Conformational Effects in 2-Deoxyglucopyranos-1-yl Radicals[1)]

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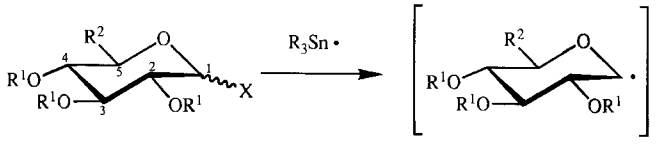
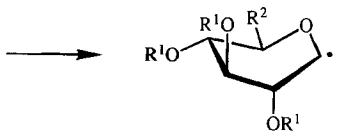
2-Unsubstituted and 2-substituted (fluoro, tosylamino, *n*-propyl) 3,4,6-tri-O-acetyl-2-deoxypyranosyl radicals are obtained by reaction of the corresponding pyranosyl bromides or phenylselenides with photolytically generated trimethyltin radicals in benzene solution. Analysis of the ESR hyperfine splittings reveals that the 2-deoxy-2-fluoroglucopyranosyl radical exists in a boat-like conformation at room temperature, whereas the others retain the $^4C_1$ chair conformation of the starting material. The observed conformational effects are explained by a "quasi-homo-anomeric" frontier orbital interaction of the n_π lone pair of the ring oxygen atom with the σ^* MO of the β-C – O bond, in which the singly occupied p orbital at C-1 acts as a mediator for this 1,3-anomeric interaction.

Recently, it has been demonstrated that radical-induced intermolecular C–C coupling reactions can serve as a useful tool in synthetic carbohydrate chemistry[2)]. *O*-protected pyranosyl compounds in which the radical center is generated at different positions of the carbon skeleton sometimes show a markedly enhanced diastereoselective preference in C–C bond formation. In the course of our ESR-spectroscopic investigations[3,4)] of the intermediate carbohydrate radicals we have observed that in non-aqueous solution π-type C-1 pyranosyl radicals, derived from all-equatorially substituted (glucosyl-type) precursors, transform into a boat-like conformation C instead of retaining the sterically more favored $^4C_1$ chair conformation **A** of the starting material. The primary radical **B** can be observed only in a low-temperature matrix[5)]. From the ESR data we have deduced a twisted $B_{2,5}$ boat conformation[3,6)] to be the most populated equilibrium conformation of the C-1 glucosyl radicals.

Our original explanation for the conformational change **B** → **C** by frontier molecular orbital arguments has been modified recently[1)]. We propose a so-called "quasi-homo-anomeric" stabilization effect to be operative when the β-C – O bond is in a parallel orientation with the singly occupied p orbital (see Discussion). Our interpretation is strongly supported by the fact that in 2-manno-pyranosyl-type systems **E**, where the β-C – O bond is already in the axial position, no conformational change can be observed[3)].



A **B**

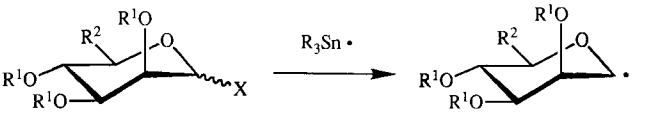


C

R^1 = Me, Ac, Bz

R^2 = H, CH_2OR^1

X = Br, I, SePh, $COBu^t$



D **E**

Regarding the quasi-homo-anomeric effect in C-1 pyranosyl radicals as a special case of the general anomeric effect[8)], we expect it to be operative also in pyranosyl radicals carrying substituents at C-2 of equal or higher electronegativity than oxygen and vice versa[8,9)]. In the present study we report on the conformation of C-1 glucopyranosyl radicals where the β-oxygen substituent is replaced by hydrogen, fluorine, *n*-propyl, or tosylamino.

Results

ESR Measurements

The pyranosyl radicals (**1R** – **8R**) have been generated in benzene solution in the cavity of the ESR spectrometer by reaction of the corresponding 1-bromo- or 1-phenylseleno-substituted compounds (**1** – **8**) with trimethyltin radicals, produced by UV photolysis of hexamethylditin. ESR spectra of the radicals **1R** – **8R** have been recorded in the temperature range from 264 to 323 K, and the analysis of their hyperfine splittings (hfs) (Table 1) has been refined by computer simulation. Assignment of the hyperfine splitting constants is based on a specific deuteration (see below) and a comparison

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with data from our previous studies[3-5]. The regiospecific generation of the radical center is obvious from the α-hydrogen hfs of 1.7–1.9 mT and the g values in the range of 2.003–2.004, representing typical data for α-alkoxyalkyl radicals.

Table 1. ESR data of 2-deoxyglucopyranosyl radicals in benzene solution

Radical	T [K]	g value[b]	Hyperfine splittings [mT][a] a(α-H)	a(β-H)	a(γ_1-H)	a(γ_2-H)	a(other)
1R	272	2.0038(2)	1.905	0.435	0.375	0.310	13.62 (1F)
2R	264	2.00328(3)	1.732	4.768	0.187	0.081	
				<0.03			
2R[c]	296	2.00329(3)	1.734	4.750	0.180	0.083	≤0.01 (δ-H)
				0.015			
3R	264	2.00323(3)	1.728	4.07(1)	0.184	0.083	<0.01 (β-D)
4R	264	2.00320(5)	1.725	4.769	-	0.079	0.028 (γ_1-D)
				0.014			0.010 (δ-H)
5R	264	2.00347(5)	1.728	4.768	0.187	0.081	5.774 (α-^{13}C)
				0.010			
6R	290	2.00313(3)	1.393	3.445	0.156	0.084	6.35(1) (α-^{13}C)
7R	323	2.0032(1)	1.700	3.733	0.190	0.080	0.055 (2γ-H)[d]
8R	257	2.0031(1)	1.633	3.580	0.190	0.073	0.185 (β-N)

[a] ±0.003 mT, unless otherwise noted. – [b] Estimated errors in the last digit are given in parentheses. – [c] At low modulation amplitude (0.01 mT). – [d] Exocyclic CH_2 group.

