Surface Behavior of Boronic Acid-Terminated Silicones

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ABSTRACT

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There is interest in developing responsive, surface-active species that can be used to confer functionality and sensing capabilities to surfaces. Controlling structure, organization and material properties of thin film coatings requires an understanding of the nature of intermolecular interactions taking place at the air-water and air-solid interfaces. With the objective of combining differential diol (sugar) binding capabilities of boronic acids with surface activity of silicones, a series of boronic acid-derived bola amphiphiles (silicone boronic acid, SiBA) have been characterized at the air-water interface as a function of silicone chain length and subphase composition. Isotherms of SiBA show similar phase transitions as poly(dimethyl)siloxane but display a sharp increase in pressure before film collapse, indicating strong tethering of boronic acid headgroups to the subphase. For comparison, hydride and amine-terminated silicones were studied. Boronic acids occupy a relatively larger molecular area at the interface than other polar headgroups, suggesting they adopt a planar orientation on the subphase possibly forming boronic acid-boronic acid complexes rather than being submerged into the subphase. SiBA showed low sensitivity for sugars in the subphase at pH 5.5 which appears to be improved by addition of amines. Testing if amines alone are responsible for the observed shifts, a series of amines in the absence of diols were added to the subphase. The addition of amines in the subphase led to isotherm shifts to higher molecular areas and decreased film stability. While generally small molecule crosslinkers in the subphase increase film stability, for SiBA, they may be disrupting the boronic acid self-complexations, making the film less resistant to collapse.

Acknowledgements

I would like to thank my parents and my husband for their unconditional love and support throughout my studies and for putting up with my ups and downs. Thanks to all my lab mates for making this such an enjoyable journey. Thank you, Rolf, for being so patient with me and for your endless help on all the instruments and programs. Last but not least, I would like to thank my supervisors, Dr. DeWolf and Dr. Brook, for their guidance and support throughout my M.Sc. and making it such a great experience.

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Chapter 1. Introduction

1.1. General Overview

In the past couple of decades, boronic acids have gained attention in the fields of chemistry and biology. From the 1980s onwards there has been a drastic increase in synthetic, biological and medicinal applications of boronic acids.[1] Exploiting their sensitivity for diol compounds, there has been a lot of interest in developing new and improved boronic acid-based biosensors such as those for sugar recognition.

Silicone polymers such as poly(dimethyl)siloxane, PDMS, have also been studied for years for their exceptional properties such as backbone flexibility, biocompatibility, thermal stability, low intermolecular interactions and low surface tension.[2] Modified with hydrophilic headgroups, silicone surfactants can be used as agricultural adjuvants,[3] foam stabilizers in polyurethane[4] and in many personal care products.[5-7]

Silicone surfactants combined with boronic acid functionality yield exceptional surface properties for macroscopic films.[8] It is essential to understand the nature of the intermolecular interactions governing these surface properties in order to control the structure and organization of these films. If nanofilms of silicone boronic acids (SiBA) exhibit similar properties as those seen for macroscopic films, they may potentially be used for applications such as thin film coatings to make biocompatible surfaces or biosensors for saccharides or other biologically relevant diol compounds.

1.2. Boronic Acids

1.2.1. Boronic Acid-Diol Binding

Boronic acids bind to 1,2- and 1,3-diol compounds by forming reversible ester linkages (Figure 1.1). At pH values below their nominal (solution) pK_a, boronic acids are sp^2 hybridized, and in their neutral state. With an empty p-orbital these boronic acids act as mild Lewis acids. At higher pH, the boronic acids adopt a tetrahedral geometry (sp^3 hybridized) leading to a negative charge on the boron atom because of their interaction with water, or more commonly, hydroxide. In this state, it is favorable to bind diol compounds forming reversible ester linkages.[1] Lorand

and Edwards first determined the association constants of boronic acids with saccharides by monitoring the drop in pH upon the addition of saccharides in solution.[9] Additionally, the use of boronic acids as saccharide sensors (under biological conditions) usually requires the presence of a Lewis base such as a tertiary amine.[10] The amine enhances boronic acid-saccharide binding at neutral pH by promoting the tetrahedral boronate anion form.

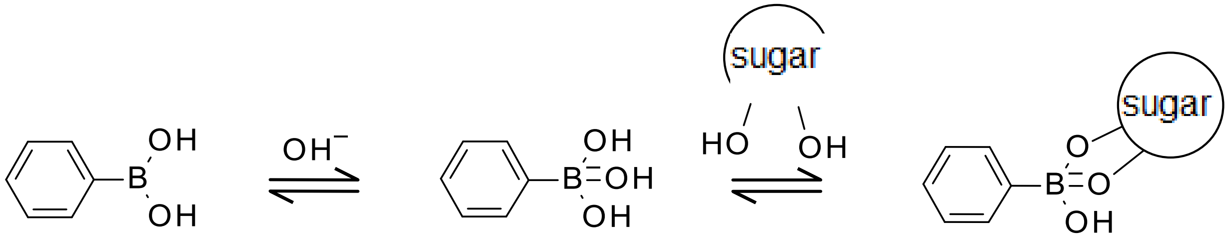


Figure 1.1. Phenylboronic acid-sugar complexation.

The properties of the boronic acid can be tuned based on the R group attached to it. Thus, the R group also plays a role in its affinity for different diol compounds. For example, the presence of a bulky substituent would decrease the likelihood of forming the tetrahedral boronate anion. Additionally, electron-withdrawing groups increase the acidity of the boronic acid by forming stable hydroxyboronate anions.[1] Phenylboronic acid has a comparable acidity to phenol with a solution pK_a of about 8.8.[1] They bind to different sugar molecules with different affinities, which gives rise to their selectivity. For example, the association constant (K_{eq}) for phenylboronic acid with glucose is 5 M^{-1} whereas for fructose it is 160 M^{-1}.[11, 12] James et al. explained that this is because the boronic acid prefers the β-D-fructofuranose form over the α-D-glucofuranose.[13] The relative affinity for boronate anions for saccharides follows this order: cis-1,2-diol > cis-1,3-diol > trans-1,2-diol[14] giving rise to the selectivity of boronic acids for one diol over another.

1.2.2. Boronic Acid Self-Complexation

The phenylboronic acids have a trigonal geometry and the boronic acids are fairly coplanar with respect to the benzene ring.[1] The x-ray crystal structure of phenylboronic acid was first reported by Rettig and Trotter in 1977 and showed that the boronic acids were crosslinked into a layered network via hydrogen bonds (Figure 1.2).[15] Boronic acids themselves are diol compounds, thus, they can self-complex to form interconnected networks.

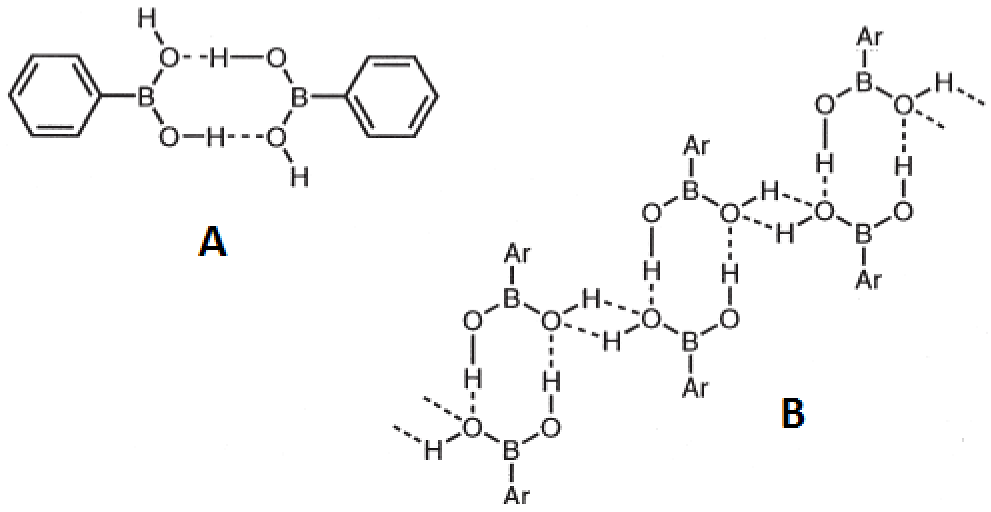


Figure 1.2. A: Dimeric boronic acid units showing hydrogen bonds; B: Extended hydrogen bonded network of boronic acids.[1]

1.2.3. Boronic Acid Applications

Utilizing their binding capability and specificity for sugars, boronic acids can be used as sugar biosensors.[14, 16-19] Boronic acid-based colorimetric sugar sensors have been proposed as replacements for the traditional enzyme-based glucose assay.[17] They may additionally be used to make biocompatible surfaces or surfaces for cell attachment.[20] Although saccharide sensors are the major application, boronic acids have also been used as fluorescence, anion and chiral sensors and their use in electrochemical processes has also been reported.[10]

1.3. Silicone Boronic Acids (SiBA)

Thin film coatings provide a route to generate sensors whose properties change upon binding. Self-assembly yields a facile method for the production of films with defined organization and properties. Boronic acid monolayers with varying hydrocarbon R groups have been previously studied with the interest to form selective saccharide sensing films.[16, 19] Chen et al. formed and characterized self-assembled monolayers of phenylboronic acid derivatives on Au surfaces and discovered by surface plasmon resonance spectroscopy that phenylboronic acids displayed a good sensitivity for monosaccharides even in the picomolar range.[16] Ludwig et al., on the other hand, studied amphiphilic diphenylmethane-3,3'-diboronic acid (two phenylboronic acids connected chemically) at the air-water interface, with the attempt to vary physical and chemical properties of the film in order to optimize the sensitivity of boronic acids for monosaccharides.[19] They determined that the selectivity of boronic acids for saccharides was dependent on the configuration of the saccharide as well as the stoichiometry of the complex at the air-water interface. Additionally, they found that the stoichiometry and the selectivity can further be tuned by the addition of polycations to the subphase. Here, the boronic acid functionality is combined with the film forming capabilities of silicones to generate a self-assembling system for creation of biocompatible films. Specifically, we have synthesized α,ω-boronic acid-functionalized silicones of various chain lengths in order to study their behavior and their tunability at the air-water interface.

1.3.1. Silicone Chain

Silicone chains are of interest due to their biocompatibility and exceptional chain flexibility. The Si-O bond is very flexible compared to the C-C bond which is found in traditional surfactant backbones. For instance, the energy of free rotation about a C-C bond in polyethylene is 13.8 kJ/mol whereas for Si-O bond in Siloxane is ~ 0 (less than 4 kJ/mol).[21] Some reasons for this exceptional flexibility (compared to C-O bond), would be the longer Si-O bond length, its highly ionic character, and a large bond energy of 452 kJ/mol.[22] Such bond characteristics of the Si-O backbone of silicones allow for the freedom of interconversion between different conformations.

1.3.2. Bola-Amphiphiles

The silicone chain was functionalized on both ends with boronic acids, making SiBA a bola-amphiphile. Bola-amphiphiles with a hydrocarbon backbone have been studied before at the air-water interface[23, 24] and, due to the rigidity of the hydrocarbon backbone, compression of the film at the air-water interface may allow for the surfactant molecules to align in an upright position, where one polar headgroup would be interacting with the aqueous subphase, and the other headgroup would be extending into the air. Similarly, the SiBA surfactants also have two polar boronic acid headgroups on either end of the chain. If one boronic acid is available at the air interface, it can potentially be used to bind to diol compounds or other molecules it may interact with, while the other polar headgroup is tethered to the subphase. If the SiBA can self-assemble analogously at the air-water interface, it should be possible transfer them onto solid substrates to make thin film coating and biocompatible surfaces.

1.3.3. Silicone Boronic acids at the macroscopic level

SiBAs display very interesting properties at the macroscopic level. A drop of the neat surfactant spreads on a water surface forming a coherent film.[8] The film is durable enough to support additional water droplets. Furthermore, when drops are applied one after another on the film, the individual drops do not mix. The SiBA film is not only strong enough to support water droplets, once a drop is in contact with the film, it spontaneously coats the drop surface with the underlying surfactant layer. Such behavior is unique to SiBA, as it is not seen for silicones functionalized with other headgroups (carboxylic acids or amines).[8]

1.3.4. Silicone behaviour in monolayers

The polymeric silicone, poly(dimethyl)siloxane, PDMS, has been widely studied at surfaces.[2, 4, 25-28] In early work, Lenk et al. proposed the formation of helices during the phase transition of non-functionalized PDMS, as well as mono-functionalized and di-functionalized PDMS, at the air-water interface in a Langmuir trough.[28] Piwowar and Gardella later performed RA-FTIR to deduce the conformation changes that occur in PDMS throughout the isotherm (Figure 1.3).[2] It is generally accepted that the PDMS chains initially (up to low surface pressures) adopt a caterpillar conformation, where molecules are stretched and lying at the water surface with the siloxane backbone immersed in the aqueous subphase and the methyl groups extending into the air. As the molecular area is reduced, molecules are forced to come into contact with one another and adopt a zigzag conformation where the backbone becomes less-solvated as some oxygen and silicon atoms are no longer in contact with water. However, the conformational changes that PDMS chains undergo during the first order phase transition was a subject of debate for several years. Based on earlier work, a transition in which the stretched chains are compressed to a point where they must form helical coils in order to occupy a smaller surface area was proposed.[2, 25, 28] The formation of helical coils at the air-water interface was suggested based on the characteristic conformation of PDMS molecules in the three-dimensional liquid state.[25] The small increase in pressure after the phase transition plateau due to further compression was suggested to correspond to the formation of very compact helices. The very small surface area may cause the helices to slide over another in the case of non-functionalized PDMS or perhaps an up-righting transition in the case of end functionalized PDMS.

