Electron Spin Resonance Spectroscopic Investigation of Carbohydrate Radicals. Part 2.[1] Conformation and Configuration in Pyranos-1-yl Radicals

Hans-Gert Korth and Reiner Sustmann *
Institut für Organische Chemie der Universität Essen, D-4300 Essen, West Germany
Jacques Dupuis and Bernd Giese *
Institut für Organische Chemie der TH Darmstadt, D-6100 Darmstadt, West Germany

Carbohydrate free radicals were regiospecifically generated at C-1 of acylated and alkylated pyranosyl derivatives in non-aqueous solution and their conformations were deduced from the hyperfine splittings of their e.s.r. spectra. The preferred conformations of the pyranosyl radicals are discussed in terms of a stabilizing interaction of the singly occupied *p*-orbital with the σ*-LUMO of the adjacent β-C–OR bond. From the α-^{13}C coupling constant of the tetra-acetylglucosyl radical it is concluded that pyranosyl radicals are of π-type.

The use of free-radical reactions in organic synthesis has received increased interest in recent years.[2] Provided that proper conditions are chosen, free-radical reactions can be of great value for the stereoselective synthesis of natural products as they are less sensitive to the presence of functional groups than are ionic reactions.[2,3]

Recently, free-radical reactions have been applied to C–C coupling reactions of carbohydrate compounds with alkenes.[4,5] For instance, a high diastereoselectivity for axial C–C bond formation was found in the reaction of tetra-acetylglucosyl radicals with acrylonitrile or methylacrylate.[4,5] This has been interpreted in terms of a preferentially axial-oriented σ-type α-oxyalkyl radical, the radical centre being at C-1 of the glucosyl moiety.[5–8] However, further studies on other glucosyl derivatives lent doubt to this interpretation.[1] In order to obtain definite information about the connection between radical structure and stereoselectivity of radical C–C bond formation we investigated the configurations and conformations of regiospecifically generated carbohydrate radicals by e.s.r. spectroscopy.

Most published e.s.r. studies on radicals deriving from carbohydrates deal with solid matrices or aqueous solutions.[9,10] In an outstanding series of papers, Gilbert *et al.*[11,12] investigated the radicals generated by reaction of carbohydrates and structurally related compounds with OH radicals in aqueous solution. The e.s.r. hyperfine splittings were interpreted on the basis of chair-like equilibrium conformations of the radicals derived from six-membered carbohydrate rings. Since OH radicals quite unselectively abstract hydrogen atoms from all positions of the substrates the recorded e.s.r. spectra were rather complex and in some cases only tentative assignments of the coupling constants could be made.

From a synthetic point of view, radical reactions of hydroxy-protected carbohydrate derivatives in non-aqueous solutions are of special interest. To the best of our knowledge, no e.s.r. spectra of specifically generated carbohydrate radicals in non-aqueous solution had been published prior to our investigation. In Part 1, we reported an e.s.r. spectroscopic study of the radicals generated at C-1 of substituted glucosyl and mannosyl compounds.[1] Here we present an extended study on radicals of this type, including galactosyl, xylosyl, and lyxosyl derivatives.

Results and Discussion

The carbohydrate radicals (**R1**—**R5**) (see Table) were regiospecifically generated in the e.s.r. cavity by reaction of the corresponding 1-bromo- or 1-phenylseleno-substituted compounds (**1**)—(**5**) with trimethyl- or tributyl-stannyl radicals, generated photolytically from hexamethyl- or hexa-n-butyl-ditin, respectively. The glucose derivatives (**1e**—**i**) and the galactose derivative (**2b**) are new compounds that were synthesized by standard procedures.

The best signal-to-noise ratio of the e.s.r. spectra was obtained in benzene or THF solution. The e.s.r. spectra were evaluated manually and the coupling constants were refined by computer simulation. E.s.r. coupling constants, *g* values, and the particular method of generation are collected in the Table. For most substrates, temperatures above 0 °C have to be applied in order to obtain good e.s.r. spectra. Generally, trimethylstannyl radicals yield more intense spectra than the bulkier tri-n-butylstannyl radicals. The e.s.r. signal intensity also strongly depends on the configuration of the radical precursor. For instance, axially bonded halogen atoms in a *trans*-arrangement to adjacent OR substituents are more easily abstracted than those bearing equatorially bonded OR groups. The *g* values of 2.0031—2.0035, found in this study, are consistent with literature data for α-alkoxyalkyl radicals.[13]

(a) *Glucosyl Derivatives.*—An e.s.r. investigation of the glucosyl radicals (**R1a**—**d** and **g**) generated from (**1a**—**d** and **g**), respectively, has already been published by us.[1] The glucosyl series was extended by the isotopically substituted derivatives (**1e**—**f**) and the bi- and tri-cyclic compounds (**1h** and **i**) (see Table).

