Scanning tunneling microscopy on cyclodextrin inclusion complexes

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Scanning tunneling microscopy on both cyclodextrins (CyDs) and their structural complex formed with a guest compound (1-adamantanemethanol) was performed on specimens obtained by deposition of CyD aqueous solutions onto highly oriented pyrolytic graphite. The CyD and guest compound image sizes were found to be satisfactorily consistent with molecular dimensions. In the absence of guest compounds, both α- and β-CyDs strongly interacted with each other, and formed regularly ordered structures. Guest compound addition resulted in a breakdown of the regular CyD structure, thus indicating that mutual CyD molecular interactions are suppressed by CyD-guest complex formations.

I. INTRODUCTION

Cyclodextrins (CyDs), doughnut-shaped molecules formed by cyclic linkage of 6–8 glucose units (Fig. 1), exhibit selective catalyses in various organic reactions, and have been widely used as artificial enzymes.[1] Additionally they have many useful applications/properties, e.g., chiral separation, stabilizing unstable compounds, and increasing water solubility of hydrophobic drugs. These specific properties can be directly attributed to the formation of an inclusion complex between the CyD and a guest compound, usually occurring in water, where the guest is accommodated in α- and β-CyD cavities having respective diameters of approximately 0.45 and 0.7 nm. Further information concerning CyDs's structures and their inclusion complexes is therefore quite important.

Methods previously employed for inclusion complex structure determination are ^{1}H-NMR (nuclear magnetic resonance) spectroscopy[2] and x-ray crystallography,[3] yet scanning tunneling microscopy (STM) has significant advantages over these methods since direct visual information can be obtained.[4-6]

Recently STM was used by Miles *et al.*[7] to observe a tosylated β-CyD lattice pattern which was found from tosyl residue images, and not from the β-CyD residue itself.

The study presented reports both the first STM observations of CyDs having no chemical modifications, and the results when using a CyD inclusion complex having a guest compound [adamantanemethanol (I)] addition.

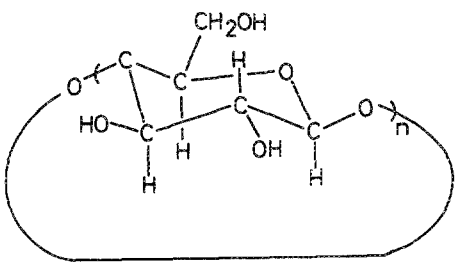
II. EXPERIMENT

STM specimens were prepared by deposition of 10^{-2} M CyD aqueous solutions (with and without a guest compound) on a freshly cleaved highly oriented pyrolytic graphite (HOPG). STM was performed by a Digital Instrument Co. microscope (in air at an ambient temperature) with Pt-Ir tips using a constant height mode. No thermal drift corrections were made.

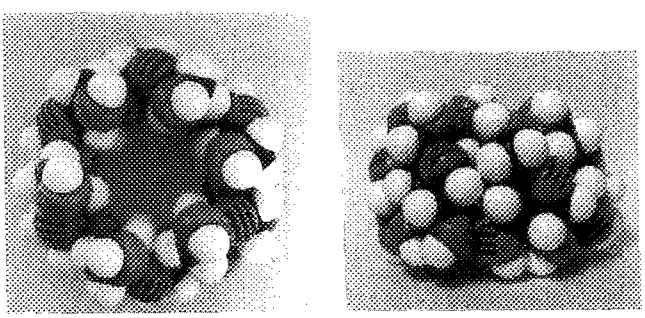
III. RESULTS AND DISCUSSION

A. "Empty" α-cyclodextrin (α-CyD-water complex)

Figure 2 shows a wide scan STM image (60 nm × 60 nm) of "empty" α-CyDs. The tip bias voltage (V_t) was -21.4 mV and the setting current (I_s) was 0.91 nA. Periodic structures can be seen over a wide area range, and in a magnified image [Fig. 3(a)], columns of parallel running protrusions



(a)



(b)

FIG. 1. Molecular structure (a) and Corey–Pauling–Koltun molecular model (b) of CyDs: the diameters of the cavities of α- and β-CyDs are, respectively, 0.45 and 0.7 nm, and the depth is 0.7 nm. The CyD outer diameters are around 1.4 and 1.65 nm.