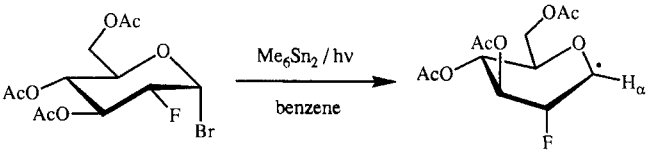
The equilibrium conformations of the radicals[10] are deduced from the angular dependence of the β-hydrogen hfs by application of the common relation (1)[11]

$$a(\beta\text{-H}) = A + B\langle\cos^2\Theta\rangle \quad (1)$$

with $A = 0.3 \pm 0.2$ mT and $B = 4.9 \pm 0.5$ mT, where Θ stands for the dihedral angle between the direction of the singly occupied p orbital and the β-C–H bond. According to eq. (1) the β-H splitting is expected to vary between values around 0 and 5 mT for orthogonal and parallel arrangement of the β-C–H bond, respectively.

Experimental β-H splittings arise from an average of rotational quantum states and, therefore, correspond to an average value of $\langle\cos^2\Theta\rangle$ rather than an average dihedral angle $\langle\Theta\rangle$[11,12]. Consequently, the application of eq. (1) leads to physically meaningful dihedral angles only in cases where the relative conformation of the –CH–CH(X)– subunit (X = H, OR, F, NHR) is reasonably rigid in the particular radical. Due to their cyclic structure and the barriers associated with the chair-boat interconversion (fairly narrow potential wells for the β-CHX rotational vibrations can be assumed) our 2-deoxypyranosyl radicals should be locked in structures rigid enough to allow an estimation of the dihedral angles from the observed β-H splittings.

3,4,6-Tri-O-acetyl-2-deoxy-2-fluoro-D-glucopyranosyl Radical **1R**. Bromine abstraction from 3,4,6-tri-*O*-acetyl-2-deoxy-2-fluoro-α-D-glucopyranosyl bromide (**1**) at –1°C yields a radical, the ESR spectrum of which (Figure 1) is dominated by a doublet splitting of 13.6 mT. Such a large coupling can only be attributed to an axially oriented β-fluoro substituent in radical **1R**. The magnitude of the β-F coupling is at the upper limit observed for β-fluoroalkyl radicals in solution[11,13] and proves that radical **1R** has been converted from the $^4C_1$ conformation of the precursor into the $B_{2,5}$ boat conformation.



1 **1R**

In addition to the almost "normal" α-H hfs, three small doublet splittings are observed in agreement with the presence of one pseudo-equatorial β-H atom and two different γ-hydrogen atoms. The relative assignment of these three hfs is based on a comparison with other C-1 pyranosyl radicals[3,4] but remains somewhat tentative. The significant increase of the γ_2-H splitting at C-3 compared with the related β-oxygen-substituted pyranosyl radicals might reflect an increased spin density at C-2 induced by the β-fluorine substituent. The $B_{2,5}$ conformation of **1R** demonstrates that this radical gains stabilization by the conformational change.

Figure 1. ESR spectrum of the 3,4,6-tri-*O*-acetyl-2-fluoro-2-deoxyglucopyranosyl radical **1R** at 273 K in benzene solution

3,4,6-Tri-O-acetyl-2-deoxy-D-glucopyranosyl Radicals **2R**–**5R**. The ESR spectrum (Figure 2) of the 3,4,6-tri-*O*-acetyl-2-deoxy-D-glucopyranosyl radical **2R**, obtained from the corresponding 1-phenylseleno compound **2** exhibits a large doublet splitting of about 4.77 mT, a value which is in the range expected for an axially oriented β-hydrogen atom. According to eq. (1), a deviation of ca. 17° from coplanarity of the direction of the SOMO and the β-C–H bond is estimated. Computer simulation reveals the presence of two additional splittings of ca. 0.015 and 0.01 mT which could not be completely resolved from the experimental linewidth at low modulation amplitudes. We assign these hfs to the equatorial β-hydrogen atom and the δ-hydrogen atom at C-4, respectively (see below). The exceptional small second β-H splitting implies a pronounced alignment of the equatorial β-C–H bond in the nodal plane of the semioccupied p orbital. The dihedral angle is estimated to be about 14°.

The conservation of the $^4C_1$ chair conformation may be deduced from the magnitude of the hfs of the two γ-hydrogen atoms at C-3 and C-5, respectively, the values of which

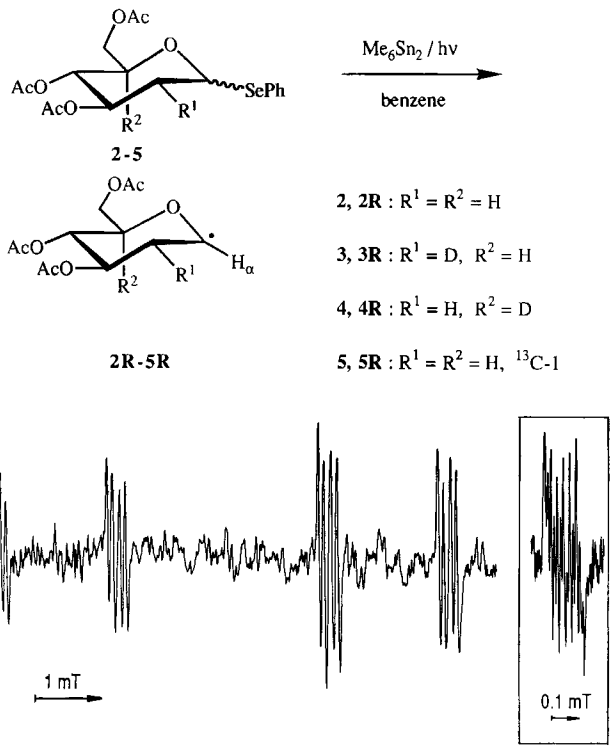
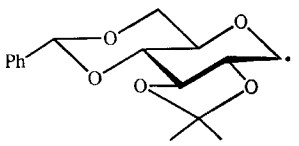


Figure 2. ESR spectrum of the 3,4,6-tri-*O*-acetyl-2-deoxyglucopyranosyl radical **2R** at 264 K in benzene solution; inset: outermost right-hand group of the 3,4,6-tri-*O*-acetyl-2-deoxy-[5-^{2}H]-glucopyranosyl radical **4R** at 283 K

are significantly smaller than those of the boat-type pyranosyl radicals[3]. A similar effect has been found in other chair-type radicals, e.g. **6R**[3b]. However, the present set of coupling constants did not allow an unequivocal discrimination to be made between chair and boat structures, since the latter are also characterized by pronounced parallel and orthogonal orientations of the β-hydrogen atoms.