The most remarkable features of the e.s.r. spectra of radicals (**R1a**—**g**) are the relatively small coupling constants of the β-hydrogen atoms at C-2 and the occurrence of two γ-hydrogen couplings of relatively large magnitude. This observation supports most reasonably the assumption of either a half-chair conformation (B), a $B_{2,5}$ boat-like conformation (C), a $^{1,4}B$ boat-like conformation (D), or a $^{1}C_{4}$ chair conformation (E) of radicals (**R1a**—**g**), in which the β-hydrogen atoms occupy the pseudoequatorial position, *i.e.*, to a large extent, the β-C–H bond adopts an orthogonal arrangement with respect to the singly occupied *p*-orbital at C-1.[11,†]

The smaller of the two γ-hydrogen couplings is assigned to C-3, caused by a W-like arrangement of the bonds in the C-1/C-3 subunit.[15] This assignment is verified by the e.s.r. spectra of radical (**R1f**), deuteriated at C-5. Here the larger of the two γ-H-couplings is replaced by a deuterium triplet

† An analogous cationic transition from the chair to the boat conformation has been discussed previously.[14]

Table. Conformations and e.s.r. data of pyranosyl radicals

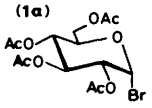
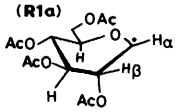
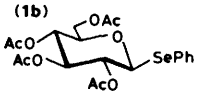
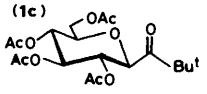
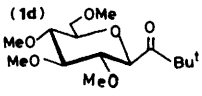
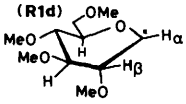
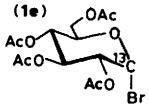
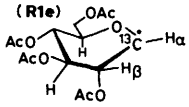
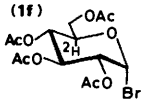
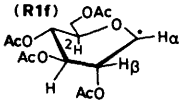
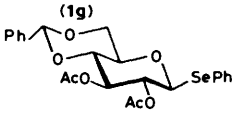
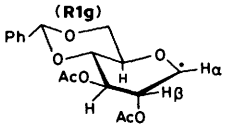
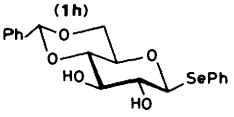
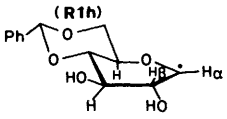
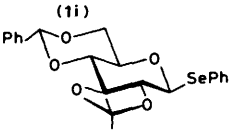
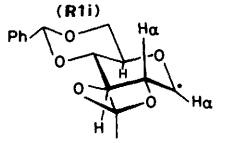
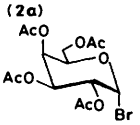
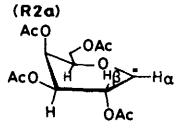
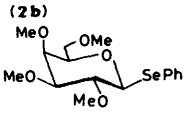
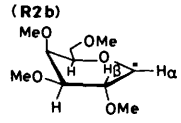
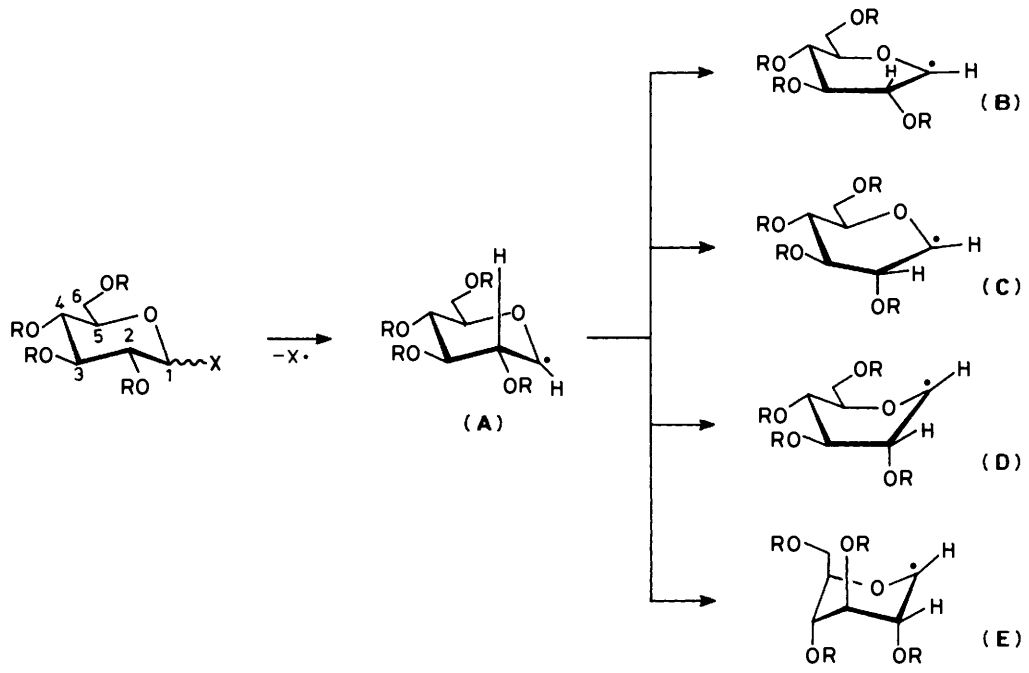
Substrate	Method[a]	Conformation	T/°C[b]	g	Hyperfine splittings (mT)[c] a(α-H)	a(β-H)	a(γ_1-H)	a(γ_2-H)	a(other)
(1a) 	A	(R1a) 	−30	2.0031	1.800	1.364	0.348	0.145	
	A		+20	2.0031	1.796	1.407	0.345	0.141	
(1b) 	B	(R1a)	+16	2.0031	1.799	1.392	0.345	0.143	
(1c) 	C[d]	(R1a)	−27	2.0031	1.844	1.179	0.377	0.173	
	C[d]		+40	2.0031	1.820	1.291	0.356	0.146	
(1d) 	C[d]	(R1d) 	−22	2.0032	1.799	1.058	0.388	0.221	
	C[d]		+3	2.0032	1.799	1.162	0.382	0.205	
	C[d]		+44	2.0032	1.792	1.274	0.359	0.184	
(1e) 	A	(R1e) 	+15	2.003 13	1.788	1.285	0.358	0.146	4.730 (^{13}C)
	A		+30	2.003 13	1.808	1.308	0.360	0.143	4.751 (^{13}C)
(1f) 	A	(R1f) 	−6	2.0032	1.815	1.172		0.154	0.047 (^{2}H)
(1g) 	B	(R1g) 	−24	2.0035	1.802	1.002	0.384	0.164	
	B		+16	2.0035	1.802	1.200	0.376	0.142	
	B		+33	2.0033	1.802	1.199	0.376	0.142	
(1h) 	A	(R1h) 	+30	2.0031	1.706	2.893	0.207	0.040	
(1i) 	D	(R1i) 	+17	2.003 13	1.393	3.445	0.156	0.084	
(2a) 	A	(R2a) 	+30	2.0031	1.684	2.759	0.253		
(2b) 	A	(R2b) 	+66	2.0031	1.712	2.597	0.243	<0.03	
	A		+75	2.0031	1.716	2.578	0.228	<0.03	
	A		+90	2.0031	1.726	2.540	0.237	<0.03	