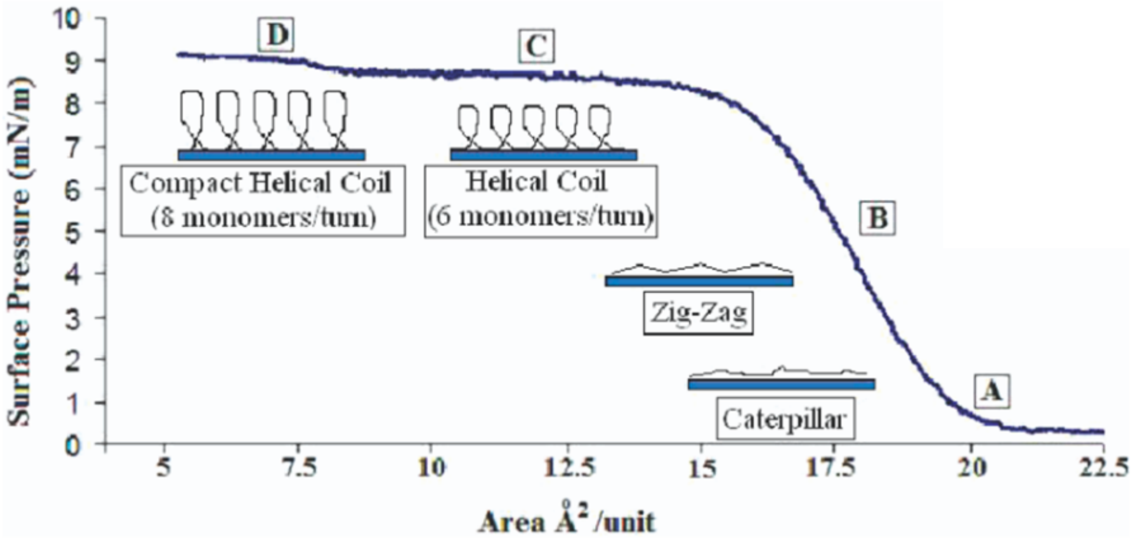


Figure 1.3. PDMS isotherm at the air-water interface showing possible conformations throughout the compression isotherm.[2]

In recent years, there has been increasing evidence against helix formation. Instead, the plateau in the isotherm is attributed to a layering transition where the chains just slide above one another and form odd numbered multilayers (Figure 1.4 C1 and D). Recent work has shown that PDMS polymers do not form helices at the surface and, even if they do form helices, it is most likely that the helices form on top of a monolayer and not just directly at the air-water interface (Figure 1.4 C2).[27, 29]

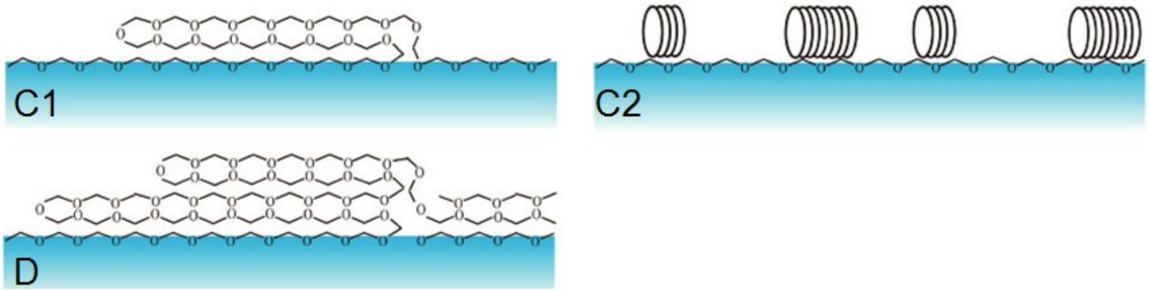


Figure 1.4. Alternate conformations adopted by PDMS chains during phase C and D of the compression isotherm as proposed in more recent work.[27]

End-functionalised PDMS have also been studied at the air-water interface (Figure 1.5).[28] Type 1 is the generally accepted isotherm for simple PDMS. Lenk et al. discovered that when PDMS chains are terminally functionalized with polar headgroups, they yield type 2 and type 3 isotherms (Figure 1.5). Type 2 isotherms are associated with high molecular weight compounds and show distinct phase transitions. Type 3 isotherms are generated by low molecular weight compounds because the isotherm occurs over a smaller range of molecular area and these phase transitions become overlapping and indistinguishable. Lenk et al. proposed that since transitions A-D are effectively the same for all types, they must be independent of the molecular weight of the compound, and must be governed by monomer-subphase interaction. However, since transitions E and F are apparent only in functionalized PDMS, these must be due to the tethering of the polar headgroup to the subphase. Additionally, when varying the type of terminal-functionality, Lenk et al. had seen that the collapse pressure of the film depended on the hydrophilicity of the headgroup. The better the headgroup interacted with the aqueous subphase, the stronger was the tethering and the higher the collapse pressure.

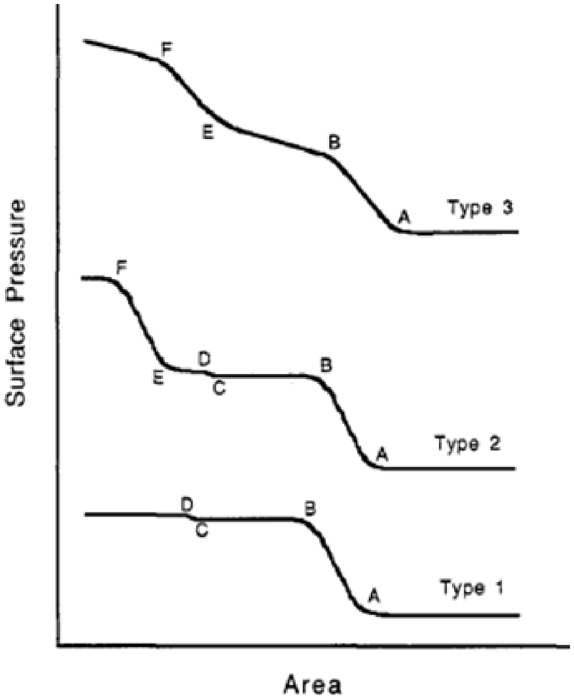


Figure 1.5. Types of isotherms observed for functionalized and non-functionalized PDMS of varying molecular weights, as described in the text.[28]

1.4. Objectives

The focus of this thesis is to evaluate the surface film-forming properties of silicone boronic acids with long term aims of determining the extent to which useful viscoelastic and/or biosensing materials can be achieved with ultrathin films (monolayers and multilayers). As a first step towards this goal, the surface phase behavior of these boronic acid-terminated silicones was characterized at the air-water and air-solid interfaces. Specifically, this work seeks to determine the following:

i) Does the boronic acid end-functionality affects the phase behavior of PDMS film, i.e., how does the boronic acid compare to other end functionalities?

ii) Do the oligomeric molecules behave any differently than the commonly studied polymeric forms, i.e., what is the impact of chain length influence on film properties?

We also attempt to tune the phase behavior of SiBA by modifying the subphase composition, including varying pH and the presence of sugars, amines, or other compounds.

1.5. Thesis Overview

This thesis focuses on the concept of combining the functionality of boronic acids with the self-assembly properties of silicone surfactants. Silicone boronic acids are studied at the air-water interface with the potential to develop new and improved saccharide sensing platforms.

Chapter 2 gives an overview of the experimental techniques used throughout the research. It describes the general principles of each instrument/technique used and what experimental data it yields.

Chapter 3 focuses on the surface characterization of the silicone boronic acid films at the air-water interface. It gives a detailed analysis of the phase transitions of the molecules upon compression, the effect of the silicone chain length, the role of the terminal boronic acid functionality and the comparison of boronic acids with other polar headgroup functionalities. This work has been published in Langmuir.

Chapter 4 focuses on boronic acid interactions with small molecules in the subphase. It attempts to disrupt the proposed boronic acid-boronic acid complexation at the air-water interface by the addition of molecules known to bind with boronic acids in the subphase. This chapter is written as a manuscript to be submitted to Langmuir.

Chapter 5 will provide an overall discussion, final conclusions of the thesis and an outlook for future work.

Chapter 2. Overview of Experimental Techniques

2.1. Monolayers at the air-water interface

The Langmuir film balance is used to study the organization and behaviour of organic monolayers at the air-water interface. The Langmuir trough is made of Teflon, consists of a well, two Teflon barriers for compression and a Wilhelmy plate for measuring the surface pressure, which is defined as the difference between the surface tension in the absence and presence of a film ($\pi=\gamma_0-\gamma$). In order to spread the surfactant on the trough, the surfactant must first be dissolved in a spreading solvent, such as chloroform, that has a high spreading coefficient on water and is relatively volatile. When spread on the water surface, the solvent evaporates, leaving behind a monolayer of the insoluble surfactant. The monolayer is then compressed by closing in the barriers. The surface pressure is measured as a function of molecular area, and the plot obtained as a result is referred to as a surface pressure - area isotherm (Figure 2.1).

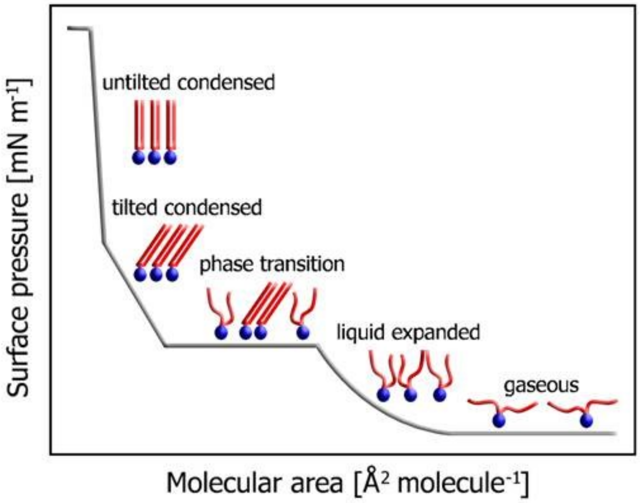


Figure 2.1. Schematic isotherm showing surface pressure as a function of molecular area and the various conformations adopted by surfactants upon compression.

The surfactants (or other film forming molecules) are spread onto the liquid surface in the gaseous phase (high molecular areas), where the molecules are considered to have little or no interaction with each other and they are oriented at the interface with the hydrophilic headgroup interacting with the aqueous subphase and the hydrophobic tails lying at the surface. Upon compression of the film beyond the critical area, molecules begin to interact and undergo a phase transition from gas to liquid expanded phase in which the chains are disordered with high mobility. Further compression can lead to a first-order phase transition where the molecules align to form an organized condensed phase. In general, high compressibility of the film is apparent from the resistance in pressure increase as the molecular area is decreased. Further compression of the film beyond a critical area eventually leads to a film collapse, where the film can no longer be compressed as a monolayer, leading to buckling of the film, loss of material to the subphase, or the formation of multilayers.

2.2. Film thickness at the air-water and air-solid interface

Ellipsometry is a versatile technique in which monolayer thicknesses can be estimated based on the optical properties of the sample. In ellipsometry at the air-water interface, p-polarized light is shined at the sample surface. As the film is being compressed, the changes in the polarization state of the light after being reflected off the sample are measured. The ellipsometric parameters measured are the angles Δ (delta) and Ψ (psi), which are related to the reflection coefficients of the polarized light, ρ_π (parallel to the plane of incidence), and ρ_σ (perpendicular to the plane of incidence). The ratio of the two reflections, ρ is defined as,

$$\rho = \frac{\rho_\pi}{\rho_\sigma} = \tan(\Psi) e^{j\Delta}$$

Due to the optical model, there is no significant change in Ψ over the thickness range we are studying (0-2 nm), therefore only changes in Δ (δΔ) are monitored. The changes in the optical thickness of the film over the course of the compression isotherm are referenced to the clean subphase (prior to the formation of a coherent film where δΔ in the gas phase is zero).

Ellipsometry at the air-solid interface requires the transfer of the film from the air-water interface on to a solid substrate (for example, silicon wafer or mica sheets). One way to transfer films onto solid substrates is using the Langmuir-Blodgett technique as shown in Figure 2.2. If the refractive index of the substrate and the deposited film are known, it is possible to determine the thickness of the film by measuring the thickness of the substrate before and after the film deposition. The change in thickness, δΔ, is reported as

$$\delta\Delta = \Delta - \Delta_o$$

where Δ_0 is the thickness measured before thin film deposition and Δ is the thickness measured after the deposition.

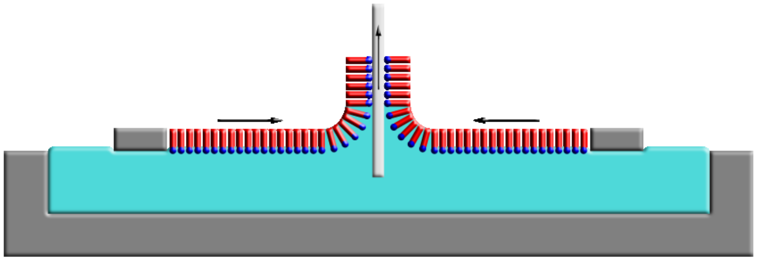


Figure 2.2. Langmuir Blodgett deposition technique at the air-water interface.

2.3. Film morphology at the air-water interface

Brewster angle microscopy (BAM) is another technique that utilizes polarized light incident at the air-water interface to visualize film morphology of nanofilms. Clean, perfect surfaces reflect light, but when p-polarized light is shined at the surface at a very specific angle, known as the Brewster angle, there is no reflection of the incident light (Figure 2.3). The Brewster angle is specific to each surface/substrate based on the optical properties of the two phases. The Brewster angle of the air-water interface is 53.15°. In the gas phase of the isotherm, there is no coherent film at the surface. As the surface area is compressed, a coherent film begins to form at the interface. As a result, the optical properties of the surface change, thus the Brewster angle of the surface is no longer that of water leading to reflection of some of the incident light. The amount of light reflected is proportional to the changes in the properties of the film, leading to a higher contrast in the image observed. Different phases have sufficiently different optical properties to produce detectable differences in reflected light.

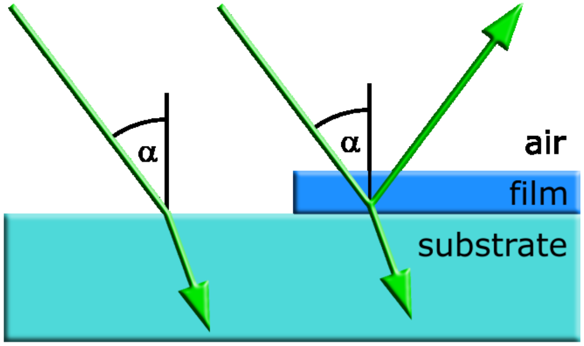


Figure 2.3. Schematic depiction of Brewster Angle Microscopy.

2.4. Surface topology of film at the air-solid interface

Atomic force microscopy (AFM) is a scanning probe microscopy that allows for a high resolution imaging of a thin film supported on a solid substrate. AFM utilizes a sharp tip (cantilever) that scans over the surface of the sample in the (x, y) direction, while the interaction forces between the tip and the sample are measured generating a three-dimensional topological image of the sample surface. A laser beam is aimed at the top of the cantilever and the reflection of the beam off the cantilever is detected in order to monitor the deflection of the cantilever (Figure 2.4). The extent of deflection of the cantilever gives information about the height differences at the surface of the sample.

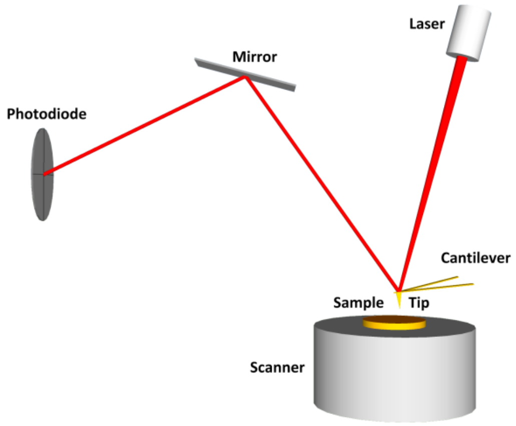


Figure 2.4. Schematic Depiction of Atomic Force Microscopy.

