

Tailoring Aqueous Solubility of Functionalized Single-Wall Carbon Nanotubes over a Wide pH Range through Substituent Chain Length

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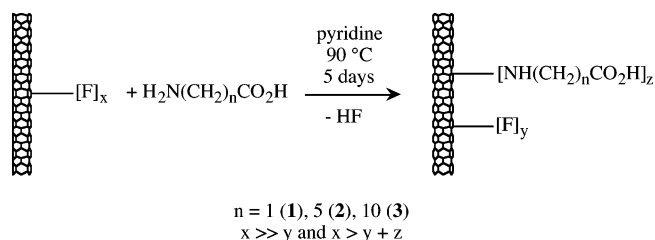
ABSTRACT

Carboxylic acid-functionalized SWNTs prepared via the reaction of an amino acid, $\text{NH}_2(\text{CH}_2)_n\text{CO}_2\text{H}$, with fluoronanotubes show similar levels of sidewall functionalization; however, the solubility in water is controlled by the length of the hydrocarbon side chain (i.e., n). The 6-aminohexanoic acid derivative is soluble in aqueous solution (0.5 mg mL^{-1}) between pH 4 and 11, whereas the glycine and 11-aminoundecanoic acid derivatives are insoluble across all pH values.

There has been increasing interest in the ability to prepare water-soluble single-walled carbon nanotubes (SWNTs) in particular under physiologically relevant conditions.^{1,2} An additional area of interest is the formation of individual SWNTs rather than bundles or aggregates. Several methods have been used to functionalize SWNT bundles with water solubilizing substituents;³ however, only some methods exfoliate the bundles.⁴ Solubilization is made possible through either wrapping (surfacting) the SWNTs,⁵ end-group functionalization,⁶ or sidewall functionalization.⁷ The majority of sidewall functionality is aimed at either solubility via poly-(ethylene glycol), ester, or cationic substituents, although Tour and co-workers have reported good results with aryl sulfonates.^{4d} We are interested in the formation of anionic substituents in order to facilitate transport through cell membranes⁸ and also substituents that can be used as the basis for attachment of peptides. In this regard we have investigated the synthesis of carboxylic acid-functionalized SWNTs. We have reported previously that fluorinated SWNTs (F-SWNTs) react with amines and other strong nucleophiles;^{9,10} this therefore suggests that amino acids will make suitable flexible reagents. Initial studies have shown that α -amino acids did not confer the desirable solubility, so in order to investigate the effect of chain length we have synthesized representative examples using glycine (GLY), 6-aminohexanoic acid (AHA), and 11-aminoundecanoic acid (AUDA).

HiPCo SWNTs produced at Rice University were purified to remove iron and other impurities,¹¹ and subsequently

Scheme 1. Functionalization of F-SWNTs.



fluorinated to a C/F ratio of approximately 2.4:1, by direct fluorination at 150°C by a procedure reported previously.¹² The fluoronanotubes were functionalized by reaction with the appropriate amino acid in the presence of a base catalyst (Scheme 1).¹³

The IR spectra of SWNTs **1–3** show bands consistent with the appropriate substituents¹⁴ and the significant reduction in the fluorine content (as indicated by the loss of the band at 1102 cm^{-1}). The carboxylic acid C=O stretch for AHA-SWNT (**2**) and AUDA-SWNT (**3**), 1710 and 1705 cm^{-1} , respectively, are typical of saturated aliphatic acids.¹⁵ However, the band observed for the glycine derivative (GLY-SWNT, **1**) at 1619 cm^{-1} is characteristic of a chelated acid, suggesting the presence of strong intraligand hydrogen bonding.

