Glycosylidene Carbenes

Part 27[1])

Glucosidation of Titanium Dioxide with 1-Aziglucoses: Preparation and Characterization of Modified Titanium-Dioxide Surfaces

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Titanium-dioxide surfaces have been glycosylated with the benzyl-, 4-fluorobenzyl-, and acetyl-protected diazirines **1**–**3**. The modified TiO_2 surfaces were characterized by contact-angle measurement, X-ray photoelectron spectroscopy (XPES), and time-of-flight secondary-ion mass spectrometry (ToF-SIMS). The main by-products of the glucosidation (mostly azines and trehaloses) were identified. Their physisorption slightly reduces the efficiency of the glucosidation by 1 mM solution of **1** or **2** in CH_2Cl_2, but this influence is neutralized by repeating the glucosidation, or by using a 100 mM solution of the diazirines. The immobilized, acetylated glucosyl moieties were deacetylated *in situ*. Calculations based on the XPES peaks of Ti 2p and F 1s for the TiO_2 surface modified with **2** indicated 1.5 ± 0.9 immobilized glucosyl moieties per nm^2.

1. Introduction. – The structure and reactivity of titanium surfaces have been the subject of detailed studies [2–5]. Titanium, upon exposure to air, forms a thin film of oxides, among which TiO_2 predominates [6]. The OH groups of the readily hydrated titanium-oxide surface are amphoteric; half of the groups are characterized by a pK_a value of *ca.* 3.8, the other half by a pK_a of 6.6 [6–8].

A number of studies about adsorption on titanium-oxide surfaces have been published, *e.g.*, the adsorption of gas molecules [2], of different reagents and solvents [8][9], and of proteins [10–12]. The nature of adsorbed molecules has a strong influence on the physical, chemical, and biochemical properties of the surface. The interest in TiO_2 surfaces with immobilized biomolecules derives from their expected higher biocompatibility. The outermost atomic or molecular layer of the biomaterial and the first molecular layer of biomolecules that forms on the implant surface after implantation [13] are critically important for the success or failure of medical implants. Immobilized carbohydrates are expected to positively influence the interaction with biomolecules, such as proteins and glycoproteins, the recruitment and attachment of cells, and the proliferation and differentiation of cells on the surface [14].

The low pK_a value and the expected weak nucleophilicity of the OH groups on the surface of oxidized titanium strongly suggest the use of 1-aziglycoses [15] for their

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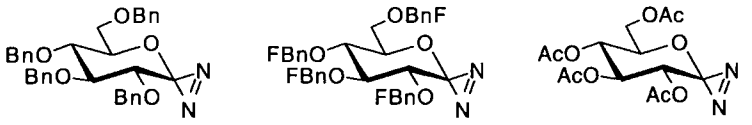
glycosidation. 1-Aziglycoses generate singulet carbenes that readily insert into H–O bonds [16–19], leading to glycosides. Glycosidation of TiO_2 by 1-aziglycoses should thus lead to a monolayer of immobilized glycosyl moieties[2]).

The TiO_2 surfaces should be generated by sputter coating glass slides. We planned to use the benzylated diazirine **1** [15] for exploratory work. Glucosidation by the 4-fluorobenzyl-protected diazirine **2** should facilitate the specific demonstration of glucosyl residues on the surface (as opposed to a contamination by organic material) and the characterization of the glucosylated surface by X-ray photoelectron spectroscopy (XPES) and time-of-flight secondary-ion mass spectrometry (ToF-SIMS), through detection of specific XPES binding energies (F 1s) and secondary-ion fragments. Finally, TiO_2 surfaces modified by unprotected glucosyl residues should be obtained by glucosidation with the diazirine **3** and deacetylation.



1 **2** **3**

Bn=$PhCH_2$, FBn=4-$FC_6H_4CH_2$

2. Results and Discussion. – *Preparation of the TiO_2 Layer.* TiO_2-Covered glass slides (12×12 mm^2) were prepared by magnetron sputtering. XPES showed that the TiO_2-sputtered layer completely covered the glass. The survey spectrum of the TiO_2 film (*Fig. 1*) indicated the presence of Ti, O and small amounts of C. The high-resolution Ti 2p spectrum showed two major peaks at 458.6 and 464.3 eV, attributed to Ti^{4+} $2p_{3/2}$ and Ti^{4+} $2p_{1/2}$, respectively. The peak positions, line shapes and oxidation states are consis-

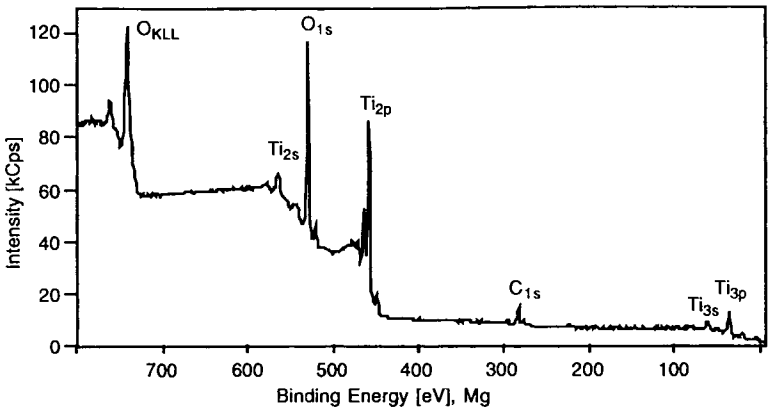


Fig. 1. *XPE Survey spectrum of the TiO_2-covered glass slide, prepared by the magnetron sputter procedure.* The TiO_2 coating completely covers the glass substrate.

[2]) The reaction of TiO_2 with CH_2N_2 has been described by *Boehm* [8].

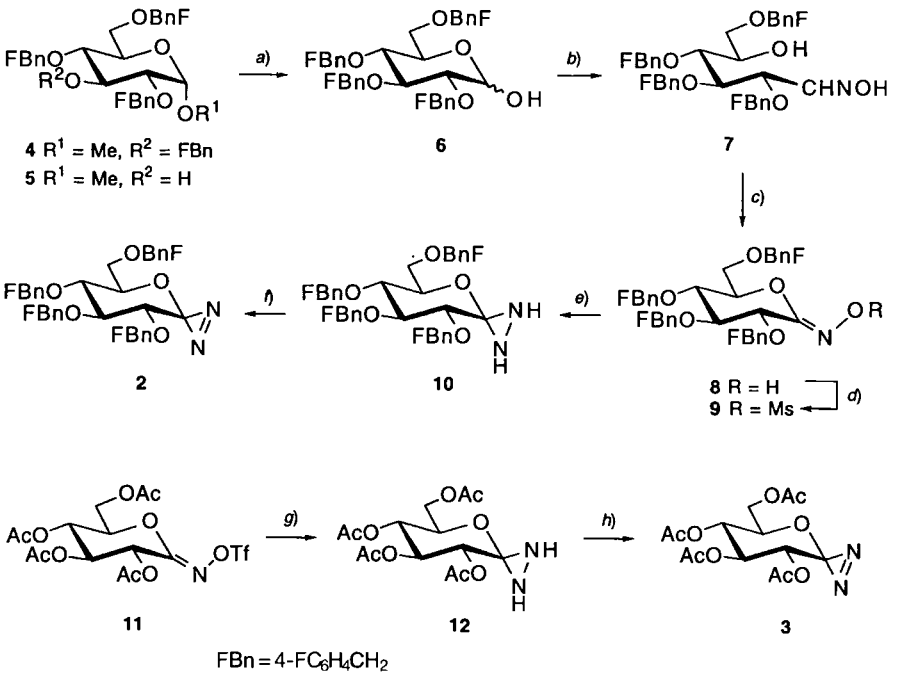
tent with those observed in TiO_2 reference spectra [6][20]. High-resolution, angle-dependent O 1s spectra showed an asymmetric broadening at the high-binding-energy side of the major peak at 530.0 eV. Varying the angle between the surface plane and the X-ray source from 90 to 20° (increasing the surface sensitivity) clearly increased the relative peak area of the low-intensity peak at 531 eV (*Table 1*). This experiment indicates that the O species, which correlates with the low-intensity/high-binding-energy peak, is located at or very close to the surface. The binding energy of 531.9–531.5 eV suggests the presence of OH groups at the outermost surface (partially hydrated TiO_2). The increase of the stoichiometric ratio O/Ti as a function of the angle of detection (*Table 1*) indicates additional O species at the surface, in keeping with previous results [6][7]. Organic contaminants containing O-atoms that may contribute to the O 1s peak at around 532 eV can not, however, been excluded.

