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Functionalized Vesicles Based on Amphiphilic Boronic Acids: A System for Recognizing Biologically Important Polyols

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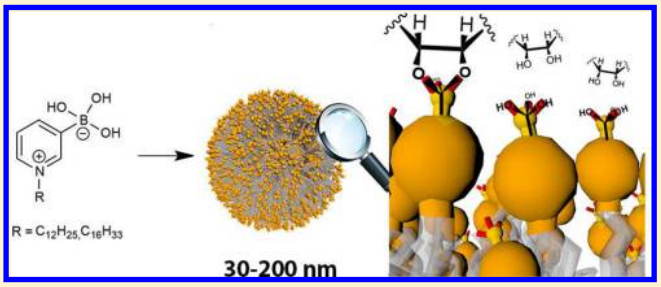
Supporting Information

ABSTRACT: We report on a new approach for creating water-soluble functionalized vesicles employing *N*-alkyl-3-boronopyridinium triflates (alkyl = Me, $C_{12}H_{25}$, $C_{16}H_{33}$) as sensors for monosaccharides. The nanoaggregate properties were studied by means of DLS, TEM, high-resolution ^{1}H NMR, and the solvatochromic dyes Reichardt's betaine and Methyl Orange. The vesicles were shown to have 30−200 nm diameters depending on the amphiphile chain length. Diol binding to the vesicles was studied by steady-state fluorescence and UV−vis using Alizarin Red S as a probe in the solution at pH 7.4 in the presence and in the absence of D-glucose and D-fructose. Strong sensing ability of boronic acid functional moieties in the order D-fructose > D-glucose was demonstrated, and apparent binding constants were estimated.



INTRODUCTION

The search and design of synthetic chemosensors for biologically important molecules have been seriously developing over recent decades.[1,2] Recognition of different small biologically important molecules is an integral part of supramolecular chemistry.[3,4] The saccharides chemistry plays a significant role in the metabolic pathways of living organisms. Detecting the presence and concentration of biologically important sugars (glucose, fructose, galactose, etc.) in aqueous solution is necessary in a variety of medicinal and industrial contexts. For instance, the quantitation of glucose plays a pivotal role in diabetes control.[5] Different approaches for sensing of glucose and other monosaccharides have been reported such as enzymatic,[6] fluorescence,[7−10] optical,[11,12] and electrochemical[13,14] methods. The most promising way to construct saccharide-sensitive molecular receptors is to use the ability of boronic acid to form covalent bonds with 1,2- and 1,3-diols.[15,16] Boronic acids and their esters are highly valuable compounds which have found extensive applications in organic and medicinal chemistry. The utility of organoboronic acids in organic synthesis has flourished in recent years, particularly through developments in Suzuki−Miyaura coupling.[17] These compounds are known as an attractive class of synthetic intermediates and structures for self-assembly and functional materials.[4] Because of the relatively low toxicity of boronic acids and their degradation into the environmentally benign boric acid, they can be considered as "green" compounds. Recently, a number of boronic acid-based sensing systems have been reported,[18] some of them based on the boron-containing cavitands derived from calyx-4-resorcines in Langmuir films,[19] monolayer films with catechol sensing selectivity,[20] sensitive thin-layer chromatography detectors,[21] dye displacement with boronate hydrogels,[22] and color chemosensors based on boronate-containing azo dye.[23] Organized molecular systems have also been proposed, namely micelles[24] or vesicles[25] of cationic surfactants solubilizing nonmicellar aryl boronic acids in the presence of fluorescence dye, or oriented molecular aggregates of porphyrin-based amphiphiles.[26] Vesicles functionalized with both boronic groups and fluorescence probes have been reported to study in the THF/water or methanol/water mixture.[27,28] To the best of our knowledge, no water-soluble, solvent-free vesicular system has been previously proposed.

