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Self-Assembling Carbohydrate-Functionalized Oligothiophenes

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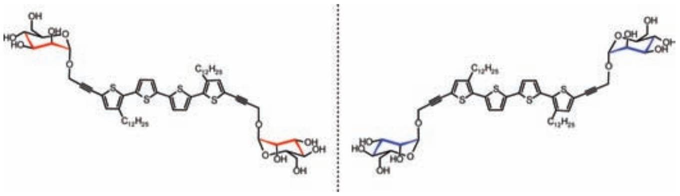
ABSTRACT



Carbohydrate-functionalized oligothiophenes have been synthesized applying mild Sonogashira cross-coupling conditions. In an aqueous environment the amphiphilic hybrids self-assemble into chiral superstructures as a result of multiple hydrogen bond interactions and the helicity of the aggregates is controllable by the configuration of the carbohydrate unit. By means of atomic force microscopy highly ordered layer arrangements on substrates were characterized.

Poly- and oligothiophenes (OTs) are multifunctional materials of great interest for application in organic electronics.[1] Because of their excellent semiconducting and optoelectronic properties they are used in organic light emitting diodes (OLEDs),[2] field-effect transistors (OFETs),[3] or solar cells (OSC).[4] OTs have also received attention as ideal models for polymers:[5] they can be isolated in a well-defined form and consequently reliable structure−property relationships can be derived in contrast to polydisperse polymeric systems. An interesting feature of OTs is their ability to self-assemble,[6] which offers a promising approach for building a wide variety of complex functional nanostructures. A highly intriguing concept appears by combination of an artificial π-conjugated system with natural biomolecules. Thus, molecular recognition can be exploited as a tool to influence self-assembling processes due to the information that is present in the biosequence, an important principle for the construction of biological sensors or electronic devices. In this respect, some nucleoside[7,8] and peptide[9−12] functionalized OTs and oligo(*p*-phenylenevinylenes)[13,14] were recently found to act as excellent probes to study self-

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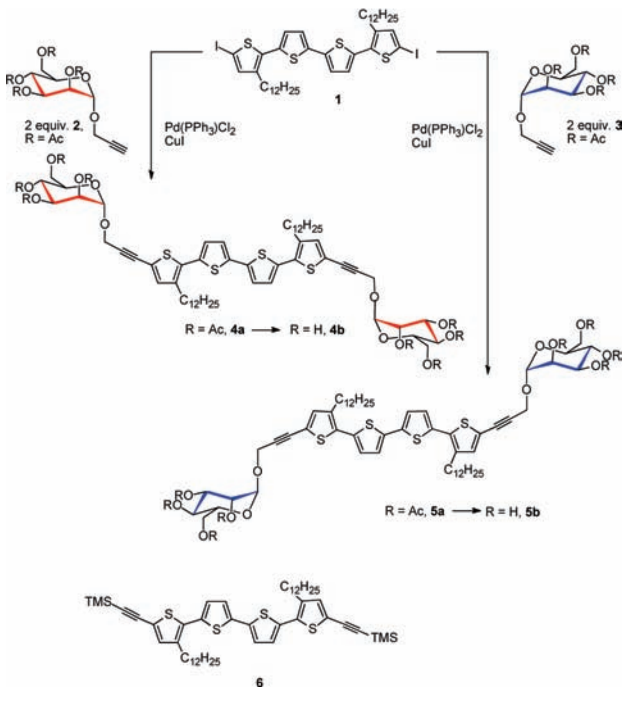
assembly mechanisms. Several dye−carbohydrate conjugates are known[15,16] and various conjugated polymer−carbohydrate hybrids comprising poly(arylene-ethynylenes),[17] poly(phenylene-vinylenes),[18] poly(*p*-phenylene-ethynylenes),[19] or polythiophenes[20] for mainly sensing applications have been reported.