Table (*continued*)

Substrate	Method[a]	Conformation	T/°C[b]	g	Hyperfine splittings (mT)[c] a(α-H)	a(β-H)	a(γ_1-H)	a(γ_2-H)	a(other)
(3)	A	(R3)	+20	2.003 07	1.852	0.353	0.307	<0.03	
	A		+95	2.0031	1.834	0.424	0.307	<0.03	
(4a)	A	(R4a)	−2	2.0031	1.816	1.189	0.176	0.176	0.048 (γ-H)
	A		+5	2.0031	1.829	1.221	0.176	0.176	0.051 (γ-H)
(4b)	E	(R4b)	+22	2.0031	1.845	1.250	0.114	0.114	
(5)	F	(R5)	+30	2.003 06	1.826	0.473	0.193	0.091	
	F		+36	2.003 06	1.833	0.486	0.209	0.099	
	F		+45	2.0031	1.835	0.499	0.210	0.106	

[a] U.v. photolysis. [b] ±2°. [c] ±0.002—±0.005 mT. [d] Ref. 1, in propan-2-ol.

A, Me_6Sn_2, THF; B, Me_6Sn_2, toluene; C, propan-2-ol; D, Bu_6Sn_2, benzene; E, Bu_6Sn_2, THF; F, Me_6Sn_2, benzene.

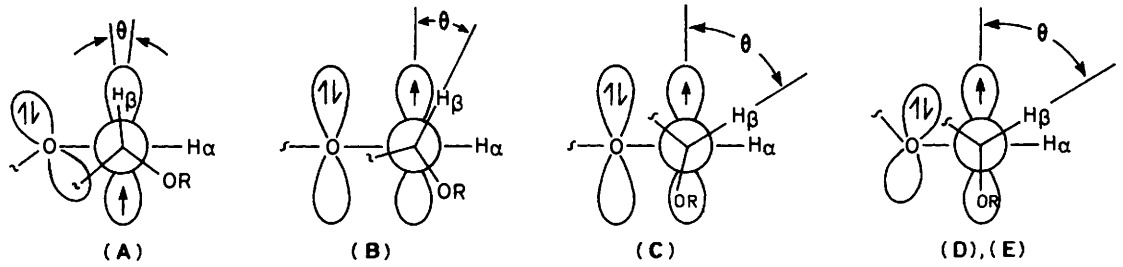


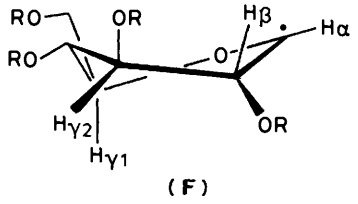
coupling of the expected value [calculated from (**R1a**), 0.053 mT; observed 0.047 mT].

The transformation of radicals (**R1a—g**) into conformations (B)—(E) can be interpreted in terms of a stabilizing interaction between the *p*-orbital of the unpaired electron and the σ*-orbital (LUMO) of the adjacent β-C–OR bond, preferring a coplanar arrangement. This interaction is increased in glucosyl radicals, since the SOMO-energy of the radical is raised by the neighbouring α-oxygen atom, so that the steric destabilization of the non-chair conformation is overcompensated by the stabilizing SOMO/LUMO interaction. Analogous preferred conformations have been observed by Gilbert *et al.* in open-chain radicals of the type R^1O–$\dot{C}H$–CHR^2OR^2.[16]

We discuss the experimental data for radicals (**R1a—g**) in terms of the three (idealized) conformations (B)—(D)[(E)] for which projections along the C-2–C-1 bond are shown. Conformations (D) and (E) display nearly identical steric arrangements in the C-1–C-2 region of the pyranosyl ring.

The stabilization of a half-filled *p*-orbital by an α-oxygen atom is believed to occur by conjugative electron delocalization





with a *p*-type lone-pair orbital at oxygen.[17,*] In this view, the half-chair conformation (B) and the $B_{2,5}$ boat conformation (C) should be energetically favoured over the $^{1,4}B$ boat and the $^{1}C_4$ chair conformations (D) and (E), since the former allow better overlap of the interacting orbitals. On the other hand, compared with (B) conformations (C)—(E) are able to achieve enhanced stabilization by the SOMO/LUMO interaction of the radical centre and the adjacent β-C–OR bond. Conformation (B) exhibits a smaller dihedral angle θ between the semi-occupied *p*-orbital and the β-C–H bond than the three other conformations, and thus a larger β-hydrogen coupling is expected for conformation (B). On the basis of the well known relation (1)[19]

$$a(\beta\text{-H}) = A + B\cos^2\theta \qquad (1)$$

for the dependence of β-hydrogen coupling constants on the dihedral angle θ, where $A = 0.3 \pm 0.2$, $B = 4.9 \pm 0.5$ mT, a dihedral angle θ of 63 ± 5° is calculated for radicals (**R1a**—**g**) [*a*(β-H) 1.3 mT]. Such a dihedral angle is in better agreement with conformations (C)—(E) than with a half-chair conformation (B). For the latter, a dihedral angle of *ca.* 30° is implied by structural models.†

