.5 equiv. of BEt_3 at 25 °C, followed by treatment with excess 30% alkaline H_2O_2 and aqueous work-up, yielded 55% of hemiacetal **5** and 13% of the *C*-ethylglucal **6**. These products suggest the intermediate formation of anomeric glycosyl boranes **4**. Treatment with alkaline H_2O_2 leads either (depending on the borane configuration?) to oxidation[6] and (after anomerisation?) to the hemiacetal **5**, or to elimination of the C(1) boron substituent and the vicinal benzyloxy group.[7] *trans*-Elimination is suggested by the observation (^{13}C NMR) that **6** is only formed after additon of alkaline H_2O_2. Thermolysis of the diazirine **1** in the presence of 1.5 equiv. of BEt_3 in oxygen-containing THF yielded 25% of the borinic acid **7** after rapid chromatography (Scheme 2). The borinic acid **7** was rapidly converted into the hemiacetal **5** (isolated in *ca.* 75%) by exposure to air, storage in oxygen–containing $CDCl_3$, or treatment with alkaline H_2O_2. The ^{11}B NMR of air-stable mixtures of **7** and 2 equiv. of PPh_3 shows a broad signal at δ 56.5, typical for dialkyl borinic acids.[8] The ^1H NMR shows a broad singlet of an exchangeable H at δ 8.16, corresponding to B–OH, two doublets of quintets at δ 1.8 and 1.6 (2 H), a triplet at δ 0.9 (3 H) for the *C*-ethyl and a multiplet at δ 1.0–0.9 (5 H) of the *B*–Et group. The ^{13}C NMR signal for the boron substituted anomeric carbon is missing, as expected.[9]



Scheme 2

The intermediate formation of a glycosyl borane was further evidenced by treating the product of thermolysis of **1** and BEt_3 in degassed THF with excess TFA, followed by aqueous work-up (Scheme 3). The resulting cyclic borinic ester **8**, isolated in 45%, showed a ^{11}B signal at δ 51, typical for *O*-alkyl borinates.[10]

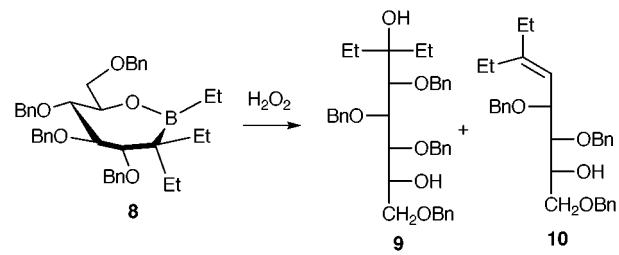


Scheme 3

The ^1H NMR spectrum of **8** shows signals for a $BC(Et)_2$ moiety and a multiplet at δ 0.9–0.7 for a BEt group. H–C(7) is strongly shifted downfield due to the R_2BO substituent [H–C(5) in **6** at δ 4.02, H–C(7) in **8** at δ 4.77].

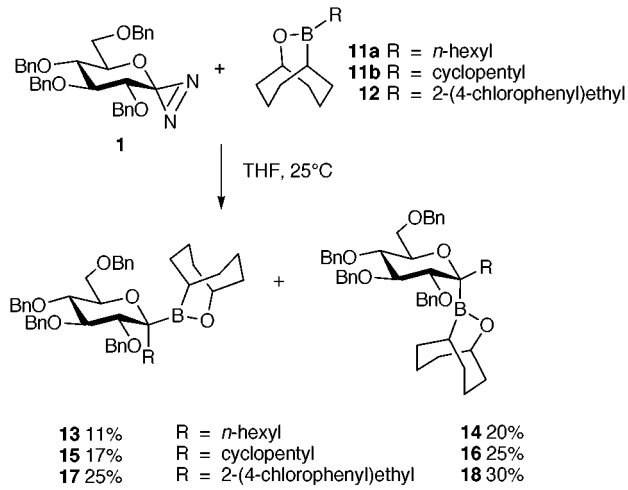
The formation of **8** is rationalised by protonation of the ring oxygen of **4**, nucleophilic attack of trifluoroacetate at boron, 1,2-migration of an ethyl substituent with concomitant ring-opening, and nucleophilic attack of HO–C(7) at boron. Treatment of **8** with alkaline H_2O_2 in THF leads to the diol **9** (37%) and the alkene **10** (39%) (Scheme 4).

