Cavitand-Functionalized SWCNTs for *N*-Methylammonium Detection

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Ⓢ *Supporting Information*

ABSTRACT: Single-walled carbon nanotubes (SWCNTs) have been functionalized with highly selective tetraphosphonate cavitand receptors. The binding of charged *N*-methylammonium species to the functionalized SWCNTs was analyzed by X-ray photoelectron spectroscopy and confirmed by ^{31}P MAS NMR spectroscopy. The cavitand-functionalized SWCNTs were shown to function as chemiresistive sensory materials for the detection of sarcosine and its ethyl ester hydrochloride in water with high selectivity at concentrations as low as 0.02 mM. Exposure to sarcosine and its derivative resulted in an increased conductance, in contrast to a decreased conductance response observed for potential interferents such as the structurally related glycine ethyl ester hydrochloride.

Carbon nanotubes (CNTs) are a desirable platform for sensor engineering, because of their electrical properties and quasi-one-dimensional structure.[1] Although very sensitive to a wide variety of chemical signals, pristine CNTs lack in selectivity.[2] Polymers,[3] metal nanoparticles,[4] and biomolecules[5] have been used to improve CNTs sensing properties. Embedding molecular recognition units is the ultimate strategy for imparting high selectivity and sensitivity into sensor systems.[6] Indeed a host–guest (receptor) approach has proved to be a powerful strategy for sensor design, and the introduction of cyclodextrins or calixarenes on the sidewall of CNTs has led to the selective recognition of small molecules.[7]

To further explore the scope of CNT sensing, we have targeted the tetraphosphonate cavitands which offer remarkable complexation capabilities toward charged *N*-methylammonium species.[8] The complex between a tetraphosphonate cavitand and *N*-methylbutyl ammonium chloride exhibits a high K_a value, ~4×10^5 M^{-1} in methanol,[9] making tetraphosphonate cavitands interesting candidates for the specific sensing of methylammonium species. Herein we explore the molecular recognition properties offered by the tetraphosphonate cavitand **Tiiii**[N_3, CH_3, **Ph**][10] **1** installed on single-walled CNTs (**SWCNTs**), toward small ammonium ions in the liquid phase. While noncovalent attachment of the receptors to the CNTs has been shown to provide good sensing results in other

systems,[7d,e] here we have chosen a covalent attachment strategy for better long-term stability of the material under liquid sensing conditions.

The introduction of an azide group at the lower rim of tetraphosphonate cavitands allows the covalent functionalization of **SWCNTS** by a thermal 1,3-dipolar cycloaddition reaction followed by nitrogen extrusion,[11] with very limited structural damage to the CNTs compared to other methods such as oxidation with nitric acid.[11a] The tetraphosphonate cavitand **Tiiii**[N_3, CH_3, **Ph**], **1**, from now onward referred to as **Tiiii**, was prepared in four steps and 45% overall yield, starting from the monohydroxy footed silyl cavitand (see the Supporting Information for details).[8,12] The key steps of the synthesis were the stereospecific introduction of four inward-pointing phosphonate bridges at the upper rim of the resorcinarene skeleton and the installation of an azide moiety (Scheme S1). The covalent aziridine groups are then installed on the SWCNTs by reaction with **Tiiii** in *o*-DCB at 160 °C for 2 days.

The covalently functionalized **Tiiii@SWCNTs** were characterized by attenuated total reflectance Fourier transform infrared spectroscopy (ATR FTIR), X-ray photoelectron spectroscopy (XPS), and ^{31}P magic-angle spinning nuclear magnetic resonance (MAS NMR). The infrared spectra (between 1000 and 1500 cm^{-1}) of **Tiiii@SWCNTs** displayed a broad band arising from the stretching of the PO bonds, P-phenyl group, and the aromatic skeleton, which overlap with one another. By comparison with **Tiiii** ATR FTIR spectra, the azide peak is no longer visible for **Tiiii@SWCNTs**, indicating that aziridination of the SWCNTs has taken place (Figure S2). XPS confirmed the presence of P 2p and N 1s peaks at a density that suggests one cavitand for every 50 CNT carbon atoms, based on the P 2p vs C 1s signal (Figures 1b and S1).