The high-resolution spectra of C 1s also showed an angular-dependence of the line shape, *i.e.*, of the ratio of the sub-peak areas at 284, 286, and 289 eV (*Table 1*). Although the dependence is weaker than that observed for the O 1s line shape, the ratio of the C 1s to Ti 2p peak areas clearly increased as the detection angle decreased from 90° (42:58) to 20° (73:27), suggesting that the C signal is (mostly) due to (natural) surface contamination.

The contact angle of ultrapure H_2O on the sputter-deposited TiO_2 surfaces (as received) with relatively low C contamination (17.6%) varied between 70 and 84°. These surfaces were treated with a 1.5M aqueous solution of H_2O_2, washed with deionized H_2O, and dried with a stream of N_2, before being immersed into a solution of the diazirines **1**–**3**. A treatment with H_2O_2 has been suggested to produce a TiO_2 surface that is capable of forming durable bonds with adhesives [21–24]. The X-ray photoelectron survey and high-resolution spectra of the H_2O_2-treated TiO_2 surfaces were qualitatively similar to the spectra of the untreated surfaces. However, the C concentration was reduced from 17.6 to 14.2% (*Table 1*), resulting in more highly hydrophilic surfaces (contact angle 25–28°). Furthermore, the O 1s to Ti 2p peak area ratio increased slightly, as the angle of detection was decreased from 90 to 20° (*Table 1*). The changes of the contact angle and the peak-area ratios are in keeping with an increased degree of hydration of the surface layer and – together with the observed reduction in surface contamination – suggest a surface more suited to chemical functionalisation.

Preparation of the Diazirines **2** *and* **3**. The *O*-fluorobenzylated 1-aziglucose **2** (*Scheme*) was synthesized according to the established method [15]. Fluorobenzylation of methyl α-D-glucopyranoside with 4.4 equiv. of 4-fluorobenzyl bromide led to a mixture of the fully fluorobenzylated **4** (53%) and the 2,4,6-tris-*O*-fluorobenzylated glucoside **5** (36%), which were separated by flash chromatography (FC). Hydrolysis of **4** with AcOH and H_2SO_4 led to the hemiacetals **6** (52%; α-D/β-D 66:34). Transformation into the oximes **7** (97%; (*E*)/(*Z*) 58:42) and oxidation with MnO_2 [25] yielded 60% of the (*Z*)-hydroximolactone **8**. Mesylation of **8** and treatment of the resulting sulfonate **9** with NH_3 in MeOH yielded 73% of the *trans*-diaziridines **10** (two *trans*-isomers in the ratio 96:4). The 1-aziglucose **2** was obtained in 78% yield by oxidation of the diaziridines with I_2 in CH_2Cl_2. The fluorobenzylated **2** is more stable than the benzylated **1** (halflife $\tau_{1/2}$ of 43 min in MeOH at 25° *vs.* $\tau_{1/2}$ 33 min [16]), and kept well for months at −78° either as a solution in CH_2Cl_2 or in the solid state.

Scheme



a) 1M H_2SO_4, AcOH, 118°; 52%. *b*) $NH_2OH \cdot HCl$, NaOMe, MeOH, 60°; 97%. *c*) MnO_2, MeOH, acetone, Et_2O, 25°; 60%. *d*) MsCl, Et_3N, CH_2Cl_2, 0°; 89%. *e*) Sat. NH_3 soln. in MeOH, 25°; 82%. *f*) I_2, Me_3N, CH_2Cl_2, −45°; 78%. *g*) Sat. NH_3 soln. in MeOH, CH_2Cl_2, −20°; 71%. *h*) I_2, Et_3N, CH_2Cl_2, 0°; 98%.

The acetylated 1-hydraziglucose **12**[3]) was obtained in 71% yield from the known triflate **11** [25], following the established method [16] (*Scheme*). Oxidation of **12** with I_2 in CH_2Cl_2 afforded the 1-aziglucose **3** (98%). It had a $\tau_{1/2}$ value of 181 min in MeOH at 25°, shorter than the 1,5-anhydro-1-azi-2,3,4,6-tetra-*O*-pivaloyl-D-glucitol ($\tau_{1/2}$ 202 min [16]), and kept well for up to two months at −25° in the solid state.

Surface Modification with the Diazirine **1**. H_2O_2-Treated, TiO_2-covered glass slides were exposed to a 1 mM or 100 mM solution of **1** in dry CH_2Cl_2, as described in the *Exper. Part.* The XPE spectra of the glycosylated samples showed an increased C amount (*Table 2*). The survey spectra indicated that O, C, and Ti were present in ratios of 60:19:21 (1 mM) and 58:24:18 (100 mM) with a minor contamination by Si and N. The amount of C detected by XPES ranged between 19.3 and 21.8% for TiO_2 surfaces treated with a 1 mM solution of **1** and between 23.6 and 24.3% for TiO_2 surfaces treated with a 100 mM solution of **1**. Repetitive treatment of the TiO_2 surface with a 1 mM solution of **1** led to 24.1–24.5% of C after three glucosidations (*Table 2*). Renewed glucosidation had no effect on the C content. The same C content was obtained whether the sufaces were rinsed with CH_2Cl_2[4]) after each treatment, or not. However, the

[3]) The ^{1}H-NMR spectrum of **12** shows N*H* signals for only a single *trans*-configured isomer.

[4]) Rinsing with acetone and MeOH had the same effect.

Table 1. *Angle-Dependent XPES Data of the TiO_2-Coated Glass Substrate as Sputtered and after H_2O_2 Treatment of the TiO_2 Surface*

Surface	Angle of detection [ ]	Binding energies [eV][a] (relative peak area [%])							Atomic concentration [at.-%]		
		O $1s_A$	O $1s_B$	Ti $2p_{1/2}$	Ti $2p_{3/2}$	C $1s_A$	C $1s_B$	C $1s_C$	Ti	O	C
Untreated (as sputtered)	20	531.9 (19.7)	530.0 (80.3)	464.3 (33.3)	458.6 (66.7)	288.8 (7.0)	286.5 (12.8)	284.9 (80.2)	15.5	42.4	42.1
	45	531.7 (13.7)	530.0 (86.3)	464.2 (33.3)	458.6 (66.7)	288.9 (6.0)	286.3 (21.6)	284.9 (72.4)	22.4	54.3	23.3
	90	531.5 (11.1)	530.0 (88.9)	464.3 (33.3)	458.6 (66.7)	289.0 (6.9)	286.4 (23.1)	285.0 (70.0)	24.1	58.3	17.6
H_2O_2-Treated	20	531.8 (23.4)	530.1 (76.6)	464.4 (33.3)	458.6 (66.7)	289.0 (10.5)	286.4 (25.0)	284.9 (64.5)	18.5	49.1	32.4
	45	531.6 (13.4)	530.0 (86.4)	464.4 (33.3)	458.6 (66.7)	289.1 (9.1)	286.7 (25.5)	285.0 (65.4)	23.7	58.8	17.5
	90	531.6 (11.9)	530.0 (88.1)	464.3 (33.3)	458.6 (66.7)	289.0 (10.4)	286.6 (23.3)	285.1 (66.3)	25.0	60.8	14.2

[a]) Referenced by setting the Ti $2p_{3/2}$ peak to 458.6 eV.

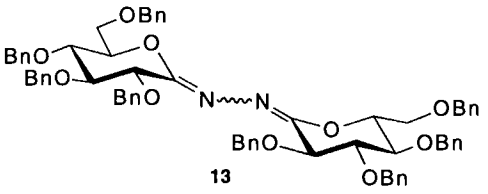
Table 2. *XPES Data of the TiO_2 Surfaces after Chemical Immobilization of 1-Aziglucoses.* Angle of detection 90°.