The ability to monitor the presence of analytes within physiological and environmental systems is of crucial importance. However, due to the scale at which recognition events occur on the molecular level, gathering this information and providing cheap and simple methods of monitoring poses a nontrivial challenge. Surfactants bearing specifically modified moieties, or functionalized surfactants,[29] open opportunities to use the advantages of nonfunctionalized organized molecular systems (bringing together analyte and a sensing molecule in water/micelle or water/vesicle interface) with the high "local" concentration of specific moieties responsible for sensitivity. Recently, we reported simple and efficient methods of synthesis of *N*-alkyl-3-boronopyridinium triflates[30] and iodides[31] (compounds **2** and **3** in Scheme 1). These surfactants are the derivatives of pyridine-3-boronic acid which is known as one of the least basic among aryl boronic acids, its pK_a (constant of

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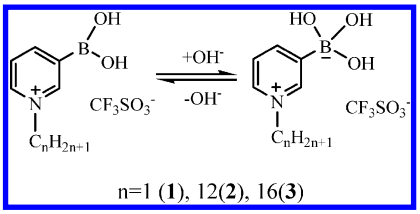
Scheme 1. *N*-Alkyl-3-boronopyridinium Surfactants in the Trigonal (left) and Tetragonal (right) Form of Boron



indirect proton transfer that characterizes the acidity of most boronic acids in water followed by trigonal–tetragonal boron transformation[4]) is as low as ca. 4.3, and its alkylation does not change the pK_a significantly.[32] At the same time, *N*-alkyl derivatives of 3-pyridineboronic acid are well soluble in water at concentrations providing micelle or vesicle formation, whereas pyridine-4-boronic acid derivatives are sparingly soluble in water. And finally, **2** and **3** have abnormally low critical aggregate concentrations of 0.158 and 0.016 mM,[30] respectively.

In the present study, we (i) characterize the formation of vesicles of surfactants **2** and **3** and (ii) analyze their ability to selectively bind the monosaccharides, D-fructose and D-glucose. We will discuss that the structure of functionalized boronopyridinium surfactants causes changes in vesicle size and play an important role in the binding of biologically important polyols.

EXPERIMENTAL SECTION

All chemicals were purchased from commercial suppliers and used as received. Solvents were purified and dried by standard methods prior to use, when needed. Boronic acids **1**–**3** were synthesized according to the previously reported method.[30,31] All solutions were prepared using water from a Millipore UltraPure system (18.2 MΩ·cm). Solutions of compounds **2** and **3** were sonicated for 20 min until they had completely dissolved and then equilibrated at 25 °C in the thermal control unit before running an experiment.

Dynamic Light Scattering (DLS) Studies. The size of the aggregates was determined from DLS measurement by using a Zetasizer Nano S (ZEN3600) light scattering apparatus (Malvern Instruments, Westborough, MA) with a He–Ne laser (632.8 nm, 4 mW). The solution was filtered directly into the scattering cell through a Millipore Millex syringe filter (Triton free, 0.2 μm). Before measurements, the scattering cell was rinsed with the filtered solution, and the sample solution was equilibrated for 5–10 min in the DLS optical system. The scattering intensity was measured normally at θ = 173°. Data acquisition was carried out for 10 min.

Transmission Electron Microscopy Studies. Transmission electron microscopic measurements were performed with a high-resolution transmission electron microscope (TEM HT 7700 Hitachi, Japan) operating at 100 keV. The transmission electron microscopic measurements were performed using aqueous solutions of the amphiphile after equilibration for 4 h. A drop of surfactant solution was put on a copper grid coated with carbon and allowed to soak for 2 min; the surface solvent on the grid was removed by trapping in a filter paper followed by staining with 1% aqueous uranyl acetate solution. The specimens were then dried in desiccators prior to the measurements.

NMR Studies. High-resolution ^{1}H NMR spectroscopy was performed for **2** at the concentrations 0.2–1 mM using a Bruker NMR 500 MHz instrument equipped with a CryoProbe with water suppression. Solutions prepared in phosphate buffer (pH = 7.4) containing 10% of D_2O. ^{11}B spectra were recorded in quartz tubes using a Bruker AVANCE 400 MHz and a Bruker 300 MHz instrument.

UV–Vis Spectroscopy and Spectrofluorometry. Absorption UV–vis spectra were recorded in 10 mm quartz cells using a HP 8452A and an Analytik Jena Specord 600, both diode array spectrophotometers equipped with a thermostated single cell holder (HP 8452A) or 8-cell changer (AJ Specord 600), and Genesys 10S UV–vis (Thermo Electron) spectrophotometer equipped with a thermostated cell unit. Steady-state fluorescence measurements were performed in aqueous solutions using PTI (Photon Technology International) Quantamaster 1 equipment. The four-side transparent quartz cells (10 mm path length) used for the measurements were equilibrated at 25 °C. The fluorescence spectra obtained by excitation at 495 nm (high-pressure Xe lamp, 419 W) were recorded between 450 and 650 nm, and total fluorescence intensities (I_F) were calculated by integration of the fluorescence band centered at ca. 565 nm. Solvatochromic dyes Reichardt's betaine (RB) and Methyl Orange (MO) were prepared as 1–10 mM stock solutions, added by microsyringe, and used at the concentrations 0.05 and 0.01 mM, respectively.

