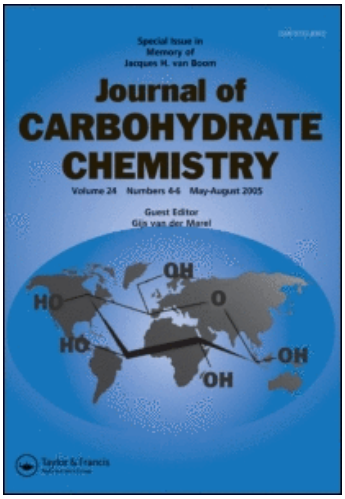

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COMMUNICATION

RIGID gt CONFORMATION OF THE C5/C6 BOND IN A GLUCO DERIVATIVE

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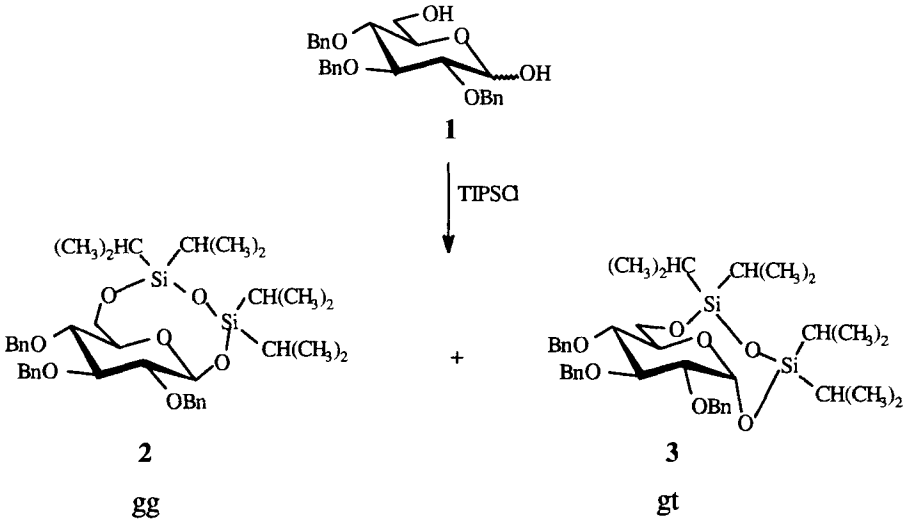
The rotational freedom of the C5/C6 bond of hexopyranosides very often governs the conformation of oligosaccharides, especially when 1→6 linkages are present in the saccharide. Conformational analysis may be complicated by the existence of a dynamic equilibrium between three staggered rotamers in the C5/C6 fragment.[1] The population of the individual rotamers can be deduced from $J_{5,6S}$ and $J_{5,6R}$ coupling constants by applying an equation that connects the experimentally derived time-averaged coupling constants to the populational equilibrium. A prerequisite for this approach is the assignment of the prochiral protons H-6R and H-6S[2] and a correct evaluation of the effects of substituents on the coupling constants.[3,4]

The accuracy of the applied approach may be determined by comparing the calculated results with experimental data of rigid derivatives of known conformations, as has been done for the fixed tg conformations of 4,6-*O*-benzylideneglucosides.[4] Unfortunately, other glucose derivatives are flexible compounds with gg and gt rotamer populations of about 60/40. As an exception to this a glucose-6-*O*-sulfate shows a gt conformation in the crystal,[5] but the same molecule adopts the normal equilibrium of gg and gt

rotamers in solution.[6] We are not aware of any gluco compound with a gt conformation in solution and, hence, any experimental evidence for the theoretical coupling constant in this rotamer. We wish to report here the synthesis of and data from two glucose derivatives **2** and **3**, that both adopt a single, defined rotameric conformation at C5/C6: the α-anomer adopts a gt rotamer, whereas the β-anomer has gg conformation.



In our attempts to prepare 1,6-bridged glycosides we treated 2,3,4-tri-*O*-benzyl-glucose **1**[7] with several dialkyldichlorosilanes. The resulting products were too reactive to survive isolation. Only when we used tipsylchloride[8,9] (1,3-dichloro-1,1,3,3-tetraisopropyl-1,3-disiloxane) did we succeed in isolating the α- and β-anomer of the corresponding 1,6-tipsyl-glucosides **2** and **3**. These 1,6-bridged saccharides are very labile towards neutral and acidic hydrolysis because the acetalic position 1 is part of the ring system. These products have to be separated immediately under basic conditions.

The β-anomer **2** was obtained in 51% yield as the main product. The C5/C6 bond adopts a gg conformation ($J_{5,6S}$ = 1.2 Hz and $J_{5,6R}$ = 5.4 Hz) with slightly distorted torsion angles from the ideal staggered positions, because of steric reasons. Since nine atoms form the bridge there is little strain imposed on the sugar ring, and unlike previously prepared 1,6-bridged derivatives,[10] both glycosides **2** and **3** remain in the $^4C_1$-conformation. The minor isomer, the α-glucoside **3**, is obtained in 5 % yield from **1.** Due to steric requirements, **3** adopts a gt conformation at the C5/C6 linkage allowing unambiguous assignment of the prochiral protons, whose coupling constants are $J_{5,6S}$ = 1.5 Hz and $J_{5,6R}$ = 9.5 Hz.

EXPERIMENTAL

General methods. The reaction was monitored by TLC on silica gel (GF_{254}, Merck) and the spots were detected by UV absorption and staining with sulphuric acid. For chromatography, silica gel 60 (70 - 230 mesh, Merck) was used. Optical rotations were determined with a Perkin-Elmer model 241 MC. ^1H NMR spectra were recorded at 300.13 MHz with an AM 300 from Bruker Analytische Meßtechnik and ^{13}C NMR spectra were obtained with the same instrument at 75.47 MHz. [D_6] benzene was used as the NMR solvent and tetramethylsilane as internal standard. Mass spectra were recorded on a MAT 212 from Finnigan Mat (70 eV, He gas support) in the chemical ionization mode(isobutane).

