1,2-Acyloxyl Migration in Pyranosyl Radicals[1]

Hans-Gert Korth and Reiner Sustmann*

Institut für Organische Chemie der Universität Essen, D-4300 Essen 1, West Germany

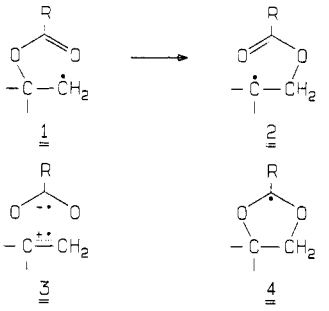
Kay Stefan Gröninger, Michael Leisung, and Bernd Giese*

Institut für Organische Chemie der TH Darmstadt, D-6100 Darmstadt, West Germany

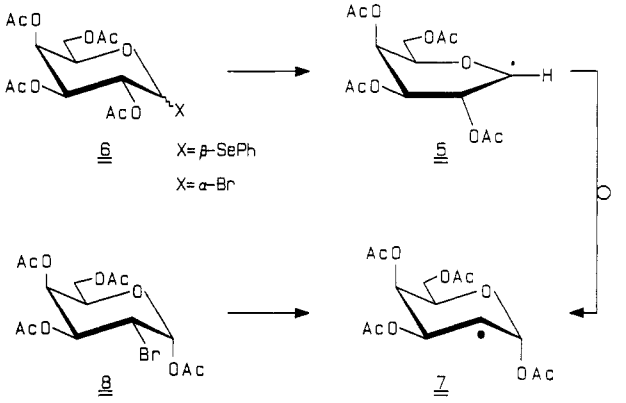
Received December 7, 1987

Tetra-*O*-acetylgalactosyl radical (**5**) and tetra-*O*-acetylglucosyl radical (**10**) undergo a 1,2-migration of acetoxyl groups to the corresponding 2-deoxytetra-*O*-acetylpyranosan-2-yl radicals. The activation parameters for the rearrangement of tetra-*O*-acetylgalactosyl radical, as determined by ESR spectroscopy, are $\Delta H^{\ddagger} = 12.2 \pm 0.3$ kcal/mol and $\Delta S^{\ddagger} = -6.7 \pm 1.0$ eu. Labeling studies with ^{18}O support a five-membered cyclic transition state for the rearrangement with exchange of the oxygen atoms of the carboxy group. The driving force for the rearrangement, which is unfavorable in terms of the stability of the radical centers, derives from the gain in anomeric stabilization of the product radical.

Since its discovery,[2] the 1,2-migration of the acyloxyl group in β-(acyloxyl)alkyl radicals has found particular attention.[3] In recent years the mechanism of this rearrangement has been studied extensively by many experimental techniques[4,5] and also by theoretical calculations.[6] Evidence has accumulated that the isomerization **1** → **2** occurs via a cyclic transition state, which might be represented by a charge-separated structure **3**, and not via an intermediate 1,3-dioxolan-2-yl radical (**4**). Support for the participation of **3** derives from the acceleration of the reaction by electronegative R groups like trifluoromethyl and by polar solvents, e.g. water. Furthermore, 1,3-dioxolan-2-yl radicals such as **4** undergo ring opening under conditions different from the rearrangement reaction. Theoretical calculations[6] also show that the structure of the transition state is geometrically and electronically different from the 1,3-dioxolan-2-yl radical (**4**).



We have recently reported ESR spectroscopical studies on carbohydrate derived radicals,[1,7-9] which are intermediates in synthetically useful radical CC coupling reactions.[10-12] In the course of these studies we detected a 1,2-acyloxyl migration when we generated the tetra-*O*-acetylgalactosyl radical **5** in benzene solution by selenophenyl abstraction from **6** with trialkyltin radicals. At temperatures above 0 °C we observe not only ESR signals due to the radical **5**, but also signals of a second radical, later identified as the 2-deoxytetra-*O*-acetylgalactopyranosan-2-yl radical (**7**). The concentration of **7** increased with increasing temperature. This rearrangement has already found a useful application in the synthesis of 2-deoxy sugars.[13] The present contribution describes a detailed mechanistic study of the rearrangement **5** → **7** and analyses other acyloxyl-substituted carbohydrate radicals for their isomerization capabilities.



Results

ESR Spectra. The tetra-*O*-acetylgalactosyl radical (**5**) was produced in nonpolar solvents by abstraction of a selenophenyl group or a bromine atom from **6** with photolytically generated trialkyltin radicals. The analysis of its ESR spectrum reveals that it adopts more or less a half-chair conformation.[8] Above 0 °C additional signals were present in the ESR spectrum. The presumption that the signals were due to the rearranged radical **7** was confirmed by independent generation of **7** from precursor **8**. The ESR spectrum of **7** (Table I) is characterized by a *g* value of 2.00263, typical for alkyl radicals, and by one large and one small β-hyperfine coupling constant pointing to equatorial and axial positions of the β-hydrogen atoms.

(1) Part 4 of Electron Spin Resonance Spectroscopic Investigation of Carbohydrate Radicals. For part 3, see: Korth, H-G.; Sustmann, R.; Gröninger, K. S.; Witzel, T.; Giese, B. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1461.

(2) Surzur, J-M.; Teissier, P. *C. R. Hebd. Seances Acad. Sci., Ser C* **1967**, *264*, 1981-1984; *Bull. Soc. Chim. Fr.* **1970**, 3060-3070.

(3) Beckwith, A. L. J.; Ingold, K. U. In *Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Academic: New York, 1980; Vol. 1, Essay 4, p 161.