Surface modified with	Binding energies [eV][a] (relative peak area [%])							Atomic concentration [at.-%]			
	O $1s_A$	O $1s_B$	O $1s_C$	C $1s_A$	C $1s_B$	C $1s_C$	F 1s	Ti	O	C	F
Benzylated 1-aziglucose **1** (once 1 mM)	532.2 (7.5)	530.8 (16.1)	530.0 (76.4)	290.6 (7.5)	285.3 (21.1)	284.1 (71.4)	–	20.7	60.0	19.3	–
Benzylated 1-aziglucose **1** (twice 1 mM)	532.2 (7.3)	530.7 (16.2)	530.1 (76.5)	290.6 (7.7)	285.2 (22.3)	284.2 (70.0)	–	19.2	58.2	22.6	–
Benzylated 1-aziglucose **1** (three times 1 mM)	532.2 (7.5)	530.7 (16.1)	529.9 (76.4)	290.5 (7.4)	285.4 (22.1)	284.0 (70.5)	–	19.0	56.5	24.5	–
Benzylated 1-aziglucose **1** (100 mM)	532.2 (8.9)	530.9 (17.8)	529.9 (73.3)	290.6 (7.6)	285.3 (22.6)	284.2 (69.8)	–	18.5	57.9	23.6	–
4-Fluorobenzylated 1-aziglucose **2** (100 mM)	532.4 (15.6)	531.0 (11.4)	530.1 (73.0)	289.1 (4.2)	286.6 (27.1)	284.8 (68.7)	687.6	17.6	56.0	24.5	1.9
Physisorbed hemiacetal **6**	532.7 (87.4)	532.2 (12.6)	–	286.6 (25.1)	284.7 (18.6)	284.6 (56.3)	687.2	–	14.7	77.3	8.0
Acetylated 1-aziglucose **3** (100 mM)	532.5 (7.6)	531.2 (7.6)	529.8 (84.8)	289.1 (15.1)	286.8 (18.1)	285.0 (66.8)	–	20.4	60.9	18.7	–
Physisorbed 2,3,4,6-tetra-*O*-acetylglucopyranose	533.2 (7.8)	532.0 (33.6)	530.1 (58.6)	288.7 (14.0)	286.9 (14.0)	285.1 (72.0)	–	11.6	46.8	41.6	–
3 and deacetylation of the immobilized sugar moieties	532.9 (19.8)	531.8 (9.6)	529.9 (70.6)	288.5 (14.0)	286.5 (57.6)	284.8 (28.4)	–	15.9	60.1	24.0	–
Physisorbed glucose	533.0 (32.8)	532.3 (20.6)	530.1 (46.6)	288.1 (13.5)	286.3 (72.5)	284.5 (14.0)	–	8.6	49.4	42.0	–

[a]) Referenced by setting the Ti $2p_{3/2}$ peak to 458.6 eV.

increase of the C content upon each of the first three glucosidation experiments appeared to depend upon the quality of the surface, as discussed below.

The supernatant of the glucosidation experiments and the solutions resulting from rinsing the TiO_2 surfaces after glycosidation were examined by analytical HPLC[5]) and TLC. This showed the formation of lactone azines **13**[6]), tri-*O*-benzyl-2-(benzyloxy)-glucal **14** [26], a mixture of anomeric octa-*O*-benzyl-trehaloses **15** [27] and 2,3,4,6-tetra-*O*-benzyl-D-glucopyranoses (**16**). The ratio of these products in the supernatant and in the washings was similar, but changed when the treatment of the surfaces with a 1 mM solution of **1** in CH_2Cl_2 was repeated. The relative amount of lactone azines **13** increased in the supernatant and washings with repetitive exposure of the TiO_2 surfaces to **1**, while the perbenzylated trehaloses **15** and hemiacetals **16** were no longer detected in the supernatant of the second and third glucosidation. A comparison of the supernatant of the first glucosidation of a range of samples showed that the amount of **15** corresponded inversely to the amount of C detected in the XPE spectrum of the TiO_2 surfaces. The trehaloses **15** must result from the glycosidation of the hemiacetals **16** by the diazirine **1**. The hemiacetals **16**, in their turn, derive from the reaction of **1** with residual H_2O on the surface. Thus, the first treatment of the TiO_2 surface by **1** is equivalent to a drying process. The inverse correlation between the amount of trehaloses **15** in the supernatant of the first glucosidation and the C content of the resulting sample shows that physisorption of **15** competes with the interaction of the surface with **1** and the carbene derived from the diazirine, slightly impairing glucosidation.



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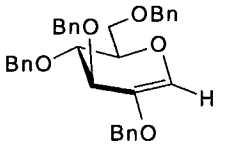

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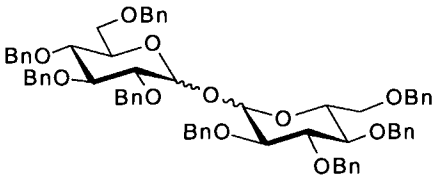

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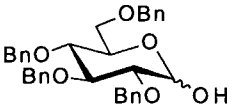

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The C amount on the TiO_2 surface treated once with a 100 mM solution of **1** in CH_2Cl_2 was 24.0 ± 0.3% and did not increase beyond 24.5%, even if the treatment with this more highly concentrated solution was repeated. Apparently, a single treatment of the samples with a 1 mM solution of **1** led to a partially glucosyl-covered surface that could be further glucosylated to reach a maximum corresponding to 24.3 ± 0.2% of C. This is obtained by a single treatment with a 100 mM solution of **1**, or by repeated treatment with a 1 mM solution.

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[5]) Column: *Spherisorb SH* 5 μm; hexane/AcOEt 3:1; flow 2.0 ml/min; UV detection at 254 nm.

[6]) Resulting from the reaction of the diazirines with the carbenes derived from them [16].

The positive ToF-SIMS of the TiO_2 surface modified with **1** showed the base peak at m/z 91 ($C_7H_7^+$), typical for benzylic ethers and evidencing the immobilized sugar molecules. The signal at m/z 181 ($C_{14}H_{13}^+$, combination of two tropylium ions, 1%) is typical for perbenzylated carbohydrates, containing at least two BnO groups adjacent to each other. Additionally, the spectrum showed signals for $C_7H_5O^+$ at m/z 105 (2%), for siloxane at m/z 147 (2%) and for phthalate at m/z 149 (0.6%). No peaks corresponding to M^+ of the carbohydrate moiety or to $(TiOC)^+$ were detected. The ToF-SIMS measurements showed also that the modified TiO_2 surface is slightly contaminated with poly(dimethylsiloxane) (PDMS, m/z 147 and 256) and phthalate (m/z 149). Measurements at different positions of the surface showed that the distribution of the glucosyl residues is homogenous on the scale of the beam diameter (50 μm).

The XPE spectra of the surface treated with **1** were compared with the spectra of reference samples. Reference samples were prepared by exposing the H_2O_2-treated, TiO_2-covered glass slides to a CH_2Cl_2 solution of the hemiacetals corresponding to the diazirines and removing the solvent *in vacuo*. In contrast to the glucosyl moieties on TiO_2 surfaces treated with **1**, those on TiO_2 surfaces that were exposed to the hemiacetals **16** were removed by rinsing with CH_2Cl_2 and/or acetone and MeOH. The line shapes of the high-resolution O 1s and C 1s spectra of the samples treated with **1** and of those treated with **16** were qualitatively similar, but the stoichiometric ratio was clearly different. For the reference samples, no signal for Ti was detected in the XPE spectra. This shows that the surface is completely covered by the – probably multilayered – hemiacetals **16**, as expected from the mode of preparation.

The contact angle for the glucosylated surface showed values in the range of 72–76°. The increase from 25–28° for the H_2O_2-treated to 72–76° for the modified surface evidences a high concentration of hydrophobic (tetrabenzyl glucosyl) groups on the surface.