Binding Constants ARS/Monosaccharides–Boronic Acid. A typical solution for the study of binding fluorescence dye Alizarin Red S (ARS) and boronic acids **1**–**3** consisted of phosphate buffer at pH = 7.4, ARS (0.01 mM) and boronic acid ranging in concentrations from 0.01 to 1 mM. For determination of binding constants with monosaccharides, the same pH and ARS concentrations were used, the concentration of boronic acid corresponding to $[D]_t$/CAC ca. 5 was fixed, and concentrations of fructose or glucose were varied. Calculations were done using the Beneshi–Hildebrand equation following previously published recommendations.[33–35]

RESULTS AND DISCUSSION

Vesicle Formation. Boronopyridinium surfactants **2** and **3** in water at physiological pH should be considered as zwitterionic surfactants. Indeed, the pK_a values of **2** (3.8 ± 0.1) and **3** (3.9 ± 0.1) determined from by UV–vis titration, and ^{11}B NMR spectra are slightly lower than the pK_a of pyridine-3-boronic acid reported in the literature.[32] Hence, at pH > 6.0 the boronopyridinium salts completely transformed into the tetragonal form (Scheme 1, structure on the right); zwitterionic nanoaggregates are expected to appear in the water solution. This may partly explain the unexpectedly low critical aggregation concentration (CAC) (0.158 and 0.016 mM for **2** and **3**, respectively) values we reported earlier,[30] compared to the critical micellar concentrations (CMCs) of cationic surfactants having the same chain length. Thus, compound **2** forms aggregates at concentrations much smaller in comparison to dodecylpyridinium halides (CMC 11.5 mM) and *N*-dodecylnicotinamide (CMC 11.0 mM).[36] The critical aggregate concentrations of **2** and **3** are quite similar to those of zwitterionic micelles formed by *N*-alkylbetaines of comparable chain length.[37]

The DLS study of the solutions of **2** and **3** in the concentration range 1 < $[D]_t$/CAC < 5 shows that there are no aggregates were found below 10 nm (e.g., micelles). At the same time, aggregates with an apparent diameter of 30–50 nm in the solution of **3** and 100–200 nm in the case of **2** were found (see Figure 1). The aggregate sizes obtained from the DLS data are considerably higher than those for spherical micelles which suggests the existence of nanoaggregates of higher hierarchy, namely spontaneous forming vesicles. Transmission electron microscopy (TEM) provides an additional support to this suggestion. In Figure 2, TEM photographs with the negative staining agent, uranyl acetate, taken at the same concentration of **2** and **3** as in the DLS study, demonstrate very similar size distributions. The nanoaggregates are sphere-like in their shape and have "halos" of the staining dye as often observed for vesicles.

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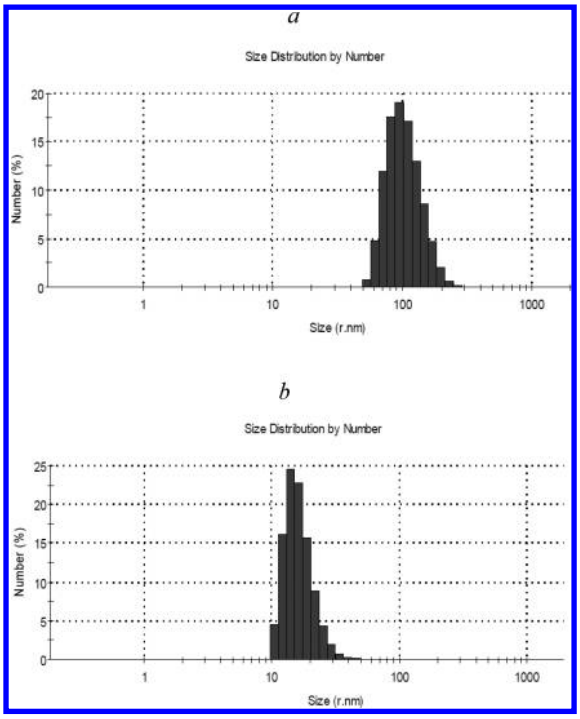

Figure 1. DLS data for solution of surfactants **2** (a) and **3** (b); concentrations of both surfactants correspond to $[D]_t$/CAC ca. 5 ($[\mathbf{2}]_0$ = 0.8 mM; $[\mathbf{3}]_0$ = 0.08 mM).