To prepare glycosyl borinates, we exposed the diazirine **1** to the exceptionally stable borinates **11**–**12**[11] derived from 10-bora-9-oxabicyclo[3.3.2]decane (Scheme 5). This led to



Scheme 4

† Glycosylidene Carbenes Part 28. For Part 27, see ref. 1(*b*).



Scheme 5

diastereoisomeric mixtures **13**/**14** (31%; 35:65), **15**/**16** (42%; 40:60) and **17**/**18** (55%; 45:55) that were isolated by flash chromatography. The isomers **15**/**16** and **17**/**18** were separated by HPLC. The glycosyl borinates **13**–**18** were characterized by FAB-MS, ^{11}B NMR, ^{1}H NMR, ^{13}C NMR and IR spectroscopy. They were stable at −10 °C for several weeks and not affected by air.

The configuration of **17** and **18** was deduced from NOE experiments (Fig. 1), with **17** showing NOEs between H–C(2) and H–C(5), H–C(2) and H–C(7), and H–C(1′) and H–C(4), indicating an axial orientation of the anomeric alkyl group. In contradistinction, a small NOE between H–C(1′) and H–C(5) and the lack of other NOEs > 1% for **18** indicate an equatorial orientation of the anomeric alkyl group.

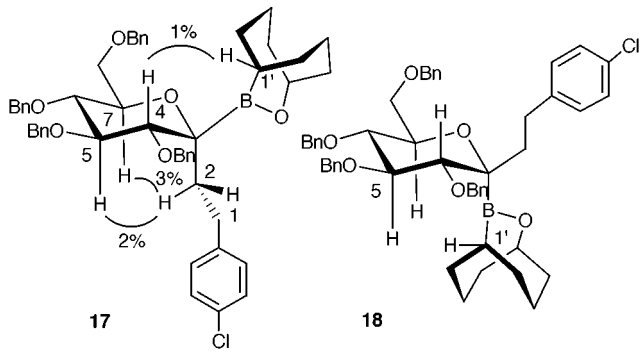


Fig. 1

We thank the Swiss National Science Foundation and F Hoffmann-La Roche, Basel, for generous financial support.

