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Fluorinated saccharides on the Si(0 0 1) surface

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ABSTRACT

The attachment of saccharide molecules directly to silicon surface has been for the first time. Oxygen free silicon surface was functionalized with monosacharides thanks to UV irradiation in acetonitryl solution (254 nm). Selected derivatives of pentofuranose were protected at the C-1 and C-2 position. The remaining hydroxyl group at C-3 or C-5 was suitable for direct attachment to H-terminated Si(0 0 1) surface via Si—O—C bonds. The binding energy of the saccharide to the Si surface was investigated by quantum mechanical calculations method. The Parametric Method 5 (PM5) calculations confirmed that the formation of Si—O—C bonds was chemically possible. Synthesis of new fluorinated carbohydrates has been described. The resulting monolayers were characterized by Atomic Force Microscopy (AFM), X-ray photoelectron spectroscopy (XPS) and Attenuated Total Reflection (ATR) infrared spectroscopy. The effect of incorporating fluorine atom or CF_3 group into self-assembled monosaccharide monolayers was studied using a water contact angle measurements. The resulting surface wettability of different fluorinated components on one kind of planar substrate enables an answer which of derivative is required for the preparation of the hydrophobic monolayer.

1. Introduction

Carbohydrates play an important role in living organisms and are significant group in organic chemistry [1]. Materials modified with carbohydrates have recently attracted great attention. Sugars were immobilized on iron oxide [2], alumina, titania [3], silica uncoated [4,5] or coated with silver [6], diamond [7], gold [8], glass [8,9], polymers [10]. Additional study was performed using silica surface – mesoporous and silica nanoparticles [11,12], nickel nanowires [4] and even macromolecules of bacterium *Pseudomonas putida* [13]. The bulk of a biomaterial presents physical and chemical properties of the sugar layer. That is why, some carbohydrates attached to surface frequently have been used as microarray chips to determinate and to detect sugars. Thanks to the specific protein–carbohydrate interactions and because of their minimal and non-specific adsorption of proteins, the carbohydrates have been used for membrane protein extraction as well [14]. Moreover these compounds tend to form diverse supramolecular structures. The structures like these are used to mimic functional biosurfaces – as it was shown for D-α-mannose and D-β-galactose analogues [15] or ion channel with surfactants having one, two or three glucose moieties [16]. The assembly of organic layers onto surfaces depends on the material surface properties such as wettability, polar or ionic interactions, chemical structures and topography of the surface. From the beginning, a specific interest has been focused on development of the immobilizations methods. A few methods of noncovalent immobilization of sugar derivatives on different surfaces have been reported. For the Si(1 0 0) surface the noncovalent attached cellulose film has been studied[17]. The standard methods for the attachment of precursor monolayers via covalent bonds to the surface, which is subsequently transformed into a bioactive monolayer involved photo- [18] or thermal reactions [19,20]. Previously, Linford et al. have reported an immobilization method of the organic compounds on Si surface [17,19–24]. In 2003 de Smet et al. announced the first functionalization of hydrogen (Si—H) terminated Si(1 0 0) surfaces with saccharides (a protected β-glucose-functionalized alkene and its sialic acid modification) by a thermal method [18]. Also Shirahata et al. have announced covalently attachment to silicon surface allyl derivatives of R-D-galactopyranoside (Allyl-Gal) [25]. Other methods have involved the 1,3-dipolar cycloaddition reactions (alkene/thiol, or alkyne/azide- [23–25], or nucleophilic substitution as used for amine and carboxylic acid derivative [26,27]. These procedures for the functionalization of well-defined hydrogen-terminated silicon surfaces allowed obtaining a monolayer via Si—C linkage [7,27].

In this paper we reported the synthesis of five monosaccharides with one unprotected OH-group (at C-3 or C-5 position) (Fig. 1). Additionally, the synthesis and properties of fluorinated

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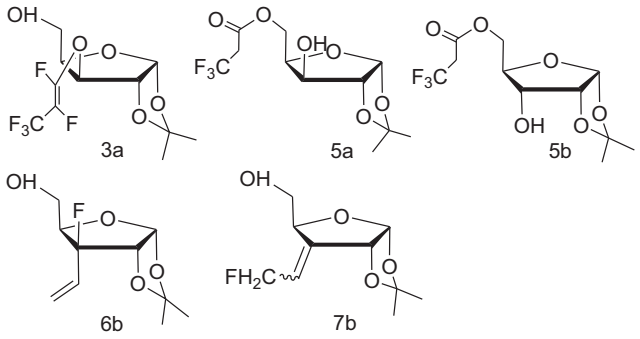

Fig. 1. Structural formula of the investigated derivatives of fluorinated pentofuranose (**3a**, **5a**, **5b**, **6b**, and **7b**).