2,3,4-Tri-*O*-benzyl-1,6-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxanediyl) α- and β-D-glucopyranose (2 and 3). A solution of 2,3,4-tri-*O*-benzyl-D-glucopyranose **1** (203 mg, 0.45 mmol) and imidazole (66 mg, 1.0 mmol) in dry pyridine (2 mL) was stirred with molecular sieve under nitrogen. 1,1,3,3-Tetraisopropyl-1,3-disiloxane-1,3-dichloride (250 µL, 0.8 mmol) was added dropwise over a period of 15 min. After an additional 30 min the reaction was complete and the solution was filtered, concentrated and products immediately separated by chromatography on silica gel which had been treated previously with 1% triethylamine (eluent : ethyl acetate / petroleum ether = 1/ 3 and triethylamine (0.5 %)).

The β-anomer **2** was eluted first (161 mg, 51 %): $[\alpha]_D^{20}$ = -7.8° (*c* 0.5 in chloroform); MS (70 eV) m/z 694 (M^+), 651 (M^+-C_3H_7), 587 (M^+-OCH_2Ph); ^1H NMR δ 7.40 -7.10 (m, 15H, aromatic), 5.015 (d, 1H, J = 11.4 Hz, CH_2Ph), 4.994 (d, 1H, $J_{1,2}$ = 7.4 Hz, 1H, H-1), 4.930 (d, 2H, J = 11.6 Hz, 2 x CH_2Ph), 4.796 (d, 1H, J = 11.2 Hz, CH_2Ph), 4.763 (d, 1H, J = 11.0 Hz, CH_2Ph), 4.620 (d, 1H, J = 11.2 Hz, CH_2Ph), 4.200 (dd, 1H, $J_{5,6S}$ =1.2 Hz, $J_{6S,6R}$ = 11.4 Hz, H-6S), 3.969 (dd, 1H, $J_{5,6R}$ = 5.4 Hz, H-6R), 3.628 (m, 2H, H-3 and H-4), 3.471(ddd, 1H, $J_{4,5}$ = 9.2 Hz, H-5), 3.470 (dd, 1H, $J_{2,3}$ = 9.6 Hz, H-2), 1.300 - 1.000 (m, 16H, $CH(CH_3)_2$ and $CH(CH_3)_2$); ^{13}C NMR δ 139.24, 139.00, 138.89 (C_q aromatic), 128.57-127.69 (15 x C aromatic), 98.09 (C-1), 84.95 (C-4), 84.23 (C-2), 77.77 (C-3), 77.12 (C-5), 75.69, 75.18, 75.04 (CH_2Ph), 62.59 (C-6), 17.72, 17.64, 17.59, 17.51 ($CH(CH_3)_2$), 14.06,13.94, 13.76, 13.69, 13.41, 13.32, 13.20, 13.14 ($CH(CH_3)_2$).

Anal. Calcd for $C_{39}H_{56}O_7Si_2$ (693.04): C, 67.59; H, 8.14. Found: C, 68.01; H, 8.24.

The second fraction contained the α-anomer **3** (16 mg, 5 %); $[\alpha]_D^{20}$ = 16.7° (*c* 0.44 in benzene); ^{1}H NMR δ 7.50 - 7.00 (m, 15H, H-aromatic), 5.489 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.973 (d, 1H, J = 12.0 Hz, C*H*$_2$Ph), 4.770 (d, 1H, J = 11.6 Hz, C*H*$_2$Ph), 4.750 (d, 1H, J = 11.6 Hz, C*H*$_2$Ph), 4.589 (d, 1H, J = 12.0 Hz, C*H*$_2$Ph), 4.503 (d, 1H, J = 11.6 Hz, C*H*$_2$Ph), 4.409 (d, 1H, J = 11.6 Hz, C*H*$_2$Ph), 4.361 (dd, 1H, $J_{5,6S}$ = 1.5 Hz, $J_{6S,6R}$ = 11.4 Hz, H-6S), 4.118 (dd, 1H, $J_{2,3}$ = 9.2 Hz, $J_{3,4}$ = 8.6 Hz, H-3), 3.790 (dd, 1H, $J_{5,6R}$ = 9.5 Hz, H-6R), 3.548 (dd, 1H, H-2), 3.213 (dd, 1H, $J_{4,5}$ = 10.4 Hz, H-4) 1.500-0.900 (m, 16H, C*H*(CH$_3$)$_2$ and CH(C*H*$_3$)$_2$); ^{13}C NMR δ 139.60, 139.45,138.93 (C_q aromatic), 130.09 - 127.68 (15 x C aromatic), 97.50 (C-1), 85.12 (C-4), 84.50 (C-2), 78.44 (C-3), 78.15 (C-5), 75.46, 74.94, 75.66 (3 x *C*H$_2$Ph), 62.46 (C-6), 17.76, 17.64 (4 x *C*HCH$_3$),14.80, 14.14, 14.00, 13.80, 13.64, 13.48 (8 x *C*H$_3$).

Anal. Calcd. for $C_{39}H_{56}O_7Si_2$ (693.04): C, 67.59; H, 8.14. Found: C, 67.80; H, 8.18.

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REFERENCES AND NOTES

1. Nomenclature used to describe the staggered rotamers gg, gt and tg: The first letter refers to the angle O-5–C-5–C-6–OH-6, the second to C-4–C-5–C-6–OH-6.
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