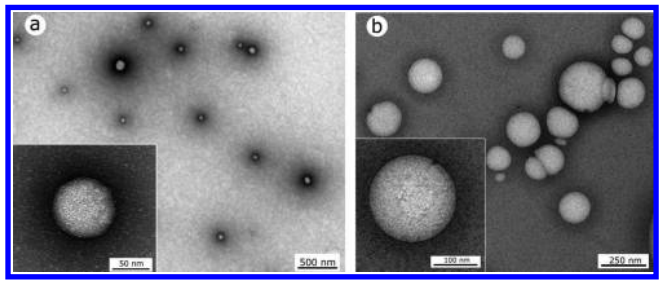

Figure 2. TEM pictures for surfactants **3** (a) and **2** (b); surfactant concentrations correspond to $[D]_t$/CAC ca. 5 ($[\mathbf{2}]_t$ 0.8 mM; $[\mathbf{3}]_t$ 0.08 mM), uranyl acetate as staining agent. Insets are the magnifications of the image.

TEM pictures revealed the existence of closed bilayer vesicles in aqueous solution. Therefore, for the first time, it was observed that a single-chain boronic acid-based amphiphile spontaneously assemblies to vesicles in aqueous solution. There are numerous reports on vesicle formation from natural amphiphiles (mainly phospholipids), and synthetic surfactants have been reported.[38,39] The organization of various bilayers of single-tail surfactants is well-known.[40] The phenomenon of vesicle formation by single-tailed surfactants[41−44] and the stability of unilamellar and multilamellar surfactant vesicles[45] have been extensively investigated. In most cases, catanionic single-tailed surfactants or mixed surfactants are used to form vesicles. At the same time, limited evidence on zwitterionic surfactants, namely betaines[46] and nicotinic acid-based amphiphiles,[47] indicates the formation of small vesicles in water. In contrast to the latter investigation,[47] we did not observe the existence of the second break in the surface tension vs concentration plot which may be explained in terms of the very narrow concentration range of the micellar solution followed by spontaneous vesicle formation.

The dodecyl derivative **2** forms considerably larger vesicles than its cetyl chain length analogue **3**, at the same normalized concentration (i.e., $[D]_t$/CAC). According to the literature data,[48,49] the longer chain length monocationic and Gemini surfactants form the larger aggregates. This surprising sensitivity of vesicle formation to chain length may be evidence of strong headgroup repulsion compared to hydrophobic forces between the tails which favors "tighter" (i.e., water-deficient) bilayers in the case of shorter chain derivatives giving significantly larger aggregates.

Note that a slight increase of the aggregate size of **3** occurred with an increase of its concentration up to $[\mathbf{3}]_t$/CAC ca. 10 (0.16 mM), a concentration close to the CAC of **2**. We can assume that in the equal total concentration of surfactant $[\mathbf{3}]_t \geq$ 0.8 mM (equal to $[\mathbf{2}]_t$/CAC ca. 5) the difference in their size is not that great. Revisiting our recent data,[30] it is worth noting that we cannot reach the CAC of the *N*-octyl-3-boronopyridinium salt within the concentration range of its solubility at 25 °C. Considering the above-mentioned, it may not be observed due to the tendency of this derivative to form a water-deficient bilayer which does not pack into vesicles within the concentration range studied. In contrast to the catanionic surfactants or Gemini surfactants, aggregates of boronopyridinium amphiphiles form when only zwitterionic (tetrahedral boron) single-chain surfactant is present. Considering relatively high A_{min} values reported for **2** and **3** earlier,[30] the driving forces of spontaneous vesicle formation should be analyzed. A remarkable property of boronic acid is the ability to form boroxines, which may also contain oligomeric acyclic analogues.[2] The thermodynamic parameters of boroxine formation in water were examined by Tokunaga et al.[50] using ^{1}H NMR spectroscopy. The reaction was found to be reversible at room temperature with a small equilibrium constant. In water, the equilibrium is predominantly shifted toward free boronic acid, whereas in the hydrophobic premicellar aggregates in the presence of high "local" concentration of head groups we could expect equilibrium formation of a condensation product. Such equilibrium formation of the boroxines or their acyclic analogues could change crucially the packing parameter and therefore favor vesicle formation. The balance of forces controlling the dispersion interactions of hydrophobic tails and Coloumbic forces controlling charged head groups attraction/repulsion directs self-organization toward a certain type of the nanoaggregates, namely toward vesicles.