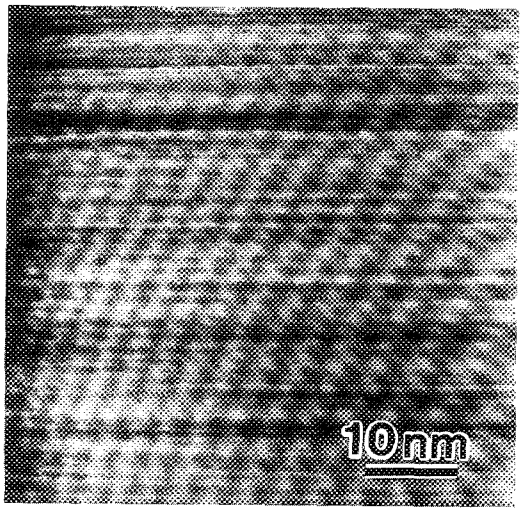


FIG. 2. STM image of "empty" α-CyDs ($V_t = -21.4$ mV, $I_s = 0.91$ nA, 60 nm$\times$60 nm).

are apparent, with all these protrusions being tilted along the column's longitudinal axis. The size of this trapezoid-shaped protrusion (estimated with no drift corrections to be $\sim$1 nm$\times$2 nm) is almost identical to the α-CyD molecule which is "lying" with its apolar outside wall on the apolar graphite substrate. This "lying" conformation is possibly more favorable than the "sitting" conformation where the α-CyD hydroxyl residues are contacting the apolar substrate [Fig. 3(b)].

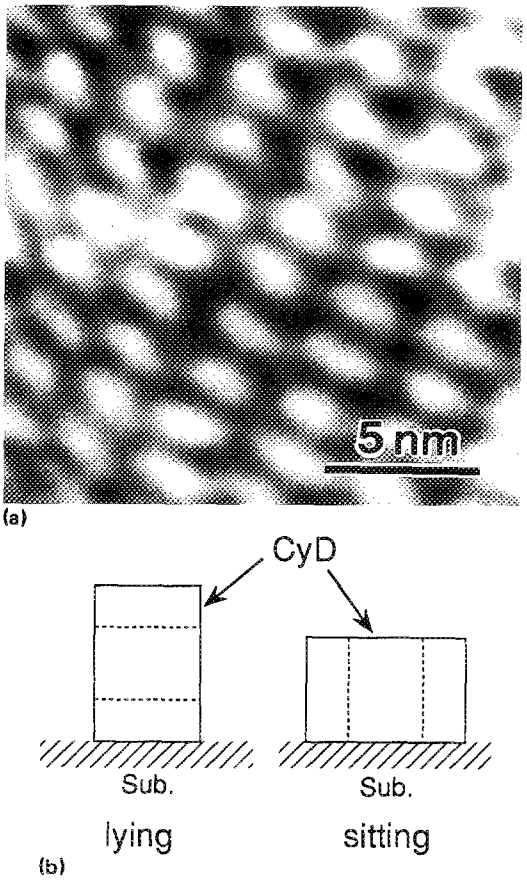


FIG. 3. (a) Magnified STM image of "empty" α-CyDs ($V_t = -24.1$ mV, $I_s = 0.91$ nA, 18 nm$\times$18 nm). (b) Conformations of CyDs on HOPG.