(4) Barclay, L. R. C.; Griller, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1982**, *104*, 4399.

(5) Barclay, L. R. C.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1984**, *106*, 1793.

(6) Saebo, S.; Beckwith, A. J. L.; Radom, L. *J. Am. Chem. Soc.* **1984**, *106*, 5119.

(7) Dupuis, J.; Giese, B.; Ruegge, D.; Fischer, H.; Korth, H-G.; Sustmann, R. *Angew. Chem.* **1984**, *96*, 887; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 896.

(8) Korth, H.-G.; Sustmann, R.; Dupuis, J.; Giese, B. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1453.

(9) Sustmann, R.; Korth, H.-G. *J. Chem. Soc., Faraday Trans. 1* **1987**, *83*, 95.

(10) Giese, B.; Dupuis, J. *Angew. Chem.* **1983**, *95*, 633; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 622.

(11) Giese, B.; Gröninger, K. *Tetrahedron Lett.* **1986**, *25*, 2743.

(12) Giese, B.; Witzel, T. *Angew. Chem.* **1986**, *98*, 459; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 450.

(13) Giese, B.; Gröninger, K. S.; Witzel, T.; Korth, H.-G.; Sustmann, R. *Angew. Chem.* **1987**, *99*, 246; *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 233.

0022-3263/88/1953-4364$01.50/0

Table I. ESR Parameters for Carbohydrate Radicals (mT)[a]

radical	T, °C	g	a_α	a_{β^1}	a_{β^2}	a_{γ^1}	a_{γ^2}
10	+13	2.003 11 (3)	1.817	1.245		0.355	0.160
12	+13	2.002 55 (3)	2.182	3.753	1.065	0.092	
5	+12	2.003 19 (3)	1.648	2.873		0.268	
7	+12	2.002 63 (3)	2.160	4.142	0.707	0.059	
14	−10		2.180	4.155	0.730	0.060	
16	+24	2.004 41 (1)	1.732	1.883		0.359	

[a] ±0.003 mT.

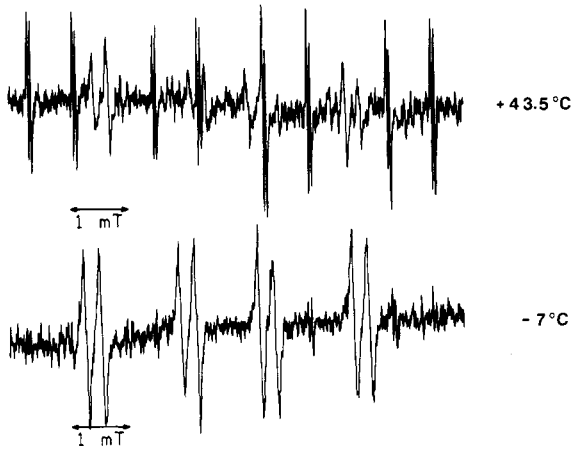


Figure 1. ESR spectra recorded during the photolysis of hexa-*n*-butylditin in the presence of **6**.

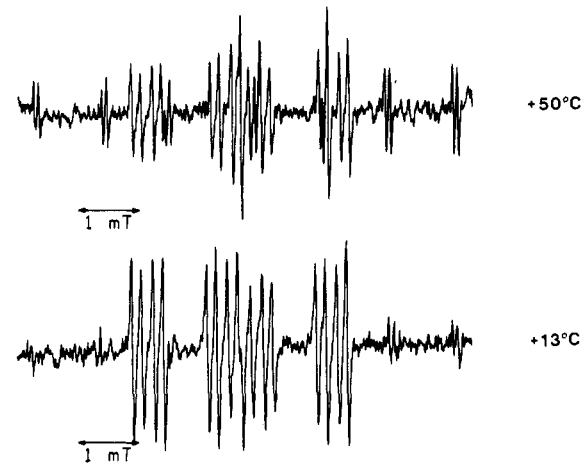
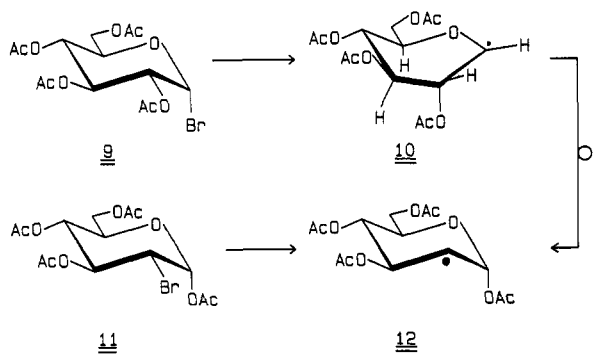


Figure 2. ESR spectra recorded during the photolysis of hexa-*n*-butylditin in the presence of **9**.