Chapter 3. Surface Behaviour of Boronic Acid Terminated Silicones

This chapter has been published in Langmuir (Mansuri, E.; Zepeda-Velazquez, L.; Schmidt, R.; Brook, M. A.; DeWolf, C. E., Surface Behavior of Boronic Acid-Terminated Silicones. *Langmuir* **2015,** *31* (34), 9331-9339. DOI: 10.1021/acs.langmuir.5b02143) and is included in this chapter as published. Dr. Laura Zepeda-Velazquez synthesized the silicone boronic acids (at McMaster University in the lab of Dr. M.A. Brook). I carried out all experimental work and wrote drafts of the manuscript under the supervision of Dr. Christine DeWolf and Dr. Michael Brook. Dr. Rolf Schmidt contributed to the discussion of the results and editing of the manuscript.

3.1. Abstract

Silicone polymers, with their high flexibility, lie in a monolayer at the air water interface as they are compressed until a critical pressure is reached, at which point multilayers are formed. Surface pressure measurements demonstrate that, in contrast, silicones that are end-modified with polar groups take up lower surface areas under compression because the polar groups submerge into the water phase. Boronic acids have the ability to undergo coordination with Lewis bases. As part of a program to examine the surface properties of boronic acids, we have prepared boronic acid-modified silicones (SiBAs) and examined them at the air-water interface to better understand if they behave like other end-functional silicones. Monolayers of silicones, aminopropyl-silicones and SiBAs were characterized at the air-water interface as a function of end-functionalization and silicone chain length. Brewster angle and atomic force microscopy confirm domain formation and similar film morphologies for both functionalized and non-functionalized silicone chains. There is a critical surface pressure (10 $mN \cdot m^{-1}$) independent of chain length that corresponds to a first order phase transition. Below this transition the film appears to be a homogeneous monolayer whose thickness is independent of chain length Ellipsometry at the air-water interface indicates that the boronic acid functionality leads to a significant increase of film thickness at low molecular areas that is not seen for non-

functionalized silicone chains. What differentiates the boronic acids from simple silicones or other end-functionalized silicones, in particular, is the larger area occupied by the headgroup when under compression, compared to other or non-end-functionalized silicones, which suggests an in-plane rather than submerged orientation that may be driven by boronic acid self-complexation.

3.2. Introduction

An important consequence of the highly flexible Si-O backbone of silicone polymers is an intrinsically low surface energy and high surface activity. When further modified with hydrophilic groups, silicone surfactants have applications ranging from agricultural adjuvants[3] to foam stabilizers in polyurethane.[4] While polyethers are frequently the hydrophiles of choice, silicones bearing other surface-active groups including phosphates, sulfates,[6] amines, carboxylic acids and amino acids[5, 7] have been developed for specific applications, particularly in personal care applications. The surface activities some of these materials can be modified at pHs away from neutrality, however, usually at conditions under which the silicones are known to undergo depolymerization.

The interfacial behavior of silicone polymers (typically poly(dimethyl)siloxane, (PDMS)), including a range of end-functionalized PDMS, has been widely studied.[2, 4, 25-28] At high molecular areas, PDMS chains are generally assumed to adopt a caterpillar conformation, where molecules are stretched and lying at the water surface with the siloxane backbone immersed in the aqueous subphase and the methyl groups extending into the air. As the molecular area is reduced, molecules are forced to come into contact with one another and adopt a zigzag conformation where the backbone becomes less-solvated as some oxygen and silicon atoms are no longer in contact with water.[27] Further compression leads to a phase transition. In early work, Lenk et al.[28] proposed the formation of helices during this phase transition for both functionalized and non-functionalized PDMS. Later work on PDMS by Kim et al.[27] suggested a multilayering rather than helix formation on the basis of vibrational sum frequency spectroscopy measurements. It is now generally accepted that the chains slide above one another and form odd numbered multilayers. If they do form helices, it is most likely that the helices form on top of a monolayer and not just directly at the air-water interface.[27, 29]

The impact of end-functionalization of both PDMS and carbon-based backbone polymers has also been studied at the air-water interface.[23, 28] Functional groups typically serve to anchor the chain to the subphase, forcing a more horseshoe-type conformation, as has also been reported for long-chain bolaform amphiphiles.[24] The strength of this type of anchoring has been shown to impact the surface pressure at small molecular areas and the surface pressure at film collapse.[23, 28]

Boronic acids are known to provide a pH-sensitive binding site for diols, specifically the 1,2- and 1,3-diols that are common in saccharides. The binding affinity for different diol-containing compounds varies significantly (over orders of magnitude), which enables differentiation of sugars.[3] Based on this selective binding, boronic acids have been proposed as drug delivery agents[30], as artificial lectins[31] and tunable saccharide sensors.[11, 12] Any changes to the local environment at boron can be 'locked in' by forcing the boron center to tetracoordination, for example, at higher pH.

Recently, we reported the preparation of boronic acid-modified silicone polymers.[32, 33] The surface activity of boronic acids at the air-water interface has been reported to be affected by the size and structure of the boronate.[34-36] Silicone boronic acid polymer behavior should be tunable by modification of the subphase constituents, including pH, presence of sugars, etc., under conditions that do not affect the silicone backbone. That is, unlike other silicone-based surfactants, it should be possible to dynamically modify interfacial behavior of silicone boronic acids under mild conditions. This paper describes an initial study on the behavior of silicone boronates at the air/water interface compared to related surface-active silicone polymers, which will allow specific applications to be identified. The silicone boronates under consideration are α,ω-boronic acid-functionalized silicones (Figure 3.1) of various molecular weights that were examined as a function of chain length, pH and temperature.

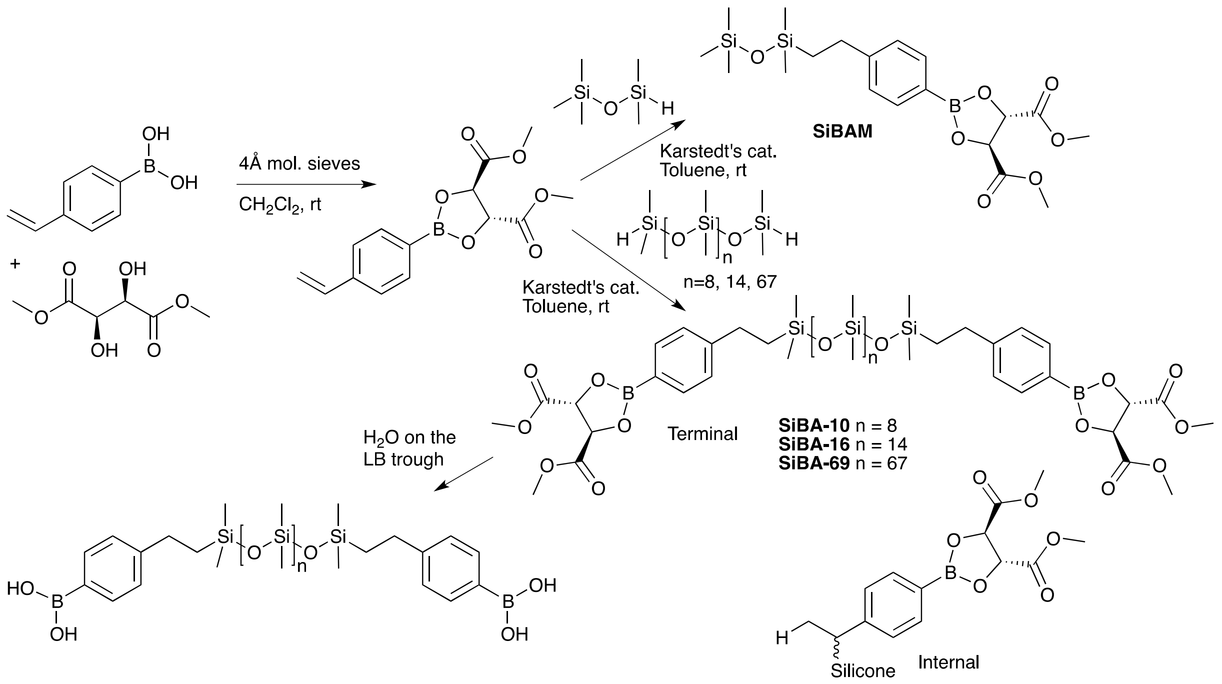


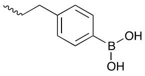
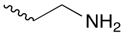
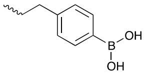
Figure 3.1. Chemical synthesis and structure of boronic acid functionalized silicones: the ratio of terminal:internal isomers in the SiBAs are ~70:30. The abbreviated name indicates the total number of silicon atoms in the central silicone block (i.e., SiBA-10: n=8).

3.3. Experimental

3.3.1. Materials

Boronic acid-terminated PDMS (difunctional SiBAs and monofunctional **SiBAM**, Figure 3.1) were synthesized as previously described.[33] The hydride-terminated silicone precursors, (**H-PDMS-m** where m = number of silicon atoms in the chain, 10, 16, or 69, respectively) and aminopropyl-terminated polydimethylsiloxane (**H_2N-PDMS-10,** m = 10) were obtained from Gelest Inc. (Morrisville, PA). Details of the functionalized silicones are provided in Table 3.1. Average number of repeat units and corresponding molecular weights were determined by ^{1}H NMR.

Table 3.1. Details of the functionalized silicones used in these studies.

	End Group*	m	n	M_n (g mol^{-1})	Trade Name
SiBA-10		10	8	~1310	-
SiBA-16		16	14	~1750	-
SiBA-69		69	67	~5680	-
H-PDMS-10	H	10	8	~650	DMS-H03
H-PDMS-16		16	14	~1100	DMS-H11
H-PDMS-69		69	67	~5030	DMS-H21
H_2N-PDMS-10		10	8	~840	DMS-A11
SiBAM		2	-	~296	-

* Note that the terminal and internal isomers are formed in a ~70:30 ratio.[4]

Spreading solutions were prepared in chloroform (HPLC grade, Fisher Scientific) with concentrations ranging from 0.5 mM to 1 mM. All solutions were stored at -4 °C and brought to room temperature before use. Ultrapure water with resistivity of 18.2 MΩ cm was obtained from an EasyPure II LF system (Barnstead, Dubuque, IA). Silicon wafers were purchased from Wafer World Inc. (West Palm Beach, FL) and cleaned using the following procedure: substrates were immersed in a 1:1 mixture of concentrated hydrochloric acid (ACS grade, EM Science) and methanol (HPLC grade, Fisher Scientific) for 30 min, rinsed abundantly with ultrapure water, immersed in concentrated sulfuric acid (Reagent grade, J.T. Baker) for 30 min, rinsed abundantly with ultrapure water, and stored in ultrapure water. Storage times never exceeded 7 days. Prior to use, silicon substrates were blown dry with nitrogen. Mica sheets were purchased from Ted Pella

Inc. (Redding, CA) and were cleaved by separating thin layers from either side of the sheet to expose a clean surface for deposition.

3.3.2. Methods

Surface pressure-area isotherms were obtained on thermostatted Langmuir film balances (140 cm^2, 6:1 length:width aspect ratio, Nima Technology Ltd., Coventry, U.K.) at varying temperatures with a compression speed of 5 $cm^2 \cdot min^{-1}$. Surface pressure measurements were made using a filter paper (Whatman No. 1) Wilhelmy plate. Monolayers of each surfactant were spread from chloroform solutions on the aqueous subphase and the solvent was allowed to evaporate for approximately 3 min before beginning compression. All isotherms and transfers were carried out under symmetric compression. All subphases were made using ultrapure water (pH $\approx$5.5) and, where noted, the subphase pH was adjusted by addition of sodium hydroxide (ACS reagent, Sigma Aldrich). Monolayers were transferred at constant pressure onto clean silicon wafers and on mica using the Langmuir-Blodgett (LB) technique with a dipping speed of 2 mm min^{-1}.

Brewster angle microscopy (BAM) and ellipsometry measurements were carried out with an I-Elli2000 imaging ellipsometer (Nanofilm Technologie GmbH, Göttingen, Germany) equipped with a 50 mW Nd:YAG laser, λ = 532 nm) using a 20× magnification with a lateral resolution of 1 μm. BAM experiments were performed at an incident angle of 53.15° (Brewster angle of water) and a laser output of 50% and 100% (analyzer, compensator, and polarizer were all set to 0). Ellipsometric measurements at the air-water interface were carried out at an incident angle of 50.00° and a laser output of 100% with the compensator set to 20.00°. The reported thickness is an average of 10 measurements each taken at a different location on the same film and is consistent for multiple samples. The ellipsometric isotherm is reported in terms of $\delta\Delta$, which is independent of the optical model. $\delta\Delta$ is defined as the difference between the ellipsometric angle Δ of the film on the subphase and the subphase alone ($\delta\Delta = \Delta_{film} - \Delta_{subphase}$). Measurements were also carried out on LB films deposited onto silicon substrates using an incident angle of 65.00° and a laser output of 1% with the compensator set to 45.00°. To determine the optical thickness of the monolayers at the air-solid interface, the silicon dioxide layer thickness was determined on clean substrates with the following two-box optical model: silicon as the substrate (n=4.15, κ=0.04) and silicon dioxide as the layer (n= 1.46, κ=0), assuming an isotropic film. The same box model was used to determine the combined thickness of the LB film and silicon dioxide after LB film deposition. All values are reported as average film thicknesses.

Atomic force microscopy (AFM) was carried out using a Nanoscope IIIa MultiMode AFM from Veeco (Santa Barbara, CA). All images were obtained using tapping mode, using V-shaped silicon nitride tips with a nominal spring constant of 0.58 N·m^{-1}. Images were analyzed using the NanoScope Analysis VERSION 1.40 software.