High-resolution ^{1}H NMR spectroscopy provided information about the microenvironment of the nanoaggregates.[51] The changes in the chemical shifts of pyridinium protons in the concentration range of surfactants $1 < [\mathbf{2}]_t$/CAC < 5 are shown in Figure 3.

Interestingly, the chemical shifts change little around the CAC, whereas at $[\mathbf{2}]_t$/CAC ≥ 3 the divergence rises and remains similar when $3 < [\mathbf{2}]_t$/CAC< 5. Broadening of the signals corresponds to water-deficient packing, either micellar or bilayer organization, whereas the low field shift of pyridinium protons (in particular, ca. 0.2 ppm for Pyr-H2 singlet signal; see Figure 3) can be considered as an evidence of *in situ* boroxine formation. At the same time, the chemical shift of cetyl derivative **3** at $[\mathbf{3}]_t$/CAC ca. 5 was found to be smaller than 0.1 ppm (Figure S3).

The phenomenon of solvatochromism has been widely employed as a useful tool for the characterization of the microenvironment of the solvent systems or self-assemblies,

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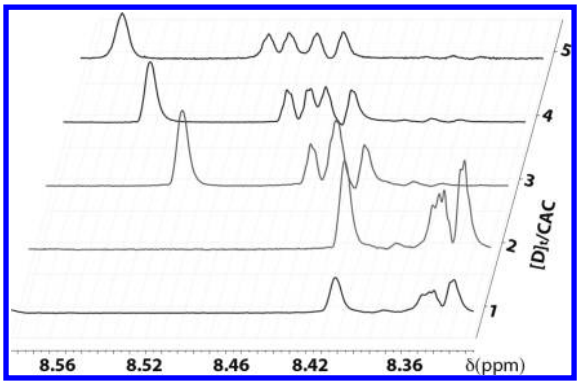


Figure 3. ^{1}H NMR spectra of **2** at different normalized concentrations ($[D]_t$/CAC); phosphate buffer (pH 7.4), 10% D_2O. 500 MHz (CryoProbe).

both in the premicellar area[52] and over the corresponding critical concentration.[53] We analyzed the UV−vis spectra of the solvatochromic dyes Methyl Orange (MO) and Reichardt's betaine (RB) at the normalized concentration of surfactants **2** and **3** equal to $[D]_t$/CAC = 5. MO is an anionic dye establishing positive solvatochromism, and RB is a probe with the negative solvatochromism. The maximum absorbance peaks for MO and RB and E_T30 values for RB are collected in Table 1.

Table 1. Absorbance Characteristics of Solvatochromic Dyes RB and MO

surfactant	MO/nm	RB/nm (E_T30/kcal/mol)
2	406	515 (55.52)
3	420	540 (52.95)
CTABr	432	538 (53.14)
DTABr	425	532 (53.74)
water	462	452 (63.25)