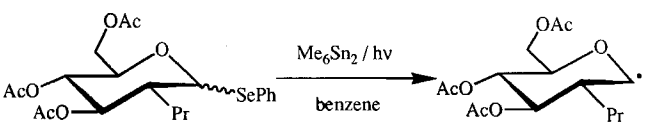
6R

An unambiguous proof for the conservation of the $^4C_1$ conformation in **2R** and also the relative assignment of the β- and γ-H hfs has been obtained from specifically deuterated material. The ESR spectrum of the radical **3R**, derived from the 2-deoxyglucopyranosyl compound **3** in which the equatorial β-hydrogen atom is replaced by deuterium, is almost indistinguishable to that of its undeuterated analog **2R**, proving that indeed the equatorial β-H atom is associated with one of the small, unresolvable hfs. Since the axial and equatorial C-2 substituents interchange their relative orientation if the radical undergoes the $^4C_1 \rightarrow B_{2,5}$ transformation one would expect a β-^{2}H splitting around $4.77 \times 0.153 = 0.7$ mT and a β-H splitting in the range of 0.3–1.3 mT, respectively. Obviously, this is not the case. Remarkably, the axial β-H splitting of 4.0 mT in **3R** is smaller by ca. 0.7 mT compared with the C-2-undeuterated radicals **2R**, **4R**, and **5R**. It would be surprising if such an effect could be due to the electronic influence of the deuterium substituent on the spin density at C-2 or a significant change of the conformation of the radical. We rather prefer to relate this interesting phenomenon to a larger amplitude of the bending vibration of the β-CH_2 group in the case of the isotopic substitution, leading to an increased population of rotational vibration states of larger dihedral angles Θ according to eq. (1).

The relative assignment of the two γ-hfs can be made on the basis of the hfs of the C-5-deuterated radical **4R** (Figure 2). A correct value of 0.03 mT for the deuterium splitting, as calculated from the 0.18 mT splitting in **2R**, has been derived from the ESR spectrum. In this case we have been able to resolve the hfs of the equatorial β- and the δ-hydrogen atom. Their values confirm our assignment for **2R**. The isotopic substitution at C-5 leads to a reduction of the ESR linewidth, making the small additional splittings resolvable.

In order to elucidate the effect of β substituents on the *configuration* of the radical center in C-1 pyranosyl radicals we have also measured the α-^{13}C hfs in the 2-deoxyglucopyranosyl system from ^{13}C-labeled material **5**. The α-^{13}C splitting in radical **5R** amounts to 5.77 mT from which an average out-of-plane bent angle of ca. 6° has been estimated, following the approach outlined before[3,14]. This bent angle corresponds to approximately 2.1% 2s character of the semioccupied p orbital, i.e. about 10% on the way from a "pure" sp^2-hybridized π radical to a "pure" sp^3- hybridized σ radical. For the 2,3,4,6-tetra-*O*-acetylglucopyranosyl radical in the boat conformation (structure **C**; R^1 = OAc, R^2 = CH_2OAc)[3] we have found a somewhat smaller α-^{13}C hfs of 4.72 mT, corresponding to ca. 4° out-of-plane bending. It seems that the additional quasi-homo-anomeric stabilization by the axially oriented β-C–O bond induces some "flattening" of the radical center, i.e. increases the π character of the radical[15]. In accordance, we observed a relatively large α-^{13}C splitting of 6.35 mT in the ESR spectrum of the tricyclic glucosyl radical **6R**. Here, the chair conformation is fixed by the *trans* fusion of the cyclic substituents, prohibiting the coplanar arrangement of the β-C–O bond and the SOMO. The pyramidalization in the latter case has been estimated to about 7° (ca. 2.7% 2s character)[16].

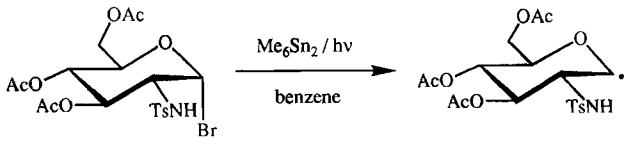
3,4,6-Tri-O-acetyl-2-deoxy-2-propyl-D-glucopyranosyl Radical **7R**. The major structural feature of radical **7R** as deduced from its ESR spectrum (Table 1) is the preservation of the $^4C_1$ chair conformation of the starting compound **7**, i.e. the *n*-propyl group at C-2 assumes the equatorial position. This fact is unequivocally indicated by the hfs of 3.73 mT for the β-hydrogen atom in the axial orientation. More-



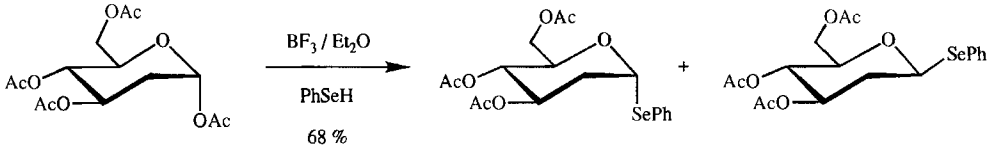
7 **7R**

over, the γ-hydrogen splittings are close to the values of those in radicals **2R**–**5R**. Thus, any quasi-anomeric interaction is too low to overcompensate the steric demands for a chair-boat interconversion.