The experimental results allow no unambiguous distinction between the $^{1,4}B$ and the $B_{2,5}$ boat conformations. Whereas in the former the singly occupied *p*-orbital is expected to overlap better with the β-C–OR bond but less with the lone-pair orbital at the ring oxygen, the reverse applies to the latter conformation. For both conformations, structural models display dihedral angles of the magnitude [θ($^{1,4}B$) 75°, θ($B_{2,5}$) 60°] predicted from the experimental β-H hyperfine splitting by equation (1).

The transformation of the $^{4}C_1$ conformation (A) of the educts (**1a**—**f**) into a boat-like conformation in radicals (**R1a**—**f**) involves an interconversion of the substituents on C-2 and C-3 from the equatorial to a pseudoaxial position. This situation cannot be distinguished from the $^{1}C_4$ chair conformation (E), in which complete interconversion of all substituents into the axial positions has occurred. However, the correspondence of the e.s.r. data for the bicyclic radical (**R1g**) with those of radicals (**R1a**—**f**) is reconcilable only with a boat-like conformation because in radical (**R1g**) the *trans*-connection of the two rings forestalls an interconversion into the $^{1}C_4$ chair conformation.

We prefer to interpret the e.s.r. spectroscopic data for the glucopyranosyl radicals (**R1a**—**g**) in terms of a slightly twisted $B_{2,5}$ boat conformation (F) because of the following arguments: (a) an optimal planar arrangement of the singly occupied *p*-orbital at C-1 with both the *p*-type lone pair at the ring oxygen and the β-C–OR bond, giving maximum electron delocalization, (b) a dihedral angle as predicted by the β-H coupling constant, and (c) a more pronounced W-arrangement of the *p*-orbital and the pseudoaxial γ-C–H bond than in the $^{1,4}B$ conformation.‡

A twist-boat conformation is structurally flexible, as is demonstrated by the temperature coefficient of the β-H couplings, and so the e.s.r. data may represent only the most populated equilibrium conformation of the glucosyl radicals at the temperature of the experiment.

Interestingly, a twisted $B_{2,5}$ boat conformation (F) is very similar to the most stable but not so puckered conformation of cyclohexene.

A remarkable conformational effect is observed in radical (**R1h**), generated from the glucosyl derivative (**1h**), carrying free hydroxy groups at C-2 and C-3. The β-H coupling constant of 1.2 mT in the corresponding radical (**R1g**) is raised to 2.9 mT in (**R1h**), accompanied by a lowering of the γ-hydrogen couplings. Values in the range 4.0—4.8 mT observed for β-H hyperfine splittings in six-membered heterosubstituted cycloalkyl radicals are explained by coplanar arrangement of axial β-C–H bonds and the *p*-orbital of the radical centre.[20] Our experimental value of 2.9 mT suggests a significant deviation from the idealized chair conformation in radical (**R1h**) and is consistent with the assumption of a more or less pronounced half-chair equilibrium conformation.

Further evidence for this interpretation is given by the tricyclic glucosyl radical (**R1i**), in which the chair conformation is more strongly fixed by the *trans*-bonding of the rings, leading to a coupling constant of *ca.* 3.4 mT for the axial β-hydrogen atoms. Similar coupling constants have been observed by Gilbert *et al.* for unsubstituted glucosyl radicals in aqueous solution.[11,12] It seems that hydrogen bonding of the hydroxy groups forces the radical skeleton into a half-chair conformation or a chair conformation flattened at the C-1 side. Consequently, the above discussed SOMO/LUMO interaction between the alkoxyalkyl radical and the β-C–O bond is just strong enough to induce the conformational change from (A) to (F) but cannot break additional hydrogen bonds.

* For a general discussion of the status of lone-pair electrons at two-co-ordinated oxygen see pp. 39, 78 of ref. 18. The collinearity of the *p*-type lone-pair orbital at the α-oxygen with the γ-C–H bond at C-5 also offers an explanation of the relatively large γ-H hyperfine coupling across oxygen in pyranosyl radicals.

† The alternative description in terms of two localized sp^3 lone-pair orbitals at oxygen gives qualitatively the same picture, though in this approach the $^{1,4}B$ conformation should be slightly favoured over the $B_{2,5}$ conformation.

‡ A $B_{2,5}$ twist-boat conformation represents an intermediate structure between the fully evolved $B_{2,5}$ and $^{1,4}B$ boat conformations and is easily reached from both sides.

The conformational dependence of the β- and γ-hydrogen coupling constants as discussed above only applies if the carbohydrate radicals are largely π-type radicals, *i.e.* possess an almost planar configuration at the radical centre.[19] With only the exception (**R1i**), the α-hydrogen couplings at C-1 of the pyranosyl radicals are in the range 1.65—1.85 mT, values normally observed for open-chain α-oxyalkyl radicals of the type R^1–$\dot{C}$H–OR^2.[13,19] The latter are regarded as only slightly bent at the radical centre. A negative temperature coefficient of the α-H-coupling constant is very common for a planar π-radical with negative sign of the coupling constant. Although such a temperature dependence is observed for radicals (**R1a**—**d**), this effect may be covered by a larger influence of vibrational ring inversion.