Surface Modification with the Fluorobenzylated Diazirine **2**. As for the glucosidation by **1**, the TiO_2-covered slides were treated by a 100 mM solution of **2** in CH_2Cl_2. The XPE survey spectrum of the glucosylated probes indicated the presence of O, C, Ti, F, and traces of Si and N. The high-resolution C 1s and O 1s spectra showed a main peak with shoulders on the high-binding-energy side. For comparison, XPE spectra were also recorded of a reference sample covered by a thin layer of the physisorbed hemiacetals **6**. The line shapes of the high-resolution O 1s and C 1s spectra of the surfaces treated with **2**, and those treated by **6** (without rinsing) were similar. The quantitative XPES data (binding energies, peak areas, and atomic concentrations) are collected in *Tables 2* and *3* for fluorobenzylated glucosyl moieties on the TiO_2 surface.

The amount of F detected by XPES ranged between 1.7 and 1.9% for TiO_2 surfaces modified with **2**. Repetitive treatment of the TiO_2 surface by a 100 mM solution of **2** in CH_2Cl_2 did not increase the amount of F (*Fig. 2*), in keeping with the results of the glucosidation with **1**. Treatment with a 1 mM solution of **2** led to a surface F content of only 0.3–0.6%. A second glucosidation of this TiO_2 surface by a 1 mM, or by a 100 mM solution of **2** in CH_2Cl_2 increased the F amount to 0.8 and 1.4–1.6%, respectively. The control experiment, where the reference sample – TiO_2 surface covered with physisorbed **6** – was rinsed with acetone and MeOH did not yield a F peak in the XPE spectra, demonstrating that the carbohydrates detected on the surface after treatment with **2** are indeed due to immobilization and not just to physisorption.

Table 3. *Atomic Concentrations of C, O, and F Calculated from XPES Peak Areas for Physisorbed and Immobilized (4-Fluorobenzyl)-Protected Glucose, in Comparison to the Calculated Stoichiometry.* Detection angle, 90° to the surface plane.

Element	Calculated concentration [atom.-%]	Observed concentration [atom.-%]	
		physisorbed[a])	immobilized[b])
C 1s	77.3	77.3	29.8
O 1s	13.6	14.7	67.9
F 1s	9.1	8.0	2.3

[a]) No Ti 2p peak observed; the titanium surface is completely covered by multilayer-physisorbed tetra-*O*-(4-fluorobenzyl)glucose. [b]) Immobilized monolayer or fractional monolayer of tetra-*O*-(4-fluorobenzyl)glucose. O-Atom is due to both TiO_2 and glucose.

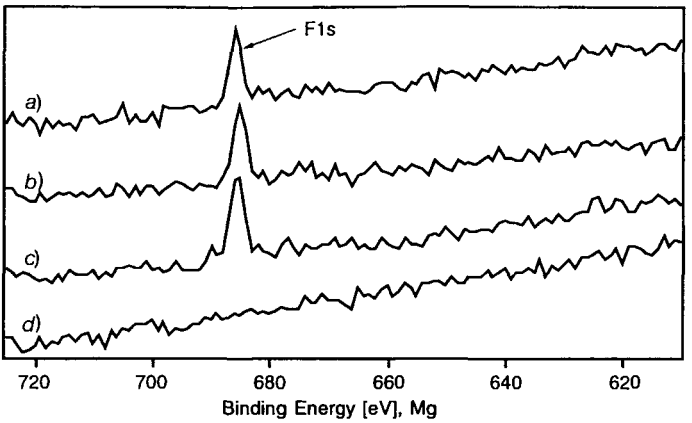

Fig. 2. *XPE Spectra in the F 1s region of TiO_2 surfaces after H_2O_2 treatment and glucosidation with 100 mM diazirine* **2** *in CH_2Cl_2* (repetitive treatment): a) *immersed once into 100 mM* **2**, b) *immersed twice*, c) *immersed three times, and* d) *blank, untreated TiO_2 surface*

A rough calculation of the F/C ratio for the immobilized surface layer, based on the XPES results in *Tables 2* and *3*, leads to a figure of 0.21 if one assumes that the initial C contaminant of the surface of H_2O_2-treated TiO_2 (14.2%) is not removed during the reaction with **2**. If it were removed, the corresponding figure would be 0.08. Since the theoretical stoichiometric F/C ratio for **6** is 4 F: 34 C (F/C 0.12), we may conclude that the hydrocarbon contaminant is partially removed during glucosidation.

The following XPES quantification model of *Madey et al.* [28] for a monolayer or a fractional monolayer (m) on a substrate (s) was used to estimate the density of carbohydrate moieties on the TiO_2 surface:

$$Y_m/Y_s = (\mu_m M_r \sigma)/(N_A \mu_s \rho \tau \cos\theta)$$

where Y is the photoelectron yield, μ_m is the mass X-ray absorption coefficient, σ is the number of atoms per cm^2, ρ is the density of TiO_2, τ is the inelastic scattering length

(mean free path), and θ is the electron take-off angle (position of the analyzer relative to the surface normal). On the basis of the XPES peaks of Ti 2p and F 1s for Y_s and Y_m, respectively, we calculated a density of 1.5 ± 0.9 glucosyl moieties per nm^2 of the modified TiO_2. This number correlates satisfactorily with the density of OH groups on the TiO_2 surface (6.1 OH per nm^2) [2][9] and the roughly calculated[7]) maximum of 1.0 ± 0.2 carbohydrate moieties per nm^2 for complete glucosidation of the TiO_2 surface.

To check if physisorbed lactone azines (main product in the supernatant and washing) impair glucosidation by a 300–600-fold excess of **2** per surface OH group (corresponding to a 1 mM solution of the diazirine), the H_2O_2-treated TiO_2 sample was exposed to a solution of lactone azines, dried, and then treated with a CH_2Cl_2 solution of **2** (100 mM). The XPE spectrum of this sample showed 1.1% of F. This is indeed less F than what was found for the sample obtained by glucosidation with a 100 mM solution of **2** (1.7–1.9%). The spectrum of the reference sample, treated with lactone azines, rinsed (MeOH and acetone), but not glucosylated with **2**, did not show any F signals. This is in keeping with the results of the repetitive treatment of the TiO_2 surfaces with a 1 mM solution of **2**, where the F amount increased from 0.3 to 0.8%, when the surfaces were treated twice without rinsing inbetween, and the results for the repetitive treatment of TiO_2 surfaces with a 1 mM solution of **1** (see above).

This shows that the physisorbed lactone azines reduce the extent of surface glucosidation, and that they are slowly desorbed by a solution of excess diazirine. Obviously, complete glucosidation of the TiO_2 surface by a 1 mM solution of **1** or **2** in one step is prevented by the by-products of the glucosidation.

The positive ToF-SIMS of the glucosylated TiO_2 surface showed the most intense mass peak at *m/z* 109 corresponding to the 4-fluorobenzyl groups of the immobilized glucosyl moieties. In addition to the main peak, the spectra showed signals at *m/z* 23 (Na^+, 15%), 39 (K^+, 4%), 48 (Ti^+, 31%), 64 (TiO^+, 14%), and 65 ($TiOH^+$, 4%). The negative SIMS showed the main signals at *m/z* 16 (O^-, 100%), 17 (HO^-, 43%), and 19 (F^-, 32%).

The contact angles measured for the TiO_2 surfaces modified by reaction with either **1** or **2** were very similar (72–76 *vs.* 65–70°).

Surface Modification with the Acetylated Diazirine **3**. Similarly as described for the glucosidation by **1** and **2**, the H_2O_2-treated, TiO_2-covered slides were also treated with a 100 mM solution of **3** in CH_2Cl_2. The duration of the contact between the solution of **3** and the TiO_2 surface (17 h), and the temperature (32°) were increased in view of the longer halflife of **3** at 25° (see above). The XPE survey spectra of the glucosylated TiO_2 surface indicated the presence of O, C, and Ti (*Table 2*). The high-resolution O 1s spectra clearly showed a second high-energy peak at 532.1 eV for the C=O group besides the major peak at 530.1 eV (O of TiO_2, *Table 2*). The C 1s spectrum exhibited a pronounced high binding energy peak at 289.1 eV, typical for C 1s of the C=O groups. A comparison of the data of the (fluorobenzyl)- and the acetylglucosylated TiO_2 surfaces (*Table 2*) showed mainly an increased intensity of the C 1s peak at 289.1 eV and of the O 1s peak

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[7]) For the calculation, we assumed a β-glucosidic linkage where the C(1)–O bond is perpendicular to the average plane of the TiO_2 surface, and a packing where there is neither free rotation around the C(1)–O bond nor interdigitation of the BnO groups. The volume of the 2,3,4,6-tetra-*O*-benzylated glucosyl residues was derived from pertinent X-ray crystal structures [29].

at 532.1 eV, and a reduced total C content for the tetraacetylglucosylated surface, as expected.

