Direct Observation of Cation Complexation of 18-Crown-6 by Atomic Force Microscopy Using Chemically Modified Tips

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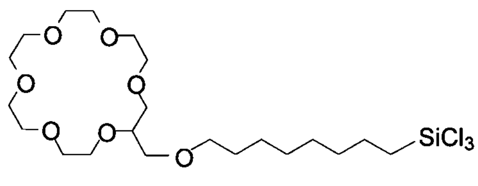
Intermolecular forces between 18-crown-6 and guest ions have been measured by atomic force microscopy using AFM tips modified chemically with an alkylsilane derivative having 18-crown-6 moiety. The greater adhesion forces were observed with the crown-ether modified tip than with bare tips on mica substrate in aqueous solutions containing K^+, probably due to the complexation between 18-crown-6 moiety on tip and K^+ in solution. Specific interactions based on cation complexation of 18-crown-6 have been observed in ethanol on mica substrate treated with (3-aminopropyl)triethoxysilane ($–NH_3^+$).

Specific intermolecular forces play important roles in molecular recognition phenomena in biological systems. Direct measurements of the intermolecular forces have attracted growing interests from fundamental and practical points of view. Recently, atomic force microscopy (AFM) has been a versatile tool for measuring specific intermolecular forces in host–guest and supramolecular systems, such as antibody–antigen conjugates,[1–3] strands of DNA,[4] DNA nucleotide base conjugates,[5] Ag^+–methylsulfide,[6] Ni^{2+}–histidine complexes,[7] and β-cyclodextrin–ferrocene,[8] and rupture forces of covalent bonding.[9] Specifically, AFM using chemically modified tips (chemical force microscopy CFM),[10–12] is very attractive because CFM allows the imaging of chemical functional groups on the substrate with high spatial resolution. For the purpose, AFM tips are often modified with target molecules by using self-assembled monolayers (SAMs) of organosilane or thiol compounds to control the tip-substrate interaction.

It is well-known that crown ethers complex guest ions by ion–dipole interaction, but specific intermolecular forces concerning their cation complexation have not been measured directly with AFM, to the best of our knowledge. In the present study, we have attempted to measure the specific intermolecular forces between 18-crown-6 and guest ions using AFM tip modified with an alkylsilane having 18-crown-6 moiety (18-crown-6/tip).

We synthesized 8-(trichlorosilyl)octyloxymethyl-18-crown-6 (**1**) by hydrosilylation of 7-octenyloxymethyl-18-crown-6 with trichlorosilane using hydrogen hexachloroplatinate(IV) hexahydrate as the catalyst. The precursor, 7-octenyloxymethyl-18-crown-6, was obtained from hydroxymethyl-18-crown-6 and 8-bromo-1-octene by Williamson synthesis.



Scheme 1. 8-(trichlorosilyl)octyloxymethyl-18-crown-6 (**1**) used for modification of AFM tip.

AFM cantilevers (length 100 μm, spring constant 0.09 N/m, Seiko Instruments, Inc.) were cleaned by soaking into piranha solution (H_2SO_4/H_2O_2=7/3) and then immersed successively into 1 M NaOH, 1 M HCl, and 1 M NaOH aqueous solutions for 5 min each. The cantilevers were rinsed with deionized water and heated at 120 °C for 10 min. Then, the cleaned AFM tips were treated with **1** by immersion into benzene solution containing **1**, which was prepared just prior to use. After rinsing with toluene, ethanol and deionized water, the resulting tips were heated at 100 °C for 30 min. (3-Aminopropyl)triethoxysilane (APTES)-modified mica substrates (APTES/mica) were prepared by immersion of freshly cleaved mica into an APTES toluene solution for 30 min, followed by rinsing and heating at 100 °C for 30 min. Protonation of APTES on the APTES/mica surface was achieved by immersion of the APTES/mica into 0.1 M HCl for 30 min and drying in air. All force-curve measurements were performed using SPA300 microscope (Seiko Instruments, Inc.) at room temperature. The substrate and cantilever were mounted in aqueous or ethanol solution using a liquid cell.