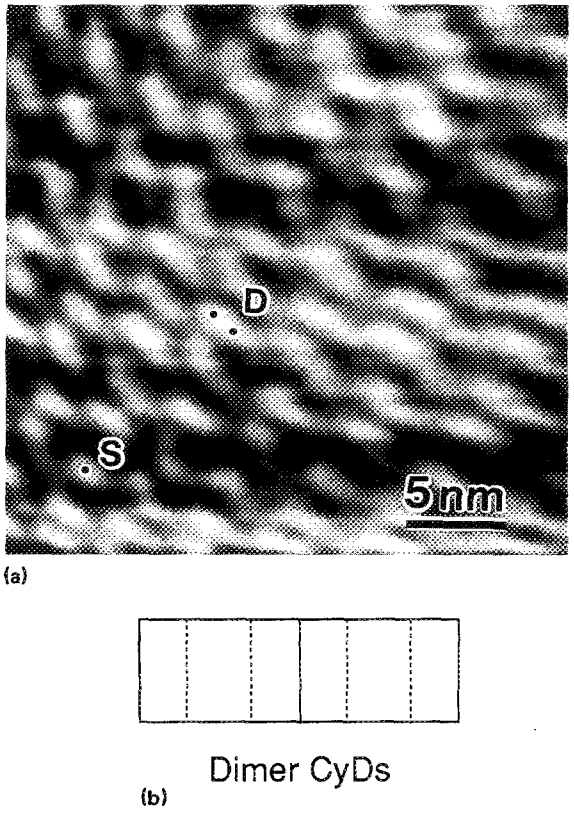


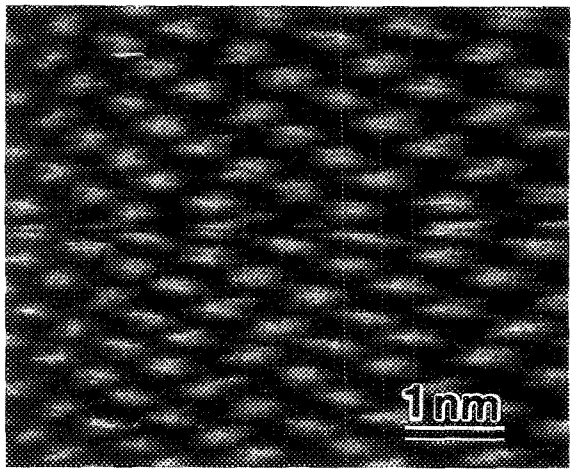
FIG. 4. (a) Magnified STM image of "empty" α-CyDs ($V_t = -24.1$ mV, $I_s = 0.91$ nA, 30 nm$\times$30 nm). (b) Dimer structure of CyDs.

Figure 4(a) shows another magnified image of "empty" α-CyDs, where CyD molecular aggregate formation is dominant. Three-dimensional mosaic-like structures which are constructed from component blocks are clearly shown. In addition to the single CyDs, labeled "S" in the figure, bigger blocks with a size of $\sim$1 nm$\times$4 nm, labeled D, can be seen, which are believed to be α-CyD dimers, consisting of two α-CyD molecules (located in the same plane and connected to each other at the cavity's apolar outside wall) [Fig. 4(b)].

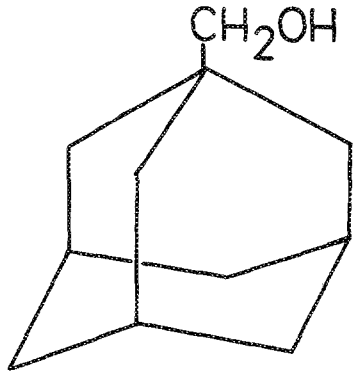
B. α-CyD inclusion complex

Figure 5(b) shows the structure of adamantanemethanol (I) which was employed as a guest compound. The adamantane moiety has a rigid spheric structure (0.6 nm diam), which promotes a simple STM result analysis. A hydroxymethyl residue was attached to increase the solubility in water. The adamantane moiety has been confirmed to be too bulky to be totally included inside the α-CyD cavity, and therefore it is located on top [Fig. 6(b)].[8]

An STM image of I/HOPG with no α-CyD is shown in Fig. 5(a). The cyclic protrusions diameters are 0.4–0.5 nm, which is consistent with I's molecular size.



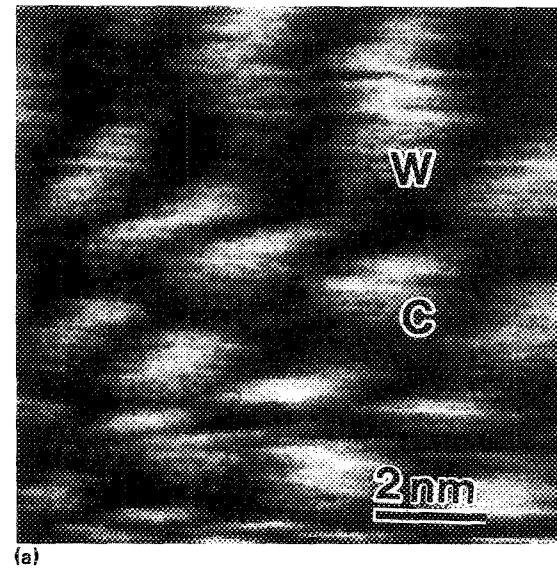
(a)