There is a good correspondence of the high-resolution O 1s and C 1s spectra of the TiO_2 surface treated with **3** and the reference surface, covered with physisorbed tetraacetyl glucose (*Table 2*). The high-resolution XPE spectra are also in good agreement with the spectra for gold substrates with a self-assembled monolayer of carbohydrates [30].

The contact angle of the acetylglucosylated surfaces showed values in the range of 56–69°. This contact angle is smaller than the one observed for the benzyl- or (fluorobenzyl)glucosylated surfaces, as expected for the less hydrophobic character of the Ac groups.

The acetylglucosylated TiO_2 surface was deprotected by treating the sample with a 0.7–1.1% solution of NaOMe in MeOH, followed by extensive washing. The XPE survey spectra of the glucosylated TiO_2 surface indicated that O, C, and Ti were present in a stoichiometric ratio of 60:16:24. The positions of the *Gaussian* model peaks and line shape of the high-resolution O 1s spectra are similar to the high-resolution spectra of the surface with the Ac-protected glucosyl moieties. The high-resolution C 1s spectra are clearly different from those reported above, reflecting the change of the surface upon deacetylation: a decrease of the hydrocarbon C 1s signal at 284.8 eV (loss of Ac groups), a dominant C 1s contribution from the singly bonded *C*–O functions (286.5 eV) and a reduction of O 1s intensity at the C=*O* position (loss of Ac groups; *Fig. 3*, *Table 2*).

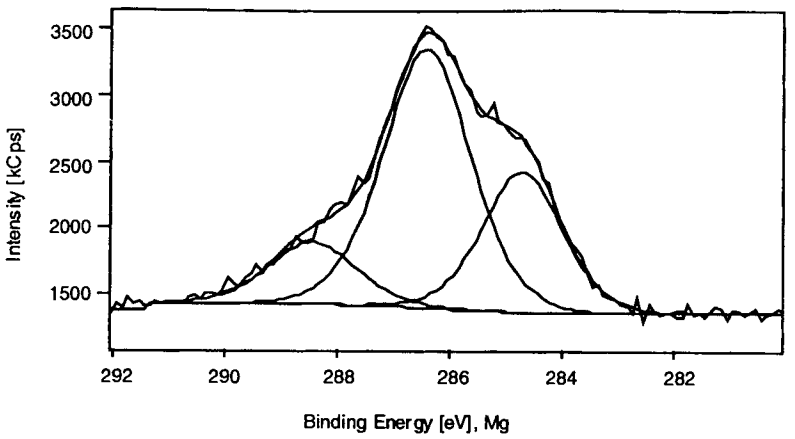

Fig. 3. *XPE C 1s High-resolution spectrum of the TiO_2 surface glucosylated with the diazirine* **3** *in CH_2Cl_2 and deacetylated with 0.7–1.1% NaOMe solution in MeOH, fitted with three subpeaks at 284.8, 286.5, and 288.5 eV*

The contact angle for the glucosylated TiO_2 surface is in the range of 27–37°. As expected for a hydrophilic layer of carbohydrates on the TiO_2 surface, the wetting behaviour of the glucosylated TiO_2 surface is similar to that of the H_2O_2-treated surface.

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Experimental Part

1. *General.* TLC: *Merck* silica gel *60 F_{254}* plates with the solvent systems indicated; detection by treating with a 5% $(NH_4)_6Mo_7O_{24} \cdot 4\,H_2O$ and 0.1% $Ce(SO_4)_2 \cdot 4\,H_2O$ soln. in 10% H_2SO_4. Flash chromatography (FC): silica gel (*Fluka* or *Merck 60*; 0.040–0.063 mm). UV Spectra (determination of the kinetic parameters): MeOH soln. in nm; ε in parenthesis. NMR Spectra: chemical shifts δ in ppm and coupling constants J in Hz. Contact angle: measurements with ultrapure H_2O (1 drop (6 µl) on surface) at 25° and ambient humidity using a *Ramé-Hart* goniometer; under these conditions, the contact angles were stable for several min. X-Ray Photoelectron Spectroscopy (XPES): MgK_α radiation at 300 W under ultrahigh vacuum ($\leq 10^{-8}$ mbar) in a *Specs-SAGE-100* spectrometer; for survey spectra, data collection over a binding-energy range of 0–1150 eV with a constant detector pass energy range of 50 eV, at a take-off angle of 90° with respect to the sample surface and *ca.* 1 cm^2 X-ray spot size; for high-resolution C 1s, N 1s, O 1s, F 1s, Si 2p, and Ti 2p spectra (pass energy 14 eV), data collection normally over 20–30 eV range; peak-area data by numerical integration after background subtraction according to [31]; the atomic concentrations of molecular species were obtained by deconvoluting and fitting the data with *Gaussian* model peaks, calculating the peak area ratios (*SpecsLab*® software), and applying sensitivity factors according to [32]; electron-binding energies were referenced by setting the titanium oxide Ti $2p_{3/2}$ peak to 458.6 eV; angle-dependent XPES were recorded with MgK_α (300 W) radiation in a *ESCA-5600* spectrometer (*Physical Electronics*, Eden Prairie, MN) at take-off angles of 20, 45, and 90°, in order to vary the depth of information. Time-of-flight secondary-ion mass spectrometry (ToF-SIMS): *Perkin-Elmer-PHI-7000* instrument using a pulsed caesium primary-ion source (8 keV); positive SIMS by keeping the ion dose below the threshold of the static regime (10^{12} ions/cm^2); a pulsed low-energy electron beam was used to neutralize the surface charges; detection of the positive secondary ions over a mass range of 1–1000 amu; mass resolution $M/\Delta M$ *ca.* 5000, using a 50-µm diameter ion beam; mass calibration by means of hydrocarbon peaks (CH_3^+, $C_2H_3^+$, $C_3H_5^+$).

2. *1-Aziglucose* **2**. *Fluorobenzylation of Methyl* α-D-*Glucopyranoside*. A soln. of methyl α-D-glucopyranoside (3.7 g, 19 mmol) in dry DMF (10 ml) was added to a mixture of NaH (2.3 g, 95 mmol) and 4-fluorobenzyl bromide (10 ml, 84 mmol) in dry DMF (25 ml) under Ar between 0–10°. After 45 min at 25°, MeOH (3 ml) and H_2O (20 ml) were added at 0°. The mixture was extracted with Et_2O and the org. layer dried ($MgSO_4$) and evaporated. FC (hexane/acetone 3:2) gave **4** (6.3 g, 53%) and **5** (4.2 g, 36%).

Methyl 2,3,4,6-Tetrakis-O-*(4-fluorobenzyl)*-α-D-*glucopyranoside* (**4**): R_f (hexane/acetone 3:2) 0.37. IR ($CHCl_3$): 3007*w*, 2955*w*, 1889*w*, 1606*m*, 1513*s*, 1464*w*, 1380*m*, 1362*m*, 1157*m*, 1044*m*, 966*w*, 827*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.36–7.21 (*m*), 7.11–6.91 (*m*, 16 arom. H); 4.90 (*d*, J = 11.2), 4.73 (*d*, J = 10.4), 4.71 (*d*, J = 12.0, 3 ArC*H*); 4.67–4.59 (*m*, H–C(1), 2 ArC*H*); 4.58 (*d*, J = 12.0), 4.43 (*d*, J = 12.8), 4.42 (*d*, J = 10.4, 3 ArC*H*); 3.94 (*t*, $J \approx 9.3$, H–C(4)); 3.76–3.59 (*m*, 3 H); 3.59 (*t*, $J \approx 9.3$, H–C(3)); 3.53 (*dd*, J = 3.3, 9.5, H–C(2)); 3.39 (*s*, MeO). ^{13}C-NMR (75 MHz, $CDCl_3$): 162.63 (br. *d*, ^1J(C,F) ≈ 246.5, 4 C); 134.77, 134.23, 133.92 (3*s*, 4 C); 130.11–129.48 (several *t*, ^3J(C,F) ≈ 8.5, 8 C); 115.71–115.30 (several *t*, ^2J(C,F) ≈ 20.7, 8 C); 98.20 (*d*, C(1)); 82.04 (*d*, C(3)); 80.08 (*d*, C(2)); 77.76 (*d*, C(4)); 75.02, 74.29, 72.92, 72.64 (4 *t*, 4 ArCH_2); 70.17 (*d*, C(5)); 68.57 (*t*, C(6)); 55.31 (*q*, MeO). ^{19}F-NMR (282 MHz, $CDCl_3$): −114.02 (*tt*, $J \approx 4.3$, 8.5, F); −114.24 to −114.39 (*m*, 2 F); −114.52 (*tt*, $J \approx 4.3$, 8.5, F). FAB-MS: 626 (20), 625 (51), 517 (14), 485 (19), 469 (6), 289 (11), 136 (10), 109 (20), 108 (100).