3,4,6-Tri-O-acetyl-2-deoxy-2-(N-tosylamino)-D-glucopyranosyl Radical **8R**. Depending on their substitution pattern, nitrogen substituents show different and less predictable anomeric behavior. Therefore, it seemed interesting to us to look for the conformational effects which nitrogen substituents might induce in pyranosyl radicals. So far, we have only been successful with the 2-tosylamino compound **8**[17]. The ESR spectrum of **8R**, produced from **8**, was rather weak

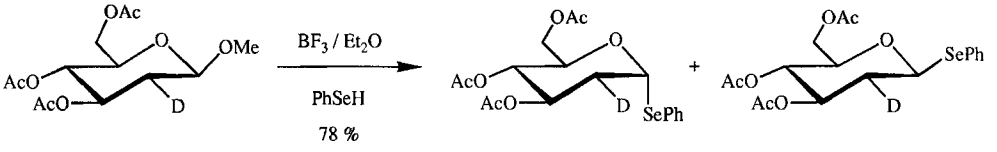


8 **8R**



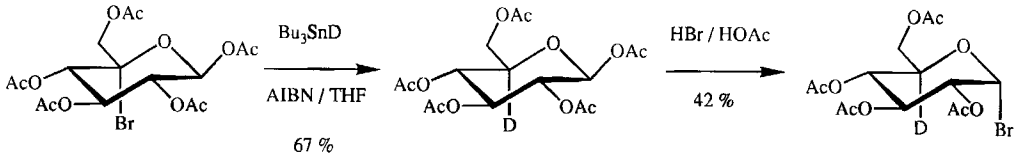
9 **2α** **2β**

2 : 1

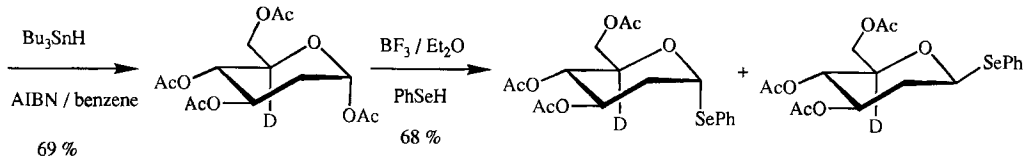


10 **3α** **3β**

5 : 1

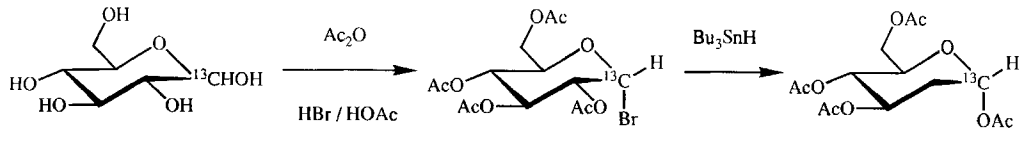


11 **12** **13**

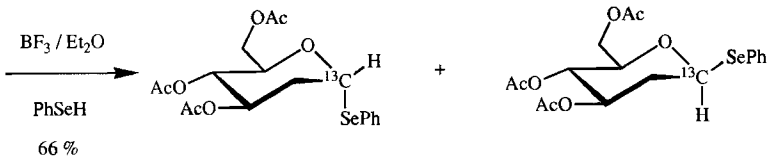


14 **4α** **4β**

5 : 1

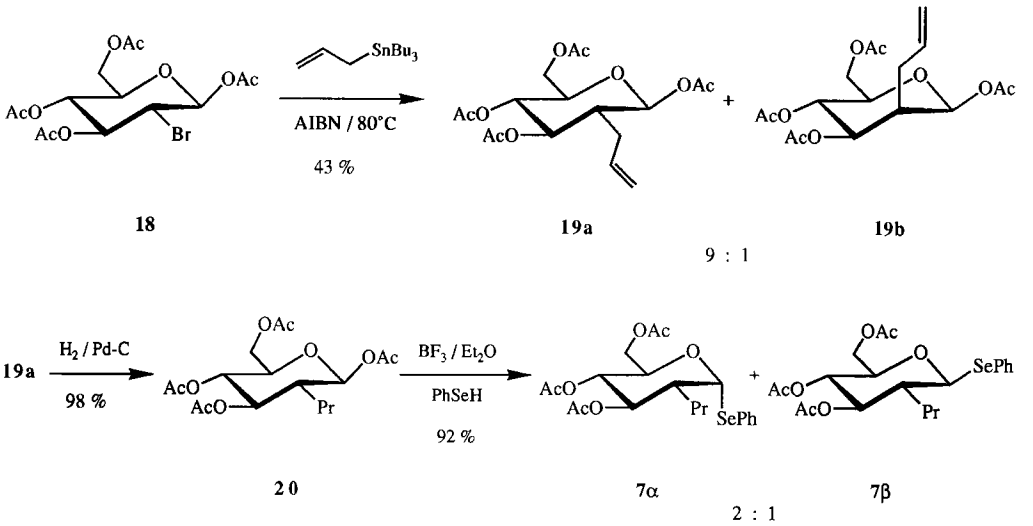


15 **16** **17**



5α **5β**

3 : 1



but could be analyzed unequivocally in terms of its structure. A doublet splitting of 3.48 mT and a small nitrogen triplet splitting of 0.19 mT clearly reflect the conservation of the $^4C_1$ chair conformation of the starting material. Thus, the interaction of the tosylamino substituent with the radical center is not strong enough to induce a change in the conformation of the pyranosyl ring. The reduction of the axial β-H splitting from the "parent" value 4.77 mT in **2R** to 3.48 mT corresponds to the effect of the β-acetoxy substituent observed in radical **6R**.

Synthesis of the Radical Precursors

The 2-deoxy sugar selenides **2**–**5** were prepared by treatment of deoxyglucosides **9**, **10**, **14**, and **17** with selenophenol and boron tifluoride.

The labeled precursors **14** and **17** may be synthesized by reductive radical rearrangement[4,18] of glucosides **13** and **16**. The radical reaction of allyltributyltin with bromide **18** introduces the allyl group into position C-2 of the carbohydrate. Because of equatorial substituents at the sugar, the equatorially allylated product **19a** is formed predominantly[19]. Isomer **19a** crystallized from the mixture and is converted into selenides **7α,β** after catalytic hydrogenation (→ **20**).

Fluoro- and amino sugars **1** and **8** have been prepared according to the literature[20].

Discussion

Our previous ESR studies[3–5] have shown that in *O*-protected C-1 pyranosyl radicals in non-aqueous solution the β-C–O substituent at C-2 tries to achieve or preserve an ecliptic, i.e. axial, orientation with respect to the singly occupied p orbital[21]. Consequently, in all-equatorially substituted pyranosyl radicals, viz. glucosyl or xylosyl radicals, the chair conformation of the precursors is converted into a more or less twisted $B_{2,5}$ conformation. Other systems, e.g. galactopyranosyl radicals, adopt intermediate structures, compromising the tendency for ecliptic orientation and opposing steric repulsions. On the other hand, mannosyl-type pyranosyl radicals retain their chair conformations since here the β-C–O bond already occupies the axial position.