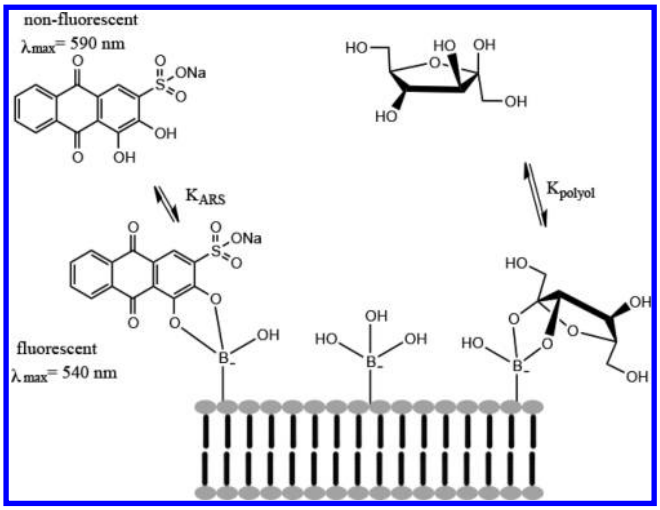
As seen in Table 1, MO undergoes a larger shift in the presence of **2**, whereas its maximum in the presence of **3** is generally similar to the wavelength corresponding to conventional cationic surfactants. The larger shift corresponds to a more hydrophobic localization site of the dye.[54] It can therefore be concluded that the microenvironment of the vesicle bilayer of **2** is more hydrophobic, enhancing its ability to form larger vesicles. This observation supports the above-discussed ^{1}H NMR spectroscopy data, suggesting that the higher hydrophobicity of **2** can lead to a higher equilibrium concentration of boronic acid condensation products which, in its turn, favors a larger size of vesicle.

Changes in the spectra of RB are less obvious. Being a negative solvatochromic probe, it usually undergoes a bathochromic shift if solvent polarity is lower. Surfactant **3** presents a shift similar to that of cationic micelles, as was the case of MO whereas the peak of RB for solutions of **2** is shifted toward more polar regions. One of the reasons for this observation could be a repulsion of the dye from the interface as has been reported for elongated micelles.[55,56]

Thus, surfactants **2** and **3** can form vesicles of different sizes and interface micropolarities. At the same normalized concentration ($[D]_t$/CAC), the shorter the chain length, the more water-deficient the interface and therefore the larger the vesicle size.

Diol Binding. To investigate monosaccharide binding, we used a method involving the competitive binding of the fluorescent probe ARS[57] by means of spectrofluorometry and UV−vis spectrophotometry. The principal mechanism of diol binding and sensing by the boronic acid moiety of functionalized vesicles of **2** and **3** is shown in Scheme 2.

Scheme 2. A Mechanism of Diol Sensing by Functionalized Vesicles of 2 and 3 with D-Fructofuranose as an Example



Interaction of the boronic acids with ARS has been the subject of numerous studies. It is generally considered that binding of biologically important polyols is more favorable if boron is tetracoordinated.[33] However, as shown by Benkovic in his recent detailed study,[58] both trigonal and tetragonal forms of the boronic acid can interact with ARS acting as fluorescent responsive species.

We studied the binding capacity of the functionalized vesicles at physiological pH (7.4) where all *N*-alkyl-3-boronopyridinium salts are entirely present in the tetragonal form and no complex interaction occurs, according to the recent time-resolved study.[59] Spectrofluorometric and spectrophotometric titration of ARS are shown in Figure 4; the determination of binding constants proceeded according to the algorithm recommended in the paper of Hargrove et al.[35] Binding constants for ARS by different techniques are collected in Table 2.

Fluorescence intensity of ARS increases about 1 order of magnitude in the presence of vesicles **2** and **3** compared to **1** taken at the same concentration, which is in agreement with data reported for nonfunctionalized micelles[24] and vesicles.[25] Interestingly, surfactants **2** and **3** demonstrated different binding abilities. The data are consistent by two different methods, and values for **1** and **2** are similar. Nevertheless, surfactant **3** demonstrated much stronger affinity toward ARS in terms of $K_{b,app}$. This could be caused by the differences in packing of the bilayers in small and large vesicles. A vesicle of **3**, due to its higher curvature, has to be less hydrophobic than a vesicle of **2** so it is seemingly able to increase its affinity to ARS by both boronic ester formation and solubilization mechanisms. Another factor influencing the affinity of the vesicles formed by **2** and **3** could be the "local" concentration of boronic hydroxyl groups affected by the concentration of boronic acid condensation products in the nanoaggregate. As it was higher with **2**, less free boronic acid was available on surface. Hence, its affinity for ARS might be lower in comparison with **3**.

