

Measuring the Stability of Supramolecular Complexes in the Proximity of Single-Walled Carbon Nanotubes

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Cet article est dédié à Jean-Marie Lehn, père de la chimie supramoléculaire, à l'occasion de son 80ème anniversaire.

The decoration of SWNTs with supramolecular motifs is a common strategy for their subsequent noncovalent functionalization. However, due to the lack of a standard methodology, there are no quantitative measurements showing the extent to which the supramolecular equilibria are affected by one of the host-guest couple being anchored to the SWNT. Here, we use a method we initially developed to quantify association of small organic molecules to the walls of SWNTs to compare association constants of two host-guest systems, a Hamilton receptor-cyanuric acid derivative and a crown ether-ammonium couple, in solution and when the host is covalently attached to the SWNTs. Our data show that association does occur, but the stability of the complexes is significantly affected, as reflected in a sizable reduction in their association constant, when compared to solution.

Measuring is the heart of the scientific method. Hypothesis are supported or disproven by experimental data. However, when the scientist cannot measure the system of interest, we resort to extrapolation of data from the closest measurable system. This is, for instance, commonplace in the biomedical field, where the complexity of living systems, and the moral implications of experimenting with them,^[1] often prevents quantitative measurements, that are instead extrapolated from *in vitro* models.^[2–4] On a much less complex level, the supramolecular chemistry of single-walled carbon nanotubes (SWNTs) has also been dominated by qualitative or extrapolated quantitative data,^[5–9] due to the lack of a standardized method to measure association constants in supramolecular equilibria involving SWNTs.^[10–11] In particular, host-guest systems with large binding constants (K_a) in solution have been routinely used to functionalize SWNTs via noncovalent forces, assuming

that the stability of the supramolecular complexes will remain intact. The following are some representative examples: Martín and cols. have recently described the covalent decoration of SWNTs to later use guanidinium-carboxylate couples to associate porphyrin chromophores.^[12] Teams led by D'Souza and Ito used ammonium-crown ether recognition to a very similar end, in this case using pyrene as a noncovalent anchor to the SWNT for the ammonium group.^[13] Earlier, Stoddart and Heath had used ammonium-crown ether, and dioxynaphthalene-“blue box” interactions to build pseudorotaxane architectures on SWNTs.^[14]

We have developed a method to directly measure K_a of small organic molecules towards SWNTs.^[15–16] Our method benefits from the insolubility of SWNTs: we allow a mixture of a soluble guest molecule and the SWNTs to reach thermodynamic equilibrium, and then filter to separate the insoluble SWNT-guest complex from the soluble free guest. We then quantify the amount of bound guest molecule through thermogravimetric analysis (TGA). By repeating this experiment at different initial concentrations of guest molecule, we can plot binding isotherms and extract association constants by using a standard binding isotherm.^[17] Using this method, we have been able to determine binding constants of a variety of pyrene-based guest molecules towards SWNTs, observing clear differences between size, solvent and electronic effects. We complemented the experimental results with comprehensive theoretical modelling by the groups of Ortí and Comer.^[16]

In this work, we directly measure K_a of host-guest pairs in which one of the molecular components is covalently connected to SWNTs, and compare it to the K_a in absence of the SWNT, to quantify the influence of the nanotube on the supramolecular equilibria (Figure 1a).

To this end, we decided to study systems featuring both large and more moderate association constants. As tight binding host-guest couple ($\log K_a > 5$), we chose a Hamilton receptor-cyanuric acid derivative pair (HR-cy in Figure 1b),^[18] which has been thoroughly studied before,^[19] and has been used by Hirsch and co-workers in a supramolecular approach to solubilise SWNTs.^[20] As weakly binding host-guest pair ($\log K_a \approx 3$), we chose a 18-crown-6-ammonium system (Crown-Am in Figure 1b), similar to those used by D'Souza and Ito in connection with SWNTs.^[13] In order to compare the K_a with and without SWNTs, we tagged the guest molecules with a tris (bipyridine)ruthenium(II) dye, while the hosts were both decorated with an aniline group for their covalent attachment to the SWNTs by means of *in situ* diazonium chemistry.^[21] To