Methyl 2,4,6-Tris-O-*(4-fluorobenzyl)*-α-D-*glucopyranoside* (**5**): R_f (hexane/acetone 3:2) 0.31. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.38–6.93 (*m*, 12 arom. H); 4.82 (*d*, J = 11.2, ArC*H*); 4.67 (*d*, J = 3.7, H–C(1)); 4.65 (br. *s*, ArCH_2); 4.59 (*d*, J = 12.0), 4.48 (*d*, J = 11.2), 4.45 (*d*, J = 12.0, 3 ArC*H*); 4.05 (*dt*, $J \approx 2.5$, 9.1, H–C(3)); 3.77–3.60 (*m*, H–C(5), 2 H–C(6)); 3.53 (*t*, $J \approx 9.1$, H–C(4)); 3.39 (*dd*, J = 3.3, 9.5, H–C(2)); 3.35 (*s*, MeO); 2.47 (br. *s*, HO–C(3)). ^{19}F-NMR (282 MHz, $CDCl_3$): −113.79 (*tt*, $J \approx 4.3$, 8.5, F); −114.31 to −114.46 (*m*, 2 F).

2,3,4,6-Tetrakis-O-*(4-fluorobenzyl)*-D-*glucopyranose* (**6**). A soln. of **4** (6.3 g, 10 mmol) in AcOH (8.5 ml) was added to a mixture of AcOH (50 ml) and 1M H_2SO_4 (13 ml) under reflux. After 2 h, the soln. was cooled to 25°, treated with ice and sat. $NaHCO_3$ soln., and extracted with $CHCl_3$. The org. layer was filtered through a cotton plug and evaporated. Crystallization from AcOH gave **6** (3.2 g, 52%). M.p. 150–152°. R_f (hexane/acetone 3:2) 0.47. IR ($CHCl_3$): 3596*w*, 3007*w*, 2922*w*, 2870*w*, 1887*w*, 1604*m*, 1511*s*, 1464*w*, 1361*w*, 1295*w*, 1156*m*, 1074*s*, 1016*w*, 854*w*, 834*m*. ^{1}H-NMR (200 MHz, $CDCl_3$; α-D/β-D 64:36): 7.31–7.10, 7.09–6.93 (*m*, 16 arom. H); 5.23 (*d*, J = 3.7, 0.64 H–C(1)); 4.91 (*d*, J = 11.2, 0.36 H), 4.86 (*d*, J = 11.2, 0.36 H, ArC*H*); 4.83 (*d*, J = 10.9, 0.64 ArC*H*); 4.77–4.41 (*m*, 0.36 H–C(1), 6.64 ArC*H*); 4.04–3.99 (*m*, 0.64 H–C(5)); 3.92 (*t*, $J \approx 9.3$, 0.64 H–C(3)); 3.68–3.47 (*m*, 4.36 H); 3.38 (br. *s*, exchange with D_2O, 0.36 HO–C(1)); 3.35 (*dd*, J = 8.1, 8.7, 0.36 H–C(2)); 3.06 (br. *s*, exchange with D_2O, 0.64 HO–C(1)). ^{13}C-NMR (75 MHz, $CDCl_3$; α-D/β-D 65:35): α-D-anomer: 162.52 (br. *d*, ^1J(C,F) ≈ 240.5, 4 C); 134.48, 133.99, 133.62 (3*s*, 4 C); 129.89–129.37 (*m*, 8 C); 115.63–115.16 (several *t*, ^2J(C,F) ≈ 22.0, 8 C); 91.19 (*d*, C(1)); 81.50 (*d*, C(3)); 80.01 (*d*, C(2)); 77.63 (*d*, C(4)); 74.83,

74.12, 72.76, 72.41 (4 *t*, 4 ArCH$_2$); 70.24 (*d*, C(5)); 68.49 (*t*, C(6)); β-D-anomer: 97.56 (*d*, C(1)); 84.33 (*d*, C(3)); 82.95 (*d*, C(2)); 74.67, 73.88 (2 *t*, 2 ArCH$_2$); 68.77 (*t*, C(6)). ^{19}F-NMR (282 MHz, $CDCl_3$; α-D/β-D 67:33): −113.82 (*tt*, $J \approx 4.3$, 8.5, 0.67 F); −114.02 (*tt*, $J \approx 4.3$, 8.5, 0.33 F); −114.19 to −114.36 (*m*, 2.33 F); −114.38 to −115.50 (*m*, 0.67 F). FAB-MS: 612 (22, M^+), 611 (56), 485 (44), 377 (22), 307 (38), 290 (25), 289 (100), 260 (29), 246 (25), 217 (40), 109 (100, $C_7H_6F^+$).

*(E/Z)-2,3,4,6-Tetrakis-*O*-(4-fluorobenzyl)-*D*-glucose Oximes* ((*E*/*Z*)-**7**). A soln. of **6** (3.2 g, 5.2 mmol) in MeOH (20 ml) was treated with a mixture of $NH_2OH \cdot HCl$ (1.8 g, 26 mmol) and NaOMe (1.4 g, 26 mmol) in MeOH (10 ml). After stirring at 60° for 7 h, MeOH was removed and the residue dissolved in $CHCl_3$ and washed with H_2O. The org. layer was filtered through a cotton plug. Evaporation gave crude (*E*/*Z*)-**7** (3.2 g, 97%). R_f (hexane/acetone 3:2) 0.45. IR ($CHCl_3$): 3582*w*, 3345*w*, 2918*w*, 2872*w*, 1888*w*, 1669*w*, 1604*m*, 1511*s*, 1466*w*, 1418*w*, 1361*w*, 1294*w*, 1156*m*, 1078*m*, 1016*m*, 933*w*, 854*m*, 826*m*. ^{1}H-NMR (200 MHz, $CDCl_3$; (*E*)/(*Z*) 58:42): 7.74 (*s*, 0.42 H, exchange with D_2O, NOH); 7.44 (*d*, $J = 7.8$, 0.58 H−C(1)); 7.36–6.93 (*m*, 16 arom. H, 0.58 NOH, 0.42 H−C(1)); 4.75–4.28 (*m*, 8 ArC*H*); 3.96–3.51 (*m*, 6 H); 2.76 (*d*, $J = 5.6$, exchange with D_2O, 0.58 HO−C(5)). ^{19}F-NMR (282 MHz, $CDCl_3$; (*E*)/(*Z*) 58:42): −113.59 to −113.72 (*m*, 0.84 F); −113.90 (*tt*, $J \approx 4.3$, 8.5, 0.58 F); −113.98 to −114.11 (*m*, 1.16 F); −114.20 to −114.42 (*m*, 1 F); −114.69 (*tt*, $J \approx 4.3$, 8.5, 0.42 F).