α-^{13}C Hyperfine coupling constants serve as a more reliable probe for the configuration at radical centres.[19] Therefore, we have recorded the e.s.r. spectrum of the α-^{13}C-enriched glucosyl radical (**R1e**). The α-^{13}C coupling constant of 4.73 mT is in good accord with values known for open-chain α-oxyalkyl radicals or even pure alkyl radicals [*e.g.* α-^{13}C(cyclohexyl) 4.14; α-^{13}C(methoxymethyl) 4.72 mT].[13] Following the approach outlined by McKelvey *et al.*,[21] the 2*s* character of the semi-occupied orbital can be estimated from the term $2\tan^2\theta$ of equation (2)[22] where $a_C(\theta)$ and $a_C(0)$ represent the α-carbon

$$a_C(\theta) = a_C(0) + 1\,190(2\tan^2\theta) \qquad (2)$$

hyperfine coupling constants for bent and planar (methyl) radicals, respectively. Taking into account the reduction of spin density at C-1 due to interaction with the α-substituents,[23] a 2*s* character of *ca.* 0.9% is estimated for radical (**R1e**), connected with an out-of-plane bent angle of *ca.* 3.9° (compared with 19.5° in an sp^3-hybridized σ-radical). Thus, the pyranos-1-yl radicals can safely be regarded as π-type radicals with almost planar radical centre.[24] This feature is of special importance for the interpretation of the stereoselectivity in carbohydrate radicals.[4–8]

(b) *Galactosyl Derivatives.*—The galactosyl radicals (**R2a** and **b**), generated from the selenides (**2a** and **b**), display β-hydrogen coupling constants of *ca.* 2.8 mT.* This value and a vanishing γ-H coupling at C-3 are consistent with a half-chair conformation (B).

This behaviour can be explained by the occurrence of steric interactions between the substituents at C-3 and C-4 if the radicals try to convert into the twisted $B_{2,5}$ boat conformation as the glucosyl radicals do. A transition into the boat conformation leads to a nearly ecliptic arrangement of the substituents at C-3 and C-4; the vicinal repulsion of such an arrangement now over-rides the stabilizing interaction of the β-C–O bond and the *p*-orbital at C-1. The transition into a half-chair conformation or a flattened $^4C_1$ chair conformation compromises the opposing interactions.

(c) *Mannosyl Derivatives.*—The e.s.r. spectrum of the mannosyl radical (**R3**) nicely fits the interpretation of the glucosyl radical spectra outlined above. Here, the e.s.r. data clearly indicate the preservation of the $^4C_1$ conformation. This is confirmed by the small β-H coupling constant of *ca.* 0.3—0.4 mT and the disappearance of one γ-H coupling. An alternative half-chair conformation should exhibit a small dihedral angle θ of *ca.* 30°, predicting a much larger β-H hyperfine splitting than is observed. By equation (1), a β-H coupling constant of 0.3—0.4 mT implies an almost orthogonal arrangement of the *p*-orbital at C-1 and the β-C–OR bond. For the mannosyl radical the stabilizing interaction of the singly occupied *p*-orbital and the β-C–OR bond is already present in the chair conformation.

The relatively strong temperature dependence of the β-H coupling constant supports the assignment, since a stronger out-of-plane vibration of the equatorial H–C-2 bond should enhance the spin delocalizing overlap with the half-filled *p*-orbital.

(d) *Xylosyl and Lyxosyl Derivatives.*—The configurations at C-1—C-4 in the xylosyl and lyxosyl derivatives (**4a** and **b**) and (**5**) are identical to those of the glucosyl and mannosyl compounds (**1**) and (**3**), respectively. This configurational conformity is also reflected in the e.s.r. spectra of the radicals (**R4a** and **b**) and (**R5**) generated from these substrates (Table). Like the glucosyl compounds, the all-equatorial xylosyl compounds yield radicals gaining stabilization by conversion into the $B_{2,5}$ boat conformation, as is indicated by the similarity of the coupling constants of the two systems. The lyxosyl radical (**R5**) largely preserves the $^4C_1$ chair conformation of the starting material, in accord with the behaviour of the related mannosyl radical (**R3**).

Conclusions.—Pyranosyl radicals could be regioselectively generated in non-aqueous solution by halogen-atom or phenylselenyl-group abstraction with trialkyltin radicals, from the corresponding alkylated and acylated carbohydrate derivatives. From the α-^{13}C e.s.r. hyperfine splitting of the tetra-acetylglucopyranosyl radical it is concluded that pyranosyl radicals exist as almost planar π-type α-alkoxyalkyl radicals. The analysis of the β- and γ-hydrogen hyperfine splittings reveals a strong conformational dependence of those radicals on the type of the parent compound. Glucosyl and xylosyl radicals prefer to attain a (probably twisted) $B_{2,5}$ boat conformation rather than to keep the $^4C_1$ chair conformation of the starting material. This interconversion is interpreted in terms of a stabilizing interaction of the singly occupied *p*-orbital (SOMO) and the σ*-LUMO of a now axially bonded β-C–OR bond, over-riding the repulsive interaction of the substituents. Galactosyl radicals most likely exist in a ^4H half-chair conformation, representing a compromise between the stabilizing SOMO–LUMO interaction and a stronger steric repulsion during the chair–boat interconversion. As the parallel arrangement of the singly occupied *p*-orbital and the β-C–OR bond is already present in the parent compounds, the mannosyl and lyxosyl radicals retain the $^4C_1$ conformation of their precursors. Substituent effects, like hydrogen bonding, can significantly alter the preferred conformation of the pyranosyl radicals.