Radical **7** exists in the $^4C_1$ chair conformation, and the migrated acetoxy group occupies the axial position at C-1. In Figure 1 we display ESR spectra recorded at two different temperatures during the photolysis of hexa-*n*-butylditin in the presence of **6**. From the spectrum of **7**, generated from precursors **8**, no sign of reversibility of this rearrangement was recognized within the limits of detectability of the ESR method.[14]

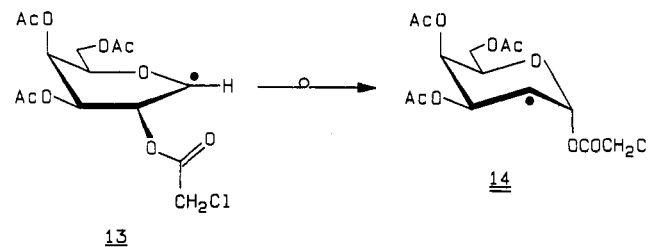
An analogous rearrangement **10** → **12** was discovered for the tetra-*O*-acetylglucosyl radical (**10**) when we photolyzed a benzene solution of hexa-*n*-butylditin, di-*tert*-butyl peroxide, and tetra-*O*-acetylglucosyl bromide (**9**) in the cavity of the ESR spectrometer. In Figure 2 we have collected the spectral evidence for this isomerization. Radical **12** was also generated independently from 2-bromo-2-deoxy-tetra-*O*-acetyl-α-D-glucose (**11**) as precursor. The ESR spectrum of **12** shows similar features to that of **7** (Table I). The coupling parameters imply a $^4C_1$ conformation for radical **12**.



In the case of the rearrangement **10** → **12**, there was also no evidence for a reverse process. Again, the equilibrium is shifted far to the side of the isomerized radicals, indicating higher thermodynamic stabilities for **7** and **12** than for **5** and **10**, respectively.

Above 40 °C several new signals appeared in the ESR spectra, which we tentatively assign to radicals produced by hydrogen abstraction from different positions of the precursors **6** and **9**. It seems reasonable that radicals **7** and **12** are the hydrogen abstracting species, since in solvents that can act as hydrogen donors, like THF or toluene, we record spectra due to the primary radicals (**5**, **10**) superimposed with spectra from radicals derived from the solvents, i.e. either α-tetrahydrofuryl or benzyl radicals. No rearranged radicals (**7**, **12**) could be detected in these solvents.

The migration of the chloroacetoxyl group in the 3,4,6-tri-*O*-acetyl-2-*O*-chloroacetylgalactosyl radical (**13**) supports the observation of Ingold et al.[4] that electron-deficient substituents in the acyloxyl group facilitate the migration process. Above −10 °C we found only signals of the isomerized radical **14** in the ESR spectrum. The hyperfine splitting constants for **14** (Table I) are in accordance with a secondary alkyl radical. A low signal to noise ratio at $T < -10$ °C prohibited the observation of the primary radical.



The tetra-*O*-acetylthioglucosyl radical **16** generated from bromide **15** constitutes an interesting radical in that it differs from **10** only by the replacement of the ring oxygen atom by sulfur. Its ESR spectrum (Table I) might signify

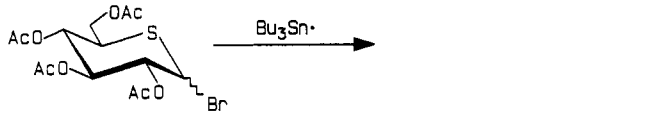
(14) With regard to the signal to noise ratio of the ESR spectra we estimate the detectability of **6** to approximately 10% relative to the signal amplitude of **7**.

Table II. Second-Order Rate Constants $2k_t$ for the Termination of 10

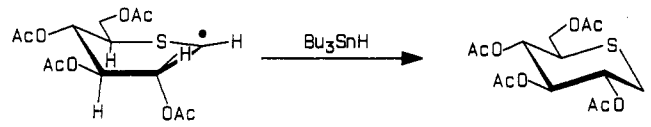
T, °C	$[5]_0$ 10^{-7} mol/L	$2k_t$,[a] 10^8 M^{-1} s^{-1}	r[2]
+7.0	1.38 ● 0.13	4.45 ± 0.32	0.989
+7.0		4.24 ± 0.21	0.995
+18.5	1.35 ± 0.11	6.21 ± 0.68	0.988
+18.5		5.86 ± 0.36	0.992
+31.2	1.03 ± 0.10	10.20 ± 0.31	0.985
+31.2		9.36 ± 0.39	0.998

[a] Each value is the average from four individual decay profiles.

a slightly different conformation for **16** than for **10**. A β-hyperfine coupling constant of 1.883 mT at +24 °C could indicate a less perfect $B_{2,5}$ boat conformation for **16**. However, the change in bond lengths and angles due to the presence of the bulkier sulfur atom may also have a significant effect on the conformation. In the context of the feasibility of the 1,2-acyloxyl migration, it is interesting to see that **16** gives only the nonrearranged product **17** on trapping with tri-*n*-butyltinhydride. Neither in the ESR spectrum nor in the product studies could we detect any sign of rearrangement.

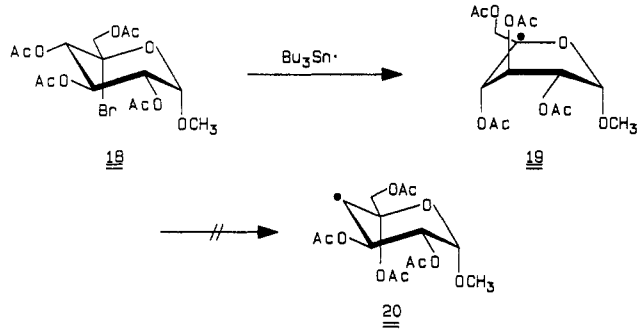


15



16 17

The tertiary radical **19** generated from bromide **18** also does not rearrange to give the secondary radical **20**. The ESR parameters in Table I indicate that **19** possesses a $B_{1,4}$ boat conformation so that the acetoxyl groups at C-3 and C-4 are axially oriented. Therefore, the acetoxyl group at C-4 is well prepared for the rearrangement. Nevertheless, a migration from C-4 to C-5 does not occur.