3.4. Results and Discussion

Surface pressure-area isotherms of silicone boronic acids with varying chain lengths (SiBA-10, SiBA-16 and SiBA-69) at the air-water interface are shown in Figure 3.2 along with isotherms for the corresponding hydride-terminated poly(dimethyl)siloxane precursors (H-PDMS-10, H-PDMS-16, H-PDMS-69) for comparison. The isotherms for the hydride-terminated PDMS are very similar to those reported for methyl-terminated PDMS,[2, 4, 27, 28] while those for the silicone boronic acids show similar transitions to other α,ω-difunctionalized PDMS.[28]

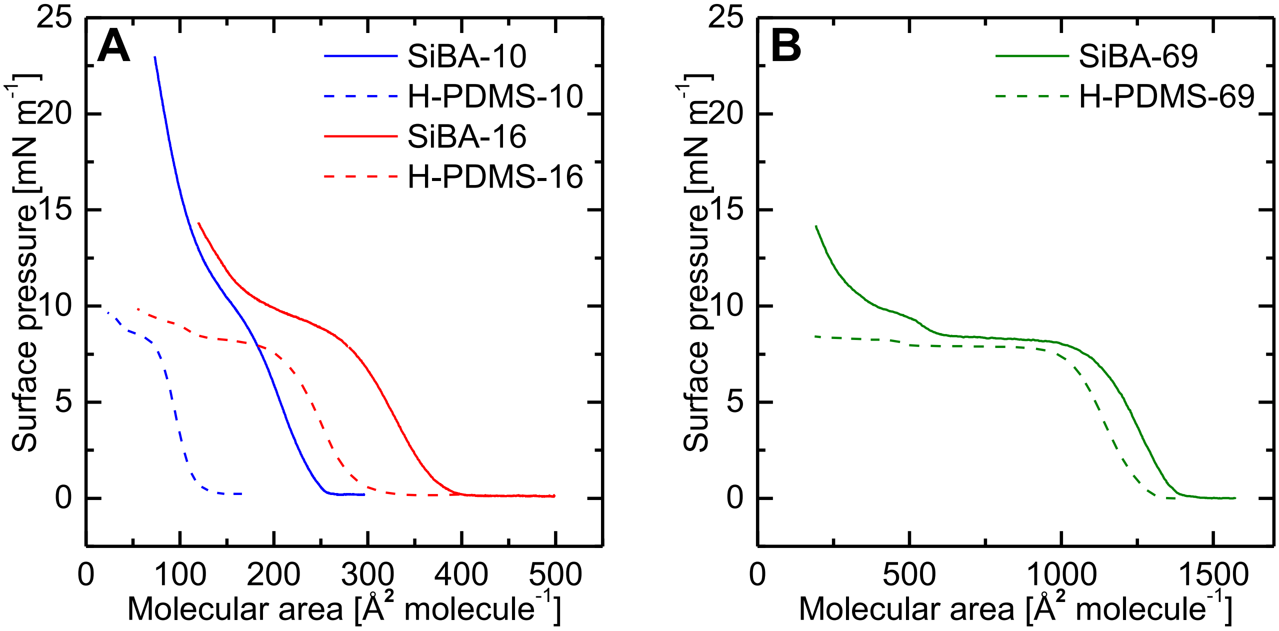


Figure 3.2 Isotherms for silicone boronic acids and hydride-terminated silicones on ultrapure water 23 °C: (A) SiBA-10 (solid blue), SiBA-16 (solid red), H-PDMS-10 (dashed blue), H-PDMS-16 (dashed red); (B) SiBA-69 (solid green), H-PDMS-69 (dashed green). Isotherms for

the high molecular weight polymer films are displayed separately for clarity given the large difference in molecular area.

In all isotherms, irrespective of end group (H versus boronic acid), there is a plateau corresponding to a first order-phase transition starting at pressures between 8 and 10 $mN\cdot m^{-1}$, with a slight increase for the low molecular weight compounds as has been previously observed.[28] Only the molecular areas for transitions and the length of the plateaus vary with chain length. The isotherms for larger molecules have a longer, flatter phase transition plateau, due to greater conformational freedom of the chain (i.e., more isoenergetic conformations).

There is the appearance of an additional transition (smaller plateau starting around 550 $Å^2\cdot molecule^{-1}$) for the higher molecular weight SiBA-69. Such transitions are commonly observed when the PDMS chain is sufficiently long, both in the presence and absence of end functional groups.[28] This secondary transition is not limited to silicones, and has also been observed in the isotherms of high molecular weight, end-functionalized polyisobutylenes.[23] The second transition may also be occurring for the oligomers SiBA-10 and SiBA-16 but may be obscured as the entire isotherm occurs over a much smaller range of molecular areas.

Finally, there is a sharp increase in surface pressure at low molecular areas for the SiBAs that is not observed for the H-terminal silicones but which is observed for aminopropyl- and other end-functionalized silicones.[28] This transition must correspond to an additional conformational change for molecules that are terminated with polar tethering groups. Without polar end functionalization, the molecules are free to slide over one another as thicker (non-monolayer) organic films are formed while the surface pressure remains constant. With the polar end functionalization, this migratory layering process is hindered as the molecule is tethered to the subphase. Longer chains may still provide enough flexibility for some layering,[27, 29] but at some point the tethering limits this process and an alternative conformation is adopted, which leads to a pressure increase at smaller molecular areas (see below). The pressure continues to increase as the film is compressed until a collapsed state is reached at approximately 38 to 40 $mN\cdot m^{-1}$. The high collapse pressure observed for SiBAs is consistent with strong tethering of the terminal group to the subphase[23, 28] and is comparable to values obtained for amine and carboxylic acid-terminated PDMS.[28]

Brewster angle microscopy images were used to follow film morphology changes throughout the compression isotherms. The formation of very bright domains towards the end of the plateau is attributed to the autophobic dewetting and/or localized collapse of the film (Appendix A). Autophobic dewetting arises when a fluid cannot spread or wet a thin film comprising the same material[37]; such dewetting processes have been reported for polymer films, such as PDMS, and result in the coexistence of regions of different thicknesses.[38, 39] Schull et al. reported polymer dewetting from a surface adsorbed (end-tethered) polymer film and noted that this process occurs more readily when the film is tethered at both ends (loops) rather than one end (tails).[37] Dewetting of droplets from a thin film of the same material has been observed for films where the first layer is more ordered than the bulk.[39] Given domains were observed for both the end-functionalized and non-end-functionalized materials, this must be a property inherent to the silicone backbone that is not impacted by tethering and is attributed to the underlying monolayer being more ordered (zig-zag conformation)[38] than the overlying layers which then spontaneously dewet to a lens of disordered material. The dewetting process only occurs after a critical film thickness is achieved, i.e. upon high compression.

Ellipsometric measurements at the air-water interface provide the means to monitor film thickness changes during compression. The ellipsometric isotherms for all three SiBAs are shown in Figure 3.3, where $\delta\Delta$ is the change in ellipsometric angle Δ and correlates to a change in optical thickness. In all cases, the films show a $\delta\Delta$ of -0.5 just before the critical area for the onset of pressure. This step change in $\delta\Delta$ corresponds to the transition from a backbone caterpillar (Si-O submerged in the subphase) to a zigzag conformation where the Si-O backbone partially desolvates and forms a thicker film on the surface.[27] The films then exhibit a slow, progressive increase in thickness (more negative $\delta\Delta$ values) until the end of the plateau, where $\delta\Delta$ reaches approximately -1.0. For all three SiBA molecules, there is a sharp increase in the average thickness of the film after the plateau (Figure 3.3D). A much smaller, less drastic increase is observed for H-PDMS-69. The differences between SiBAs and H-PDMSs observed by ellipsometry at these low molecular areas must therefore be attributed to thickness increases due to conformational restriction in the underlying SiBA film induced by the boronic acid interaction with the subphase.

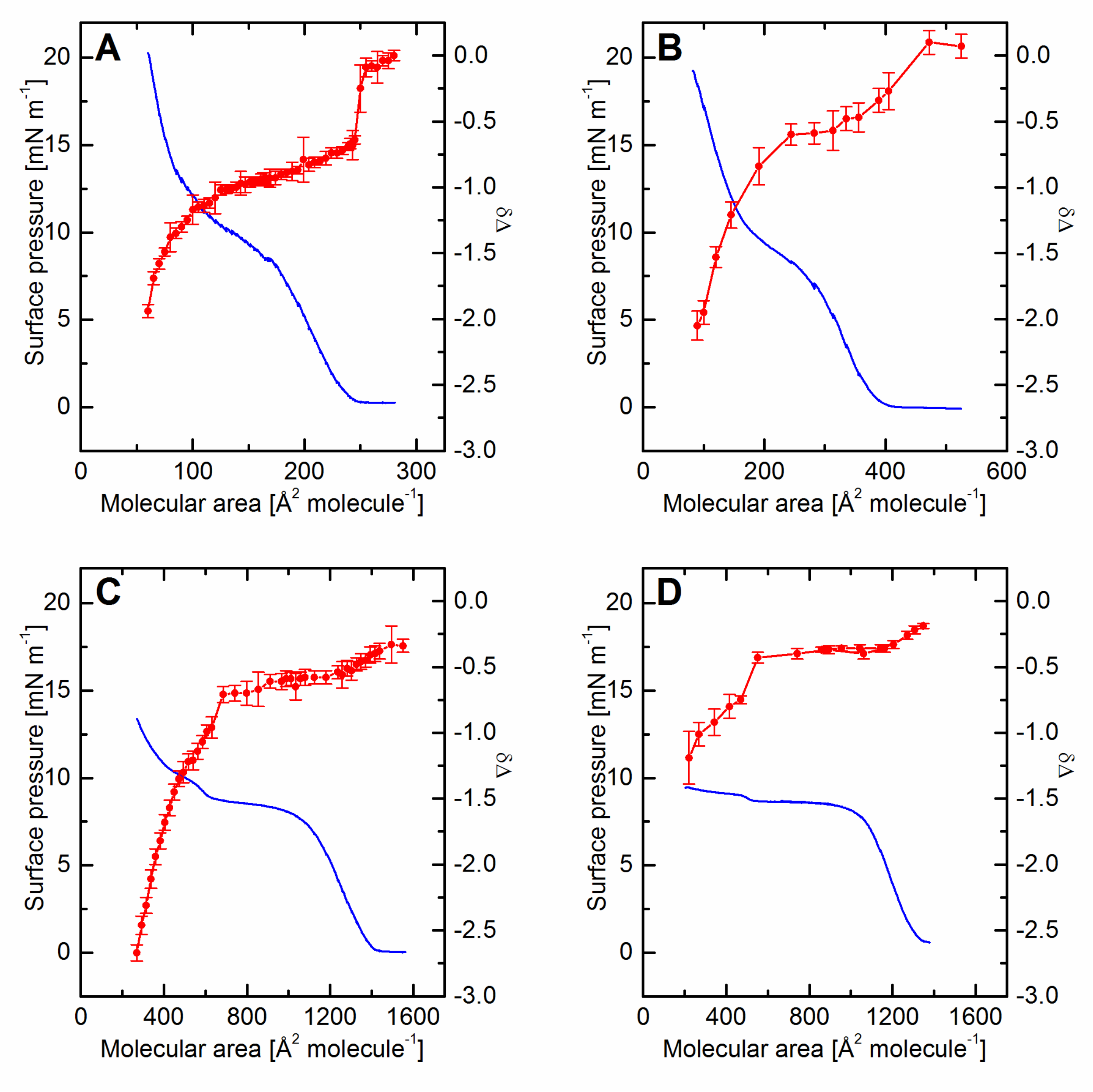


Figure 3.3. Ellipsometric isotherms at air-water interface (surface pressure: blue; ellipsometric measurement (δΔ): red): (A) SiBA-10; (B) SiBA-16; (C) SiBA-69; (D) H-PDMS-69.

The absolute thicknesses of the film below the transition pressure, where the film is homogeneous by BAM) were established by depositing Langmuir-Blodgett films onto silicon wafers. The thicknesses of the deposited films were determined by fitting ellipsometric angle changes to a two-box model and are shown in Table 3.2. All three SiBA films have approximately the same thickness, 0.5 to 0.6 nm, i.e., the thickness is independent of chain length, and correlates well with the thickness determined by Mann and Langevin[40] for a PDMS monolayer. This thickness is comparable to the silicone chain dimensions and confirms the SiBA chains are lying flat at the air-water interface and gradually rise above the surface as the area is compressed, as might be expected for a polymer with a flexible backbone. These observations are quite different from end-functionalized polymers with a less flexible carbon-backbone, which were reported to be standing at an angle to the surface, and show a defined chain-length dependence.[23]

Table 3.2. Film thickness of LB deposited monolayers on silicon wafers at 5 mN·m^{-1} measured by ellipsometry at the air-solid interface.

Surfactant	**Average Film Thickness (nm)**
SiBA-10	0.5 ± 0.1
SiBA-16	0.6 ± 0.1
SiBA-69	0.6 ± 0.1

Ellipsometric measurements on PDMS films by Mann and Langevin revealed an average thickness of 1.4 nm over the phase transition plateau,[40] which correlates well with the ellipsometric isotherms (Figure 3.3) at the air-water interface showing a significant change in $\delta\Delta$. Ellipsometry measurements on solid substrate are not reported here for higher pressures given the inhomogeneity of the film. For these systems, atomic force microscopy (AFM) was used to more accurately determine the height differences between the domains and the surrounding film (Figure 3.4). Films of SiBA-10 were deposited onto silicon and mica from the air-water interface using Langmuir-Blodgettry. The films were deposited at surface pressures above the transition plateau (25 mN·m^{-1}) where the onset of domain formation (BAM) was observed. The films exhibit the formation of domains of varying lateral and vertical dimensions. Small sub-200 nm domains are distributed throughout the background matrix (note that these domains would not be observed by BAM, which has a limit of resolution of 1 to 2 microns). The majority of these domains vary between 1 to 3 nm above the background film, although a second population of domains with heights from 7 to 11 nm was also observed. Additionally, larger domains of the order of 2 to 3 microns in diameter were observed; these are likely the domains that are observed by BAM. Upon closer examination, it can be seen that these domains comprise clusters of domains (ranging from 15 to 30 nm above the background film) often surrounded by a thick corona (2 to 7 nm above the background film). These extremely high domains are likely due to the autophobic dewetting mentioned earlier.

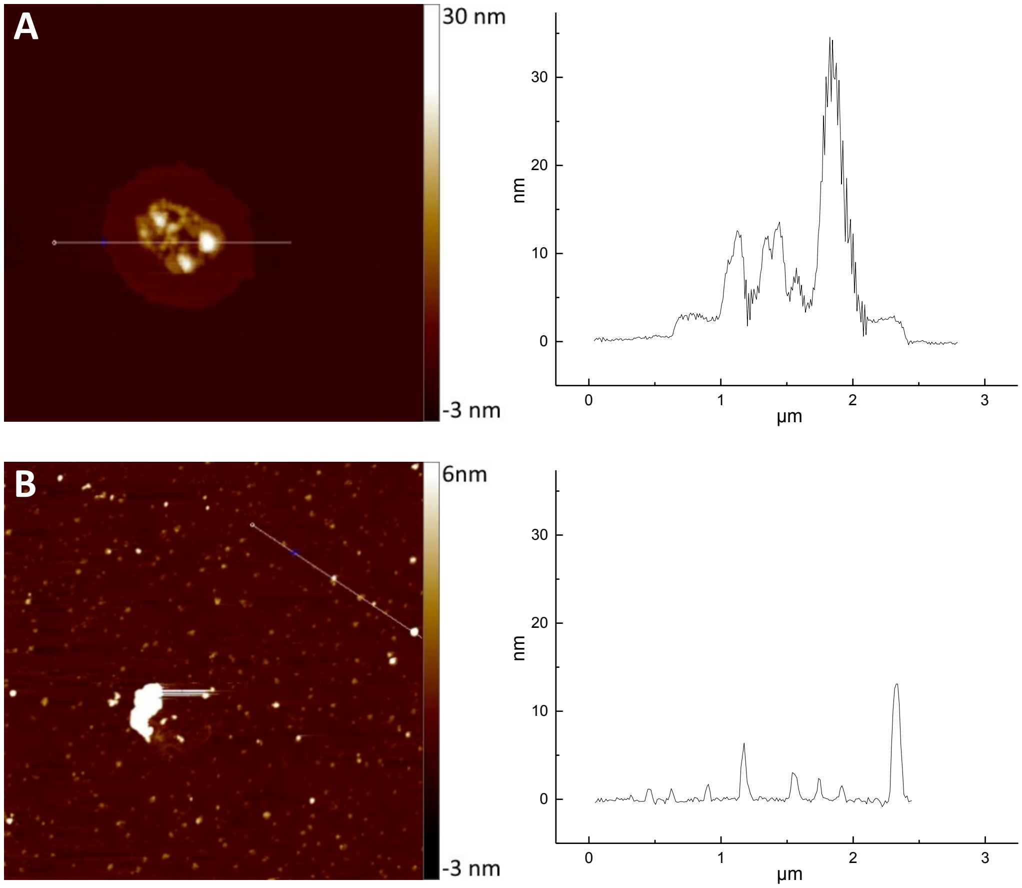


Figure 3.4. AFM images and corresponding height profiles of SiBA-10 transferred onto solid substrate at 25 mN·m^{-1}: (A) film transferred on mica; (B) film transferred on silicon wafer. The width of both images is 5 µm.