Herein, we describe first examples of α,ω-carbohydrate-functionalized OTs, which were accessible by connecting a semiconducting quaterthiophene (4T) building block and ester-protected propargylglycosides,[22] using Sonogashira cross-coupling.[21] Removal of the ester groups resulted in biohybrids with highly amphiphilic character. The presence of various functional groups should qualify the hybrid compounds to interact via an ensemble of noncovalent forces, such as π-stacking, van der Waals interaction, or H-bonding, to benefit under appropriate conditions self-assembly in solution and in the solid state. Ester-protected D-(+)-mannose-linked 4T derivative **4a** (D-(+)-ManOAc-4T) was obtained anomerically pure in good yield (75%) by Pd^0-catalyzed coupling of bis-iodinated 3,3‴-didodecylquaterthiophene (4T) **1**[12] and 2 equiv of acetyl-protected propargyl-α-D-(+)-mannoside **2** (Scheme 1). Lewis acid-catalyzed glycosylation of peracetylated D-(+)-mannose with propargyl alcohol provided α-anomeric pure sugar−alkyne component[23] **2** as a suitable starting material (see Supporting Information). Novel amphiphilic system **4a** comprises a variety of functionalities, i.e. a rod-like hydrophobic quaterthiophene backbone combined with polar, acetyl-protected monosaccharides. The ethynyl functions extend the π-conjugated system of the OT whereas the lateral dodecyl chains enhance solubility in lipophilic solvents. By applying Zemplen conditions and using a catalytic amount of sodium methanolate in a methanol/tetrahydrofuran (THF) mixture, the ester functions of **4a** were removed resulting in OT-carbohydrate hybrid **4b** D-(+)-ManOH-4T in 93% yield. L-(−)-Enantiomeric counterparts **5a** L-(−)-ManOAc-4T and **5b** L-(−)-ManOH-4T were accessible in appropriate yields (62%, 97%) following the route described above, but starting with L-(−)-mannose. As a reference, trimethylsilyl (TMS)-protected bisethynylated quaterthiophene **6** without carbohydrate units was synthesized in 78% yield from diiodoquaterthiophene **1** and TMS-acetylene according to a literature protocol.[12]

Scheme 1



Photophysical characterization of OT-hybrids **4a**, **4b**, **5a**, and **5b** and parent compound **6** in THF (see Supporting Information) resulted in almost identical absorption spectra with two broad bands peaking at 263−280 and 398−406 nm. The latter band is unequivocally assigned to the typical $\pi-\pi^*$ transition of the OT backbone. Fluorescence spectra showed vibronically fine structure bands at 483−487 nm indicative of an increased planarization of the OT-backbone in the excited state.

In contrast to **4a**, **5a**, and **6**, solubility of the deprotected compounds **4b** and **5b** improves in more polar solvents. Absorption spectra of the freshly deprotected enantiomeric hybrids **4b** and **5b** dissolved in MeOH or MeOH:H$_2$O (1:1) displayed absorption bands which are hypsochromically shifted with respect to the THF measurements. In Figure 1, absorption and emission spectra of OT-mannoside **4b** in MeOH are shown as well as the absorption spectra in MeOH:H$_2$O (1:1). In the latter more polar mixture the absorption band indicates an asymmetric shape, including a hypsochromic shift of the maximum to 389 nm and a broadening extending up to 550 nm (Figure 1, black arrows) suggesting the formation of H-aggregates.[24]

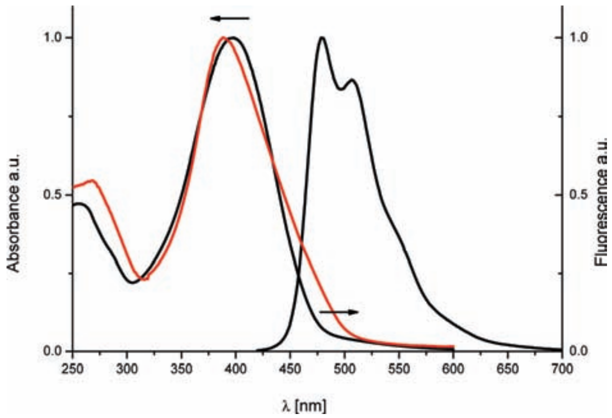


Figure 1. Absorption and emission spectra of OT-mannoside **4b** (D-(+)-ManOH-4T) in MeOH (black lines) and in MeOH/H$_2$O (1:1) mixture (red line). The arrows underline the asymmetric shift of the absorption in the solvent mixture.