18 19 20

Kinetic Measurements. The kinetics of the rearrangements **5** → **7** and **10** → **12** were analyzed according to the following reaction scheme where Z and U denote the unrearranged and the rearranged radicals.

$$R'_6Sn_2 \xrightarrow{h\nu} 2R'_3Sn^\bullet$$

$$R'_3Sn^\bullet + ZX \xrightarrow{k_a} Z^\bullet + R'_3SnX$$

$$Z^\bullet \rightarrow U^\bullet$$

$$2Z^\bullet \xrightarrow{2k_t} Z\text{–}Z$$

$$2U^\bullet \xrightarrow{2k_t} U\text{–}U$$

$$Z^\bullet + U^\bullet \xrightarrow{2k_t} Z\text{–}U$$

Steady-state analysis of these reactions leads either to eq 1[5] or eq 2[15] depending on the degree of reformulation of the initial rate equations. In order to determine the

$$\frac{k_r}{2k_t} = [U]\left[\frac{[U]}{[Z]} + 1\right] \quad (1)$$

$$\log \frac{[U]}{[Z]} = \log \frac{A_r}{(IA_t)^{1/2}} - \frac{E_r - E_{t/2}}{2.3RT} \quad (2)$$

rate constant k_r in eq 1, the rate constant $2k_t$ for termination, the absolute concentration of the rearranged radical U, and the relative ratio of the concentrations of Z and U have to be measured. Equation 2 circumvents the determination of absolute radical concentrations, only the relative concentrations of rearranged and original radicals have to be known as a function of temperature. The Arrhenius activation energy E_r for the isomerization can be calculated from the slope of the plot of the logarithm of the ratio [U]/[Z] vs $1/T$. The activation energy E_t for termination is the additional quantity that is necessary in this case. A_t and A_r in eq 2 stand for the corresponding frequency factors, I represents the rate of formation of radicals Z.

Both equations require information about the termination step, either $2k_t$ or E_t. Even though it might be anticipated that the termination kinetics will be close to diffusion control and, therefore, one could make reasonable guesses of $2k_t$ and E_t, we measured these values for the tetra-*O*-acetylglucosyl radical (**10**). We assume in our further analysis that the quantities thus obtained will be valid also for radicals **5**, **7**, and **12**. The rate constant $2k_t$ for **10** was evaluated in the range from +7 to +31 °C by the rotating sector method, i.e. we monitored the decay of **10** after intermittant irradiation of a solution of hexa-*n*-butylditin, di-*tert*-butyl peroxide and tetra-*O*-acetylglucosyl bromide in benzene. The measurements were performed in a slow-flow system in order to avoid a decrease of reactant concentrations upon prolonged photolysis time. In Table II we present the results for the rate constants, determined twice at each temperature, and the absolute concentration of Z at the appropriate temperatures. The decay curves were analyzed on the basis of a second-order rate law and showed a good linear relationship for the plot of $1/[Z]$ vs T. The range of the rate constants of 10^8–10^9 is in accordance with an almost diffusion controlled termination. However, the Arrhenius parameters obtained from these values should only be regarded as good estimates because we could only use the values at +7 °C and at +18.5 °C for their calculation. We did not consider $2k_t$ determined at 31.2 °C to be reliable since the plot of $1/[Z]$ vs T shows a slight progressive curvature at this temperature. This may be an indication of a significant rearrangement reaction at higher temperatures. Signal to noise problems at temperatures below 0 °C prohibited experiments at lower temperatures. The kinetics of the termination reaction is described by eq 3

$$\log (2k_t) = (12.2 \pm 0.4) - (4.5 \pm 0.5)/2RT \quad (3)$$

from which a rate constant $2k_t$ at 298 K of 7.0×10^8 M^{-1} s^{-1} is calculated. The experimental rate constants were compared with those obtained from a measurement of the solution viscosity as a function of temperature by application of the von Smoluchowsky equation[16] for diffusion-

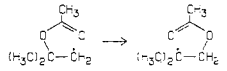
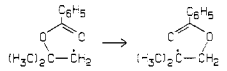
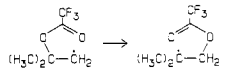
(15) Hamilton, E. J.; Fischer, H. *Helv. Chim. Acta* **1973**, *56*, 795. Korth, H.-G.; Müller, W.; Sustmann, R.; Christl, M. *Chem. Ber.* **1987**, *120*, 1257.

Table III. Experimental and Calculated Data for the Rearrangement 5 → 7

T, °C	[7],[a] 10^{-7} mol/L	[7]/[5]	$2k_t$,[b] 10^8 M^{-1} s^{-1}	k_1,[c] s^{-1}
+2	1.08	0.0485	3.68	41.6
+3	1.12	0.0529	3.79	44.7
+4	1.16	0.0614	3.90	48.0
+8	1.45	0.0690	4.39	68.0
+10	1.50	0.1889	4.65	82.9
+14	1.68	0.1250	5.20	98.3
+15	1.82	0.1677	5.35	113.7
+23	2.56	0.2035	6.63	204.2
+26	3.60	0.2440	7.16	320.7
+29	3.32	0.2904	7.73	331.1
+33	3.58	0.3660	8.53	417.2
+36	4.30	0.3246	9.18	522.5

[a] Obtained from a linear least-squares fit of $[7]_0$ vs T. [b] Calculated from the Arrhenius equation for the termination of **10**. [c] Determined from eq 1.