The thermogravimetric analysis (TGA) of the sample shows a steady mass loss between 200 and 600°C in a manner typical of sidewall functionalization.^{3,4,10,11} The extent of sidewall functionalization is often estimated from the relative mass loss associated with the thermogravimetric analysis (TGA). In the present case we can also determine

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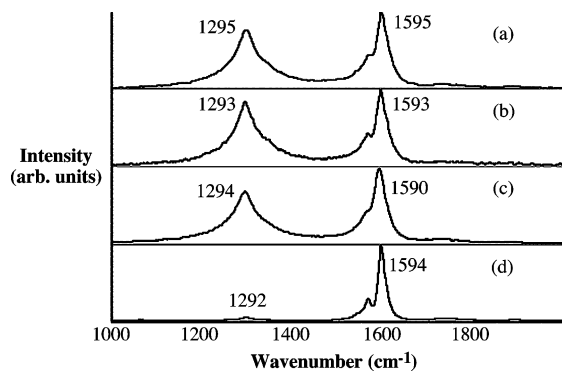


Figure 1. Raman spectrum of (a) GLY-SWNT (**1**), (b) AHA-SWNT (**2**), (c) AUDA-SWNT (**3**), and (d) pristine SWNTs using 780-nm excitation, showing the relative intensity of the D (disorder) mode at ca. 1295 cm^{-1} versus the tangential G mode at ca. 1595 cm^{-1} .

the functionalization by the relative intensities of the C, O, and N peaks in the XPS. On the basis of XPS, the SWNT-C substituent ratios may be calculated to be 18:1 (**1**), 16.8:1 (**2**), and 15:1 (**3**). These compare favorably with the ratios calculated from TGA measurements (15:1 (**1**), 16:1 (**2**) and 20:1 (**3**)), suggesting that TGA does provide a reasonable measure of sidewall functionalization.

The Raman spectra using 780-nm (red laser) excitation for SWNTs **1–3** (along with unfunctionalized SWNTs) are shown in Figure 1. The presence of a significant D (disorder) mode at ca. 1295 cm^{-1} is consistent with sidewall functionalization.¹⁶ We have shown that the relative intensity of D mode versus the tangential G mode (ca. 1595 cm^{-1}) is a measure of both the level of substitution and the distribution of substituents.⁹ The similarity in the magnitude of the D mode, and the calculated substituent concentrations, suggests that the substituents are similarly distributed for all three derivatives.

Figure 2 shows a representative atomic force microscopy (AFM) image and the height measurements of **2**, confirming the presence of individual SWNTs showing the presence of regions of functionalization along the SWNT. We have shown previously that such variations are common for reactions of F-SWNT,⁹ and based upon the discussion above we propose that SWNTs **1** and **3** would have a similar sidewall functional group distribution.¹⁷ The measured heights of the functionalized regions for **2** (ca. 2.0 nm, see Figure 2b) as compared to the SWNT diameter (ca. 1 nm) are consistent with the calculated length of N(H)(CH₂)₅CO₂H (molecular modeling with PC Spartan) in an extended conformation (1 nm). Transmission electron microscopy (TEM) confirms the presence of surface-roughened functionalized SWNTs (Figure 3).

The glycine and 11-aminoundecanoic acid-derivatized SWNTs (**1** and **3**) show no solubility in water. In contrast, AHA-SWNT (**2**) is highly soluble in aqueous solution and solutions of ca. 0.5 mg mL^{-1} are formed readily at room temperature (Figure 4). We note that no precipitation of **2** is observed over extended time or with centrifugation. Thus, although the analyses of SWNTs **1–3** show them to have similar levels of functionalization, their solubilities are quite