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 Supporting information for this article is available on the WWW under <https://doi.org/10.1002/open.202000018>

 An invited contribution to a Special Collection dedicated to Functional Supramolecular Systems

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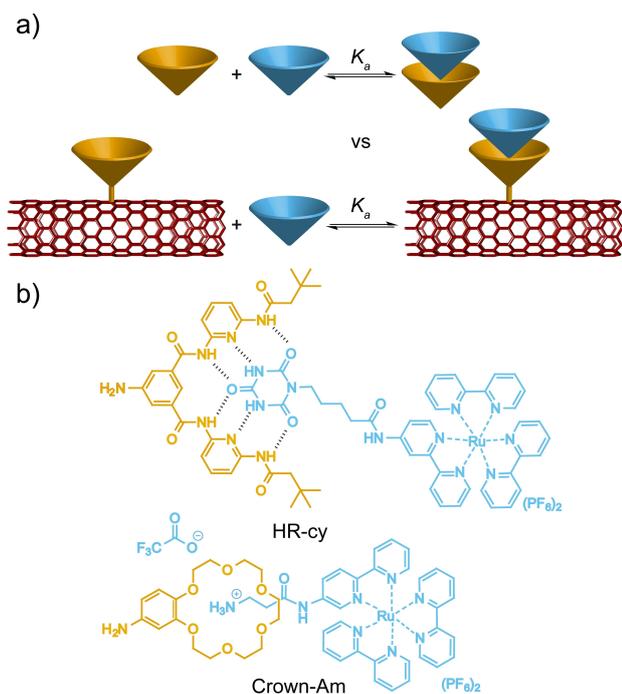


Figure 1. a) Schematic representation of a host-guest binding process (top) and a host-guest binding process where the host is covalently attached to a SWNT (bottom). b) Chemical structure of the Hamilton receptor-cyanuric acid derivative pair (HR-Cy) and the 18-crown-6-ammonium system (Crown-Am).

that end, a mixture of SWNTs ($1 \text{ mg} \cdot \text{mL}^{-1}$) in NMP was ultrasonicated for 20 min. After this time, the corresponding host molecule (the aniline derivatized Hamilton receptor or the 4'-Aminobenzo-18-crown-6) and boron trifluoride diethyl etherate were added. Isoamyl nitrite was used as oxidant. The mixture was stirred for 5 h, filtered through a $0.2 \text{ }\mu\text{m}$ -pore PTFE membrane and washed several times with THF to ensure the total removal of adsorbed host molecules. The SWNTs products showed a relatively large degree of functionalization through TGA (20% for SWNT-HR and 14% for SWNT-Crown, see SI, S4) while Raman was supportive of the covalent attachment, showing a significant increase in the I_D/I_G ratio, from 0.06 in the pristine SWNTs to 0.12 in both SWNT-HR and SWNT-Crown.

With all the molecular host-guest systems in our hands, we first determined the K_a of the host-guest couples in solution, without attachment to the SWNTs, by means of UV-vis titrations (see SI, S5 for details). For the HR-cy system we measured $\log K_a = 5.8 \pm 0.4$ in CH_3CN at room temperature, a value that is in the range of those determined for similar systems.^[22–24] In the case of Crown-Am, we measured $\log K_a = 3.6 \pm 0.5$, also in CH_3CN at room temperature, again in very good agreement with precedents in the literature.^[25–26]

To measure the binding constants of SWNT-HR-Cy and SWNT-Crown-Am, we followed the procedure we have described above,^[15–16] which we originally designed to study direct adsorption of organic molecules to the SWNT walls, but should also be applicable to the present problem, as it is based purely on mass balance. The experimental procedure can be summar-

ized as follows: covalently functionalized SWNTs ($1 \text{ mg} \cdot \text{mL}^{-1}$) were suspended in a solution of known concentration of the host molecule in CH_3CN . This mixture was stirred for 2 h to allow it to reach equilibrium. After this time, the suspension was filtered through a $0.2 \text{ }\mu\text{m}$ -pore PTFE membrane, retaining the guest-SWNTs complex. The solid obtained was analysed by TGA (air, $10^\circ\text{C} \cdot \text{min}^{-1}$) to quantify the amount of guest attached. We measure the weight loss between 250 and 475°C , where all the host-guest complex has been burned off, and take the initial SWNT-HR and SWNT-Crown as references. From the degree of functionalization and the mass of the sample analysed, we calculate the total mass of guest attached to the host, from which its free concentration in equilibrium is immediate. The same procedure is repeated for several initial concentrations of the guest molecule, ranging from 0 to near saturation in the solvent under study. A blank experiment, in which no guest is added, is run in all cases in order to determine the adsorbed/encapsulated solvent and this data is subtracted to the total weight loss. All the experiments were performed at room temperature.