Figure 3.5 shows isotherms obtained from repeated compression-expansion cycles for SiBA-10 (similar results were also obtained for SiBA-16, Appendix A) and SiBA-69. Recompression yielded the same isotherm but shifted to smaller molecular areas. This shift was greater when the film was compressed to pressures above the plateau. The isotherms for other bis-end-functionalized silicones have been reported to display little or no hysteresis for molecular weights above 1200 g·mol^{-1} films[28] suggesting multilayer formation is highly reversible. Additionally, BAM measurements carried out during the repeated compression-expansion cycles showed that the domains, which only become visible at the end of the plateau during the first compression, can still be seen when the film is expanded. During this expansion, the domains lose brightness abruptly, however, they can still be seen below the main phase transition pressure. Upon further expansion into the gaseous phase, the domains are no longer visible either because the multilayer domains have all relaxed or the surface density and/or size of remaining domains is sufficiently low to limit their resolution in the field of view. Upon recompression, the reappearance of these domains occurs even before the phase transition (unlike the first film compression). The greater shifts in the isotherm after multilayer formation for all chain lengths and the BAM measurements suggest that the boronic acid end groups may not be able to readily diffuse away from one another, once in contact, as will be discussed in more detail below.

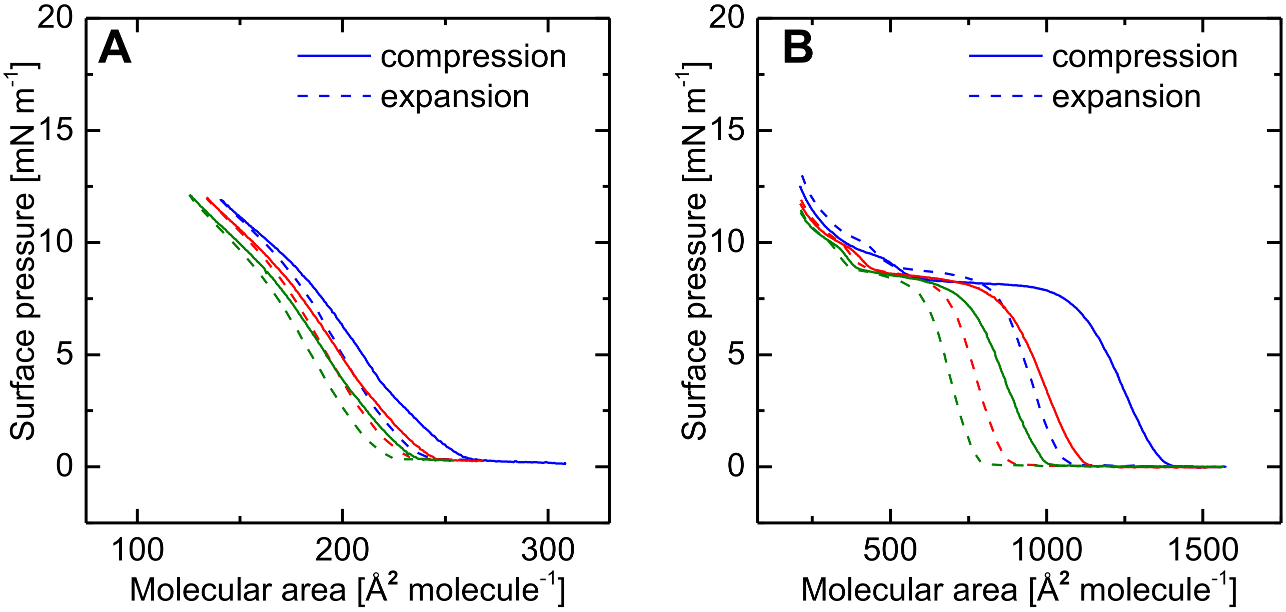


Figure 3.5. Isotherms for repeated compression-expansion cycles for SiBA films. SiBA-10 (A), SiBA-69 (B) on water at 23 °C where solid lines represent film compressions and dashed lines of the same color the corresponding film expansion. Recompression starts immediately after expansion without any equilibration time.

In order to further probe the nature of the boronic acid headgroup with the subphase, the pH was varied (Figure 3.6). The nominal (solution) pK_a of boronic acids is ~ 8.9;[1] the surface pK_a may be shifted to higher pK_a.[41] Furthermore, as a result of the multiple equilibria that exist between the trigonal and tetrahedral (charged) forms of boronic acid and their self-complexed forms, the system may not exhibit a single sharp pK_a but the charged state may vary over a very broad range pH values. [42] Subphase pH 12 was selected as it is sufficiently high that the boronic acid headgroups should be predominantly negatively charged, which in principle could lead to charge repulsion between the co-localized headgroups and/or disruption of any potential network or dimerization occurring between adjacent boronic acids at the air-water interface, causing an increase in molecular area as was reported for polymerizable surfactants with a boronic acid headgroup (these experiments were undertaken over short reaction times, where essentially no silicone depolymerization is anticipated).[35] However, for both SiBA-10 and SIBA-69, there was no difference in the isotherm at high molecular areas and low pressures and the shift in the isotherm only becomes apparent at the phase transition.

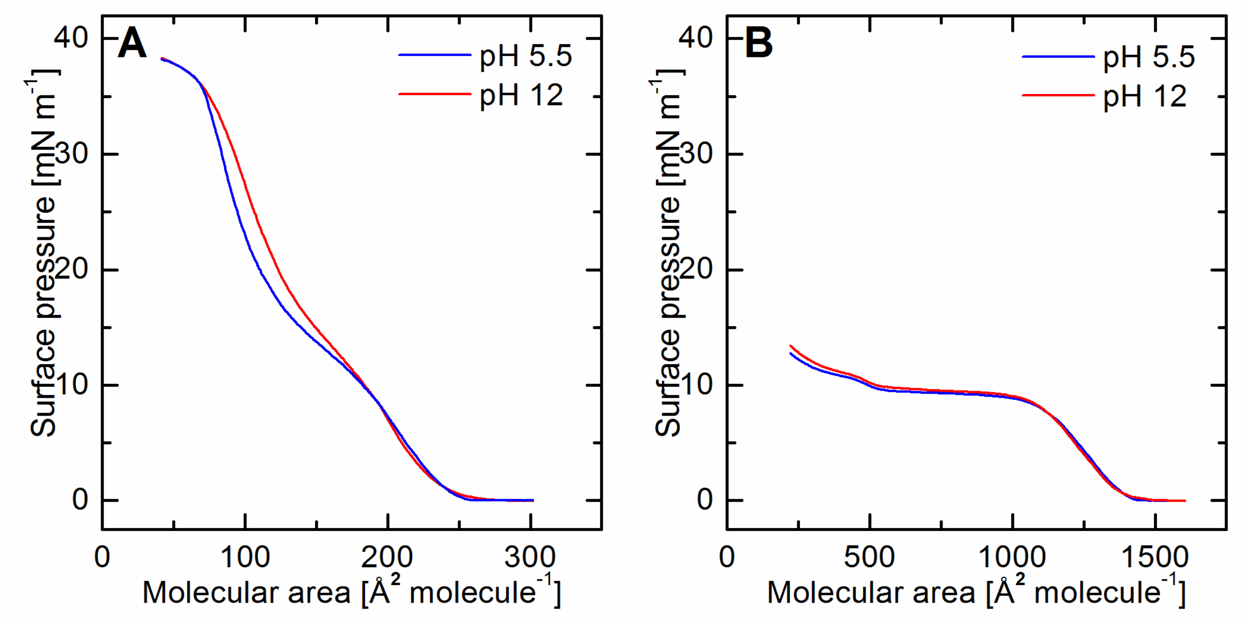


Figure 3.6. SiBA isotherms on subphases with varying pH. Blue: pH 5.5 subphase (ultrapure water); Red: pH 12 subphase, pH adjusted with sodium hydroxide. Note: the absolute shift (in Å^2·molecule^{-1}) in the isotherm to higher molecular areas above the phase transition pH 12 is similar for both chain lengths but is more prominent in the isotherms for SiBA-10 due to the scale.

The observations described above suggest that silicone boronic acids are rather different in their behavior at air-water interfaces from either simple silicones or those bearing hydrophilic functional groups at their termini. When the isotherms for SiBA and H-PDMS are normalized for chain length as shown in Figure 3.7, the impact of the boronic acid headgroup becomes much more apparent. It should be noted that the specific area of the functional end-group has not been estimated or removed prior to normalization so the areas per Si-O monomer include an additional area for these headgroups. The isotherms and values for A_0 (the critical area defined by extrapolation of the straight line region of the initial pressure increase to 0 $mN \cdot m^{-1}$) of the polymeric forms and the longest of the oligomers, H-PDMS-16, are comparable with the A_0 of 18.8 $Å^2 \cdot molecule^{-1}$ for methyl-terminated PDMS reported by Kessel et al.,[43] including the slight deviation and broadening of the isotherm at low pressure for H-PDMS-16 that was also observed for PDMS with an average chain length of 23 silicon atoms. The normalized isotherm of the shortest oligomer, H-PDMS-10, shifts to significantly smaller areas per molecule. The impact of the smaller terminal group (H vs CH_3) is much greater for a short chain, where the size differences are amortized over a smaller number of repeat units (monomers).

To examine the relative contributions to the molecular area by different headgroups, the normalized isotherms for short chain oligomers of 9 siloxane units with three different terminal functionalities were directly compared. The relative areas occupied by the molecules follow the order: terminal hydride < aminopropyl < phenylboronic acid (Figure 3.7C). The behavior of the aminopropyl-terminated silicone H_2N-PDMS-10 with its pronounced phase transition corresponds very well to the literature.[28] The normalized isotherm yields an A_0 value of 17.5 $Å^2 \cdot monomer^{-1}$, which is just slightly less than that of methyl-terminated PDMS despite the three carbon linker (rather than a methyl group), suggesting that the head group orientation is such that the amine must be fully solvated and extending into the subphase. Other end-functional silicones exhibit similar or smaller areas.[28]

For the boronic acid-terminated silicones, only the largest polymeric compound SiBA-69 converges to a monomer critical area of 19 $Å^2 \cdot monomer^{-1}$. This is, in part, because of the lower density of end functional groups: the longer the chain, the lower the impact of the terminal tethering groups on the conformational changes of the chain and the smaller the proportional contribution of the boronic acid to the molecular area. For the shorter-chain oligomeric surfactants SiBA-10 and SiBA-16, A_0 was found to be 28 and 30 $Å^2 \cdot monomer^{-1}$, respectively.

Phenylboronic acids are effectively much larger anchoring terminal groups than other functionalities such as aminoalkyl or carboxyl groups.

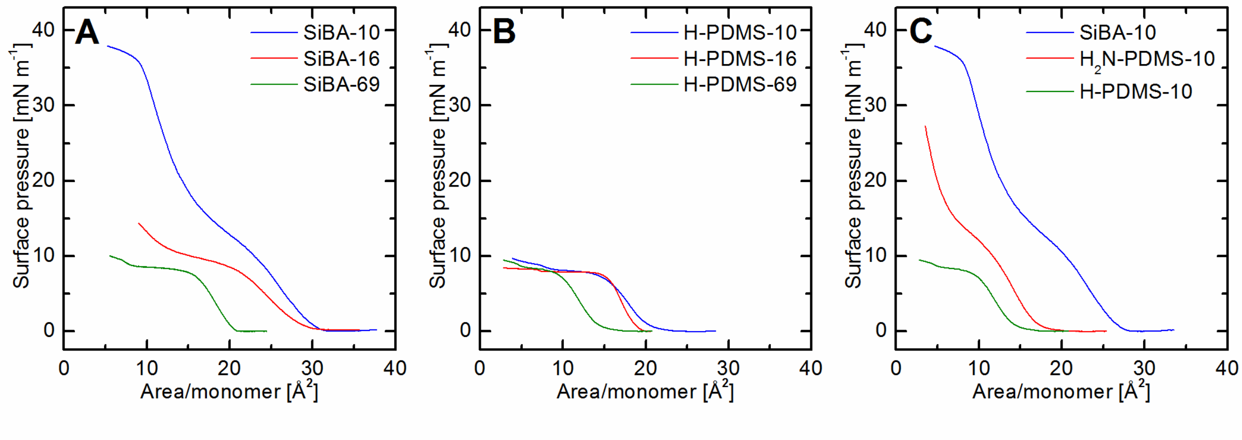


Figure 3.7. Isotherms normalized for the average chain length and reported as the area per Si-O monomer repeat unit (i.e., n-1): (A) SiBA-10 (blue), SiBA-16 (red), SiBA-69 (green); (B) H-PDMS-10 (blue), H-PDMS-16 (red), H-PDMS-69 (green). (C) Isotherms normalized for chain length for silicones with different terminal functionalities. SiBA-10 (blue), H2N-PDMS-10 (red), H-PDMS-10 (green). H2N-PDMS-10: aminopropyl-terminated PDMS.

To account for these differences it is necessary to investigate the effect of the end groups separately from the behavior of the silicone backbone. The role of the PDMS backbone is best seen with high molecular weight compound SiBA-69. It exhibits many of the characteristics of non-functional PDMS (Figure 3.8A and B), lying flat as a monolayer (0.5 to 0.6 nm thick) when uncompressed, and then increasing in thickness with compression, forming di- to trilayers (1.1 to 1.4 nm thick). The key distinguishing feature is the larger area SiBAs exhibit under compression (Figure 3.8D) when compared to non-functional PDMS, including H-PDMS or end-functional polymers such as aminopropylsilicones (Figure 3.8C), which actually take up smaller areas.