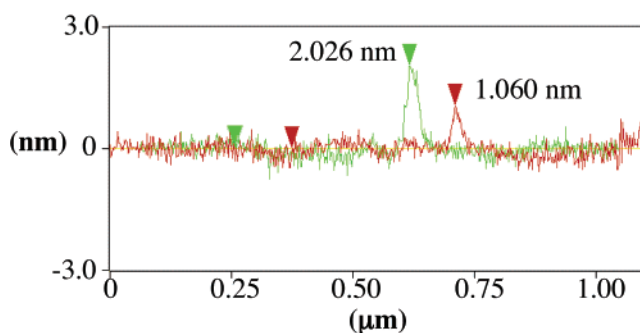
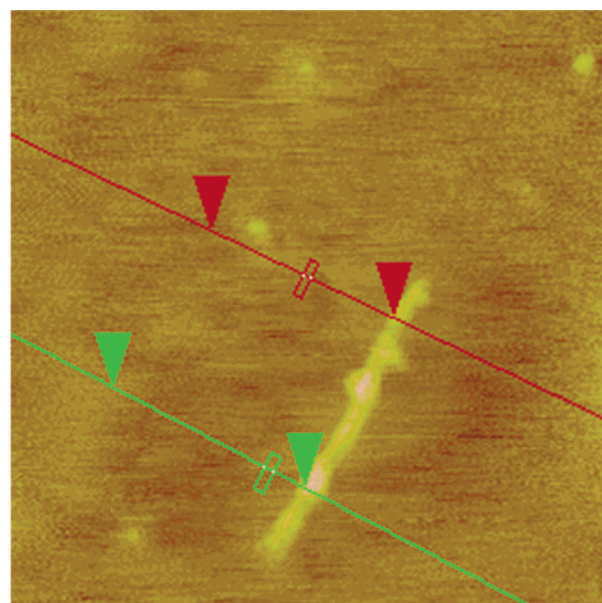


Figure 2. Representative tapping-mode AFM image and height profile of AHA-SWNT (**2**).

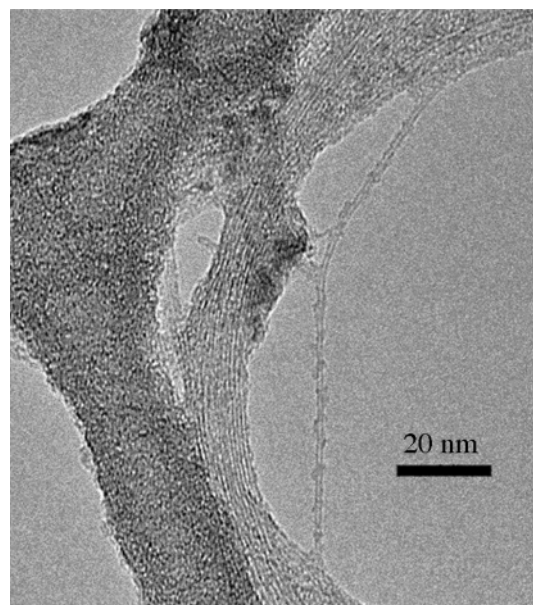


Figure 3. TEM of AHA-SWNT (**2**) suspended from lacy carbon TEM grid.

different. We propose that the lack of solubility of **1** is due to the presence of intramolecular hydrogen bonding (vide

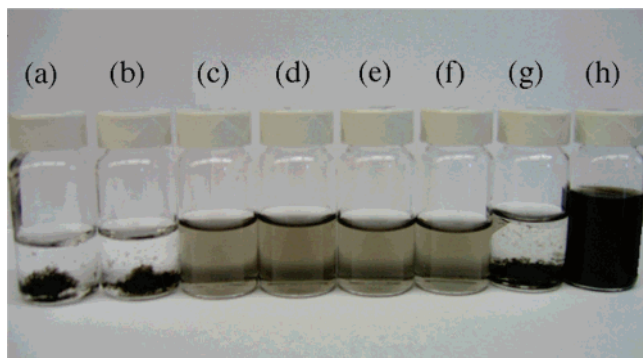


Figure 4. Photograph of AHA-SWNT (**2**) samples at pH 1, 3, 5, 7, 9, 11, and 13 (a–g, respectively), and a concentrated (0.5 mg mL^{-1}) solution in di- H_2O (h).