Table IV. Rate Constants for 1,2-Acyloxy Migrations at 75 °C

rearrangement	solvent	k_R, s^{-1}	ref
	C_6H_5-$C(CH_3)_3$	5.1×10^2	5
	H_2O	2.1×10^4	5
	C_6H_5-$C(CH_3)_3$	2.5×10^2	5
	Freon 113	7.0×10^4	5
5 → 7	C_6H_6	5.4×10^3	*a*
10 → 12	C_6H_6	4.0×10^2	*a*

[a] This work.

controlled processes. The viscosity-dependent activation energy was determined to be 2.61 ± 0.05 kcal/mol from which a value $2k_t^{298}$ of 1.79×10^9 M^{-1} s^{-1} was calculated, i.e. the value from the termination kinetics is smaller by a factor of 2.5 than this value. We might interpret this as some manifestation of slight steric hindrance in the dimerization of the carbohydrate radicals.

The data for the rearrangement **5** → **7** are collected in Table III. Application of eq 1 leads to an Arrhenius activation energy of E_r = 12.8 ± 0.3 kcal/mol and a log A_r value of 11.8 ± 0.2 for the rearrangement. The corresponding Eyring parameters are $\Delta H^{\ddagger}$ = 12.2 ± 0.3 kcal/mol, $\Delta S^{\ddagger}$ = −6.7 ± 1.0 eu and $\Delta G^{\ddagger}$ = 14.2 ± 0.1 kcal/mol. Evaluation according to eq 2 gives E_r = 12.3 ± 0.6 kcal/mol. There is thus good agreement between the two procedures.

The isomerization **10** → **12** was evaluated in an analogous manner. The plot of k_r vs $1/T$ according to eq 1 shows good linearity (r^2 = 0.994) and leads to the following activation parameters: Arrhenius activation energy of E_r = 8.7 ± 0.2 kcal/mol, log A_r = 8.1 ± 0.2, $\Delta H^{\ddagger}$ = 8.0 ± 0.2 kcal/mol, $\Delta S^{\ddagger}$ = −23.6 eu, and $\Delta G^{\ddagger}$ = 15.2 ± 0.1 kcal/mol. On the basis of eq 2 we calculated E_r = 9.0 ± 0.2 kcal/mol. Surprisingly, the values E_r and $\Delta H^{\ddagger}$ are significantly lower than for the rearrangement of **5** → **7** even though observation of the process required higher temperatures. We believe that some reversibility of the rearrangement and/or more likely, additional termination of the isomerized radical by hydrogen abstraction from the radical precursor at higher temperatures might have reduced the steady-state concentration of **10**. This results in a less pronounced temperature dependence of the [U]/[Z] ratio than would otherwise be the case.

(16) Noyes, R. M. *Progr. React. Kinet.* **1961**, *1*, 129.

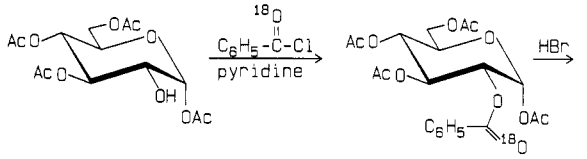
Labeling Experiments. In a recent report[17] it was claimed that the acyloxyl rearrangement may not only occur via a five-membered transition state **21** but also via a three-membered transition state **22** leading to a 1,2-shift of the ether oxygen of the acyloxyl group. In order to

21 **22**

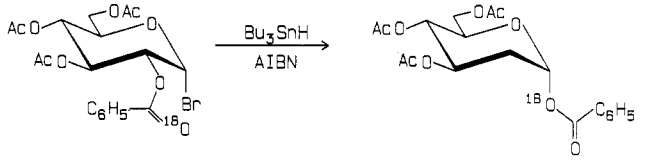
$$2CH_3OH \longrightarrow CH_2(OH)_2 + CH_4$$

$$CH_3OH + CH_3SH \longrightarrow CH_4 + HSCH_2OH$$

distinguish between these two possibilities in our systems we have synthesized the glucosyl bromide **25** enriched with 45% ^{18}O in the benzoyl group. Radical reaction with tri-*n*-butyltin hydride at 80 °C showed that the benzoyl group migrates without scrambling of the ^{18}O atom. The carbonyl oxygen of the benzoyl group in **25** becomes exclusively the alkoxy oxygen in the rearranged product **26**.



23 **24**



25 **26**

The rearrangement of the carbohydrate radical therefore proceeds exclusively via a five-membered ring transition state.

Discussion

Before we discuss the peculiarities of the acyloxyl rearrangement in the carbohydrate radicals it might be useful to compare the rate of these reactions with those reported in the literature for other systems. Ingold et al.[4,5] studied the rearrangement as a function of R in the acyloxyl group and considered different solvents. In Table IV we list values for k_r at a temperature of 75 °C, calculated from the Arrhenius equation. For R = methyl or phenyl similar rate constants are found for the cases studied by Ingold[5] and for the carbohydrate examples. The acceleration by the trifluoromethyl group and by polar solvents was taken as evidence for the stabilization of the transition state by polar interactions. This view is supported by the more facile rearrangement of the chloroacetyl-substituted glucosyl radical **13**. There is, however, a remarkable difference between our examples and those described in the literature. The driving force in the latter cases is the conversion of a primary or secondary into a tertiary carbon radical, whereas in our case an alkoxy-substituted secondary carbon radical, which is stabilized by the interaction of the unpaired electron with the alkoxy

(17) Kocovsky, P.; Stary, I.; Turecek, F. *Tetrahedron Lett.* **1986**, *27*, 1513.

group, is transformed into another secondary alkyl radical. As the rearrangement must be governed by the stability of the product radical, we have to explain the greater stability of **7** and **12** as compared to **5** and **10**.