Experimental

N.m.r. spectra were obtained with a Bruker WM 300 spectrometer, using tetramethylsilane as internal reference. I.r. spectra were recorded on a Perkin-Elmer 297 spectrometer. The e.s.r. measurements were performed on a Bruker ER-420 X-band spectrometer equipped with a variable-temperature unit. Optical rotations were recorded at 20 °C using a Perkin-Elmer 141 polarimeter. M.p.s were determined with a Büchi SMP 20 apparatus.

Materials.—Acetobromoglucose (**1a**),[25] phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-selenoglucopyranoside (**1b**),[26] acetobromogalactose (**2a**),[27] acetobromomannose (**3**),[28] acetobromoxylose

* Additionally, the e.s.r. spectra from (**2a**) displays the signals of a secondary radical, which could be identified as the corresponding 2-deoxypyranosan-2-yl radical, presumably formed by a 1,2-migration of the β-acetoxy group. A detailed analysis of this and similar 1,2-acetoxy migrations in carbohydrate radicals will be published elsewhere.

(**4a**),[29] benzoylbromoxylose (**4b**),[30] and acetobromolyxose (**5**)[31] were prepared by standard procedures.

[1-^{13}C]-2,3,4,6-*Tetra*-O-*acetyl*-α-D-*glucopyranosyl Bromide* (**1e**).—Acetic anhydride (1.20 g, 20 mmol) was added to a stirred solution of [1-^{13}C]glucose (250 mg, 1.38 mmol; IC Chemicals) in pyridine (1.8 ml) at 0 °C. After 30 min at 0 °C and 2 h at room temperature the solution was evaporated twice under reduced pressure after adding a few ml of toluene. The resulting oil was stirred for 3 h at room temperature with a solution of hydrogen bromide in acetic acid (1.4 ml; 33%). The mixture was dissolved in chloroform (20 ml) and washed with ice–water, hydrogencarbonate solution, and ice–water again (20 ml each). After drying (Na_2SO_4) and evaporating the solvent, the [^{13}C]glucosylbromide (**1e**) crystallized (450 mg, 79%). The physical data correspond to that of the non-labelled glucosyl bromide (**1a**).

2,3,4,6-*Tetra*-O-*acetyl*-5-*deuterio*-α-D-*glucopyranosyl Bromide* (**1f**).—A mixture of 1,2,3,4,6-penta-*O*-acetyl-5-bromo-α-D-glucopyranose[32] (2.7 g, 5.8 mmol) and Bu^n_3SnD (2.1 g, 7.2 mmol) in THF (50 ml) was irradiated for 1 h by a 125 W mercury lamp. The solution was then evaporated under reduced pressure, the remaining oil was dissolved in ether (80 ml), and potassium fluoride (4.0 g) was added. After stirring for 30 min, the mixture was filtered and the solution evaporated under reduced pressure. The residue was treated at 4 °C with hydrogen bromide in acetic acid (25 ml; 33%) for 12 h. Ether (100 ml) was added and the solution washed twice with water, hydrogencarbonate solution, and water again (50 ml each). After drying (Na_2SO_4) and evaporation of the solvent the deuteriated glucosylbromide (**1e**) remained as an oil (1.0 g, 42%); $\delta_H(CDCl_3)$ 2.00 (3 H, s), 2.02 (3 H, s), 2.10 (6 H, s), 4.05 (1 H, d, *J* 12.0 Hz), 4.35 (1 H, d, *J* 12.0 Hz), 4.76 (1 H, dd, *J* 4.9, 9.2 Hz), 5.15 (1 H, d, *J* 9.2 Hz), 5.50 (1 H, t, *J* 4.0 Hz), and 6.60 (1 H, d, *J* 4.0 Hz).

Phenyl 4,6-O-*Benzylidene*-β-D-*selenoglucopyranoside* (**1h**).—A DMF solution (30 ml) of phenyl β-D-selenoglucopyranoside[26] (6.0 g, 28.8 mmol), αα-dimethoxytoluene (3.0 g, 18.8 mmol), and toluene-*p*-sulphonic acid (100 mg) was heated to 50 °C. Methanol, formed during the reaction, was continuously distilled off under reduced pressure. After 1 h the mixture was poured into ice–water (50 ml) and the precipitate was filtered off. The solid product (**1h**) was purified by recyrstallization from propan-2-ol (7.0 g, 91%), m.p. 150—151 °C; $[\alpha]_D^{20}$ −33° (*c* 0.9 in $CHCl_3$) (Found: C, 55.9; H, 4.5. $C_{19}H_{20}O_5Se$ requires C, 56.0; H, 4.3%); $\delta_H([^2H_6]DMSO)$ 3.34—3.53 (4 H, m), 3.67 (1 H, t, *J* 9.94 Hz), 4.19 (1 H, t, *J* 9.94 Hz), 5.04 (1 H, d, *J* 9.87 Hz), 5.45 (1 H, d, *J* 4.79 Hz, OH), 5.58 (1 H, s), 5.59 (1 H, d, *J* 6.02 Hz, OH), and 7.25—7.70 (10 H, m).