Originally, we have explained this interesting phenomenon on the basis of the frontier orbital theory by a so-called "quasi-anomeric effect", where the SOMO is thought to undergo a stabilizing interaction with the σ* LUMO of the β-C–O bond. As the conformational effect has also been observed in C-5, but not in C-2, C-3, or C-4 pyranosyl radicals, we have proposed the necessity of the simultaneous interaction of the SOMO with the n_π lone pair of the ring oxygen atom. The latter process raises the energy level of the SOMO, thus making it more favorable for the interaction with the β-C–O LUMO.

However, the similar conformational behavior of pyranosyl radicals carrying additional radical-stabilizing substituents at the radical center has prompted us to modify our interpretation[1]. In order to obtain a consistent picture, the interaction of the π-type lone pair at the ring oxygen atom and the σ* orbital of the β-C–O bond also has to be considered explicitly, i.e. such an interaction may be called "homo-anomeric". Examples for such a 1,3 stabilization are indeed known in closed-shell systems[22]. According to the FMO picture, the homo-anomeric interaction is favorably transmitted by the p orbital at C-1. Hence, the combination of the SOMO-σ* and the n_π-σ* interactions constitute the driving force for the conformational change. Therefore, we use the term "quasi-homo-anomeric effect".

The results of the present study on 2-deoxypyranosyl radicals are in full agreement with the above explanation. The β-fluorine substituent in **1R** undoubtedly adopts the axial position, i.e. within the time scale of the ESR experiment the initial chair conformation has been largely converted into a boat-like conformation[23]. This fact strongly suggests that the quasi-homo-anomeric interaction is governed by the electronegativity, or σ acceptor strength, of the β substituent just in the same way as is the normal anomeric effect[8,9]. Experimental[8] and theoretical[9] studies have shown that fluorine as substituent exerts one of the strongest anomeric effects.

The 2-deoxypyranosyl radicals **2R**–**5R** may be regarded as a standard set for the assessment of the influence of β-substituents on the conformation of pyranosyl radicals. The

ESR data of **2R**–**5R** imply that apart from the sp^2 hybridization of the radical center no apparent change of the $^4C_1$ chair conformation has occurred. The estimated 17° deviation of the axial β-H bond from the perfect ecliptic orientation and the 14°-dihedral angle between the directions of the equatorial β-H bond and the nodal plane of the singly occupied p orbital agree surprisingly well with the geometry as deduced from simple framework models.

The anomeric effect associated with alkyl substituents is generally found to be too weak to overcompensate the steric preference for an equatorial orientation[8]. Therefore, a fundamental conformational change in the 2-*n*-propyl-substituted glucosyl radical **7R** has not been expected. This is confirmed by its experimental hfs. Since the two γ splittings at C-3 and C-5 remain almost unchanged compared with those of **2R**, the distortion of the initial $^4C_1$ chair should be relatively small. The reduction of the axial β-H hfs by about 1.0 mT compared with those of **2R**–**5R** may be attributed to the electronic influence of the alkyl substituent and/or a larger amplitude of the β-CHR bending vibration rather than a conformational change.

Amino substituents are weaker σ-acceptor groups than oxygen substituents, as can be deduced from their group electronegativities[22]. This fact and the higher π-donor ability of the amino groups should render them less effective for anomeric stabilizations[8,9]. We expect them to represent borderline cases, depending on the particular substitution pattern at nitrogen. For radical **8** the conservation of the chair conformation suggests that the quasi-homo-anomeric stabilization of the *N*-tosylamino group is insufficient to enforce a conformational change, even with regard to a supposed increase of the σ-acceptor strength of the nitrogen atom by the tosyl group. Another reasonable factor which favors the equatorial orientation is the bulkiness of the tosylamino group.

It would be interesting to see if the introduction of smaller and more electronegative substituents at the β-nitrogen atom finally will lead to a change of the conformation in these systems. Unfortunately, we have not been able to produce any identifiable ESR spectra for several other functionalized β-amino substituents[17].

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Experimental

^{1}H NMR: Bruker WM 300, $CDCl_3$, TMS as internal standard. – MS: Finnigan MAT 311A. – ESR: Bruker ER-420. – Polarimeter: Perkin-Elmer 141 (589 nm).

Materials

1) *Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-1-seleno-D-arabino-hexopyranoside* (**2**): To a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranose[18] (**9**) (3.80 g, 11.4 mmol) in chloroform (30 ml) were added Et_2O-BF_3 (1.60 g, 11.4 mmol) and selenophenol (2.10 g, 13.7 mmol). After 3 h at 20°C the mixture was washed with aqueous sodium hydrogen carbonate (50 ml), dried with sodium sulfate, and the solvent was removed under reduced pressure. Chromatography on silica gel [pentane/ether (2:1)] gave α-selenide **2α** (2.1 g, 45%) of m.p. 84.0–84.5°C and β-selenide **2β** (1.1 g, 23%) as a colorless oil.

α *Isomer* **2α**: $[\alpha]_D^{20} = +260.0$ ($c = 1.0$ in chloroform). – ^{1}H NMR ($CDCl_3$): δ = 2.03, 2.04, 2.07 (s, 3H each, OAc), 2.28 (ddd, J = 5.5, 11.6, 12.5 Hz, 1H, 2′-H), 2.54 (ddd, J = 1.1, 5.2, 12.5 Hz, 1H, 2-H), 4.02 (dd, J = 2.2, 12.2 Hz, 1H, 6′-H), 4.34 (dd, J = 5.1, 12.2 Hz, 1H, 6-H), 4.48 (ddd, J = 2.2, 5.1, 9.8 Hz, 1H, 5-H), 5.04 (t, J = 9.8 Hz, 1H, 4-H), 5.25 (ddd, J = 5.2, 9.8, 11.6 Hz, 1H, 3-H), 5.97 (dd, J = 1.1, 5.5 Hz, 1H, 1-H), 7.26–7.62 (m, 5H, aromatic H).