Lenk et al. proposed that end-functional silicones, such as aminopropyl or carboxyalkyl compounds are pinned to the water interface.[28] The smaller areas occupied by these compounds arise because the polar groups penetrate into the water, which allows the silicone chains to come into closer proximity (Figure 3.8C). These differences are magnified with shorter silicones, for which the end groups represent a larger fraction of the molecule. On the other hand, the boronic acid-terminated silicones exhibit significant shifts to higher molecular areas. This can only be accounted for by assuming that the boronic acids do not extend into the subphase. Rather, we propose that they form dimeric structures that lie on the water surface (Figure 3.8D), a proposal supported by the actual area taken up with boronic acids, which is in the same order of magnitude and range as the estimated area from the molecular dimensions for two phenylboronic acid end groups.

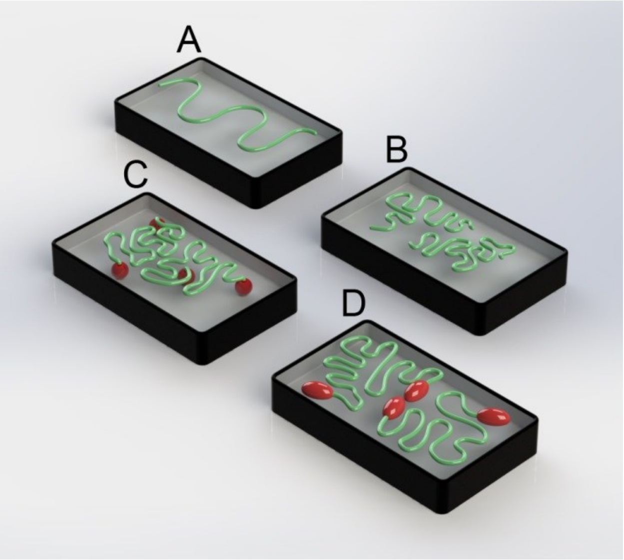


Figure 3.8. Schematic depictions at the air-water interface of: A: simple silicones at high molecular areas (gas phase); B: simple silicones upon compression; C: di-end functionalized silicones with vertical headgroup orientation observed for most end-functional silicones (e.g., aminopropylsilicones) at all non-zero pressures, and for SiBAs at high pressures; D: boronic acid functionalized silicones with horizontal headgroup orientation at low to moderate pressures.

To test this hypothesis, a monofunctional silicone boronate SiBAM was prepared. The isotherms for SiBAM and its mixtures with SiBA-10 are shown in Figure 3.9. The isotherm of SiBAM displays the same shape as the other SiBAs with a transition starting at approximately 10 $mN·m^{-1}$ despite the short chain. The critical area is 43 $Å^2·molecule^{-1}$, which matches well the cross-sectional area of the ethylphenylboronic acid if it were lying flat at the interface (approximately 40 $Å^2·molecule^{-1}$). A submerged headgroup would be expected to generate a much smaller areal footprint (approximately 16 $Å^2·molecule^{-1}$). Mixtures of SiBAM with SiBA-10 were prepared in both 1:1 mole and headgroup ratios (the latter being 2 SiBAM molecules:1 SiBA-10 molecule). Both generated isotherms displaying close to ideal mixing behavior (A_{mix} =

$x_{\text{SiBA-10}}*A_{\text{SiBAM}} + x_{\text{SiBA-10}}*A_{\text{SiBA-10}}$, where x is the mole fraction and A is the area in the single component isotherm) below the phase transition with a slight positive deviation (indicating repulsive interactions), which increases with increasing amounts of SiBAM.

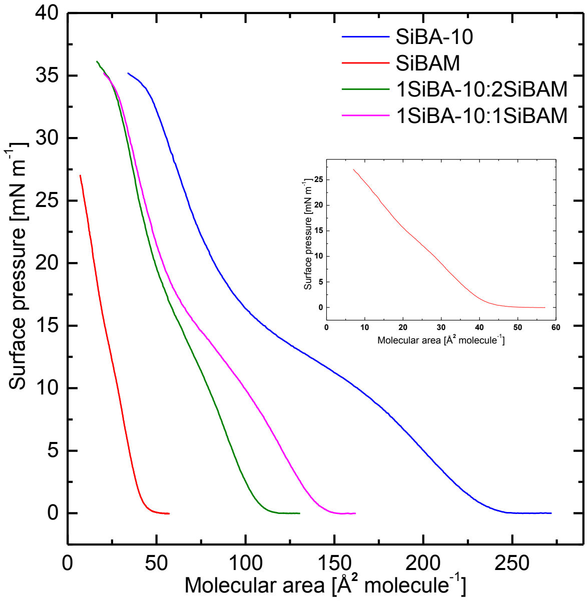


Figure 3.9. Isotherms of SiBA-10, SiBAM and mixtures of SiBA-10 and SiBAM (1:1 and 1:2 molar ratios, as indicated in the legend). The inset shows an expanded view of the SiBAM isotherm to better see the phase transition.

This orientation may be driven by headgroup complexation: the ability of boronic acids to form dimeric and higher order complexes is well known, and has been exploited as a tool for organization of self-assembled materials.[44] At the air-water interface the presence of the Lewis base water can enable this flat dimeric structure, by forming tetracoordinate boron, which is facilitated by relief of angle strain,[6] and which stabilizes it from substitution compared to the tricoordinate analogue. This configuration (Figure 3.10) could explain the lack of response to pH changes in the subphase. Increased basicity would simply pin the boron to the water interface more efficiently (Figure 3.8B). Only at very high pressures can the boron dimer be coerced into extending into the subphase with increased solvation. Such complexation would also explain the hysteresis exhibited by all three SiBAs (not observed for other highly polar end functionalizations): sufficiently strong headgroup interactions could inhibit the complete respreading, an effect that is compounded with each cycle as more headgroups come into contact.

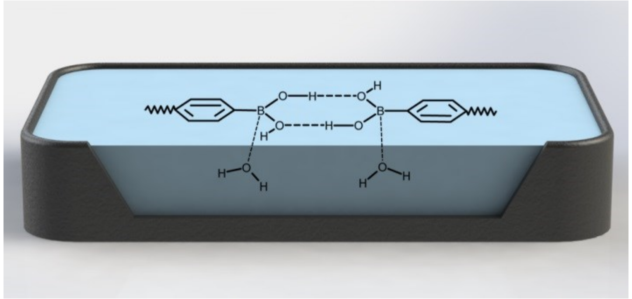


Figure 3.10. Schematic representation of proposed boronic acid-boronic acid complexation leading to a planar headgroup orientation at the air-water interface.

The phenylboronic acids are used to confer chemical sensing and electrical conductivity to thin film coatings[34-36, 45] and are ideal self-assembly building blocks due to their propensity for self-complexation, electron deficiency and co-planar structure. We have demonstrated that these self-organization properties extend to the air-water interface, where headgroup complexation induces a planar orientation at the interface permitting them to take up more area than either non- or end-functionalized silicones, which can only be disrupted through re-orientation at high surface pressures in the absence of agents that compete for the boronic acid. This different behavior when compared to other silicone surfactants, both in terms of interactions between the hydrophiles themselves and hydrophiles with water, provides new opportunities to target specific applications that involve the formation of robust hydrophobic films at aqueous interfaces, including coatings applications. Attempts to exploit this behavior will be the subject of future reports.

3.5. Conclusion

Boronic acid-terminated silicones show behaviors associated with strong tethering of the end functionalization to the subphase. Despite hindering the layering process, tethering does not affect the PDMS autophobic dewetting. However, unlike most bis end-functionalized PDMS compounds that take up less surface area than PDMS under compression, the SiBAs occupy more space. This is ascribed to planar orientation, possibly induced by boronic acid/boronic acid complexation at the air-water interface, which can only be overcome at much higher pressures that force the boronic acids into the water.

Supporting Information

Brewster Angle Spectroscopy images of SiBA-10, SiBA-69 and H-PDMS-69, and isotherms for repeated compression-expansion cycles for SiBA-16, provided as supporting information for the journal article, are found in Appendix A.

Chapter 4. Interfering with Headgroup Organization of Silicone Boronates at the Air-Water Interface

This chapter has been prepared to be submitted to Langmuir as a manuscript with the following authors: Mansuri, E., Zepeda-Velazquez, L., Schmidt, R., Brook, M.A., DeWolf, C.E. Dr. Laura Zepeda-Velazquez synthesized the silicone boronic acids (at McMaster University in the lab of Dr. M.A. Brook). I carried out all experimental work and wrote drafts of the manuscript under the supervision of Dr. Christine DeWolf and Dr. Michael Brook. Dr. Rolf Schmidt contributed to the discussion of the results and editing of the manuscript.

4.1. Abstract

Ultrathin films of boronic acid-terminated silicones at the air-water interface were studied for their potential to interact with small molecule diols and amines with differential selectivity. At low pH, the films showed no discernible interaction with either fructose or glucose, which may be a function of the low pH or an indication of strong self-complexation between the boronic acid headgroups. If an amine such as tris is introduced into the subphase in addition to the sugar, however, the isotherms shift to higher molecular areas. Evidence is presented which suggests that rather than facilitating the binding of the diols, the amine itself is responsible for changes to the isotherm. Addition of small molecules to the subphase comprising multiple amine functionalities gives the possibility of bridging the silicone polymers via the boronic acid headgroups in either linear or branched arrangements. This bridging has the effect of lowering the resistance of the film to collapse but also inducing changes to the collapse mechanism.

4.2. Introduction

Exploiting the selective and highly tunable binding of boronic acids with 1,2- and 1,3-diols has been the driving force behind much of the research into boronic acid-derived materials. For example, boronic acids have been proposed as saccharide biosensors,[11, 12] drug delivery agents,[30] and artificial lectins.[31] The selectivity and affinity of their binding to diols can be tuned by varying environmental properties such as pH of the solution, as well as varying the size and structure of the boronate.[34-36]

Boronic acids bind to diols by forming reversible ester linkages. Due to the presence of a vacant p orbital, they act as mild Lewis acids, able to accept a lone pair of electrons from a Lewis base.[17] At pH values below their pK_a, boronic acids are found in their trigonal geometry, sp^2 hybridized. The increase in pH yields a sp^3 hybridized boronate anion with a tetrahedral geometry and a negative charge on the boron atom after binding of water or, more commonly, hydroxide. Lorand and Edwards first determined the binding constants of boronic acids with saccharides by monitoring the drop in pH upon the addition of saccharides in the solution.[9] The boronic acid association with sugars occurs when the boronic acid is in this tetrahedral geometry. Thus, in neutral pH conditions, the boronic acid-saccharide linkage is favored in the presence of an amine, as the interaction with amines shifts the pK_a allowing for the formation of the tetrahedral boronate anion at lower pH values, which then in turn promotes the conditions of forming reversible ester linkages with saccharides. Therefore, the addition of amines allows for more practical applications of boronic acids where they may be used as saccharide biosensors under physiological conditions.[10]

We recently reported the synthesis of boronic acid-modified silicone polymers[32, 33] and the characterization of their surface behavior at the air-water interface.[46] It was proposed that boronic acids at the air-water interface may engage in dimerization or self-association via hydrogen bonding when the headgroups are in close enough proximity yielding a planar arrangement of the headgroups. This differentiates boronic acid from other di-end-functional headgroups and provides new opportunities to target applications involving the formation of robust hydrophobic films, including coating applications. Herein, we explore the interaction of boronic acid headgroups at the air-water interface with soluble diols and amines and hydrogen bond disrupters in the subphase.

4.3. Experimental

4.3.1. Materials

Boronic acid-terminated silicones (Figure 4.1) were synthesized as previously described.[33] The average number of repeat units and corresponding molecular weights were determined by ^1H NMR.

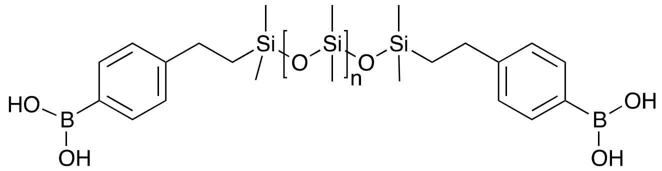


Figure 4.1. Chemical structure of boronic acid-functionalized silicone. The abbreviated name indicates the total number of silicon atoms in the central silicone block (i.e. SiBA-10: n=8).

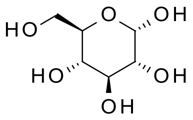
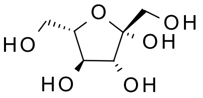
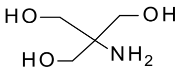
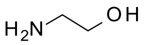
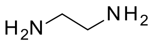
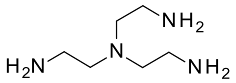
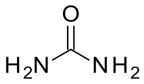
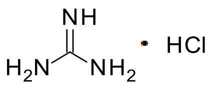
Spreading solutions were prepared in chloroform (HPLC grade, Fisher Scientific) with concentrations ranging from 0.5 mM to 1 mM. All solutions were stored at -4 °C and brought to room temperature before use. Ultrapure water with resistivity of 18.2 MΩ·cm was obtained from an EasyPure II LF system (Barnstead, Dubuque, IA). Glucose and fructose were purchased from BioShop Canada Inc. (Burlington, ON). Ethanolamine (ACS reagent, purity ≥ 99.0%), ethylenediamine (analytical reagent, purity ≥99.5%), tris(2-aminoethyl)amine (purity ≥ 95.5%), and tris(hydroxymethyl)aminomethane (ACS reagent, purity ≥ 99.8%) were purchased from Sigma Aldrich (Oakville, ON).

4.3.2. Methods

Surface pressure-area isotherms were obtained on temperature-controlled Langmuir film balances (140 cm^2, 6:1 length:width aspect ratio, Nima Technology Ltd., Coventry, U.K.), under ambient conditions, with a compression speed of 5 $cm^2 \cdot min^{-1}$. Surface pressure measurements were made using a filter paper (Whatman No. 1) Wilhelmy plate. Monolayers of the surfactant were spread from chloroform solutions on the aqueous subphase and the solvent was allowed to evaporate for approximately 3 min before beginning compression. All isotherms were carried out under symmetric compression. All subphases (Table 4.1) were made using ultrapure water (pH ≈5.5) and, where noted, the subphase pH was adjusted by addition of sodium hydroxide (ACS reagent, Sigma Aldrich).

Isotherms for each system were repeated at least 3 times with a ± 2.6 $Å^2$ $molecule^{-1}$ variation in the critical area with the exception of GdnHCl which had a ± 4.4 $Å^2$ $molecule^{-1}$ variation. The slope after the main phase transition plateau, which is associated with a localized collapse/multilayer formation, varied with solution and age but was consistent within a given series. For this reason, isotherms on water were always collected with the isotherms on a given subphase so that shifts could be assessed; the control isotherm is presented in each figure.

Table 4.1: Details of subphases studied with SiBA-10.