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To analyze in detail the nature of aggregates of **4b** D-(+)-ManOH-4T and **5b** L-(−)-ManOH-4T circular dichroism (CD) spectra were taken in MeOH:H_2O (1:1) mixture and are shown in Figure 2. A bisignate Cotton effect can be observed at the $\pi-\pi^*$ transition band with a zero-crossing of the CD signal located at the absorption maximum of the chromophore. Bisignate CD curves typically indicate excitonic coupling as a result of chiral aggregation. The shape of the CD curve for D-(+)**4b** (Figure 2, black curve: negative θ at 406 nm; positive θ at 366 nm) indicates self-assembly of the OT backbones into left-handed supramolecular stacks induced by the chiral carbohydrate moieties. The L-mannosidic counterpart L-(−)-**5b** displayed an almost perfect mirror image behavior (Figure 2, red curve), confirming the formation of well-ordered aggregates with opposite, right-handed helicity. Thus, the handedness of the observed superstructures of the π-conjugated oligomer stacks could obviously be tuned by the introduction of suitable D-(+)- or L-(−)-mannosidic building blocks. The formation of chiral aggregates is rationalized as a result of the "free" OH-groups in **4b** and **5b** being capable of forming intermolecular hydrogen bonding, forcing the π-systems into well-ordered helical assemblies. This conclusion found evidence by the study of optical properties of the protected OT-hybrids **4a** and **5a** and the parent compound **6**, which undergo conventional positive solvatochromism and did not show clear CD effects pointing to chiral aggregation phenomena.

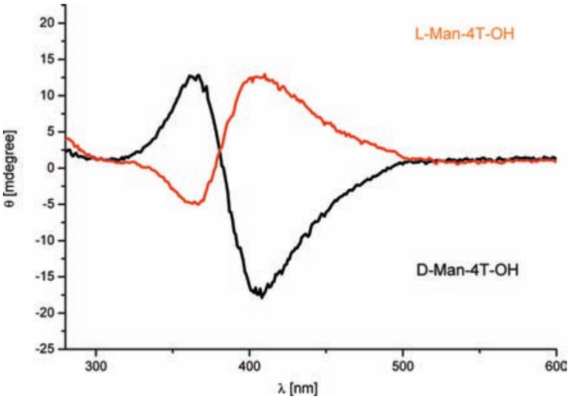

Figure 2. CD data of OT-mannosides **4b** (D-(+)-ManOH-4T, black curve) and **5b** (L-(−)-ManOH-4T, red curve) in MeOH:H_2O (1:1) mixture.

The specific optical rotations $[\alpha]_D$ of protected hybrids D-(+)-ManOAc-4T **4a** [+42.5° ($c = 0.12$ g/dL)] and L-(−)-ManOAc-4T **5a** [−48° ($c = 0.15$ g/dL)] were measured in dichloromethane. With respect to sign and magnitude, these values correspond well to those of tetraacetylated *O*-propargylmannoside building blocks **2** [+57.8° ($c = 0.27$ g/dL)][21c,22a] and **3** [−59.6° ($c = 0.27$ g/dL)] characterized as well in this work. These results corroborate the rationale that the chirality of the carbohydrate units is preserved in the hybrid systems.

OT-carbohydrate derivatives **4a** and **4b** and reference compound **6** were further characterized by cyclic (CV) and square wave voltammetry in dimethylformamide, using tetrabutylammonium hexafluorophosphate (0.1 M) as electrolyte. In the CVs of the hybrids, two reversible oxidation waves indicate the formation of stable OT radical cations ($E°_1 = 0.57$ V) and dications ($E°_2 = 0.67$ V). Due to the electron-withdrawing effect of the *O*-glycoside unit the redox potentials of the OT hybrids were higher than those of TMS-protected parent compound **6** ($E°_1 = 0.48$ V, $E°_2 = 0.60$ V) (see Supporting Information).

Solid state morphologies of adsorbates of ester-protected OT-carbohydrate hybrid **4a** and deprotected **4b** on mica were studied using tapping mode atomic force microscopy (AFM). Amphiphilic derivative **4a** adsorbed in a terrace-like multilayered structure with up to 84% coverage of the surface, indicating a Volmer−Weber growth-mode.[25] The number of layers increased with longer delay time (T_d) between deposition of the solution and start of the spin-coating process. The well-defined layered structure was not found in the case of the parent compound **6**, which undergoes cluster formation under identical conditions. In contrast, **4a** exhibited very uniform and stable layers whose thicknesses (3.5 ± 0.2 nm) perfectly correlated with the calculated length of the molecule (Figure 3a,b). Modifying the deposition procedure to a dip-coating process and subsequent evaporation of the solvent resulted in the formation of circular structures (insert in Figure 3a) formed by molecules arranged in up to four terraces of exactly the same height as in the former case. Semiempirical calculations for **4a** D-(+)-