MAS NMR was utilized to further analyze the functionalized CNTs. The use of this technique is increasing for the characterization of modified CNTs based on the ^{13}C nucleus.[13] However, obtaining high-resolution ^{13}C NMR spectra of CNTs remains a challenge due to the low isotopic abundance (1.1%, ^{13}C) and great variability of carbon sites with different chemical shifts commonly seen in a CNT sample. In contrast to this, a
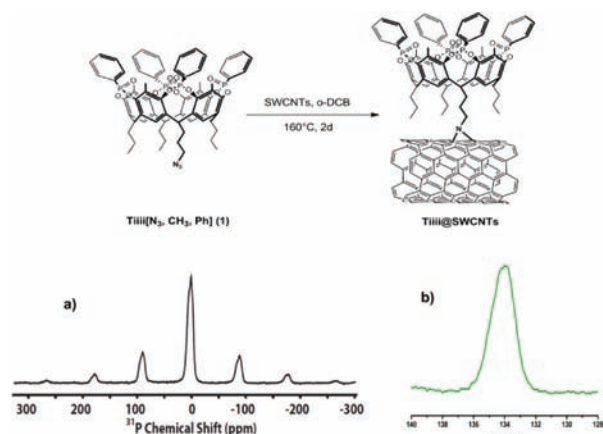
Figure 1. SWCNTs functionalization with **Tiiii[N₃, CH₃, Ph] (1)**; (a) ^{31}P MAS NMR spectra of **Tiiii@SWCNTs**; (b) XPS analysis: P 2p region.

very clear ^{31}P MAS NMR spectrum of **Tiiii@SWCNTs** was obtained of the SWCNT bound cavitand, which benefited from high ^{31}P natural abundance (100%) and its high gyromagnetic ratio, both of which lead to greater sensitivity (Figure 1a).

In order to evaluate the molecular recognition capabilities of **Tiiii@SWCNTs**, we treated a dichloromethane suspension of the functionalized SWCNTs with 4-bromo-*N*-methylbutylammonium bromide **2**, which binds as a guest and has an XPS diagnostic bromide signal.[14] After washing to remove any unbound **2**, the CNTs were analyzed by XPS. The presence of the Br 3d XPS signals confirmed successful binding of **2** to **Tiiii@SWCNTs** (Figure 2, red trace; Figure S3). Finally, the sample was washed with 1,8-diazabicyclo[5.4.0]undec-7ene (DBU). In previous experiments, it has been shown that DBU deprotonates the guest thereby breaking the cavitand–
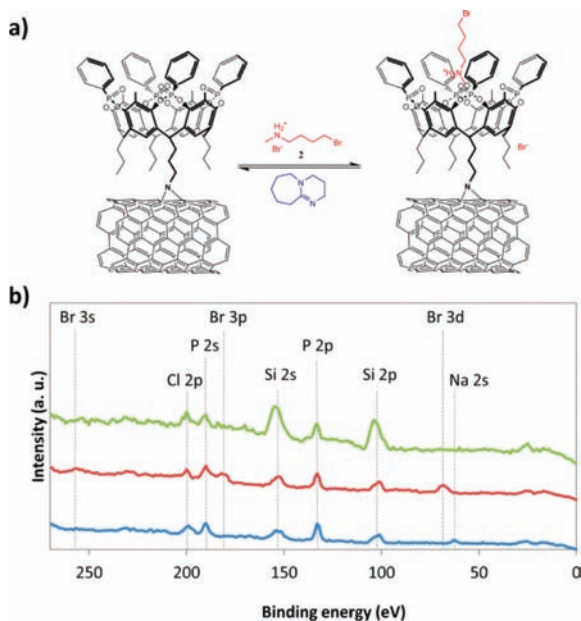

Figure 2. XPS binding study with **Tiiii@SWCNTs**. (a) Reversible binding of guest **2**; (b) XPS analysis of **Tiiii@SWCNTs** before exposure to **2** (blue), after exposure to **2** (red), and after subsequent washing with DBU (green). Si signals are due to the utilized Si substrate.

guest complex.[15] Protonated DBU cannot interact with the cavity as a result of steric hindrance and thereby produces a guest-free host (Figure 2 green trace; Figure S4). Pristine SWCNTs were used as an additional control experiment, and no Br signals were detected after similar treatments with **2**, thus ruling out nonspecific binding to the CNTs (Figure S5).