Phenyl 2,3-*Di*-O-*acetyl*-4,6-O-*benzylidene*-β-D-*selenoglucopyranoside* (**1g**).—A solution of selenoglucopyranoside (**1h**) (4.0 g, 9.8 mmol) in pyridine (60 ml) was treated at room temperature with acetic anhydride (45 ml). After stirring for 3 h the solution was poured into ice–water (500 ml), the precipitate filtered off, and recrystallized from ether (1.8 g, 38%), m.p. 176—177 °C; $[\alpha]_D^{20}$ −66.2° (*c* 1.2 in $CHCl_3$) (Found: C, 56.1; H, 4.7. $C_{23}H_{24}O_7Se$ requires C, 56.2; H, 4.9%); ν(KBr) 1 740 and 1 580 cm^{-1}; $\delta_H(CDCl_3)$ 3.54 (1 H, m), 3.64 (1 H, t, *J* 9.35 Hz), 3.76 (1 H, t, *J* 10.3 Hz), 4.37 (1 H, dd, *J* 4.86, 10.3 Hz), 4.97 (1 H, d, *J* 10.1 Hz), 5.31 (1 H, t, dd, *J* 3.5, 9.35 Hz), 5.47 (1 H, s), and 7.27—7.65 (10 H, m).

Phenyl 2,3-O-*Isopropylidene*-4,6-O-*benzylidene*-β-D-*selenoglucopyranoside* (**1i**).—Selenoglucopyranoside (**1h**) (3.0 g, 7.0 mmol) and toluene-*p*-sulphonic acid (20 mg, 0.1 mmol) were dissolved in 2,2-dimethoxypropane (60 ml) and DMF (2 ml). Every 4 h 2,2-dimethoxypropane (10 ml each) was added and the methanol formed was continuously distilled off at 100 Torr. After 14 days the mixture was neutralized with hydrogencarbonate solution, poured into water (100 ml), and extracted five times with ether (50 ml each). The combined solutions were dried (Na_2SO_4), evaporated under reduced pressure, and the remaining oil chromatographed over silica gel (ether–triethylamine 100:1). The product (**1i**) was recrystallized from ether (688 mg, 22%), m.p. 141—142 °C; $[\alpha]_D^{20}$ −47.8° (*c* 1.0 in $CHCl_3$) (Found: C, 59.3; H, 5.45. $C_{22}H_{24}O_5Se$ requires C, 59.1; H, 5.4%); ν(KBr) 2 880 and 1 570 cm^{-1}; $\delta_H(CDCl_3)$ 1.42 (3 H, s), 3.46—3.51 (1 H, m), 3.75—3.80 (2 H, m), 3.85 (1 H, t, *J* 10.4 Hz), 4.41 (1 H, dd, *J* 4.8, 10.4 Hz), 5.11 (1 H, d, *J* 9.9 Hz), 5.54 (1 H, s), and 7.29—7.75 (10 H, m).

Phenyl 2,3,4,6-*Tetra*-O-*methyl*-β-D-*selenogalactopyranoside* (**2b**).—A solution of KOH (3.8 g, 6.9 mmol) and selenophenol (9.9 g, 69 mmol) in ethanol (150 ml) was added to acetobromogalactose[27] (28.0 g, 69 mmol) in $CHCl_3$ (150 ml). After refluxing for 4 h, the solution was washed with NaOH (100 ml; 5%) and water (100 ml), dried ($MgSO_4$), and distilled. The resulting oil (9.7 g) was dissolved in benzene (100 ml) together with $Bu^n_4NHSO_4$ (680 mg, 2.0 mmol), NaOH (33.0 g, 880 mmol), and methyl bromide (20.0 g, 213 mmol). After stirring for 72 h at room temperature, the mixture was filtered over silica gel. The filtrate was washed three times with water (100 ml each), dried (Na_2SO_4), and evaporated to afford the crystalline selenogalactoside (**2b**) (6.3 g, 84%), m.p. 64—65 °C; $[\alpha]_D^{20}$ −35.8° (*c* 0.7 in $CHCl_3$) (Found: C, 51.3; H, 6.4. $C_{16}H_{24}O_5Se$ requires C, 51.2; H, 6.4%); $\delta_H(CDCl_3)$ 3.18 (1 H, dd, *J* 2.46, 9.77 Hz), 3.36 (3 H, s), 3.46 (1 H, t, *J* 9.77 Hz), 3.52 (3 H, s), 3.55 (3 H, s), 3.57 (3 H, s), 3.47—3.63 (3 H, m), and 3.70 (1 H, d, *J* 2.46 Hz).

E.s.r. Measurements.—Radicals were generated by u.v. irradiation of the solutions in sealed Suprasil quartz tubes (outer diameter 4.0 mm) with the filtered light of a Hanovia 977-B1 1 kW Hg–Xe high-pressure lamp. The e.s.r. solutions were composed of the sugar derivative (*ca.* 50 mg), absolute solvent (THF, toluene, or benzene) (0.2 ml), and hexamethyl- or hexa-n-butyl-ditin (0.2 ml). Addition of di-t-butyl peroxide (0.02 ml) in some cases gave increased signal intensities. Oxygen was removed from the solutions by purging with dry nitrogen for 30 min.

E.s.r. hyperfine coupling constants were refined by simulation of the manually solved e.s.r. spectra on a PDP-11/34 computer. *G* Values were determined with the aid of a microprocessor-controlled device, using the digital output of a microwave frequency counter and a n.m.r. field-measuring unit.