ester and ether derivatives of sugar were studied [28]. The results of the attachment of these sugar derivatives to the hydrogen-terminated surface are discussed. The monosaccharides we have selected were used to produce the well-defined monolayers via Si—O—C bonds. The photochemical method was used to attain this aim and a one structure property was required i.e. only one free hydroxyl group at C3 or C5 position, which can be reacted with hydrogen-terminated surface. The protection of hydroxyl groups has prevented the other reaction between these groups and the silicon surface. Another relevant difference between literature reports and procedure presented in this note is the absence of the long-chain alkyl as a linker between monosaccharide ring and surface. Thanks to the free hydroxyl group (at C3 or C5 position) the saccharide rings were attached to crystalline Si surface without a linker. The fluorinated saccharides were chosen since the fluoroorganic molecules have attracted particular attention in biomaterial science because of a number of unusual properties [29–33]. The incorporation of one, two, three or several fluorine atoms into an organic compound modifies the geometry of the molecule, bonds polarity and others physical properties (e.g. surface energies, dielectric constants and refracting indexes) changing also their chemical and biological properties [33,34]. Fluorinated vinyl ether is mainly associated with monomers for homo- or copolymerization [35,36], a replacement of one or two hydrogen or oxygen by fluorine atom(s) in sugar or its derivatives has found a lot of application in medicinal chemistry (e.g. [^{18}F]-2-fluoro-2-deoxy-D-glucose–FDG [37] and 2′,2′-difluoro-2′-deoxycytidine-gemcitabine inhibitors of RNR [38–40]. The presented fluorinated monolayers of sugar could be used as substrates for glycosylation, to give a surface that could play important roles in biological system. Surface glycosylation in biological systems is essential, in artificial arrangements have been used in cell recognition [41–46], blood coagulation [47] or as carriers for drug delivery [41,48].

2. Experimental

2.1. Materials and measurements

The ^{1}H (Me_4Si) NMR spectra were recorded in $CDCl_3$ solutions at 400 MHz, ^{13}C (Me_4Si) at 100.6 MHz and ^{19}F NMR (CCl_3F) at 376.4 MHz. Low-resolution and high-resolution mass spectra were recorded by electron impact (MS-EI) techniques using AMD-402 spectrometer unless otherwise noted. IR spectra were performed using spectrometer FT-IR IFS 66 v/s from Bruker. Optical rotations were measured using a 243 B PerkinElmer polarimeter [α] *D* values were determined at 589 nm and 25 °C. Reagent grade chemicals were used and solvents were dried by refluxing with sodium metal-benzophenone (THF), with $CaCl_2$ (CH_2Cl_2) and distilled under an argon atmosphere. All moisture sensitive reactions were carried out under an argon atmosphere using oven-dried glassware. Reaction temperatures below 0 °C were performed using a cooling bath (CO_2/*iso*-propanol). TLC was performed on Merck Kieselgel 60-F_{254} with EtOAc/hexane as developing systems, and products were detected by inspection with a phosphomolybdic acid solution. Merck Kieselgel 60 (230–400 mesh) was used for column chromatography. Hexafluoropropene (HFP) and pentafluoropropane (PFP) were obtained from SynQuest Labs, Inc. PFPDEA was prepared as reported [49], distilled under reduced pressure and the purity of PFPDEA was conveniently evaluated by ^{19}F NMR in $CDCl_3$. Carbohydrate substrates have to be well dried prior to use. Compound **1** was obtained from Aldrich, compounds **4a** [50], **4b** [51], **6a**, **7a** [52], were prepared as described.

2.2. Synthesis

2.2.1. 1,2,5,6-Di-O-isopropylidene-3-O-perfluoroprop-1-enyl-α-D-glucofuranose *2a/2b* and 1,2-O-isopropylidene-3-O-(E)-perfluoroprop-1-enyl-α-D-xylofuranose