$C_{18}H_{22}O_7Se$ (429.3) Calcd. C 50.48 H 5.18
Found C 50.24 H 5.11

β *Isomer* **2β**: ^{1}H NMR ($CDCl_3$): δ = 1.89–1.99 (m, 1H, 2′-H), 2.00, 2.03, 2.08 (s, 3H each, OAc), 2.53 (ddd, J = 4.5, 12.0, 12.7 Hz, 1H, 2-H), 3.63 (ddd, J = 2.4, 5.3, 9.6 Hz, 1H, 5-H), 4.13 (dd, J = 2.4, 12.1 Hz, 1H, 6′-H), 4.24 (dd, J = 5.3, 12.1 Hz, 1H, 6-H), 5.02 (dd, J = 2.1, 12.0 Hz, 1H, 1-H), 4.92–5.05 (m, 2H, 3-, 4-H), 7.29–7.65 (m, 5H, aromatic H).

2) *Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-1-seleno[2-^{2}H]-D-glucopyranoside* (**3**): To a solution of the deuterated methyl glucoside **10**[25] (396 mg, 1.3 mmol) in chloroform (5 ml) were added Et_2O-BF_3 (184 mg, 1.3 mmol) and selenophenol (245 mg, 1.5 mmol). After 12 h at 20°C the reaction mixture was washed with aqueous sodium hydrogen carbonate (20 ml), dried with sodium sulfate, and the solvent was removed under reduced pressure. Chromatography on silica gel [pentane/ether (1:2)] gave selenoglucoside **3** (436 mg, 78%) as an α,β mixture (α:β = 5:1). From this mixture NMR spectra were recorded and elementary analysis was carried out.

α *Isomer* **3α**: ^{1}H NMR ($CDCl_3$): δ = 2.03, 2.04, 2.07 (s, 3H each, OAc), 2.29 (dd, J = 5.1, 11.7 Hz, 1H, 2-H), 4.02 (dd, J = 2.1, 12.2 Hz, 1H, 6′-H), 4.35 (dd, J = 5.1, 12.2 Hz, 1H, 6-H), 4.48 (ddd, J = 2.1, 5.1, 9.6 Hz, 1H, 5-H), 5.04 (t, J = 9.6 Hz, 1H, 4-H), 5.25 (dd, J = 9.4, 11.7 Hz, 1H, 3-H), 5.97 (d, J = 5.1 Hz, 1H, 1-H), 7.26–7.62 (m, 5H, aromatic H).

β *Isomer* **3β**: ^{1}H NMR ($CDCl_3$): δ = 1.89–1.99 (m, 1H, 2-H), 2.00, 2.03, 2.08 (s, 3H each, OAc), 3.63 (ddd, J = 2.4, 5.6, 9.6 Hz, 1H, 5-H), 4.13 (dd, J = 2.4, 12.2 Hz, 1H, 6′-H), 4.25 (dd, J = 5.3, 12.2 Hz, 1H, 6-H), 5.02 (d, J = 12.0 Hz, 1H, 1-H), 4.92–5.05 (m, 2H, 3-, 4-H), 7.29–7.65 (m, 5H, aromatic H).

$C_{18}H_{21}DO_7Se$ (430.3) Calcd. C 50.24 H 5.39
Found C 50.24 H 5.33

3) *Synthesis of Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-1-seleno[5-^{2}H]-α-D-arabino-hexopyranoside* (**4**): Because the synthesis of the deuterated pyranoside **4** from the 5-bromoglucopyranoside **11**[26] follows known procedures of undeuterated sugars, the intermediate compounds **12**–**14** were used without further characterization or purification for the next synthetic steps.

a) *1,2,3,4,6-Penta-O-acetyl[5-^{2}H]-β-D-glucopyranose* (**12**): 1,2,3,4,6-Penta-*O*-acetyl-5-bromo-β-D-glucopyranose[26] (**11**) (4.0 g, 8.5 mmol) was dissolved in tetrahydrofuran (50 ml) under argon in a 100-ml three-necked flask equiped with a septum and a reflux condenser. Tributyl[^{2}H]stannane (3.0 g, 10.2 mmol) was added dropwise with a syringe through the septum. When the mixture began to reflux, irradiation with a 125-W low-pressure mercury lamp was started. After 1 h, the solvent was removed under reduced pressure and the oily residue dissolved in acetonitrile (30 ml). This solution was extracted with pentane (4 × 20 ml) and the acetonitrile phase concentrated in vacuo. The product (2.2 g, 67%) was obtained after chromatography on silica gel [ethyl acetate/pentane (1:2)].

b) *2,3,4,6-Tetra-O-acetyl[5-^{2}H]-α-D-glucopyranosyl Bromide* (**13**): **12** (2.2 g, 5.6 mmol) was mixed without further purification with 25 ml of a 33% solution of hydrobromic acid in acetic acid in the dark. After 12 h, the reaction mixture was diluted with ether (100 ml) and washed with water (2 × 50 ml), aqueous sodium hydrogen carbonate (2 × 50 ml), and again with water (50 ml). The organic phase was dried with sodium sulfate, filtered, and the solvent was removed under pressure. The product (1.1 g, 42%) was obtained as a colorless oil.

c) *1,3,4,6-Tetra-O-acetyl-2-deoxy[5-^{2}H]-α-D-arabino-hexopyranose* (**14**): A solution of tributylstannane (910 mg, 3.1 mmol) and azo(bisisobutyronitrile) (90 mg) in benzene (10 ml) was added dropwise under an inert atmosphere over 8 h to a refluxing solution of **13** (1.1 g, 2.6 mmol) in benzene (20 ml). The solvent was removed under reduced pressure, the residue dissolved in acetonitrile (30 ml), and extracted with pentane (4 × 20 ml). The acetonitrile phase was concentrated in vacuo and chromatographed on silica gel [ether/pentane (2:1)]. The purified product (598 mg, 69%) was used as such in the following step.

d) *Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-1-seleno[5-^{2}H]-D-arabino-hexopyranoside* (**4**): To a solution of **14** (598 g, 1.8 mmol) in chloroform (10 ml) were added Et_2O-BF_3 (254 mg, 1.8 mmol) and selenophenol (339 mg, 2.1 mmol). After 4 h at 20°C, the reaction mixture was washed with water (10 ml), aqueous sodium hydrogen carbonate (10 ml), and again with water (10 ml). The organic phase was dried with magnesium sulfate and the solvent removed under reduced pressure. Chromatography on silica gel [pentane/ether (1:1)] gave selenopyranoside **4** (418 mg, 54%) as a mixture (α:β = 5:1). From this mixture NMR spectra were recorded and elementary analysis was carried out.