Acknowledgements

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

References

1 Part 1, J. Dupuis, B. Giese, D. Rüegge, H. Fischer, H.-G. Korth, and R. Sustmann, *Angew. Chem.*, 1984, **96**, 887; *Angew. Chem., Int. Ed. Engl.*, 1984, **23**, 896.
2 D. I. Davies and M. J. Parrott, 'Free Radicals in Organic Synthesis,' Springer Verlag, Berlin, 1978; B. Giese, *Angew. Chem.*, 1983, **95**, 771; *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 753; D. J. Hart, *Science*, 1984, **223**, 883; B. Giese, *Angew. Chem.*, 1985, **97**, 555; *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 553.
3 D. H. R. Barton and W. B. Motherwell, *Pure Appl. Chem.*, 1981, **53**, 15; H. H. Henning, F. Pragst, and J. Fuhrmann, *Z. Chem.*, 1984, **24**, 1; G. Stork in 'Selectivity—A Goal for Synthetic Efficiency,' eds. W. Bartmann and B. M. Trost, Verlag Chemie, Weinheim 1984, p. 281.
4 B. Giese and J. Dupuis, *Angew. Chem.*, 1983, **95**, 633; *Angew. Chem., Int. Ed. Engl.*, 1983, **22**, 622; B. Giese and K. Gröninger, *Tetrahedron*

Lett., 1984, **25**, 2743; J. Dupuis, B. Giese, J. Hartung, M. Leising, H. G. Korth, and R. Sustmann, *J. Am. Chem. Soc.*, 1985, **107**, 4332.
5 R. M. Adlington, J. E. Baldwin, A. Basak, and R. P. Kozyrod, *J. Chem. Soc., Chem. Commun.*, 1983, 944.
6 F. Baumberger and A. Vasella, *Helv. Chim. Acta*, 1983, **66**, 2210.
7 J. P. Praly, *Tetrahedron Lett.*, 1983, **24**, 3075.
8 B. Giese and J. Dupuis, *Tetrahedron Lett.*, 1984, **25**, 1349.
9 For leading references see: 'Electron Spin Resonance,' Specialist Periodical Report, The Royal Society of Chemistry, London, 1985, vol. 9, p. 151; *ibid.*, 1983, vol. 8, p. 225; C. von Sonntag, *Adv. Carbohydr. Chem. Biochem.*, 1980, **37**, 7.
10 R. O. C. Norman and R. J. Pritchett, *J. Chem. Soc. B*, 1967, 1329; P. R. West, G. Schnarr, and L. Sitwell, *Tetrahedron Lett.*, 1977, 3869.
11 B. C. Gilbert, D. M. King, and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 2*, 1980, 1821; 1982, 169; *Carbohydr. Res.*, 1984, **125**, 217.
12 B. C. Gilbert, D. M. King, and C. B. Thomas, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1186; 1983, 675; in these papers, values of *ca.* 1.2 and 3.0 mT were reported for the coupling constants of equatorial and axial hydrogen atoms, respectively, in six-membered carbohydrate radicals.
13 'Landolt-Börnstein, New Series,' vol. II/9b, eds. H. Fischer and K. H. Hellwege, Springer Verlag, Berlin, 1977.
14 R. U. Lemieux, K. B. Hendricks, R. V. Stick, and K. James, *J. Am. Chem. Soc.*, 1975, **97**, 4056; see also P. Deslongchamps, 'Stereoelectronic Effects in Organic Chemistry,' Pergamon Press, Oxford, 1983, pp. 29, 211.
15 F. W. King, *Chem. Rev.*, 1977, **77**, 157.
16 A. J. Dobbs, B. C. Gilbert, and R. O. C. Norman, *J. Chem. Soc., Perkin Trans. 2*, 1972, 786; B. C. Gilbert, J. P. Larkin, and R. O. C. Norman, *ibid.*, p. 794; B. C. Gilbert, M. Trenwith, and A. J. Dobbs, *ibid.*, 1974, 1772.
17 V. Malatesta and K. U. Ingold, *J. Am. Chem. Soc.*, 1981, **103**, 609; A. J. L. Beckwith and J. C. Easton, *ibid.*, p. 615.
18 A. J. Kirby, 'The Anomeric Effect and Related Stereoelectronic Effects at Oxygen,' Springer Verlag, Berlin, 1983, p. 128.
19 For reviews see J. K. Kochi, *Adv. Free-Radical Chem.*, 1975, **5**, 189; P. D. Sullivan and E. M. Menger, *Adv. Magn. Reson.*, 1977, **9**, 1.
20 Ref. 13, pp. 271, 289*f*.
21 R. D. McKelvey, T. Sugawara, and H. Iwamira, *Magn. Reson. Chem.*, 1985, **23**, 330.
22 R. W. Fessenden and R. H. Schuler, *J. Chem. Phys.*, 1965, **43**, 2704.
23 A. J. Dobbs, B. C. Gilbert, and R. O. C. Norman, *J. Chem. Soc. A*, 1971, 124.
24 In a recent low-temperature ESR/ENDOR study, a slight out-of-plane bent angle of *ca.* 2.3 ± 1° was determined in a prototypal $^{\bullet}CH_2OR$ radical; W. A. Bernhard, T. L. Horning, and K. R. Mercer, *J. Phys. Chem.*, 1984, **88**, 1317.
25 R. U. Lemieux, *Methods Carbohydr. Chem.*, 1963, **2**, 221.
26 W. A. Bonner and A. Robinson, *J. Am. Chem. Soc.*, 1950, **72**, 354.
27 R. W. Jeanloz and P. J. Stoffya, *Methods Carbohydr. Chem.*, 1962, **1**, 221.
28 H. G. Fletcher, jr., *Methods Carbohydr. Chem.*, 1963, **2**, 198.
29 F. Weygand, *Methods Carbohydr. Chem.*, 1962, **1**, 182.
30 H. G. Fletcher, jr., and C. S. Hudson, *J. Am. Chem. Soc.*, 1947, **69**, 921.
31 P. L. Durette and D. Horton, *Carbohydr. Res.*, 1971, **18**, 57.
32 R. D. Ferrier and R. Blattner, *J. Chem. Soc., Perkin Trans. 1*, 1980, 1523.

Received 6*th November* 1985; *Paper* 5/1951