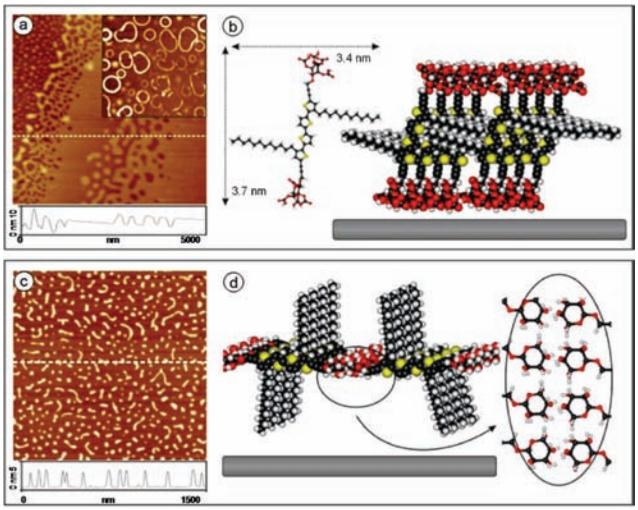

Figure 3. AFM micrographs of **4a** and **4b** absorbed on mica. (a) Height image of **4a** spin-coated from dichloromethane, 5 × 5 μm^2 (bottom: corresponding cross-section, $\Delta z = 10$ nm). Inset: Structures after dip-coating setup, 5 × 5 μm^2. (b) Calculated geometry of compound **4a** and molecular model of the adsorption geometry. (c) Amplitude image of **4b** deposited from MeOH, 1.5 × 1.5 μm^2 (bottom: corresponding cross-section, $\Delta z = 5$ nm). (d) Calculated model of **4b** and detailed view of the intermolecular H-bonding.

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ManOAc-4T suggest an *all-trans* conformation of the quaterthiophene backbone and carbohydrates stretched following the molecular axis (Figure 3b).

Due to the amphiphilic character of the molecules the aggregation model should take into account stabilization due to phase separation. The semiempirical calculated model presented in Figure 3b considers not only the intermolecular phase separation, but also the preferred interaction between the hydrophilic substrate and the polar part of the molecule. The monolayer formed in this model is additionally stabilized by $\pi-\pi$ interaction of the conjugated backbones and by van der Waals interactions of the alkyl chains.

Deprotected hybrid **4b** adsorbed from methanol on mica at $T_d = 0$ (instantaneous coating) in a monolayer structure covered by small clusters. With an increase in the delay time, fiber-like structures ($T_d = 20$ s, Figure 3c) and finally large clusters ($T_d = 60$ s) appeared. The monolayer formed at $T_d = 0$ evidenced instabilities and a height of only 0.7 nm, suggesting that the molecules were lying on the mica surface. The lack of a stable and compact monolayer structure as well as the dependence of the size of the aggregates on T_d implies strong molecule−molecule interactions, as a result of H-bonding induced by the deprotection of the carbohydrates. The observed small fibers (Figure 3c) have a uniform height of about 3.4 nm being in accordance with the width of the molecule, considering that hydrogen bond formation of the carbohydrate-functionalized termini took place parallel to the surface (Figure 3d). In the calculated model, the OT backbones are separated to 0.6 nm leading to less efficient $\pi-\pi$ stacking.

In conclusion, an efficient and convenient protocol based on Sonogashira cross-coupling for the construction of novel α,ω-end-capped α-D-(+)- and α-L-(−)mannose oligothiophene hybrids has been developed. Investigation on optical properties of amphiphilic deprotected hybrids **4b** and **5b** in polar solvents revealed self-assembly into chiral superstructures of the π-conjugated oligomer blocks whose handedness depend on the stereochemistry of the pending mannosidic bioblocks. Characterization of the self-assembly behavior of α-D-(+)mannosidic hybrids **4a** and **4b** in the solid state on mica resulted in a highly ordered layer arrangement.

These findings now allow that the developed synthetic strategy can be exploited to rationally design novel biocompatible and self-assembling (semi)conducting materials by a combination of miscellaneous ethynylated saccharides and halogenated π-conjugated building blocks. Thus, self-assembly of these materials into chiral superstructures can be tuned by the choice of saccharidic building blocks with suitable stereochemistry.

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Supporting Information Available: Characterization data for all new compounds and experimental protocols as well as optical, redox, and NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.

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