Radical **5**, which exists in a ^4H conformation between −15° and +70° according to its ESR spectrum, is formed from **6**, which exists in a $^4C_1$ chair conformation. For the tetra-*O*-acetylglucosyl radical it was demonstrated that the initial conformation after bromine abstraction at 77 K retains the $^4C_1$ chair structure **27** of the precursor.[18] In the latter example a transformation to the $B_{2,5}$ conformation occurs on warming. The conformational change was explained by the stabilizing interaction of the σ^*-orbital of the β-CO bond with the singly occupied π-orbital.[6-9] Since no radical of the original $^4C_1$ structure **27** could be detected by ESR spectroscopy between −30 and +60 °C radical **10** with the $B_{2,5}$ conformation should be at least 1.0–1.2 kcal/mol more stable than **27**.[14] The stereoelectronic effect, which arises by the interaction of the SOMO of the alkoxyalkyl radical center and the LUMO of the adjacent C–O bond has to be larger than 1.0–1.2 kcal/mol, because in the equilibrium between radicals **27** and **10** this stereoelectronic effect is reduced by the strain energy of the boat **10**. In the rearrangement **10** → **12** the 1.0–1.2 kcal/mol anomeric stabilization and an additional 1.5 kcal/mol due to α-oxygen radical stabilization[19] are lost. According to these arguments, radical **10** should be about 2.5 kcal/mol more stable than radical **12**. But we could not observe any radical **10** when we generated **12** under conditions of the rearrangement. This means that radical **12** is at least 1.0–1.2 kcal/mol more stable than radical **10**. Summing up these individual data leads to the conclusion that a stabilizing effect of at least 3.5 kcal/mol has to be found in radical **12**, which cannot be caused by the radical center (stabilization of the unpaired electron). In radical **10** each carbon atom is connected with one oxygen atom, whereas in radical **12** C-1 is connected with two oxygen atoms. Schleyer[20] has recently calculated for the isodesmic reaction (4) that a molecule gains 17 kcal/mol in stabilization if a second C–O bond is formed at an oxygen-substituted carbon atom. This stereoelectronic effect could make radical **12** more stable than radical **10**. In contrast to this case with two oxygens at one carbon atom, Schleyer calculated a stabilization energy of less than 6 kcal/mol if one of the carbon–heteroatom bonds is a carbon–sulfur bond (5) Our observation that radical **16** does not rearrange is in accord with this small electronic effect, which in this case is not able to overcompensate the loss of stabilization of the radical center. We also could not detect a migration of an acyloxyl group in radical **19** at temperatures up to +80 °C. In this rearrangement the secondary radical **20**, which would have been formed from the tertiary radical **19**, probably incorporates too much internal strain because of the two bulky groups at C-5.

$$2CH_3OH \rightarrow CH_2(OH)_2 + CH_4 \quad (4)$$

$$CH_3OH + CH_3SH \rightarrow CH_4 + HSCH_2OH \quad (5)$$

The present case is a nice demonstration of the fact that stabilization of the radical center being formed is not always the dominant factor for a rearrangement. In view of the stabilization of the radical center, the C-1 pyranosyl radicals **5** and **10** are obviously the more stabilized radicals compared to the pyranosan-2-yl radicals **7** and **12**. However, the facile migration of the acetoxyl group shows that the pyranosan-2-yl radicals are the more stabilized molecules, gaining stabilizing from interactions independent of their radical nature.

Experimental Section

Reduction of 2,3,4,6-Tetra-*O*-acetyl-5-thio-α,β-glucosyl Bromide (15). To a boiling solution of thioglucosyl bromide **15** (430 mg, 1.0 mmol) in benzene (25 mL) was added under N_2 over 20 h a solution of tributylstannane (0.37 mL, 1.1 mmol) and azoisobutyronitrile (50 mg) in benzene (20 mL). After distilling off benzene and chromatography on silica gel (diethyl ether–pentane, 2:1), **17** (318 mg, 92%) with mp 100–102 °C was isolated. Rearranged products could not be detected. ^1H NMR ($CDCl_3$): δ 2.01 (s, 3 H, OAc), 2.02 (s, 3 H, OAc), 2.03 (s, 3 H, OAc), 2.07 (s, 3 H, OAc), 2.67 (dd, 1 H, $J_{1a,2}$ = 10.1, $J_{1a,1e}$ = 12.8 Hz, H_{1a}), 2.88 (dd, 1 H, $J_{1e,2}$ = 3.9, $J_{1e,1a}$ = 12.8 Hz, H_{1e}), 3.17 (ddd, 1 H, $J_{5,6}$ = 3.3, $J_{5,6'}$ = 5.9, $J_{4,5}$ = 9.5 Hz, H_5), 4.14 (dd, 1 H, $J_{5,6}$ = 3.3, $J_{6,6'}$ = 11.9 Hz, H_6), 4.25 (dd, 1 H, $J_{5,6}$ = 5.9, $J_{6,6'}$ = 11.9 Hz, $H_{6'}$), 5.03 (m, 2 H, H-2, H-3), 5.21 (dd, 1 H, $J_{4,5}$ = 9.5, $J_{3,4}$ = 10.1 Hz, H_4). Anal. Calcd for C, 48.23; H, 5.78. Found C, 48.32; H, 5.65.

Reduction of 5-Bromo-1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose (18). To a boiling solution of bromide **18** (300 mg, 0.64 mmol) in benzene (15 mL) was added under N_2 over 20 h a solution of tributylstannane (0.2 mL, 0.7 mmol) and azoisobutyronitrile (20 mg) in 15 mL of benzene. After distilling off the solvent and chromatography on silica gel (diethyl ether–pentane, 2:1), 1,2,3,4,6-penta-*O*-acetyl-α-D-glucopyranose (270 mg, 89%) was isolated. Rearranged products could not be detected.