The binding isotherms are obtained by plotting the degree of functionalization against the concentration of free host. Both the case of the SWNT-HR-Cy and the SWNT-Crown-Am showed the characteristic Langmuir-type shape and fitted very satisfactorily ($R^2 > 0.99$) to the standard 1:1 isotherm (Figure 2).^[15–16] From three independent titration experiments for each equilibrium, we obtained $K_a = (9.0 \pm 0.7) \cdot 10^3 \text{ M}^{-1}$, that is, $\log K_a = 3.95 \pm 0.03$, for SWNT-HR-Cy, and $K_a = (5.0 \pm 0.6) \cdot 10^2 \text{ M}^{-1}$, or $\log K_a = 2.7 \pm 0.6$, for SWNT-Crown-Am.

In order to evaluate the relevance of non-specific physisorption between the Ru-derivative guest and the SWNTs, the binding isotherms between guest and non-functionalized SWNTs were measured. Figure 3 shows the plots obtained for both guest molecules. Interestingly, the curves are very far from saturation, in the linear region of the isotherm. Consequently, the calculated association constants are small. In particular, we obtained: $K_a = 37 \text{ M}^{-1}$, that is, $\log K_a = 1.6$, for SWNT-HR-Cy, and $K_a = 0.013 \text{ M}^{-1}$, or $\log K_a = -1.9$, for SWNT-Crown-Am. The small association constants indicate that the physisorption of the guest is negligible when compared to the specifically bonded guest. These data validate the strategy of attaching specific supramolecular motifs to SWNTs to further functionalize them in a later stage using host-guest chemistry.

In conclusion, we show that the procedure previously described by our group for the determination of association constants towards SWNTs can be used as a reliable method for the determination of association constants between host-guest pairs attached to SWNTs. We confirm that binding does occur, and that it is significantly larger than non-specific physisorption. The obtained host-guest association constants involving SWNTs are smaller from that obtained in solution (from $\log K_a = 5.8 \pm 0.4$ to $\log K_a = 3.95 \pm 0.03$ for SWNT-HR-Cy and from $\log K_a = 3.6 \pm 0.5$ to $\log K_a = 2.7 \pm 0.6$, for SWNT-Crown-Am). This decrease in K_a is an important fact to consider when functionalizing SWNTs via noncovalent forces. The covalent bond SWNT-host destabilizes the further attachment of the guest in the binding sites, compromising the stability of the final complex.