To further confirm that the guest binds directly to the cavitand on the CNTs, **Tiiii@SWCNTs** were treated with a solution of *N*-methylbutylammonium chloride, **3**, and subsequently analyzed by ^{31}P MAS NMR. The ^{31}P signals are sensitive to the structural changes associated with the binding of an ammonium ion to the **Tiiii@SWCNTs** (Figure 3b, green
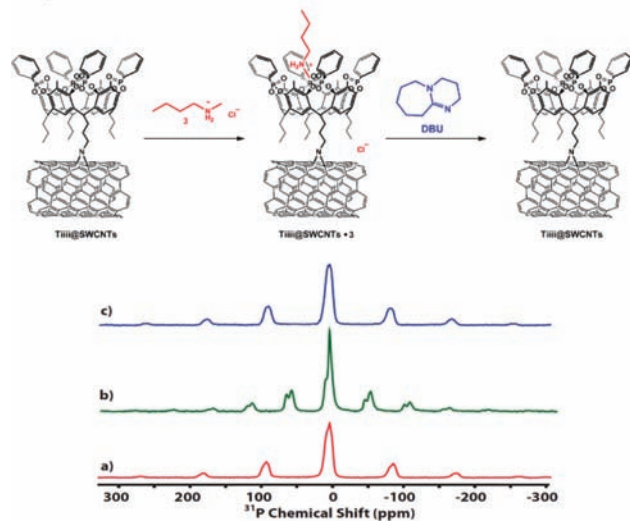

Figure 3. Host–guest binding studies using ^{31}P MAS NMR showing reversibility of the host molecule. (a) **Tiiii@SWCNTs**, (red trace); (b) after treatment with **3** (green trace); (c) after base treatment (blue trace).

trace), and a second downfield-shifted resonance is observed. This shift was expected for the host–guest complex and is consistent with solution NMR studies of the base cavitand complex.[8b]

To further confirm the binding of ammonium ions to the cavitand, the sample was treated with DBU. MAS NMR of the product after this washing step showed a similar spectrum as was obtained for the pristine **Tiiii@SWCNTs** confirming the successful removal of the guest (Figure 3c, blue trace). Based upon the reversibility of these associations we can conclude that host–guest association displays the expected pH dependence.

Given the selective ammonium ion binding to functionalized SWCNTs we have created a chemoresistive sensor for the detection of sarcosine, the *N*-methylated derivative of glycine. Sarcosine is structurally related to the previously studied guests and is a potential biomarker for the progression of prostate cancer.[16,17] In aqueous environments, **Tiiii** binds sarcosine over glycine with complete selectivity.[18] The source of this exquisite selectivity is the presence of water insensitive CH₃–π interactions between the *N*-methyl residue of sarcosine and the hydrophobic internal surface of the **Tiiii** cavity. Binding between the cavitand and sarcosine is facilitated by the formation of two H-bonds (NH···O=P), hydrophobic interactions, and cation–dipole interactions.

To prepare the sensor, an aliquot of the reaction solution of **Tiiii@SWCNTs** was directly drop cast onto a glass slide

decorated with two Au electrodes. After the device was washed to remove any excess of reagent and subsequently dried, it was analyzed by scanning electron microscopy (SEM) and atomic force microscopy (AFM) (Figure S6–S7) and then put into an enclosure that was connected to a syringe pump (see Figure S9 for a diagram). Using this experimental platform, the device was alternatingly exposed to Milli-Q water and an analyte solution (1−0.22 mM) while the current through the CNT network (at V_{app} = 50 mV) was measured.

Initial measurements with sarcosine showed an increase in current when a device with **Tiiii@SWCNTs** was exposed to the analyte at pH 7 (Figure S10). The magnitude of the change in current was however strongly dependent on the pH of the solution, and at pH 5, no change in current was observed upon exposure of the device to sarcosine (Figure S11). We attribute this strong pH dependence to the zwitterionic nature of the analyte. Our data may suggest that the protonation of the carboxylate can affect its nonspecific interaction with the SWCNT surface. In order to eliminate the effect of the carboxylate, we investigated the hydrochloride salt of sarcosine ethyl ester (**4**). The measurements were performed at pH 5 to ensure protonation of the amine. As controls, the weaker binding glycine ethyl ester hydrochloride (**5**) and tetraethylammonium chloride (**6**) that is too bulky for binding[9] were chosen.