Synthesis of 3,4,6-Tri-*O*-acetyl-2-*O*-benzoyl-[^{18}O]-α-D-glucopyranosyl Bromide (25). To a solution of 1,3,4,6-tetra-*O*-acetyl-α-D-glucopyranose (10.0 g, 28.7 mmol) in dichloromethane (30 mL) and pyridine (10 mL) was added at 0 °C a dichloromethane solution (30 mL) of [^{18}O]benzoyl chloride (5.00 g, 35.5 mmol), which was generated from thionyl chloride and [^{18}O]-benzoic acid, obtained after hydrolysis of benzoyl chloride with water (^{18}O content = 91%). After 14 h at 20 °C the reaction mixture was poured into ice water (150 mL) and extracted with chloroform (150 mL). After being washed with water, 1 M HCl solution, a saturated $NaHCO_3$ solution, and water, the chloroform solution was dried over Na_2SO_4 and flash chromatographed on silica gel (toluene–ethyl acetate, 3:1). The benzoate **24** (6.01 g, 46%) was obtained as a syrup, which contained 44% ^{18}O at the benzoate carbonyl oxygen. This was deduced from the intensity of the carbonyl signals of the benzoate in the ^{13}C NMR spectrum. The carbonyl carbon atom of the ^{16}O-benzoyl absorbs at δ 165.085, whereas the C atom of the carbonyl group of the [^{18}O]benzoyl group shows a signal at δ 165.129. In the IR spectrum the ester carbonyl absorptions appear at 1750 and at 1697 cm^{-1}. A solution of the ^{18}O and ^{16}O benzoate mixture **25** (3.50 g, 7.33 mmol) in dichloromethane (40 mL) was treated with a HBr solution (33%) in acetic acid (20 mL) at 20 °C. After 5 h, chloroform (100 mL) was added, and the solution was washed with ice water, saturated $NaHCO_3$ solution, and ice water again. Distilling off the solvent gave a syrup, which crystallized by treatment with *tert*-butyl methyl ether. The ^{18}O content of the benzoyl group remained 44%. The carbonyl carbon of the ^{16}O benzoate group shows a signal at δ 165.074 and that of the ^{18}O benzoate at δ 165.105 in the ^{13}C NMR.

Rearrangement of 3,4,6-Tri-*O*-acetyl-2-*O*-benzoyl-[^{18}O]-α-D-glucopyranosyl Bromide (25). To a solution of

(18) Chandra, H.; Symons, M. C. R.; Korth, H.-G.; Sustmann, R. *Tetrahedron Lett.* **1987**, *28*, 1455.
(19) Korth, H.-G.; Lommes, P.; Sicking, W.; Sustmann, R. *Chem. Ber.* **1985**, *118*, 4627.
(20) Schleyer, P. v. R.; Jemmis, E. D.; Spitznagel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6393.

bromide **25** (1.80 g, 3.80 mmol) in boiling benzene (80 mL) was added under argon over 8 h a solution of tributyltinhydride (1.40 g 4.80 mmol) and azoisobutyronitrile (80 mg) in benzene (20 mL). After the solvent was distilled off, crystallization (*tert*-butyl methyl ether–hexane, 1:1) gave the 2-deoxyglucose **26** (1.17 g, 76%) with ^{18}O exclusively at the alkoxy group of the benzoate. Mp: 115.5 °C. ^1H NMR ($CDCl_3$): δ 2.06 (s, 3 H, OAc), 2.07 (s, 6 H, OAc), 2.10 (ddd, 1 H, $J_{1,2a}$ = 3.7, $J_{2a,3}$ = 11.6, $J_{2a,2e}$ = 13.6 Hz, H_{2a}), 2.45 (ddd, 1 H, $J_{1,2e}$ = 1.2, $J_{2e,3}$ = 5.3, $J_{2a,2e}$ = 13.6 Hz, H_{2e}), 4.06 (dd, 1 H, $J_{5,6}$ = 2.2, $J_{6,6}$ = 5.3 Hz, H_6), 4.17 (ddd, 1 H, $J_{2e,3}$ = 5.3, $J_{2a,3}$ = 11.6 Hz), 4.35 (dd, 1 H, $J_{5,6}$ = 4.0, $J_{6,6}$ = 12.4 Hz, H_6), 5.16 (dd, 1 H, $J_{3,4}$ = 9.6, $J_{4,5}$ = 10.1 Hz, H_4), 5.47 (ddd, 1 H, $J_{2e,3}$ = 5.3, $J_{3,4}$ = 9.6, $J_{2a,3}$ = 11.6 Hz, H_3), 6.53 (dd, 1 H, $J_{1,2e}$ = 1.2, $J_{1,2a}$ = 3.7 Hz, H_1), 7.48 (t, 2 H, aromat), 7.63 (t, 1 H, aromat), 8.09 (d, 2 H, aromat). ^{13}C NMR ($CDCl_3$): δ 20.64, 20.87, 34.09, 61.90, 68.62, 68.79, 70.50, 91.465 (C-1), 91.495 (C-1), 128.64, 129.33, 129.86, 133.67, 164.26 (C=O, benzoyl, no splitting of the signal), 165.63, 170.14, 170.51. Anal. Calcd for $C_{19}H_{22}O_{8.5}{}^{18}O_{0.5}$ (395.3): C, 57.73; H, 5.61. Found: C, 57.61; H, 5.68.