α *Isomer* **4α**: ^{1}H NMR ($CDCl_3$): δ = 2.04, 2.06, 2.07 (s, 3H, each, OAc), 2.29 (ddd, *J* = 5.1, 11.6, 13.6 Hz, 1H, 2′-H), 2.53 (ddd, *J* = 1.1, 5.1, 13.6 Hz, 1H, 2-H), 4.02 (d, *J* = 12.3 Hz, 1H, 6′-H), 4.34 (d, *J* = 12.3 Hz, 1H, 6-H), 5.03 (d, *J* = 9.4 Hz, 1H, 4-H), 5.26 (ddd, *J* = 5.1, 9.4, 11.6 Hz, 1H, 3-H), 5.97 (dd, *J* = 1.1, 5.1 Hz, 1H, 1-H), 7.21–7.55 (m, 5H, aromatic H).

The signals for the β isomer **4β** in the mixture were weak. But they were in agreement with the signals of the undeuterated compound **2β**, except for the coupling to 5-H.

$C_{18}H_{21}DO_7Se$ (430.3) Calcd. C 50.24 H 5.39
Found C 50.24 H 5.17

4) *Synthesis of Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-1-seleno-[1-^{13}C]-D-arabino-hexopyranoside* (**5**): [1-^{13}C]Glucose (**15**) (500 mg, 2.8 mmol) was dissolved in pyridine (3.6 ml), cooled to 0°C, and acetic anhydride (2.5 ml) added. After stirring at 0°C for 30 min and then at room temp. for 2 h, the solvent was removed under reduced pressure. Toluene (20 ml) was added twice to the residue and removed each time under reduced pressure. After addition of a 33% solution of hydrogen bromide in acetic acid (2.8 ml), the mixture was stirred at room temp. for 3 h. It was diluted with chloroform (20 ml), and washed twice with ice-cold water (20 ml), aqueous sodium hydrogen carbonate (20 ml), and again with ice-cold water (20 ml). The organic phase was dried with sodium sulfate and concentrated in vacuo to yield an oil. The 2,3,4,6-tetra-*O*-acetyl-1-bromo[1-^{13}C]-α-D-glucopyranose (**16**) so obtained was dissolved in benzene (20 ml) under an inert atmosphere and heated to reflux. A solution of tributylstannane (810 mg, 2.8 mmol) and azo(bisisobutyronitrile) (50 mg) in benzene (10 ml) was added dropwise over 8 h. The solvent was removed in vacuo and the residue chromatographed on silica gel [pentane/ether (2:1)] to give 1,2,3,4,6-tetra-*O*-acetyl-2-deoxy-[1-^{13}C]-α-D-*arabino*-hexopyranose (**17**) (780 mg, 84%) as a colorless oil, which was used without further purification. The oil was dissolved in chloroform (10 ml) under an inert atmosphere and stirred with selenophenol (370 mg, 2.3 mmol) at room temp. for 18 h. The reaction mixture was then washed with aqueous sodium hydrogen carbonate (20 ml), dried with magnesium sulfate and purified by chromatography on silica gel [pentane/ether (1:1)]. **5** (650 mg, 66%) was obtained as a colorless oil as a mixture of isomers (α:β = 3:1). From this mixture NMR spectra were recorded and elementary analysis was carried out. The ^{1}H-NMR spectra are in agreement with the unlabeled compounds **2α** and **2β**.

$C_{17}{}^{13}CH_{22}O_7Se$ (430.3) Calcd. C 50.48 H 5.15
Found C 50.33 H 5.13

5) *Synthesis of Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-2-C-propyl-1-seleno-D-glucopyanoside* (**7**)

a) *1,3,4,6-Tetra-O-acetyl-2-C-allyl-2-deoxy-β-D-glucopyranose* (**19**): A solution of azo(bisisobutyronitrile) (280 mg, 1.7 mmol) in anhydrous benzene (20 ml) was added dropwise to a solution of 1,3,4,6-tetra-*O*-acetyl-2-bromo-2-deoxy-β-D-glucopyranose[27] (**18**) (7.0 g, 17.0 mmol) and allyltriphenylstannane (13.0 g, 34.0 mmol) in anhydrous benzene (100 ml) at 80°C for 7 h. After the addition was complete, the solvent was removed under reduced pressure, the residue dissolved in acetonitrile (100 ml), and extracted five times with pentane (50 ml). After evaporation of the acetonitrile, the crude product (consisting of a 9:1 mixture of **19a**:**19b**) was purified by flash chromatography on silica gel [ether/pentane/chloroform (2:2:1)]. 1,3,4,6-Tetra-*O*-acetyl-2-*C*-allyl-2-deoxy-β-D-glucopyranose **19a** (2.5 g, 39%) with m.p. 79–80°C was obtained after fractional crystallization from ether/pentane.

Isomer **19a**: $[\alpha]_D^{20}$ = +50.0 (*c* = 1.0 in chloroform). – ^{1}H NMR ($CDCl_3$): δ = 2.01, 2.03, 2.07, 2.13 (s, 3H each, OAc), 2.00–2.19 (m, 3H, 2-H, allylic H), 3.75 (ddd, *J* = 2.2, 4.6, 9.8 Hz, 1H, 5-H), 4.06 (dd, *J* = 2.2, 12.4 Hz, 1H, 6′-H), 4.30 (dd, *J* = 5.6, 12.4 Hz, 1H, 6-H), 4.94–5.13 (m, 4H, 3-, 4-H, allylic H), 5.57 (d, *J* = 8.9 Hz, 1H, 1-H), 5.60–5.79 (m, 1H, allylic H). – MS (FD): *m/z* = 372 [M^+].