Notes and references

‡ *Synthesis* of **17** and **18**: at 25 °C, a solution of **12** (R,R′ = H, 4-ClC_6H_4, 116 mg, 0.42 mmol) in abs. THF (3 ml) was treated portionwise with a cooled (dry ice, *ca.* −60 °C) solution of **1** (77 mg, 0.14 mmol) in dry CH_2Cl_2 (0.8 ml) within 140 min, stirred for 2 h at 25 °C until complete disappearance of **1**. Evaporation at 20 °C and flash chromatography (hexane–AcOEt–CH_2Cl_2 18:1:1) gave **17**/**18** (61 mg, 55%, 45:55), which were separated by preparative HPLC (hexane–AcOEt 12:1; 9 ml min^{-1}). *Selected data* for **17**: R_f (hexane–AcOEt–CH_2Cl_2 4:1:1) 0.36; $[\alpha]_D^{25}$ +51.4 (*c* 1.16, CH_2Cl_2); ν_{max}(CH_2Cl_2)/cm^{-1} 3032*w*, 2927*m*, 2963*m*, 1604*w*, 1493*m*, 1453*m*, 1420*m*, 1364*m*, 1092*s*, 1027*s*; δ_H(300 MHz, $CDCl_3$) 7.62–7.11 (*m*, 20 arom. H), 4.87 (*d*, *J* 10.6, PhC*H*), 4.85 (*d*, *J* 10.9, PhC*H*), 4.83 (*d*, *J* 10.9, PhC*H*), 4.77 (*d*, *J* 10.9, PhC*H*), 4.71 (*d*, *J* 12.1, PhC*H*), 4.70–4.66 (*m*, BOCH), 4.68 (*d*, *J* 10.9, PhC*H*), 4.66 (*d*, *J* 10.9, PhC*H*), 4.64 (*d*, *J* 12.1, PhC*H*), 3.91 [*t*, *J* 8.7, H–C(5)], 3.74 [*dd*, *J* 11.2, 4.0, H–C(8)], 3.73 [*dd*, *J* 11.2, 1.9, H′–C(8)], 3.68 [*d*, *J* 9.0, irrad. at 3.91 → *d*, *J* ≈ 4, H–C(4)], 3.67–3.63 [*m*, H–C(7)], 3.58 [*t*, *J* 8.4, irrad. at 3.91 → *dd*, *J* ≈ 9, 3, H–C(6)], 2.65–2.56 [*m*, 2 H–C(1)], 2.37–2.27 [*m*, irrad. at 2.6 → *d*, *J* ≈ 10, H–C(2)], 2.22–2.18 (*m*, BCH), 2.01–1.91 [*m*, irrad. at 2.6 → *d*, *J* ≈ 10, H′–C(2)], 2.01–1.46 (*m*, 12 H); δ_C(75 MHz, $CDCl_3$, assignment based on ^{1}H/^{13}C COSY) 142.03 (*s*), 139.00 (2*s*), 138.69, 138.29, 131.12 (3*s*), 129.79–127.12 (several *d*), 84.42 [*d*, C(5)], 81.57 [*d*, C(4)], 79.53 [*d*, C(6)], 75.60, 75.13, 74.73 (3*t*, 3 PhCH_2), 74.19 (*d*, BOCH), 73.51 (*t*, PhCH_2), 72.24 [*d*, C(7)], 69.99 [*t*, C(8)], 32.41 (*t*), 30.63 (*t*), 30.19 [*t*, C(1)], 28.91 [*t*, C(2)], 27.54 (*t*), 25.63 (*t*), 22.89 (*t*), 21.91 (*t*), 21.30 (small br *d*, HCB), signal of C(3) hidden by noise; δ_B(160 MHz, $CDCl_3$) 52.02 (br *s*); *m*/*z* (FAB) 821 (< 1%, [*M* + Na]$^+$), 799 (< 1, [*M* + H]$^+$), 599 (38), 553 (43, [*M* − $BnOBOC_8H_{14}$ + H]$^+$), 447 (44), 181 (100). For **18**: R_f (hexane–AcOEt–CH_2Cl_2 10:1:1) 0.32; $[\alpha]_D^{25}$ +12.0 (*c* 0.65, CH_2Cl_2); ν_{max}(CH_2Cl_2/cm^{-1} 3032*w*, 2927*m*, 1492*m*, 1453*m*, 1418*w*, 1364*m*, 1093*s*, 1027*m*, 1015*m*; δ_H(300 MHz, $CDCl_3$) 7.38–6.99 (*m*, 20 arom. H), 4.98 (*d*, *J* 11.8, PhC*H*), 4.85 (*d*, *J* 10.9, PhC*H*), 4.84 (*s*, PhCH_2), 4.70 (*d*, *J* 11.8, PhC*H*), 4.71–4.67 (*m*, HCOB), 4.68 (*d*, *J* 12.1, PhC*H*), 4.62 (*d*, *J* 10.9, PhC*H*), 4.60 (*d*, *J* 12.1, PhC*H*), 3.96 [*dt*, *J* ≈ 9.6, 4.0, H–C(7)], 3.78–3.70 [*m*, H–C(5), 2 H–C(8)], 3.60 [*t*, *J* 9.6, irrad. at 3.96 → *d*, *J* ≈ 9, H–C(6)], 3.50 [*d*, *J* 9.4, H–C(4)], 2.74–2.67 [*m*, 2 H–C(1)], 2.25–2.21 (*m*, BCH), 2.05–1.95 [*m*, irrad. at 2.70 → *d*, *J* ≈ 12, H–C(2)], 1.99–1.26 (*m*, 13 H); δ_C(75 MHz, $CDCl_3$, assignment based on ^{1}H/^{13}C COSY) 141.75 (*s*), 139.26 (2*s*), 138.2, 137.8, 133.6 (3*s*), 129.9–127.14 (several *d*), 85.93 [*d*, C(5)], 84.90 [*d*, C(3)], 79.54 [*d*, C(6)], 76.00 [*d*, C(7)], 75.37, 75.09, 74.80 (3*t*, 3 PhCH_2); 74.06 (*d*, BOCH), 73.22 (*t*, PhCH_2), 69.93 [*t*, C(8)], 37.14 [*t*, C(2)], 31.82 (*t*), 30.91 (*t*), 29.33 [*t*, C(1)], 26.79 (*t*), 25.77 (*t*), 23.38 (small br *d*, BCH), 22.48 (*t*), 21.92 (*t*), signal of C(3) hidden by noise; δ_B(160 MHz, $CDCl_3$) 53.8 (br *s*); *m*/*z* (FAB) 821 (< 1%, [*M* + Na]$^+$), 799 (< 1, [*M* + H]$^+$), 553 (43, [*M* − $BnOBOC_8H_{14}$ + H]$^+$), 461 (28), 401 (41), 325 (60), 281 (87), 181 (100).

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