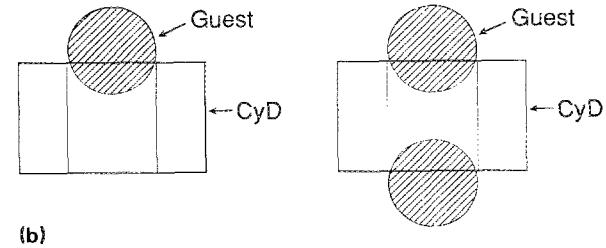
Adamantane
-methanol

(b)

FIG. 5. STM image of adamantanemethanols (I) without CyD ($V_t = 38.5$ mV, $I_s = 0.23$ nA, 6 nm×5 nm) (a) and its molecular structure (b).



(a)



(b)

FIG. 6. STM image of (α-CyD)-I complexes ($V_t = 31.4$ mV, $I_s = 0.91$ nA, 10 nm×10 nm) (a) and its molecular structures: (b) I/(α-CyD), (c) I/(α-CyD)/I.

Figure 6(a) shows the STM image of the α-CyD-I complexes. The periodic pattern observed in the absence of I (Figs. 2 and 3) is not visible due to the complex formation between α-CyDs and the guests, suppressing the interaction between the two α-CyD molecules. Due to the weaker interaction written above, the molecules are not stable against the measurement, thereby the molecular images obtained here are not so clear as those obtained for the CyDs without guests. Cyclic images, although not very clear, are evident near some α-CyD molecules, labeled "C" in the figure, and are probably results of the guests being located on the cavity's top [Fig. 6(b)]. The image labeled "W" at the top right-hand side of Fig. 6(a), is concluded to be associated with a 1:2 complex formation between α-CyD and the guest compound [Fig. 6(c)]. In order to obtain a more stable and clearer image, the interactions between the CyD compounds and the substrates are being studied.

C. "Empty" β-cyclodextrin (β-CyD-water complex)

"Empty" β-CyDs also exhibited a regular STM pattern as shown in Fig. 7. The size for each protrusion was 0.6 nm×0.9 nm (no drift correction), and is nearly identical with β-CyD's molecular dimension.

A significant difference between α-CyD and β-CyD images is the fact that the molecular packing of β-CyD is more tight, i.e., β-CyD molecules are seen by STM to be virtually contacting each other. This is considered to be attributable to the fact that the interactions between the two β-CyD molecules are stronger than those between the two α-CyD molecules. This conclusion is supported by the fact that β-CyD's

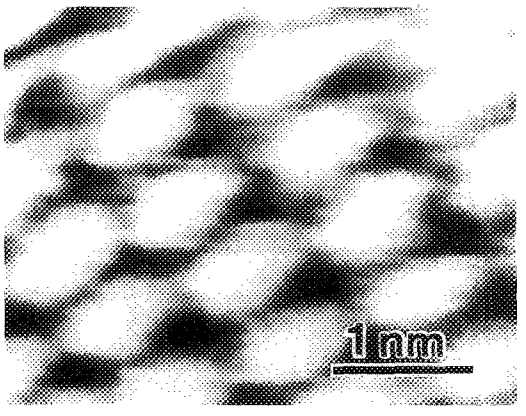


FIG. 7. STM image of "empty" β-CyDs ($V_t = 31.1$ mV, $I_s = 0.54$ nA, 4 nm×3 nm).

solubility (1.85 g/100 ml) is considerably smaller than α-CyD's (14.5 g/100 ml).

IV. CONCLUSION

The study presented showed that CyD molecular arrangements, either with or without a guest compound, can be clearly visualized by STM, and also that unique information can be obtained on the structural arrangement of the complex that is formed between CyD and a guest compound. Image resolution improvements which will aid in further research are in progress.

ACKNOWLEDGMENTS

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