*(Z)-2,3,4,6-Tetrakis-*O*-(4-fluorobenzyl)-*D*-gluconohydroximo-1,5-lactone* (**8**). A soln. of crude (*E*/*Z*)-**7** (3.2 g, 5.1 mmol) in MeOH/acetone/Et_2O 20:4:5 (20 ml) was treated with MnO_2 (2.5 g, 28.7 mmol) and stirred at 25° for 4 d. Filtration through *Celite*, evaporation, and FC (hexane/acetone 1.5:1) gave **8** (1.94 g, 60%). R_f (hexane/acetone 3:2) 0.39. IR ($CHCl_3$): 3585*m*, 3346*w*, 3006*w*, 2916*w*, 2873*w*, 1889*w*, 1669*w*, 1605*m*, 1511*s*, 1460*w*, 1362*w*, 1242*w*, 1156*w*, 1080*m*, 1015*w*, 934*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.33–6.93 (*m*, 16 arom. H); 6.81 (*s*, NOH); 4.66 (*d*, $J = 11.8$), 4.60 (*d*, $J = 12.1$, 2 ArC*H*); 4.55-4.47 (*m*, H−C(5), 3 ArC*H*); 4.44 (*d*, $J = 11.8$), 4.42 (*d*, $J = 11.5$), 4.33 (*d*, $J = 11.5$, 3 ArC*H*); 4.03 (*d*, $J = 2.0$, irrad. at 3.84 → *s*, H−C(2)); 3.84 (*dd*, $J = 2.2$, 4.6, irrad. at 4.03 → *d*, $J = 4.7$, H−C(3)); 3.83–3.38 (*m*, 3 H). ^{13}C-NMR (75 MHz, $CDCl_3$): 162.58 (br. *d*, ^1J(C,F) ≈ 246.6, 4 C); 151.16 (*s*, C(1)); 133.69, 133.38, 132.95, 132.78 (4*s*); 130.16–129.60 (several *t*, ^3J(C,F) ≈ 8.5, 8 C); 115.59–115.16 (several *t*, ^2J(C,F) ≈ 21.9, 8 C); 81.55 (*d*, C(3)); 77.29 (*d*, C(2)); 75.98 (*d*, C(4)); 73.08 (*d*, C(5)); 72.76, 72.26, 70.90, 69.75 (4*t*, 4 ArCH$_2$); 67.88 (*t*, C(6)). ^{19}F-NMR (282 MHz, $CDCl_3$): −113.62 to −113.75 (*m*, 2 F); −113.92 (*tt*, $J \approx 4.3$, 8.6, F); −114.40 (*tt*, $J \approx 4.3$, 8.6, F). FAB-MS: 1252 (4, $[2M + 1]^+$), 735 (7), 626 (95, $[M + 1]^+$), 500 (5), 154 (10), 109 (100, $C_7H_6F^+$).

*2,3,4,6-Tetrakis-*O*-(4-fluorobenzyl)-*N*-[(methylsulfonyl)oxy]-*D*-gluconimido-1,5-lactone* (**9**). A soln. of **8** (970 mg, 1.55 mmol) in CH_2Cl_2 (10 ml) was treated with Et_3N (0.52 ml, 3.72 mmol) and MsCl (0.16 ml, 2.0 mmol) under Ar at 0°. After 15 min, the mixture was treated with sat. $NaHCO_3$ soln. and extracted with CH_2Cl_2. The org. layer was filtered through a cotton plug and evaporated. FC (hexane/acetone 3:2) and crystallization (Et_2O/hexane) gave **9** (975 mg, 89%). M.p. 91°. R_f (hexane/acetone 3:2) 0.52. IR ($CHCl_3$): 2916*w*, 2872*w*, 1888*w*, 1653*m*, 1604*m*, 1511*s*, 1458*w*, 1371*s*, 1326*w*, 1295*w*, 1178*m*, 1157*m*, 1076*m*, 1016*w*, 969*m*, 834*s*. ^{1}H-NMR (200 MHz, $CDCl_3$): 7.36–6.88 (*m*, 16 arom. H); 4.70 (*d*, $J = 12.0$, ArC*H*); 4.65–4.44 (*m*, H−C(5), 6 ArC*H*); 4.33 (*d*, $J = 11.6$, ArC*H*); 4.10 (br. *s*, H−C(2)); 3.90–3.64 (*m*, 4 H); 3.14 (*s*, MsO). ^{13}C-NMR (50 MHz, $CDCl_3$): 162.71 (br. *d*, ^1J(C,F) ≈ 249.0, 4 C); 157.41 (*s*, C(1)); 133.73, 133.35, 132.78, 132.24 (4*s*); 130.62–129.67 (several *t*, ^3J(C,F) ≈ 8.8, 8 C); 115.98–115.38 (several *t*, ^2J(C,F) ≈ 20.7, 8 C); 80.91 (*d*, C(3)); 77.95 (*d*, C(4)); 77.57 (*d*, C(2)); 72.87, 72.59 (2*t*, 2 ArCH$_2$); 72.59 (*d*, C(5)); 71.25, 70.59 (2*t*, 2 ArCH$_2$); 67.32 (*t*, C(6)); 36.33 (*q*, MsO). ^{19}F-NMR (282 MHz, $CDCl_3$): −113.07 to −113.09 (*m*, F); −113.30 to −113.35 (*m*, F); −113.64 to −113.69 (*m*, F); −114.35 to −114.42 (*m*, F). FAB-MS: 1407 (3, $[2M + 1]^+$), 704 (100, $[M + 1]^+$), 109 (66, $C_7H_6F^+$).

*1,5-Anhydro-2,3,4,6-tetrakis-*O*-(4-fluorobenzyl)-1-hydrazi-*D*-glucitol* (**10**). A soln. of **9** (929 mg, 1.3 mmol) in CH_2Cl_2 (4 ml) was treated with a sat. NH_3 soln. in MeOH (20 ml) and stirred for 15 h at 25° in a closed flask. Evaporation and crystallization of the residue from Et_2O/hexane gave **10** (573 mg, 69%). FC (hexane/AcOEt 1:1) of the mother liquor gave a further crop of **10** (108 mg, 13%). M.p. 85–87°. R_f (hexane/AcOEt 1:1) 0.42. IR ($CHCl_3$): 3272*w*, 3007*m*, 2872*m*, 1887*w*, 1771*w*, 1605*s*, 1511*s*, 1464*w*, 1360*m*, 1271*m*, 1125*s*, 1082*s*, 1039*s*, 1016*m*, 854*s*, 825*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.31–6.93 (*m*, 16 arom. H); 4.81 (*d*, $J = 11.2$), 4.80 (*d*, $J = 10.6$), 4.74 (*d*, $J = 10.6$), 4.70 (*d*, $J = 10.9$), 4.59 (*d*, $J = 10.6$), 4.58 (*d*, $J = 12.1$), 4.48 (*d*, $J = 10.9$), 4.42 (*d*, $J = 12.1$, 8 ArC*H*); 4.04 (*d*, $J = 9.3$, H−C(2)); 3.87–3.58 (*m*, 5 H); 2.61 (*d*, $J = 9.3$, 0.96 NH); 2.35 (*d*, $J = 9.3$, 0.96 NH′); 2.31 (*d*, $J = 9.0$, 0.04 NH); 1.97 (*d*, $J = 9.0$, 0.04 NH′). ^{13}C-NMR (75 MHz, $CDCl_3$): 162.58 (br. *d*, ^1J(C,F) ≈ 246.6, 4 C); 134.19, 133.83, 133.44 (3*s*, 4 C); 130.39–129.34 (several *t*, ^3J(C,F) ≈ 8.0, 8 C); 115.44 (br. *t*, ^2J(C,F) ≈ 23.9, 8 C); 84.05 (*d*, C(3)); 82.94 (*s*, C(1)); 77.29 (*d*, C(4)); 76.84 (*d*, C(5)); 74.87 (*d*, C(2)); 74.87, 74.71, 74.24, 72.81 (4*t*, 4 ArCH$_2$); 67.70 (*t*, C(6)). ^{19}F-NMR (282 MHz, $CDCl_3$): −113.85 (*tt*, $J \approx 4.3$, 8.5, F); −114.05 to −114.19 (*m*, 2 F); −114.27 (*tt*, $J \approx 4.3$, 8.5, F). FAB-MS: 1874 (8, $[3M + 1]^+$), 1842 (7), 1249 (41, $[2M + 1]^+$), 1217 (33), 625 (35, $[M + 1]^+$), 109 (100, $C_7H_6F^+$).