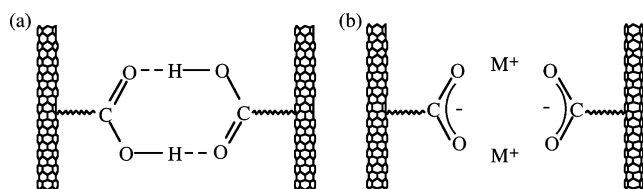


Figure 5. Schematic representation of the proposed aggregation of AHA-SWNT (**2**) under (a) acidic and (b) basic conditions.

supra). In an analogous manner to long-chain aliphatic self-assembled monolayers (SAMs), the lack of solubility of AUDA-SWNT (**3**) is presumably due to the substituents being of sufficient length to allow folding over, creating a hydrophobic appearance to the functionalized SWNT's surface. We propose that the length of **2** is sufficient to preclude folding and results in the carboxylic acid substituents being exposed, creating hydrophilic regions on the functionalized SWNT. Thus, we can show that with similar functional groups and levels of functionalization the length of the substituent's side groups control the solubility.

The pH dependence of the solubility of **2** is worthy of mention. Under acidic conditions ($\text{pH} \leq 3$), SWNT **2** is insoluble (Figure 4). Neutralization of the sample causes the SWNTs to dissolve (unless the ion concentration is too high, see below), whereas subsequent reacidification causes *rapid* precipitation. In contrast, raising the pH of a solution above pH 11 results in the *slow* precipitation of the SWNTs over 5 h (Figure 4). The resulting solid does not redissolve once the pH is reduced by the addition of acid. Analysis of the dried SWNTs isolated from a pH 13 solution shows it to be identical to the starting sample, and no decomposition of the sample has occurred. If the solute is decanted from a pH 13 sample and the solid is filtered it will redissolve in neutral water. On the basis of the foregoing and the relative $\text{p}K_a$ of aliphatic carboxylic acids, we propose that SWNT **2** is fully protonated below pH 3, that is, AHA-SWNTs are close to neutral. The intermolecular hydrogen bonding of carboxylic acids is well known and we propose that under acidic conditions the AHA-SWNTs form hydrogen-bonded aggregates that are insoluble (Figure 5a). This aggregation is reversed readily by alteration of the pH. For $3 < \text{pH} < 11$, the AHA-SWNTs are anionic and as such repel each other

to form a homogeneous solution. The lack of solubility under basic conditions is not due to any chemical alteration of the SWNTs but is a function of the ionic strength of the solution. Precipitation can occur with addition of NaOH ($\text{pH} = 13$) and equally well with NaCl at $\text{pH} = 9$. In both cases, the precipitation reaction is slow and not reversed by addition of acid. We propose that in these cases the insolubility is due to aggregation of SWNTs mediated by the presence of a critical concentration of cations (Figure 5b).

In summary, we report that the aqueous solubility of amino acid functionalization SWNTs, prepared readily from F-SWNTs, may be controlled through the length of the substituents aliphatic chain. The pH stability of the solution appears to be limited only by the $\text{p}K_a$ of the acid and the ionic strength of the solution. The stability of the solutions of AHA-SWNT (**2**) under physiologically relevant conditions merits further study.

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Supporting Information Available: TGA and IR spectra of functionalized SWNTs. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (13) F-SWNTs (ca. 30 mg) were sonicated in DMF (100 mL) for 10 min, resulting in complete dispersion to form a dark solution. 6-amino-hexanoic acid (600 mg) that was well dispersed in DMF (200 mL) and 4–5 drops of pyridine (catalyst) was added to this. The reaction mixture was stirred (under N_2) for 5 days at 90°C . The reaction

mixture was filtered through a 0.2- μm Cole Palmer Telfon membrane and washed with water and acetone to ensure complete removal of unreacted 6-aminohexanoic acid, reaction byproducts, and solvent. The AHA-SWNTs (2) were dried overnight in vacuum at 70 °C. Glycine-SWNT (1) and AUDA-SWNT (3) were made by a similar method.

- (14) The magnitude of the C–H stretch bands follows the expected trend for the length of the aliphatic chains.

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