Figure 1 shows typical force curves observed with a bare tip (Figure 1a) and 18-crown-6/tip (Figure 1b) on mica in 0.1 M HCl aqueous solution containing 10 mM $KClO_4$. With 18-crown-6/tip, the greater adhesion force was observed than with the bare tip. In the absence of K^+ or in the presence of Li^+, such a great adhesion force was not observed. These results suggest that the appearance of the adhesion force as shown in Figure 1b would be caused by complexation of the 18-crown-6 moiety on tip with K^+ in solution. Since mica has the cation exchange ability, the increase in adhesion force is probably explained by the interaction between K^+ complexed with 18-crown-6 on tip

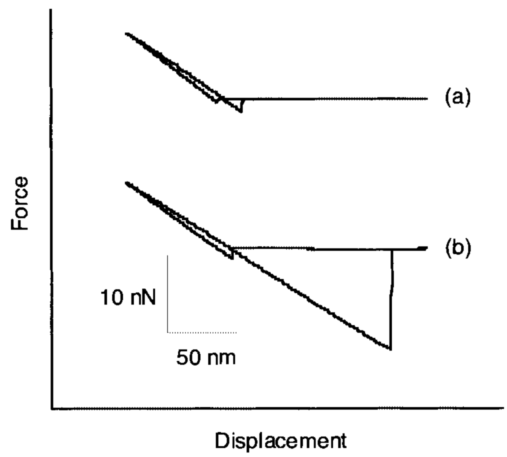


Figure 1. Force curves observed with bare tip (a) and 18-crown-6/tip (b) on mica substrate in 0.1 M HCl aqueous solution containing 10 mM $KClO_4$.

and negatively charged cation-exchange sites on mica surface. Some K^+ adsorbed on mica may be replaced when the tip approaches mica. The K^+ addition effect is supported by the fact that 18-crown-6 derivatives have a powerful complexing ability with K^+.

Figure 2 shows histograms of adhesion forces observed using 18-crown-6/tip on protonated APTES/mica in ethanol solution. Figure 2a was obtained at the force-curve measurements in a measuring bath without K^+. The distribution of adhesion forces observed in the presence of K^+, as shown in Figure 2b, was very different from that observed in the absence of K^+ (Figure 2a). The smaller adhesion forces were observed in the presence of K^+, indicating the blocking effect by K^+, i.e., the added K^+ in solution interferes the complexation of the 18-crown-6 moiety on tip with $–NH_3^+$ sites on APTES/mica. In the control force-measurements using 18-crown-6/tip on mica substrate modified with octadecyltrichlorosilane, which cannot show any ion–dipole interaction with 18-crown-6 moiety, observed adhesion forces were smaller than on APTES/mica and the histogram of them was similar to Figure 2b. These smaller adhesion forces, which may be due to non-specific interactions such as van der Waals interaction, imply that non-specific interaction hardly exists between tip and substrate in ethanol. These observations may suggest that the specific interaction forces between 18-crown-6 and ammonium ion would be measured by AFM using 18-crown-6/tip. The multiple pull-off events[3,8] were sometimes observed at force measurements on APTES/mica. This supports that such adhesion forces as shown in Figure 2a are based on specific interactions.

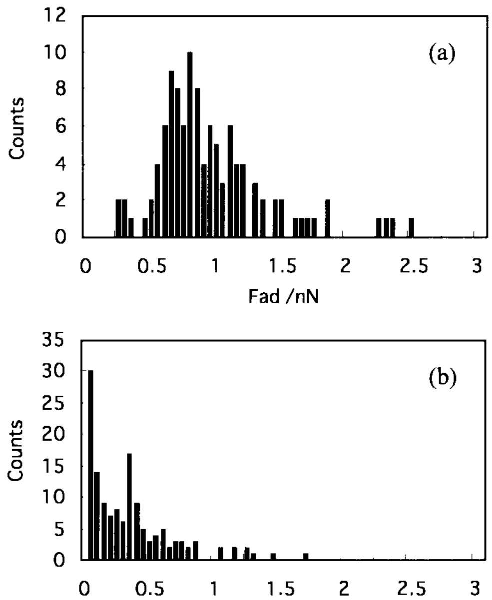


Figure 2. Histograms of adhesion forces observed on protonated APTES/mica with 18-crown-6/tip in ethanol (total counts = 110) (a), and in ethanol solution containing 10 mM CF_3SO_3K (total counts = 139) (b).

The adhesion forces (force curves) obtained with 18-crown-6/tip changed from one tip-substrate combination to another. The relatively low reproducibility may be attributed to some uncertainty of tip modification with **1**, due to the low density of silanol groups on tip surface and/or the formation of polymeric siloxane on tip in the modification process. Interestingly, when 18-crown-6/tips were used on mica substrate, the force curves often had multiple pull-off steps, showing "saw-tooth" patterns[13] in the retraction region. The "saw-tooth" patterns were never observed in the absence of K^+. The appearance of these unique force curves implies the presence of polymeric siloxane chains on tip surface, which might in turn bring about the multiple interactions between tip and substrate, based on the cation complexation of the 18-crown-6 moiety on tip with guest ions.

Further observation and analysis of these force curves could allow the evaluation of single intermolecular force between 18-crown-6 and guest ions. This technique may also be applicable to other host–guest systems.

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