Isomer **19b**: ^{1}H NMR ($CDCl_3$): δ = 2.06, 2.07, 2.09, 2.11 (s, 3H each, OAc), 2.25–2.51 (m, 3H, 2-H, allylic H), 3.84 (ddd, *J* = 3.1, 5.1, 9.0 Hz, 1H, 5-H), 4.20 (dd, *J* = 3.1, 12.2 Hz, 1H, 6′-H), 4.27 (dd, *J* = 5.1, 12.2 Hz, 1H, 6-H), 5.00–5.15 (m, 4H, 3-, 4-H, allylic H), 5.73–5.86 (m, 1H, allylic H), 5.90 (d, *J* = 2.4 Hz, 1H, 1-H). – MS (FD): *m/z* = 372 [M^+].

b) *1,3,5,6-Tetra-O-acetyl-2-deoxy-2-C-propyl-β-D-glucopyranose* (**20**): Allylglucopyranose **19** (40.0 g, 10.7 mmol) was dissolved in ethyl acetate (200 ml), and hydrogenated with hydrogen over a palladium/carbon catalyst (10% w/w, 500 mg). After 3 h the reaction mixture was filtered through celite. Removal of the solvent gave product **20** (40.0 g, 100%) with m.p. 81.0–81.5°C. – $[\alpha]_D^{20}$ = +30.5 (*c* = 1.0 in chloroform). – ^{1}H NMR ($CDCl_3$): δ = 0.86 (t, *J* = 7.0 Hz, propyl CH_3), 1.28–1.37 (m, 4H, propyl CH_2), 2.02, 2.05, 2.08, 2.15 (s, 3H each, OAc), 2.03–2.09 (m, 1H, 2-H), 3.75 (ddd, *J* = 4.6, 9.7, 12.4 Hz, 1H, 5-H), 4.06 (dd, *J* = 2.2, 12.4 Hz, 1H, 6′-H), 4.31 (dd, *J* = 4.6, 12.4 Hz, 1H, 6-H), 4.98 (dd, *J* = 9.1, 9.7 Hz, 1H, 4-H), 5.08 (dd, *J* = 9.1, 10.7 Hz, 1H, 3-H), 5.59 (d, *J* = 9.3 Hz, 1H, 1-H). – MS (FD): *m/z* = 374 [M^+].

c) *Phenyl 3,4,6-Tri-O-acetyl-2-deoxy-2-C-propyl-1-seleno-D-glucopyranoside* (**7**): Selenophenol (1.6 g, 10.2 mmol) and Et_2O-BF_3 (60 mg, 4.3 mmol) were added at room temp. to a stirred solution of **20** (3.2 g, 8.5 mmol) in anhydrous chloroform (50 ml). After 2 h the reaction mixture was washed with saturated aqueous sodium hydrogen carbonate (2 × 50 ml), twice with water (50 ml), and dried with magnesium sulfate. After removing the solvent under reduced

pressure, chromatography on silica gel [pentane/ether (2:1)] gave the α isomer **7a** (1.8 g, 45%) of m. p. 65.0–65.5°C and β isomer **7β** (900 mg, 22%) as an oil in addition to a mixture of both isomers of **7** (1.0 g, 25%).

α Isomer **7α**: $[\alpha]_D^{20} = +274.3$ ($c = 1.1$ in chloroform). – ^{1}H NMR ($CDCl_3$): δ = 0.93 (t, $J = 7.0$ Hz, propyl CH_3), 1.17–1.58 (m, 4H, propyl CH_2), 2.03, 2.04, 2.05 (s, 3H each, OAc), 2.13–2.28 (m, 1H, 2-H), 3.97 (dd, $J = 2.1$, 12.2 Hz, 1H, 6'-H), 4.33 (dd, $J = 5.0$ Hz, 12.2 Hz, 1H, 6-H), 4.53 (ddd, $J = 2.1$, 5.0, 9.3 Hz, 1H, 5-H), 5.00 (t, $J = 9.3$ Hz, 1H, 4-H), 5.07 (t, $J = 9.3$ Hz, 1H, 3-H), 5.81 (d, $J = 4.8$ Hz, 1H, 1-H), 7.22–7.63 (m, 5H, aromatic H).

$C_{21}H_{28}O_7Se$ (471.4) Calcd. C 53.46 H 6.15
Found C 53.66 H 6.06

β Isomer **7β**: ^{1}H NMR ($CDCl_3$): δ = 0.93 (t, $J = 7.0$ Hz, 3H, propyl CH_3), 1.17–1.58 (m, 4H, propyl CH_2), 2.03, 2.04, 2.05 (s, 3H each, OAc), 2.13–2.28 (m, 1H, 2-H), 3.98 (dd, $J = 2.1$, 12.1 Hz, 1H, 6'-H), 4.31 (dd, $J = 5.0$, 12.1 Hz, 1H, 6-H), 4.53 (ddd, $J = 2.1$, 5.0, 9.2 Hz, 1H, 5-H), 5.00 (t, $J = 9.2$ Hz, 1H, 4-H), 5.07 (t, $J = 9.2$ Hz, 1H, 3-H), 5.81 (d, $J = 4.8$ Hz, 1H, 1-H), 7.22–7.63 (m, 5H, aromatic H).

$C_{21}H_{28}O_7Se$ (471.4) Calcd. C 53.46 H 6.15
Found C 53.73 H 6.12

ESR Measurements: Precursors of the radicals were the α-bromide **1** and the selenides **2**–**5** and **7** either as α isomers or as α,β mixtures. Detailed description of the procedures is given in ref.[3,4].

CAS Registry Numbers

1: 34245-85-7 / **1R**: 127381-90-2 / **2** (α anomer): 115408-34-9 / **2** (β anomer): 115408-35-0 / **2R**: 127381-91-3 / **3** (α anomer): 127381-76-4 / **3** (β anomer): 127381-85-5 / **3R**: 127381-92-4 / **4** (α anomer): 127381-77-5 / **4** (β anomer): 127381-86-6 / **4R**: 127381-93-5 / **5** (α anomer): 127381-78-6 / **5** (β anomer): 127381-87-7 / **5R**: 127381-94-6 / **7** (α anomer): 127381-79-7 / **7** (β anomer): 127381-88-8 / **7R**: 127381-95-7 / **8**: 78151-17-4 / **8R**: 127381-96-8 / **9**: 16750-06-4 / **10**: 117486-47-2 / **11**: 69534-61-8 / **12**: 127381-81-1 / **13**: 106023-49-8 / **14**: 127399-00-2 / **15**: 40762-22-9 / **17**: 127381-82-2 / **18**: 2946-11-4 / **19a**: 127381-83-3 / **19b**: 127381-89-9 / **20**: 127381-84-4 / hexamethylditin: 661-69-8

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