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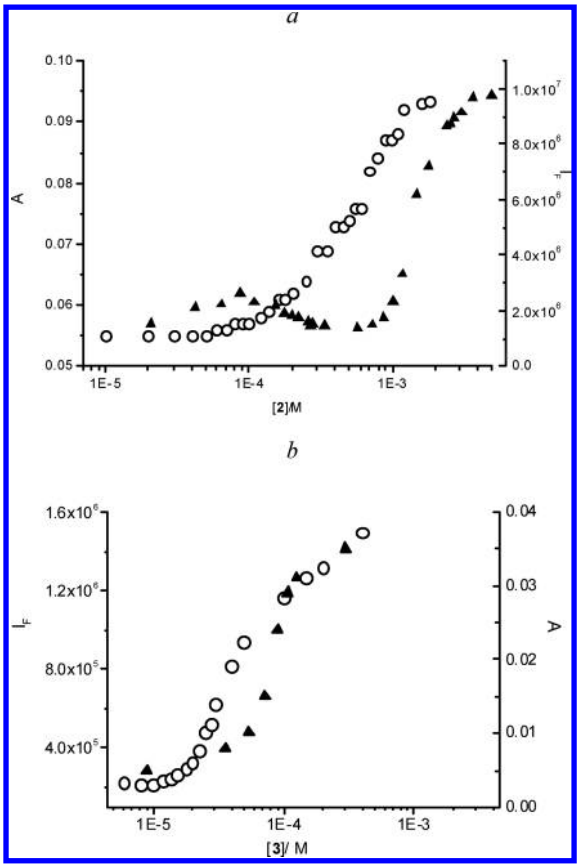

Figure 4. Fluorescence intensity (▲) and absorbance (○) for interaction of ARS with **2** (a) and **3** (b); [ARS] = 0.05 mM.

Table 2. Apparent Binding Constants $K_{b,app}/M^{-1}$ of ARS with Functionalized Vesicles 2 and 3

method	1	2	3
UV−vis	850 ± 30	810 ± 30	10100 ± 400
fluorescence	770 ± 20	625 ± 20	11000 ± 500

The binding of monosaccharides was monitored by two methods. The apparent binding constants calculated from UV−vis data are presented in Table 3.

Table 3. Apparent Binding Constants $K_{b,app}/M^{-1}$ of D-Glucose and D-Fructose with Functionalized Vesicles of 2

$[2]_t$/CAC	D-fructose	D-glucose
1	40 ± 5	5 ± 1
2	35 ± 5	5 ± 1
3	29 ± 4	5 ± 1
4	20 ± 3	6 ± 1
5	10 ± 3	6 ± 1

The apparent binding constant of fructose was low even at the CAC and gradually decreased as the surfactant concentration was increased. The K_b obtained for glucose was comparable to data from the literature for water solutions and did not change within the concentration range studied. This suggests that the equilibrium in larger vesicles between ARS, polyol, and boronic moieties can be more complicated than shown in Scheme 2. The binding constant for fructose by vesicles of **3** was constant at 25 ± 10 M^{-1} within the normalized concentration range $2 < [3]_t/CAC < 10$.

In spite of the low values of $K_{b,app}$, observed polyol sensing effects were significant. We report the relative values of the fluorescence quenching upon addition of the corresponding sugar to the vesicle−ARS mixture in Figure 5.

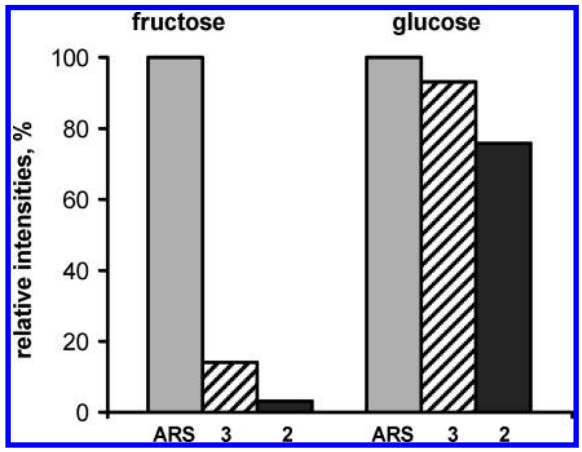

Figure 5. Binding characteristics of the solutions of **2** (0.8 mM) and **3** (0.08 mM) by introduction of fructose and glucose in phosphate buffer solutions (pH 7.4). Surfactant concentrations correspond to $[D]_t$/CAC ca. 5; monosaccharide concentration is 0.02 M.