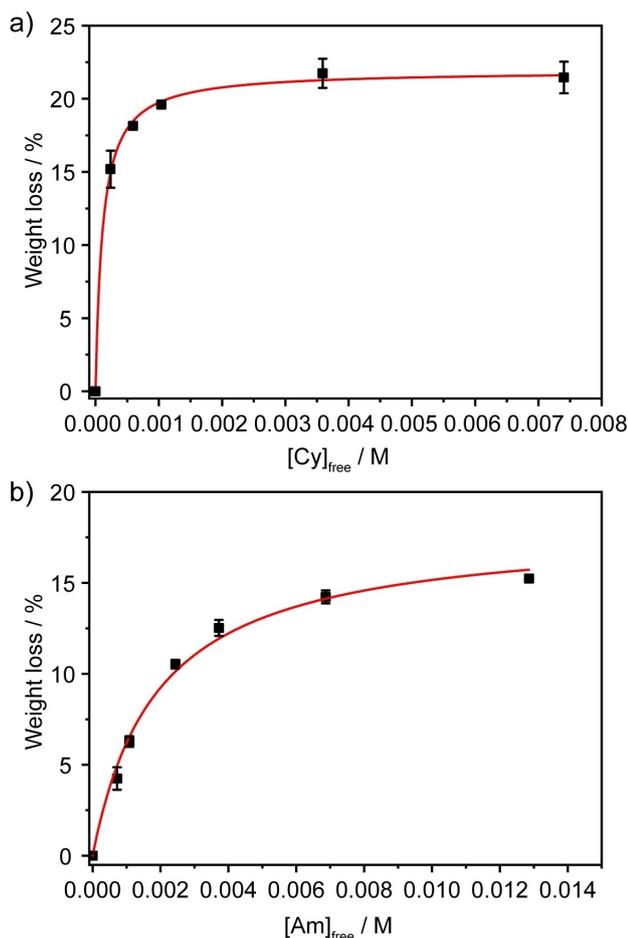


Figure 2. a) Titration of the Ruthenium dye-derived cyanuric acid (Cy) vs SWNT-HR and b) titration of the Ruthenium dye-derived ammonium (Am) vs SWNT-Crown.

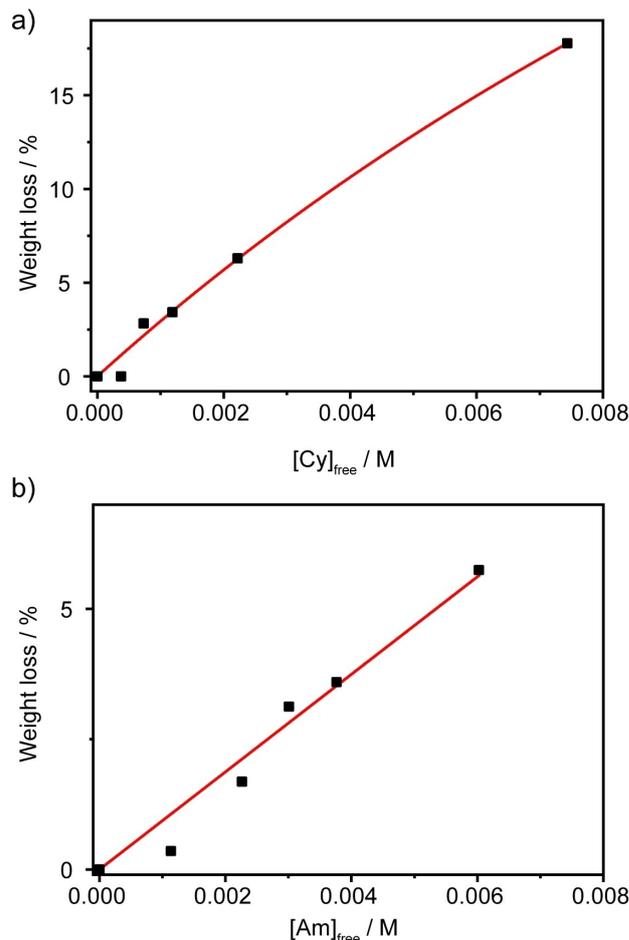


Figure 3. a) Titration of the Ruthenium dye-derived cyanuric acid (Cy) vs pristine SWNT and b) titration of the Ruthenium dye-derived ammonium (Am) vs pristine SWNT.

Overall, our quantitative analysis confirms that it is a valid strategy to covalently attach host molecules to the walls of SWNTs to later functionalize them via host-guest chemistry. However, when choosing this strategy, the chemist should consider that, once attached to the SWNTs, the host-guest association constants are probably smaller than those measured in solution.

Acknowledgements

We acknowledge funding from the European Union (ERC-StG-307609, ERC PoC 842606), MINECO (CTQ2014-60541-P and CTQ2017-86060-P), and the Comunidad de Madrid and the European Structural Funds for their financial support through FotoArt-CM project (S2018/NMT-4367) and MAD2D-CM S2013/MIT-3007. IMDEA Nanociencia acknowledges support from the "Severo Ochoa" Programme for Centres of Excellence in R&D (MINECO, grant SEV-2016-0686).

Conflict of Interest

The authors declare no conflict of interest.

Keywords: SWNTs · host-guest chemistry · supramolecular chemistry · nanoscience

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Manuscript received: January 18, 2020

Revised manuscript received: February 24, 2020