ESR Measurements. Radicals were generated by UV irradiation of 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 ESR solutions were composed of the sugar derivative (ca. 50 mg), dry benzene (0.2 mL), and hexamethylditin (0.2 mL). The addition of di-*tert*-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. ESR spectra were recorded on a Bruker ER-420 spectrometer with use of a double cavity. ESR hyperfine coupling constants were refined by simulation of the manually evaluated ESR 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 NMR field measuring unit.

The ESR kinetic experiments with the rotating sector method were carried out as described elsewehre.[11] Radical concentrations were determined by numerical double integration of simulated spectra, best fitted to the experimental spectra, and comparison with the signals of a calibrated standard.[21]

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

(21) Korth, H.-G.; Trill, H.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483. Sustmann, R. *Kinetische-(KESR) und Modulations-(MESR) Spektroskopie*; Forschungsberichte des Landes Nordrhein-Westfalen, Nr. 3087, Westdeutscher Verlag, Opladen, 1981.

Photoacetylation of 2-Substituted Adamantanes. Stereochemistry and Substituent Effects

Koushi Fukunishi,*[†] Atsuya Kohno,[†] and Shosuke Kojo[‡]

Department of Chemistry, Kyoto Institute of Technology, Matsugasaki, Sakyo-ku, Kyoto 606, Japan, and Department of Public Health, Faculty of Medicine, Kyoto University, Kyoto 606, Japan

Received January 25, 1988

Photoacetylation of 2-substituted adamantanes with biacetyl gave regiospecifically syn- and anti-4-substituted 1-acetyladamantanes. Competitive reactions for two syn and anti δ-hydrogen abstractions by triplet biacetyl showed that the ρ^* values were −0.50 and −0.79, respectively. The carbon-13 NMR was studied in order to assign stereoisomers. The observed magnitude of the field-effect transmission for two series of substituent effects was understandable on the basis of the geometrical relationships (bond length and angle) between the reaction center and a substituent.

Introduction

Rigid and symmetrical adamantanes have a wide applicability for mechanistic and preparative studies for free-radical reactions as well as ionic reactions. It has been possible at least qualitatively to partition a substituent effect into the electronic (a direct or field effect and an inductive effect)[1,2] and steric effects[3] in free-radical reactions generally, by evaluating the substituent effect of hydrogen abstraction on the 1.2, 1.3, or 1.4 adamantane systems. From a synthetic viewpoint, it is very important to be able to introduce a substituent selectively into adamantanes. The direct functionalizations of adamantanes are most often achieved by ionic substitution[4] which affords bridgehead products exclusively, whereas a free-radical process generally yields both the bridgehead and bridge products.[5]

It has been found that the direct regiospecific functionalizations of adamantanes have been successfully carried out via free-radical routes.[2,6] Among them, photoacetylation for the regiospecific bridgehead substitution is one of the most excellent procedures.[2,7] The elegant photoacetylation is interesting and noteworthy because of bridgehead hydrogen abstraction from adamantanes by the excited state of biacetyl.[2] When δ-hydrogen abstraction (two remote bridgehead hydrogens) for 2-substituted adamantane proceeds exclusively, the photoacetylation can yield only two stereoisomers.[7] The knowledge on the relative reactivity for the abstraction of two hydrogens, which are not equivalent in the length and angle from substituent X, may be useful to investigate the effect of substituents on direct or indirect interaction between the

[†] Kyoto Institute of Technology.
[‡] Kyoto University.

(1) (a) Owens, P. H.; Gleicher, G. J.; Smith, L. H., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4122. (b) Gleicher, G. J.; Jackson, J. L.; Owens, P. H.; Unruh, J. D. *Tetrahedron Lett.* **1969**, 833.
(2) (a) Tabushi, I.; Kojo, S.; Yoshida, Z. *Tetrahedron Lett.* **1973**, 2329. (b) Tabushi, I.; Kojo, S.; Fukunishi, K. *J. Org. Chem.* **1978**, *43*, 2370.
(3) Aoyama, Y. Doctor's Thesis, Kyoto University, 1974, p 116.
(4) (a) Stetter, H.; Schwarz, M.; Hirschborn, A. *Chem. Ber.* **1959**, *92*, 1629. (b) Koch, H.; Haaf, W. *Org. Synth.* **1964**, *44*, 1. (c) Kovacic, P.; Roskos, P. D. *J. Am. Chem. Soc.* **1969**, *91*, 6457. (d) Olah, G. A.; Chi-hung Lin, H. *Ibid.* **1971**, *93*, 1259.
(5) Smith, G. W.; Williams, H. D. *J. Org. Chem.* **1961**, *26*, 2207. (b) Tabushi, I.; Yoshida, Z.; Takahashi, N. *J. Am. Chem. Soc.* **1970**, *92*, 6670. (c) Tabushi, I.; Hamuro, J.; Oda, R. *Ibid.* **1967**, *89*, 7127. (d) Tabushi, I.; Hamuro, J.; Oda, R. *J. Org. Chem.* **1968**, *33*, 2108. (e) Breslow, D. S.; Edwards, E. I.; Leone, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1968**, *90*, 7097. (f) Perkins, R. R.; Pincock, R. E. *Can. J. Chem.* **1978**, *56*, 1269.
(6) Tabushi, I.; Fukunishi, K. *J. Org. Chem.* **1974**, *39*, 3748.
(7) Tabushi, I.; Aoyama, Y. *J. Org. Chem.* **1973**, *38*, 3447.

0022-3263/88/1953-4369$01.50/0