Exposing the device to **4** at pH 5 resulted in an increase in current similar to exposing it to sarcosine, while exposure to **5** or **6** led to a current decrease (Figure 4; Figures S12–S14). In many chemoresistive sensing systems a current change in the same direction is observed for the desired analytes and controls,

albeit usually stronger for the target molecule. Instead, a current switch in opposite directions for the target analyte and interferents is rare, especially for compounds as closely related as **4** and **5**. Observing a change with a different sign provides a powerful level of selectivity as it can potentially distinguish between analytes regardless of their concentration. Although the magnitude of the response to **4** varied from device to device (Figures S18–S22), an increase in current when exposed to **4** was observed in all cases. Exposing the device to **4** at pH 7, on the other hand, resulted in a current decrease similar to the response to **5** and **6** at pH 5 (Figure S23). Previous studies at the silicon−water interface[18] showed that surface complexation by Tiiii is effective only at a pH low enough to ensure complete guest protonation. This suggests that specific binding between **4** and the cavitand is reduced as a result of the change in pH and nonspecific interactions of **4** and the SWCNTs predominate.

Controls with pristine SWCNTs showed a decrease in current for all investigated analytes (Figure 4; Figures S15–S17). In order to minimize the effect of a changing ionic strength of the solution on the sensing response, a device with **Tiiii@SWCNTs** was alternatingly exposed to a 1 mM solution of **4** and **5** (instead of an analyte solution and water). An increasing current was observed in this case as well when switching to **4** (Figure 4d). Finally, the detection limit for **4** was determined to be 0.02 mM (Figure 4c). It should be noted that the devices exhibited very good stability and no significant change in sensitivity was observed over several months of regular operation.

In summary, we have illustrated the use of covalent functionalized SWCNTs as a selective sensor in water. By introducing a tetraphosphonate cavitand as a specific molecular receptor, it was possible to selectively recognize the *N*-methylammonium species. The covalent functionalization resulted in the **Tiiii@SWCNTs**-based device's high stability and allowed for the formation of a robust liquid sensing device. As a proof of concept experiment we demonstrated the selective detection of sarcosine ethyl ester hydrochloride, at concentrations as low as 0.02 mM. Interestingly, the sign of the current change upon exposure to the analyte is opposite for the controls, allowing selective detection of the analytes, regardless of their concentration. Studies concerning the sensing mechanism are ongoing in our laboratories.
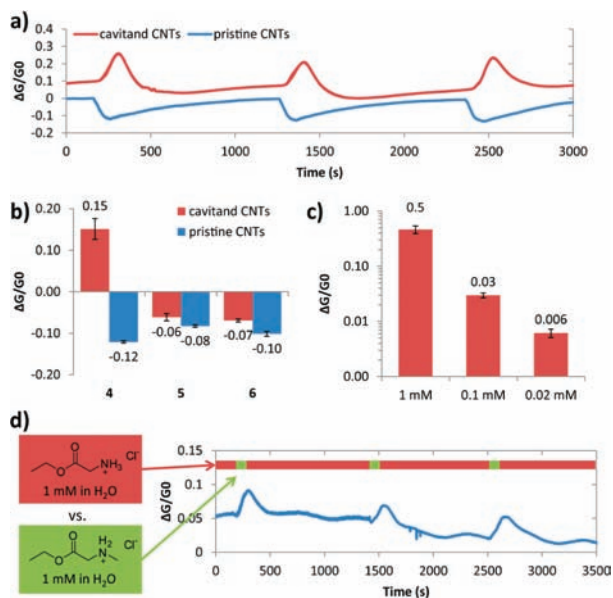

Figure 4. Liquid flow sensing experiments with **Tiiii@SWCNT**-based devices at pH 5. (a) **Tiiii@SWCNTs** and pristine SWCNTs show opposite responses upon exposure to a 1 mM solution of **4**. (b) Comparison of the current change upon exposure of **Tiiii@SWCNT** and pristine SWCNT devices to **4** (sarcosine ethyl ester hydrochloride), **5** (glycine ethyl ester hydrochloride), and **6** (tetraethylammonium chloride); error bars are based on three consecutive measurements. (c) Response of **Tiiii@SWCNT** devices to different concentrations of **4**; error bars are based on three consecutive measurements. (d) Response of **Tiiii@SWCNT** devices to alternating exposure to **4** and **5**.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and analytical data for synthesized **Tiiii[N₃, CH₃, Ph]**; XPS and ATR-FTIR characterization of **Tiiii@SWCNTs**; XPS complexation studies; SEM and AFM images of devices, device setup, and operation mode; liquid flow sensing experimental traces. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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