Subphase	Structure	Concentration (M)	pH of solution
Glucose		0.1	5.0
Fructose		0.1	4.9
Tris(hydroxymethyl)aminomethane (Tris)		0.1	9.8
Glucose + Tris	As above	0.1	7.4
Fructose + Tris	As above	0.1	7.4
Ethanolamine		0.01	10.3
Ethylenediamine		0.01, 0.1	10.6
Tris(2-aminoethyl)amine		0.01	10.5
Urea		1, 4	6.3 (1 M) 8.4 (4 M)
Guanidine Hydrochloride		0.1, 4	5.6

4.4. Results and Discussion

Boronic acid-boronic acid interactions have been postulated to affect the headgroup orientation of boronic acid end-functionalized silicones at the air-water interface.[46] The introduction of species into the subphase with which boronic acids are known to interact (e.g., 1,2-diols, amines and hydrogen bond disrupters) may serve to disrupt these interactions and/or to anchor the headgroup more strongly to the subphase. Moreover, molecules that are able to bind multiple boronic acids may serve to bridge the head groups, effectively forming physical crosslinks in the film, yielding changes in the film physicochemical and viscoelastic properties.[47-49]

Urea and guanidine hydrochloride (GdnHCl), both hydrogen bond disrupters, were added to the subphase. Isotherms on a 0.1 M GdnHCl subphase exhibited little or no shift from those on water (appendix B). Higher concentrations, often required to disrupt the hydrogen bonding in biological systems, were also tested. At concentrations of 1 M and 4 M, shifts in the isotherm were still not observed for urea but significant shifts to higher molecular area were observed for GdnHCl (Figure 4.2). Since both should disrupt hydrogen bonding but only GdnHCl exhibits an influence on the isotherm, it is likely that the interaction is via an alternative mechanism. Specifically, both compounds contain amines which can act as Lewis bases. However, the Lewis basicity of the urea amide is reduced due to resonance which likely reduces its binding strength with boronic acids. On the other hand GdnHCl has two primary amines which may bind to the boronic acid headgroups: this latter system could be charged unlike urea.

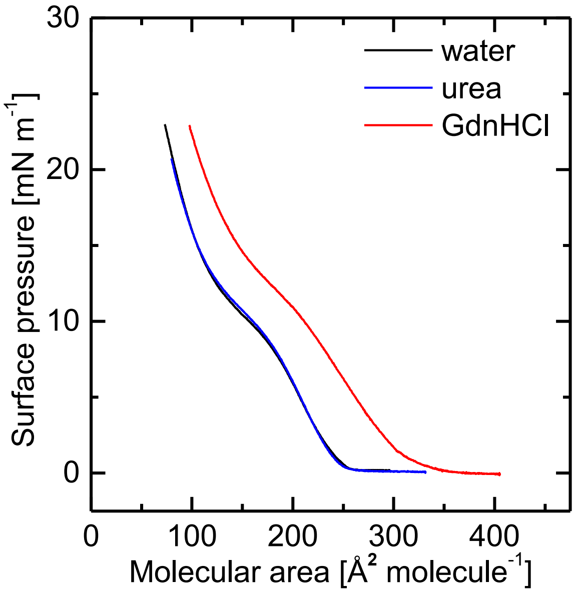


Figure 4.2. SiBA-10 on 4 M urea at pH 8.4 (blue) and 4M GdnHCl at pH 5.6 (red).

Since boronic acids are also known to bind 1,2-diol and 1,3-diol with differential binding strengths[1, 11] isotherms of the SiBA-10 were first obtained in the presence of glucose and fructose as shown in Figure 4.3A and C. Boronic acid-saccharide binding is known to occur at higher pH, but the addition of sugars decreases the apparent pK_a of boronic acids in solution, in which case the boronic acid-sugar binding may occur at lower pH values.[17] Here, the boronic acid-sugar binding at the air-water interface was tested on ultrapure water of pH approximately 5.5, without any additional change in pH of the subphase. It can be seen that in the presence of sugars at this pH, the isotherms do not show any shift, implying either no binding or very weak binding. This may be due to the low pH, but it may also be because of the boronic acid-boronic acid complexes at the interface[1, 46] which are so strong that the sugars are unable to disrupt the self-complexation.

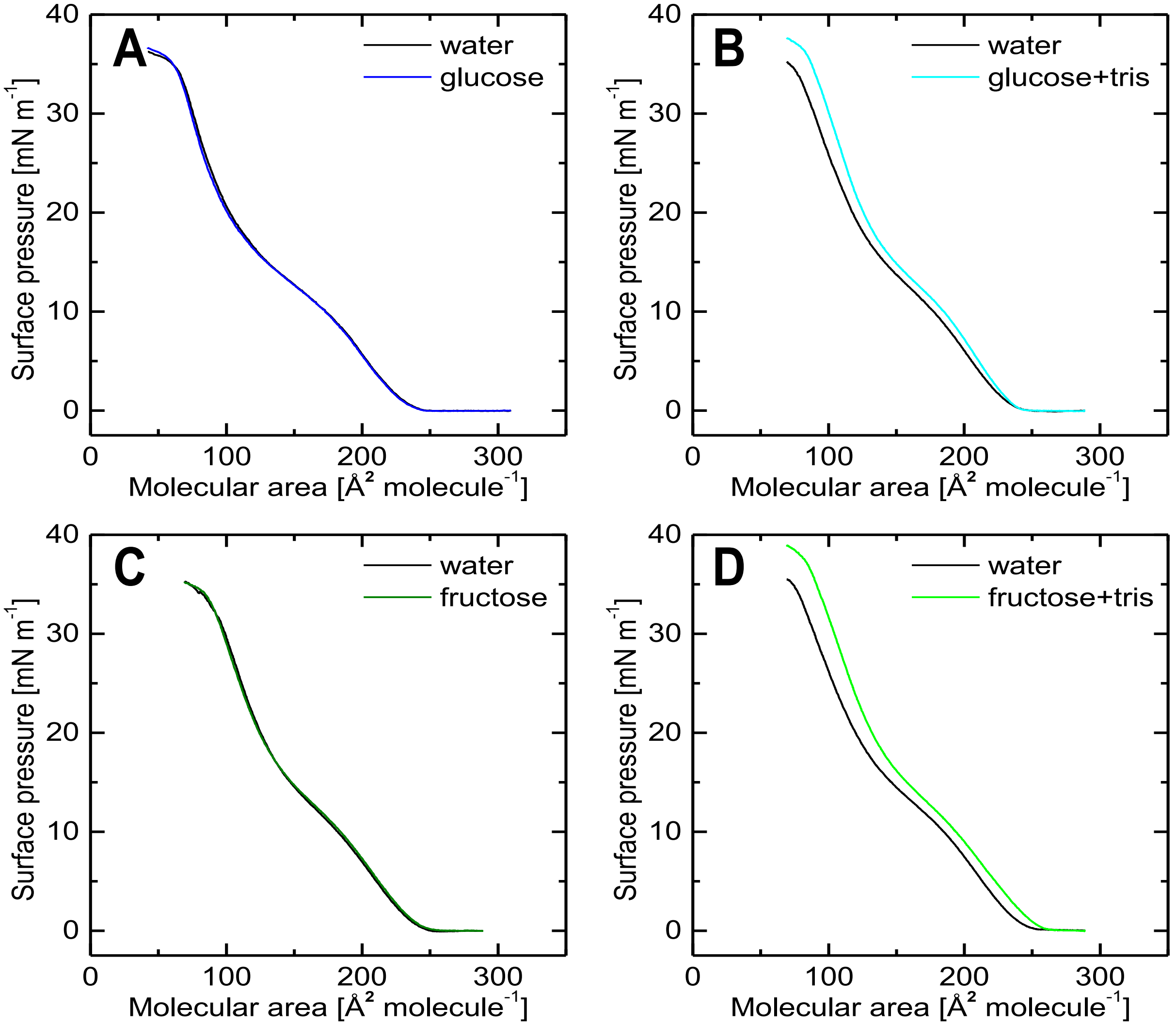


Figure 4.3. Isotherms of SiBA-10 on A) 0.1 M glucose (pH 5.0), B) 0.1 M glucose + 0.1 M tris (pH 7.4), C) 0.1 M fructose (pH 4.9) and D) 0.1 M fructose + 0.1 M tris (pH 7.4). In all cases the isotherm for SiBA-10 on water (control isotherm at pH 5.5) is also shown in black. Isotherms are plotted individually for clarity of relatively small shifts.

When the subphase additionally contained tris(hydroxymethyl)aminomethane (tris), the isotherm shifted distinctly to higher molecular areas (Figure 4.3 B and D). As mentioned before, tris is known to enhance sugar binding by promoting its tetrahedral boronate anion form.[1, 10] To determine if boronic acids were interacting with tris independently at the air-water interface, isotherms were obtained in the presence of tris without the sugars in the subphase. The isotherm in the presence of tris alone shifted to higher molecular areas (Figure 4.4) similar to those observed for the tris plus glucose system indicating that the tris interacts with the boronic acid headgroup at the air-water interface with a stronger affinity than the sugars. The tris amine effectively acts as a Lewis base and facilitates the formation of the tetrahedral boronate, enhancing the binding of sugars. It simultaneously provides the polyol to which the boronic acid can bind, negating the need for sugar molecule (although it is not clear if the boronic acid binds a diol and, if so, to which diol the boronic acid binds in the mixed subphase), exhibiting a type of autocatalysis for chemistry at boron.

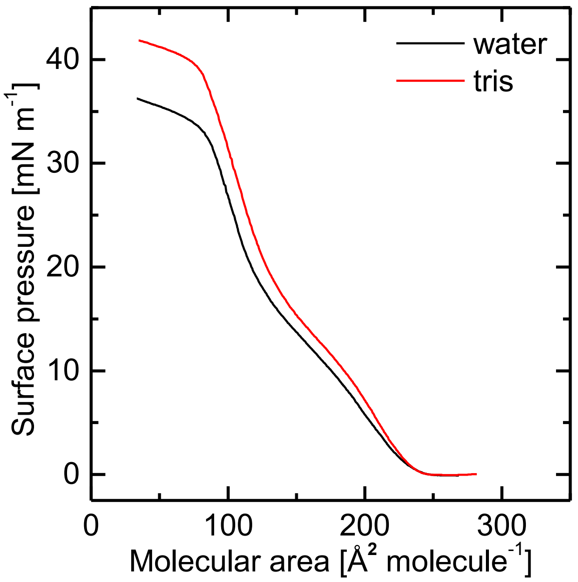


Figure 4.4. SiBA-10 isotherm on ultrapure water at pH 5.5 (black) and 0.1 M tris at pH 9.8 (red).

In order to further investigate the interactions of amines with boronic acids, including potential bridging, a selection of amines varying in the number of Lewis base moieties was studied (see Table 4.1) and the isotherms are presented in Figure 4.5. In all cases, the presence of an amine in the subphase had a significant impact on the collapse pressure and the isotherms, which show a shift towards higher molecular areas beginning from the phase transition plateau. Although the change to higher pH can also induce such shifts,[46] no significant impact on the collapse region of the isotherm has previously been reported for pH variations of the subphase (i.e., changing the charged state of the headgroups has not been shown to affect the collapse).

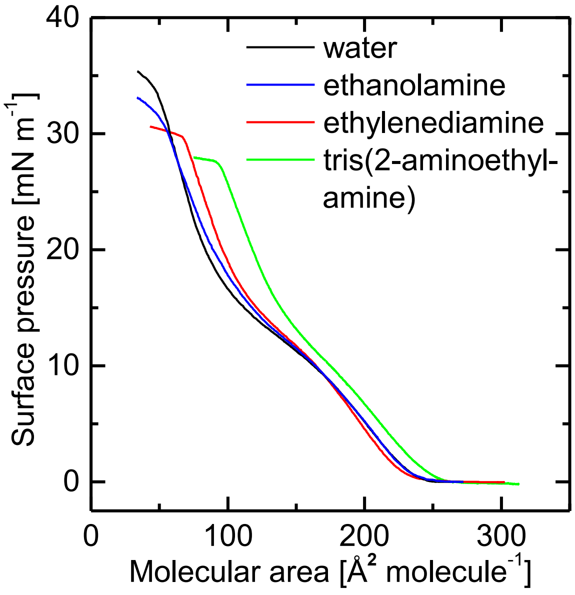


Figure 4.5. SiBA-10 with various different amines in the subphase. All subphase concentrations were 0.01 M and pH was approximately 10.5. Isotherm on ultrapure water at pH 5.5 (control) is shown in black.

Ethanolamine, which contains both an amine and a hydroxyl group, produced a slight shift in the isotherm towards higher molecular areas. With ethylenediamine (which has two amines and can potentially act as a boronic acid bridge at the air-water interface) present in the subphase, the isotherm is slightly shifted to lower molecular areas at the critical area, but shifts significantly to higher molecular areas at and above the phase transition plateau. Reducing the concentration tenfold from 0.1M to 0.01M of ethylenediamine in the subphase decreased the shift in the isotherm (Figure 4.6) even though the pH remained the same.

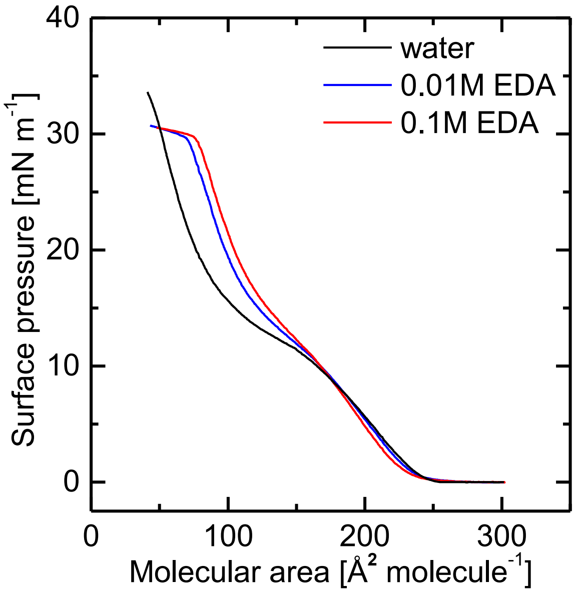


Figure 4.6. SiBA-10 on 0.01 M (blue) and 0.1 M (red) ethylenediamine (EDA) subphase. Isotherm on ultrapure water at pH 5.5 (control) shown in black.

Tris(2-aminoethyl)amine contains three primary amines, which can potentially bridge the boronic acids at the air-water interface forming more complex crosslinks, whereas ethylenediamine would only form linear linkages. In this case, the isotherm exhibits a larger shift to higher molecular areas at all surface pressures and the collapse pressure is further reduced. From these measurements, it would appear that the tris(2-aminoethyl)amine inserts between the boronic acid headgroups at the air-water interface, pushing the SiBA molecules further apart. In addition to the size difference between the two bridging molecules (ethylenediamine and tris(2-aminoethyl)amine), the nature of the bridging impacts the shifts. For ethylenediamine, linear chains are generated upon bridging that retain a high degree of conformational flexibility in the arrangements they can adopt at the air-water interface. On the other hand tris(2-aminoethyl)amine bridging forms a branched network that may limit the ability of the molecules to occupy all available space and shifts the isotherm to higher molecular areas even at low pressures.