An advantage of functionalized vesicles **2** and **3** is clearly visible in comparison with the nonfunctionalized vesicular sensor reported previously.[25] The ARS displacement method has been applied for phenylboronic acid (PBA) solubilized by the vesicles of 4-(4-dodecyloxybiphenyl-4-yloxy)-butyltrimethylammonium (DBBTAB). As it was mentioned, the transfer of ARS/boronic acid from water into the micellar[24] of vesicular[25] pseudophase causes about 10-fold increase in the fluorescent intensity. On the addition of monosaccharides, fluorescence quenching occurs due to competitive binding of the nonfluorescent diols with boronic acid. The DBBTAB/ARS/PBA system showed a relative fluorescence decrease of less than 3% for 0.02 M added glucose in 4 mM DBBTAB solution. Herein, we report a ca. 10% ($[3]_{tot}$ ca. 0.4 mM) to ca. 20% ($[2]_{tot}$ ca. 3.6 mM) fluorescence quenching in the presence of 0.02 M glucose and 85% ($[3]_{tot}$ ca. 0.4 mM) to >95% ($[2]_{tot}$ ca. 3.6 mM) quenching in the presence of 0.02 M fructose. The main reason for the difference in the sensing ability of these two vesicular systems is that boronic acid should be incorporated in a micelle or vesicle to work as a sensor. Functionalized surfactants **2** and **3** provide complete binding ("solubilization") of the boronic moieties to the vesicle. At the CAC, the nanoaggregate surface of **2** and **3** already contains as high "local" concentration of functional groups as possible.[29] In the case of PBA,[25] it cannot be bound to the DBBTAB vesicle by more than 50−70% at total surfactant concentration of 4 mM.

Binding of the monosaccharides studied was different, the apparent binding constant of fructose being higher than that of glucose, as often reported.[5,16,60] Because the B−O bond is short, boron bonds best to compounds where the diol oxygen atoms are close together in space; the best bonding is to *cis*-diols on five-membered (furanose) rings. In aqueous solution, glucose mostly exists as the pyranose, the furanoside form occurring in negligible amounts. At the same time, fructose exists as an equilibrium mixture with about 22% fructofuranose which facilitates its detection using boronic acids in comparison

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with glucose. In the case of glucose, it is difficult to bind the molecule selectively via an interaction of one monosaccharide molecule per one boronate moiety so an approach to use more than one boronic acid moiety per binding site has been explored.[4,16] In spite of high *sensitivity* of proposed functionalized vesicular systems, we did not observe an increase in the *selectivity* toward glucose. In the present study, we did not observe an increase in selectivity of the vesicular sensing system toward glucose in spite of high "local" concentration of functional moieties. This suggests that it might be connected with a decrease of the free boronic hydroxyl groups responsible for the diol binding caused by the equilibrium formation of the boroxines or their acyclic analogues.

Therefore, the proposed vesicular system can be considered as a new type of a broad-spectrum polyol-recognizing system in water at physiological pH characterized by high "local" concentration of a boronic acid moiety which increases its sensing ability toward monosaccharide species at low concentrations.

CONCLUSION

We synthesized *N*-alkyl-3-boronopyridinium salts with a single chain which spontaneously form vesicular structures in water. To our knowledge, this is the first report of the formation of vesicles by a boronopyridinium-based amphiphile. We have developed a novel functionalized vesicular system providing sensing ability toward biologically important compounds, D-glucose and D-fructose. The *N*-alkyl-3-boronopyridinium triflates form vesicles whose size (from 30 to 200 nm) is controllable by adjusting the surfactant chain length. The vesicles bind efficiently a fluorescent dye, Alizarin Red S, with different apparent binding constants for the different types of vesicles formed (ca. 10^3 M^{-1} for **2** and 10^4 M^{-1} for **3**) but consistent when different monitoring techniques are applied. Competitive binding of monosaccharides to ARS-boronic acid esters demonstrates a higher affinity for D-fructose than for D-glucose. Addition of a monosaccharide can be selectively detected by UV−vis and spectrofluorometry and provides significant quenching of the dye fluorescence at low concentrations of functionalized surfactant.

ASSOCIATED CONTENT

Supporting Information

Figure S1 (UV−vis titration of initial salts), Figure S2 (UV−vis spectra at different concentrations of ARS and monosaccharides), and Figure S3 (^{1}H NMR spectra of **3**). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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