3a

Step A. To 1,2,5,6-di-*O*-isopropylidene-α-D-glucofuranose **1** (260 mg, 1 mmol) dissolved in THF (2 mL) NaH (60% suspension in oil, 60 mg, 1.5 mmol) was added. The reaction was carried till disappearance of the substrate (confirmed by TLC analysis). Then the mixture was cooled out to −78 °C and hexafluoropropene (870 mg, 5.8 mmol) was added. The reaction was stirred for 2 h at −78 °C and then at room temperature overnight. Then the reaction mixture was partitioned (H_2O/HCl//CH_2Cl_2) and the separated organic layer was washed saturated aqueous $NaHCO_3$, brine, dried (Na_2SO_4) and evaporated. Carefully column chromatography (5 → 20% EtOAc/hexane) gave two fractions: pure isomer *E* (**2a**) (220 mg, 56%) and a mixture of two isomers *E* and *Z* (**2a**/**2b** in ratio 1.5/1) (80 mg, 21%) as slightly yellow oils. Compound **2a** had $[\alpha]_D^{25} = -33^\circ$ (c 0.3, $CHCl_3$); ^{1}H NMR *δ*: 1.33 (3H, s, *i*-Pr), 1.34 (3H, s, *i*-Pr), 1.43 (3H, s, *i*-Pr), 1.52 (3H, s, *i*-Pr), 3.92 (1H, dd, J_{6-5} = 4.9 Hz, $J_{6-6'}$ = 8.7 Hz, H-6), 4.09 (1H, dd, $J_{6'-5}$ = 2.9 Hz, $J_{6'-6}$ = 9.0 Hz, H-6′), 4.16–4.24 (2H, m, H-4/5), 4.60 (1H, d, J_{2-1} = 3.6 Hz, H-2), 4.79 (1H, d, J_{3-4} = 2.7 Hz, H-3), 5.91 (1H, d, J_{1-2} = 3.8 Hz, H-1), ^{19}F NMR *δ*: −67.70 (dd, J_{CF3-F} = 13.3 Hz, J_{CF3-F} = 22.1 Hz, 3F, CF_3), −110.00 (dq, J_{F-F} = 120.4 Hz, J_{F-CF3} = 22.1 Hz, 1F), −190.25 (dq, J_{F-F} = 120.4 Hz, J_{F-CF3} = 13.3 Hz, 1F); ^{13}C NMR *δ*: 24.8 (*i*-Pr), 26.1 (*i*-Pr), 26.6 (*i*-Pr), 26.7 (*i*-Pr), 67.5 (C-6), 71.8 (C-5), 80.3 (C-2), 82.5 (C-4), 83.4 (C-3), 105.1 (C-1), 109.6 (*i*-Pr), 112.7 (*i*-Pr), 119.51 (qdd, *J* = 269.6, 33.1, 6.6 Hz, *C*F_3). 124.02 (ddq, *J* = 233.1, 57.7, 42.5 Hz, *C*F), 152.3 (ddq, *J* = 284.5, 34.7, 2.7 Hz, *C*FCF_3); MS *m*/*z* (rel. int.) 390 $[M]^+$ (3), 375 $[M - Me]^+$ (1 0 0). Compound **2b** had ^{1}H NMR *δ*: 1.33 (3H, s, *i*-Pr), 1.34 (3H, s, *i*-Pr), 1.43 (3H, s, *i*-Pr), 1.52 (3H, s, *i*-Pr), 3.97–4.18 (3H, m, H-5/6/6′), 4.27 (2H, dd, J_{4-3} = 2.5 Hz, J_{4-5} = 4.9 Hz, H-4), 4.65 (1H, d, J_{2-1} = 3.6 Hz, H-2), 4.82 (1H, d, J_{3-4} = 2.7 Hz, H-3), 5.95 (1H, d, J_{1-2} = 3.8 Hz, H-1). ^{19}F NMR *δ*: −67.20 (dd, J_{CF3-F} = 13.2 Hz, J_{CF3-F} = 9.6 Hz, CF_3), −95.50 (qd, J_{F-CF3} = 19.1 Hz, J_{F-F} = 9.6 Hz, 1F), −184.00 (dq, J_{F-F} = 17.6 Hz, J_{F-CF3} = 13.2 Hz, 1F). *Step B.* A suspension of compound **2a** (100 mg, 0.26 mmol) in dried AcOEt (2.5 mL) and H_5IO_6 (70 mg, 0.31 mmol) was stirred for 2 h. The reaction mixture was filtered, and the filtrate was evaporated. The residue was dissolved in EtOH abs. (2.5 mL) and $NaBH_4$ (15 mg, 0.38 mmol) was added. Stirring was continued for 30 min, excess of AcOH (58 μL, 61 mg, 1.02 mmol) was added and volatiles were evaporated. The residue was dissolved in AcOEt, washed (H_2O), dried (Na_2SO_4), evaporated and column chromatographed (9: 1, hexane: ethyl acetate) to give **3a** with 60% yields. Compound **3a** had $[\alpha]_D^{25} = -11^\circ$ (c 0.5, $CHCl_3$), IR (KBr/neat) *ν* 3435, 2993, 2943, 1760, 1457, 1379, 1278, 1194, 1143, 1091, 1046, 890, 853, 651 cm^{-1}; ^{1}H NMR *δ*: 1.35 (3H, s, *i*-Pr), 1.53 (3H, s, *i*-Pr), 2.52 (1H, br s, OH), 3.89 (1H, dd, $J_{5'-4}$ = 5.6 Hz, $J_{5'-5}$ = 11.5 Hz, H-5′), 3.98 (1H, dd, J_{5-4} = 6.7 Hz, $J_{5-5'}$ = 11.5 Hz, H-5), 4.47 (1H, ddd, J_{4-3} = 3.0 Hz,