1,5-Anhydro-1-azi-2,3,4,6-tetrakis-O-(4-fluorobenzyl)-D-glucitol (**2**). A soln. of **10** (573 mg, 0.9 mmol) in CH_2Cl_2 (10 ml) and Me_3N (2 ml) was treated dropwise with a soln. of I_2 (255 mg, 1.0 mmol) in CH_2Cl_2 (5 ml) under Ar at −45°. The resulting mixture was filtered through SiO_2 (CH_2Cl_2), evaporated at 0°, and dried at −45°: **2** (445 mg, 78%). R_f (CH_2Cl_2) 0.58. UV: 347 (58). IR ($CHCl_3$): 2923*w*, 1604*m*, 1561*w*, 1511*s*, 1360*w*, 1261*m*, 1156*m*, 1082*m*, 1016*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.27–6.93 (*m*, 16 arom. H); 4.80 (*d*, *J* = 11.2), 4.77 (*d*, *J* = 10.6), 4.72 (*d*, *J* = 11.29), 4.50 (br. *d*, *J* = 12.1), 4.38 (*d*, *J* = 11.8, 6 ArC*H*); 4.12–4.10 (*m*, 2 ArC*H*); 4.06 (*d*, *J* = 8.7, H–C(2)); 3.92 (*t*, *J* ≈ 8.7, H–C(3)); 3.82 (*t*, *J* ≈ 9.6, H–C(4)); 3.73–3.68 (*m*, H–C(5)); 3.64 (*dd*, *J* = 3.4, 10.9, H–C(6)); 3.50 (*dd*, *J* = 1.9, 11.4, H′–C(6)). ^{19}F-NMR (282 MHz, $CDCl_3$): −113.64 (*tt*, *J* ≈ 4.3, 8.6, F); −113.99 (*tt*, *J* ≈ 4.3, 8.6, F); −114.14 to −114.45 (*m*, 2 F).

3. *1-Aziglucose* **3**. *2,3,4,6-Tetra-O-acetyl-1,5-anhydro-1-hydrazi-D-glucitol* (**12**). A sat. NH_3 soln. in MeOH (5 ml) was added to a soln. of **11** [25] (810 mg, 1.64 mmol) in dry CH_2Cl_2 (20 ml) under Ar at −20°. The mixture was stirred at −25° for 40 min and kept in a closed flask at −25° for 12 h. Evaporation below 0°, FC (hexane/AcOEt 2:3), and crystallization (Et_2O/pentane) gave **12** (570 mg, 71%). M.p. 43°. R_f (hexane/acetone 1.8:1) 0.13. $[\alpha]_D^{25}$ = +19.0. IR ($CHCl_3$): 3277*w*, 2961*w*, 1756*s*, 1429*w*, 1368*m*, 1325*w*, 1123*m*, 1076*m*, 1038*s*, 976*w*, 901*w*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.68–5.63 (virtual couplings, H–C(2)); 5.31–5.26 (*AB*, H–C(3), H–C(4)); 4.28 (*dd*, *J* = 4.2, 12.7, H–C(6)); 4.11 (*dd*, *J* = 2.2, 13.0, H′–C(6)); 4.06 (*ddd*, *J* = 2.1, 4.0, 10.3, H–C(5)); 2.47 (*d*, *J* = 9.4, NH); 2.40 (*d*, *J* = 9.4, NH); 2.08, 2.04 (2*s*, 2 AcO); 2.03 (*s*, 2 AcO). ^{13}C-NMR (75 MHz, $CDCl_3$): 170.65, 170.25, 169.46, 168.92 (4*s*); 81.58 (*s*, C(1)); 74.15 (*d*, C(3)); 72.37 (*d*, C(4)); 67.80 (*d*, C(5)); 65.86 (*d*, C(2)); 61.13 (*t*, C(6)); 20.50, 20.28 (2*q*, 4 Me). FAB-MS: 721 (19, $[2M + 1]^+$), 361 (100, $[M + 1]^+$), 333 (20), 289 (11).

2,3,4,6-Tetra-O-acetyl-1,5-anhydro-1-azi-D-glucitol (**3**). A soln. of I_2 (48 mg, 190 µmol) in dry CH_2Cl_2 (3.0 ml) was added dropwise to a soln. of **12** (50 mg, 140 µmol) in Et_3N (220 µl) in dry CH_2Cl_2 (4.0 ml) under Ar at 0°. The soln. was stirred for 30 min at 0°, and then washed with a cold aq. 5% $Na_2S_2O_3$ soln. and cold H_2O. The org. layer was filtered through a cotton plug and evaporated. FC (hexane/acetone 1.8:1) at 0° gave **3** (49 mg, 98%). R_f (hexane/acetone 1.8:1) 0.32. UV: 237 (367), 340 (44). IR ($CHCl_3$): 3038*m*, 2956*w*, 1756*s*, 1569*m*, 1430*m*, 1369*s*, 1071*s*, 1041*s*, 972*m*, 906*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.57–5.48 (*m*, H–C(2), H–C(3)); 5.28 (*dd*, *J* = 7.4, 9.6, H–C(4)); 4.20 (*dd*, *J* = 5.2, 13.2, H–C(6)); 4.04–3.95 (*m*, H–C(5), H′–C(6)); 2.05 (*s*, 2 AcO); 2.01, 1.86 (2*s*, 2 AcO). ^{13}C-NMR (50 MHz, $CDCl_3$): 170.73, 170.16, 169.53, 168.74 (4*s*); 73.67 (*d*, C(3)); 72.15 (*d*, C(4)); 67.35 (*d*, C(5)); 64.88 (*d*, C(2)); 60.59 (*t*, C(6)); 55.83 (*s*, C(1)); 20.63 (*q*, Me); 20.57 (*q*, 2 Me); 20.12 (*q*, Me).

4. *Determination of the Activation Energy of the Diazirines* **2** *and* **3**. A soln. of **2** (12 mg, 0.019 mmol) or **3** (16 mg, 0.044 mmol) in dry MeOH (3.0 ml and 5.0 ml, resp.) was placed in a *Pyrex* immersion cell. As soon as the indicated temp. were constant, 10 readings of absorption at λ 290–400 nm were taken. k_1 was calculated using a least-square-fit linear regression.

2: *T*(1) 291.2 K, $k_1(1) = 1.020 \cdot 10^{-4}$; *T*(2) 298.2 K, $k_1(2) = 2.684 \cdot 10^{-4}$; *T*(3) 301.6 K, $k_1(3) = 4.190 \cdot 10^{-4}$. E_A = 99.3 kJ/mol, log*A* = 13.8, τ(298) 43 min; $\Delta S^{\neq}$ = 11.4 J/mol · K; $\Delta H^{\neq}$ = 96.8 kJ/mol.

3: *T*(1) 290.2 K, $k_1(1) = 2.302 \cdot 10^{-5}$; *T*(2) 298.2 K, $k_1(2) = 6.850 \cdot 10^{-5}$; *T*(3) 306.2 K, $k_1(3) = 1.559 \cdot 10^{-4}$. E_A = 90.2 kJ/mol, log*A* = 11.6, τ(298) 181 min; $\Delta S^{\neq}$ = −31.3 J/mol · K; $\Delta H^{\neq}$ = 87.7 kJ/mol.

5. *Sample Preparation and Glucosidation.* The TiO_2-covered slides were prepared by magnetron sputter coating float glass (12 × 240 mm^2) with 20 nm (± 10%) of titanium using a *Z-600-Leybold* coater, operating at a pressure of $5 \cdot 10^{-5}$ mbar of O_2 during evaporation. The TiO_2 surfaces were treated with 1.5M H_2O_2 (*Merck*, 30% *pro analysi*) for 5 min, extensively rinsed with deionized H_2O, and dried in a stream of N_2. The TiO_2-covered glass slides were then dipped into a soln. of the diazirine in dry CH_2Cl_2 (3.0 ml; distilled from CaH_2) under Ar in a closed flask for 3–4 h at 25° (**1** or **2**; 1–100 mM), and for 17 h at 32° for **3** (100 mM). The slides were removed from the soln., extensively rinsed with acetone and MeOH, and dried in a stream of N_2. Until characterization, the slides were wrapped in aluminium foil and stored in a desiccator under N_2.

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