Binding to the amines in the subphase impacts the collapse of the films: the greater the number of primary amines on the bound molecule, the greater the reduction in collapse pressure. Additionally, if the amines can bridge two or more headgroups, the collapse also becomes sharper. For PDMS films, it was noted that the stronger the tethering to the subphase (via end functionalization), the higher the collapse pressure.[46] We have previously found that boronic acid end-functionalization yields a collapse pressure similar to that of carboxylic acid end-functionalization.[28] On the other hand, monolayer studies of alkyl chain-based surfactants have shown that bridging of headgroups yields more stable films, which again results in an increase in collapse pressure.[47-50] In contrast, here the presence of crosslinkers in the subphase resulted in decrease in the collapse pressure suggesting that the boronic acid headgroups are strongly interacting with each other at the air-water interface and that this self-complexation is stronger than crosslinking with a bridging molecule. With regards to the sharper collapse observed with bridging molecules, Ludwig et al. showed that a steroidal phenyl boronic acid can be bridged in a 2:1 complex with sugars at the air-water interface leading to a similarly sharp collapse.[51] On the other hand, they also showed that an amphiphilic diphenylmethane-3,3’-diboronic acid, (where two phenylboronic acids are chemically connected) forms a 1:1 complex with the sugar and exhibits a less well-defined collapse.

4.5. Conclusion

Silicone boronic acid thin films have been studied at the air-water interface for their differential interaction with diols and amines. Boronic acids do not show much sensitivity for sugars in the subphase, which may be due to the low pH of the ultrapure subphase (formation of tetrahedral boronate anions is disfavoured), or due to the boronic acid-boronic acid complexation at the air-water interface. While boronic acids did appear to show increased sensitivity to sugars when they were present along with amines in the subphase, similar shifts are also observed for amines alone. However, the presence of amines without sugars also impacted the film collapse. The greater the number of primary amine moieties, the greater disruption to the film stability, evident from the larger reduction in collapse pressure. While small molecule crosslinkers in the subphase generally increase film stability of surfactants, here, the already strong boronic acid-boronic acid complexation at the air-water interface are disrupted by the amines in the subphase, making the film less resistant to collapse upon compression.

Chapter 5. Conclusions and Future Work

The objective of this work was to evaluate the film-forming properties of silicone boronic acids for potential long-term applications in materials chemistry, biosensing and biocompatible materials. Silicone boronic acids show similar phase behaviour at the air-water interface to both non-functionalized and end-functionalized PDMS. As with other polar end-functionalized silicones, SiBAs show a significant increase in surface pressure when the film is compressed to small molecular areas suggesting that the boronic acids are strongly tethered to the aqueous subphase. What differentiated the boronic acids from other polar headgroups (end functionalization) is that SiBAs occupy a relatively larger surface area at the air-water interface than other functional groups. Where other polar headgroups are more commonly submerged into the subphase, boronic acids are likely oriented planar to the subphase, possibly forming boronic acid-boronic acid complexes at the interface. Hydrogen-bond disrupters such as urea and guanidine hydrochloride had essentially no impact on the isotherm at moderate concentrations. Very high concentrations of guanidine hydrochloride were able to induce shifts in the isotherm to higher molecular areas indicative of an interaction. However, it must be considered that both these hydrogen bond disrupters also contain an amine moiety. Future work should investigate the impact of a non-amine-derived hydrogen bond disrupter. Preliminary work with sodium chloride subphases (data not shown) has shown that the effects are not due to a simple counterion effect.

The strong boronic acid-boronic acid complexation may define the extent to which the boronic acids can bind to small molecules in the subphase. The boronic acids do not show sensitivity for sugar molecules in the subphase, although it is likely that the pK_a is not shifted sufficiently for the boronic acid to adopt a tetrahedral form required for binding at the pH of ultrapure water (pH 5.5). This is in agreement with previous studies of alkyl and cholesterol derived phenylboronic acid and diphenylboronic acids, where binding to sugars was only observed at pH values >10.[19, 51] The addition of a Lewis base (tris) appeared to increase the sensitivity towards diols even at pH values as low as 7.4, however, this work showed that amines alone may be responsible for the observed shifts and changes to the film collapse.

Amines in the subphase appear to interfere with the boronic acid-boronic acid complexation at the air-water interface, which results in a larger occupied molecular area, and decrease in the stability of the film, evidence from the decrease in the collapse pressure. This implies that the boronic acid self-complexation is strong enough that simple diol molecules cannot break apart, but rather, one needs an acid-base reaction to disrupt the complexation.

In order to further probe the boronic acid-boronic acid complexation at the air-water interface, mixed surfactant films containing a mixture of SiBA with amine or diol surfactants may also be studied. It has been reported that the sensitivity of boronic acids can be altered by diluting a phenylboronic acid monolayer with amphiphilic quaternized ammonium ions.[19] Boronic acid interactions with adjacent diol or amine headgroups may yield different properties at the air-water interface. Those interactions may also be subjected to disruption by small molecules in the subphase to determine if they also yield similar surface properties as boronic acid-boronic acid complexation.

Isotherm shifts are determined by multiple factors include pH, counterions (as a function of pH) and bound crosslinkers. Future work should include a more comprehensive study of competing factors. It is noted though that the collapse region may be a useful indicator of both the strength of tethering and crosslinking of the headgroups. Since boronic acid-sugar binding is highly pH dependent, silicone boronic acid interactions with sugar molecules as a function of subphase pH may also be studied. Additionally, there is vast amount of literature with boronic acid-saccharide binding studies, but boronic acid binding is not limited to sugars, there are many other biologically relevant diol compounds which may be targeted using boronic acids. Thus, boronic acid binding with other diol compounds, other than sugars, such as catechol or dopamine should also be an interaction of interest for biosensing applications.

Last but not least, physical crosslinkers are known to give rise to elastic behavior,[49] thus the viscoelastic properties if SiBA films with and without crosslinkers in the subphase would be useful to study. Due to the complexation at the air-water interface, the SiBA films are more stable, as well as more rigid, the presence of small molecules in the subphase result in a change in the viscoelastic properties of the film, leading to a buckling mechanism of collapse (sharper collapse). Film properties may be tuned based on variations in parameters such as amines/sugars/diols of varying concentrations in the subphase, subphase pH and a combination thereof. Compression-expansion cycles of the film in presence of crosslinkers in the subphase may also shed light onto the elastic properties of the film. Also the viscoelastic properties of mixed films with varying subphase properties may also be studied in order to determine optimum conditions for developing robust, SiBA thin films for practical applications.

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Appendix

Appendix A: Supplementary information for Chapter 3 (Surface behavior of Boronic-Acid Terminated Silicones)

Brewster angle microscopy

Brewster angle microscopy is used to follow film morphology changes throughout the compression isotherms; images obtained for functionalized and non-functionalized PDMS at the air-water interface are shown in Figure A.1. At very low pressures two-dimensional foam can be observed as has previously been reported.[29, 52] Beyond the critical area at which pressure begins to increase, no contrast can be observed within the films, even across most of the plateau region. For both end-functionalized and non-functionalized PDMS, small, very bright domains are observed starting at mid-way through the plateau region, although it should be noted that the density of domains in not uniform across the film, i.e. there are regions of a high and low density of domains. The formation of such domains for PDMS has been previously reported in literature, and are associated autophobic dewetting of PDMS.[38, 39, 52, 53] From the BAM images, it can be seen that these domains grow in density and brightness as the film is compressed, the latter indicating that they are much thicker than the rest of the film. Both the functionalized and non-functionalized films display similar morphologies despite the differences in the isotherms and in ellipsometry in this region.

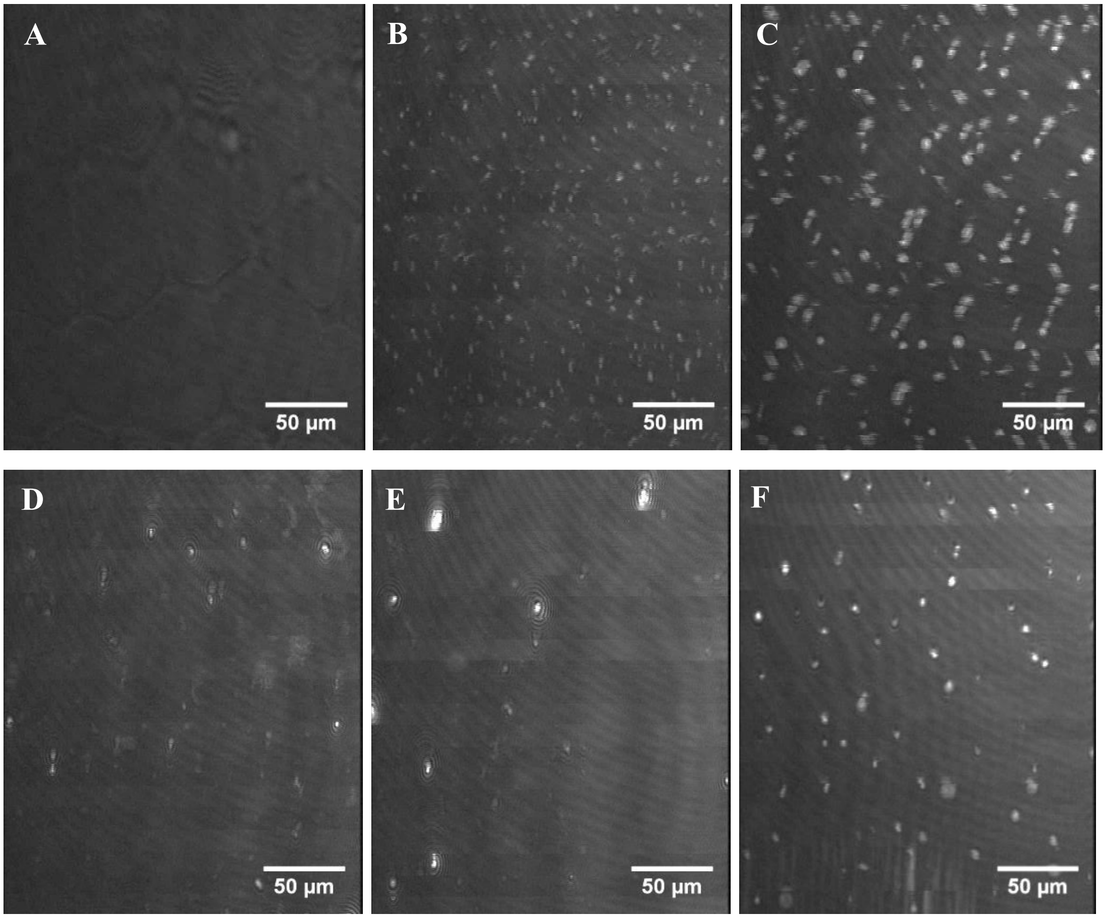

Figure A.1. *Top row* (images A-C), BAM images for SiBA-10 (A: 246 Å^2·molecule^{-1}, 0.2 mN·m^{-1}; B: 64 Å^2·molecule^{-1}, 23 mN·m^{-1}; C: 48 Å^2·molecule-^{1}, 26 mN·m^{-1}. *Bottom row* (images D-F), BAM images for SiBA-69 (D: 349 Å^2·molecule^{-1}, 11 mN·m^{-1}; E: 267 Å^2·molecule^{-1}, 12 mN·m^{-1}) and H-PDMS-69 (F: 377 Å^2·molecule^{-1}, 8 mN·m^{-1}).

Recompression isotherms

Figure A.2 shows the recompression isotherms for SiBA-16. The overlapping expansion and subsequent recompression isotherms indicate that the hysteresis is generated by a slow respreading rather than a partial solubility of the SiBAs.

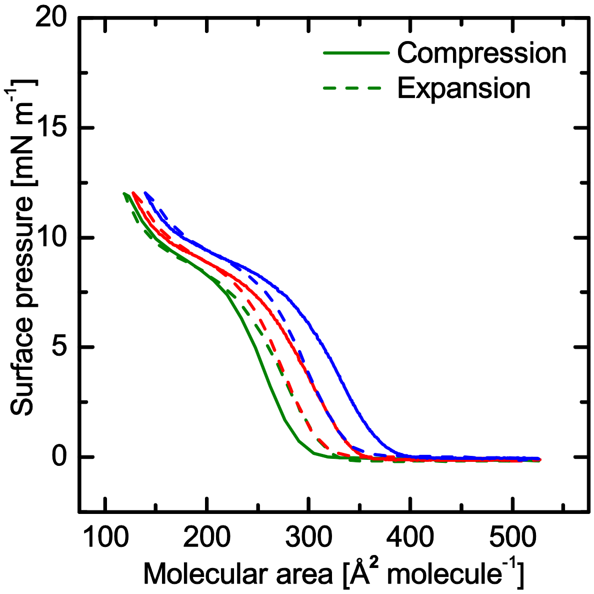

Figure A.2. Isotherm for repeated compression-expansion cycles for SiBA-16 on water at room temperature where solid lines represent film compressions and dashed lines of the same color the corresponding film expansion. Recompression starts immediately after expansion without any equilibration time.

Appendix B: Supplementary information for Chapter 4 (Interfering with Headgroup Organization of Silicone Boronates at the Air-Water Interface)

The isotherm of SiBA-10 on 0.1 M GdnHCl is presented in figure A.3. The control isotherm (on ultrapure water subphase) is shown in black. At low concentrations of GdnHCl, the isotherms do not seem to be affected by the presence of the hydrogen bond disruptor in the subphase.

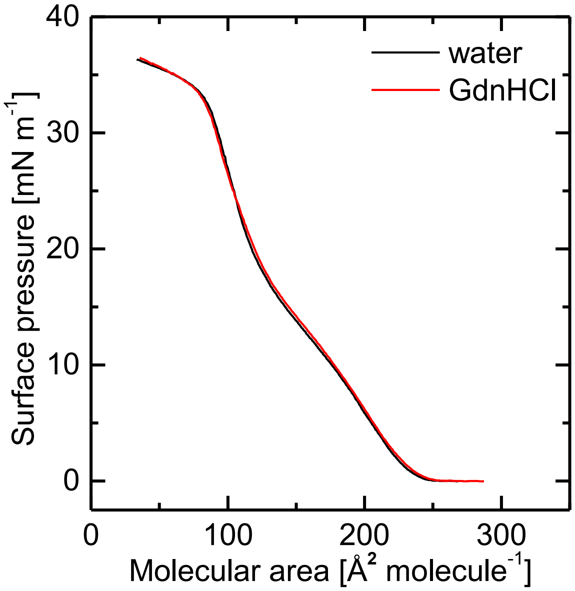

Figure A.3. SiBA-10 on ultrapure water at pH 5.5 (black) and 0.1 M GdnHCl at pH 5.6 (red).