An Isothiouronium-derived Organized Monolayer at the Air–Water Interface: Design of Film-based Anion Sensor Systems for $H_2PO_4^-$

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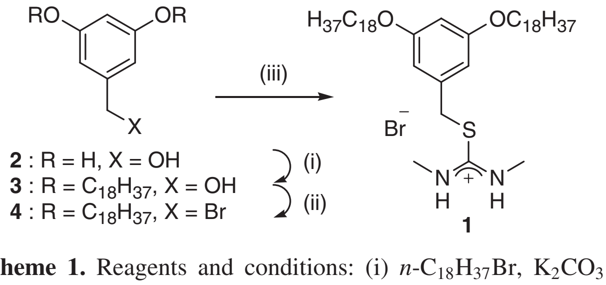
We have prepared for the first time an organized monolayer with long-chain amphiphiles possessing an isothiouronium segment. Interactions between the monolayer and anions in aqueous subphase have been investigated and show a significant selectivity of $H_2PO_4^-$. Also, by fabricating the Langmuir–Blodgett (LB) films under competitive conditions of the anions used and picrate as an indicator, we can read out $H_2PO_4^-$ recognition using UV–vis spectroscopy, providing a potential application for the design of film-based anion sensor systems.

The family of isothiouronium salts has great potential for use as an anion-binding site in supramolecular chemistry,[1] because 1) it has a similar structure to guanidinium; 2) it enhances NH acidity compared to the corresponding thiourea; 3) the chemical modification is easy using synthetic methods to make several types of functional molecular systems. Here, taking advantage of these properties, we have synthesized cationic isothiouronium amphiphiles with long alkyl-chains, and then fabricated organized monolayers at the air–water interface. We thereby develop film-based anion receptors enabling to recognize the anions in water, since hydrogen bonding at the air–water interface is not only stronger than that in bulk water,[2] but also at the interface a highly ordered structure could be oriented[3] to give rise to an effective host/guest complexation. In this work, it has been interestingly found that the organized molecular film shows a significant selectivity for $H_2PO_4^-$ over AcO^-, even though $H_2PO_4^-$ is less basic than AcO^- (pK_a: 2.16 for $H_2PO_4^-$, 4.76 for AcO^- in water at 25 °C)[4] and $H_2PO_4^-$ is more hydrophilic than AcO^- (Hofmeister series). This phenomenon might be useful in the design of $H_2PO_4^-$-selective receptors,[5] which have potential applications in chemical, biological, and environmental research.[6] Further, we tried to read out the $H_2PO_4^-$-recognition over AcO^- and Cl^- by fabricating the LB films in the presence of picrate as an indicator; the result is also reported here.

The synthesis of compound **1** is shown in Scheme 1: 3,5-dihydroxybenzyl alcohol (**2**) was allowed to react with 1-bromooctadecane in DMF at 70 °C in the presence of K_2CO_3 to give dialkoxybenzyl alcohol (**3**), and then bromination of **3** with PBr_3 in THF yielded dialkoxybenzyl bromide (**4**); reaction with dimethylthiourea in EtOH at 60 °C then gave **1**.[7]



Scheme 1. Reagents and conditions: (i) n-$C_{18}H_{37}Br$, K_2CO_3, dry DMF, 44%; (ii) PBr_3, dry THF, 94%; (iii) dimethylthiourea, EtOH, 71%.

Figure 1A shows the surface pressure versus area per molecule (π-A) isotherms for the monolayers of **1** on pure water (Milli-Q, pH 5.8) and the aqueous subphases containing NaH_2PO_4 (1, 10, and 100 μM) at 20 °C. The monolayer at 20 °C on pure water has a clearly condensed phase with the molecular limiting area of ca. 0.52 nm^2 $molecule^{-1}$. By adding to these incremental amounts of $H_2PO_4^-$ as a possible oxoanion in the subphase, the monolayer showed an expansion of up to ca. 0.55 nm^2 $molecule^{-1}$ above 10 μM of $H_2PO_4^-$. This suggests that $H_2PO_4^-$ interacted with the isothiouronium-containing monolayers at the air–water interface.[8] In contrast, other anions (AcO^- and Cl^-) did not induce any expansion even with excess amounts of these anions (Figure 1B). The absence of expansion with AcO^-, having pK_a value higher than that of $H_2PO_4^-$, may be because the highly ordered isothiouronium units at the air–water interface can participate in multiple hydrogen bondings with tetrahedral $H_2PO_4^-$. This is due to the fact that tripodal isothiouronium receptors significantly bind tetrahedral oxoanions.[1a] On the other hand, we discovered that when hydrophobic picrate is added to the aqueous subphase the monolayer of **1** expanded remarkably below 10 $mN\,m^{-1}$; the large expansion of molecular area at 0.95 nm^2 $molecule^{-1}$ reflects the fact that the monolayer interacts with a bulky picrate. Therefore, picrate could act as an indicator to monitor the selective binding of $H_2PO_4^-$ (vide infra).

To investigate the film structure, we fabricated Langmuir–Blodgett (LB) films by transferring the monolayer on pure water onto hydrophobic plates at 24 $mN\,m^{-1}$ and 20 °C. The molecular orientation in the film was estimated by polarized FTIR spectra

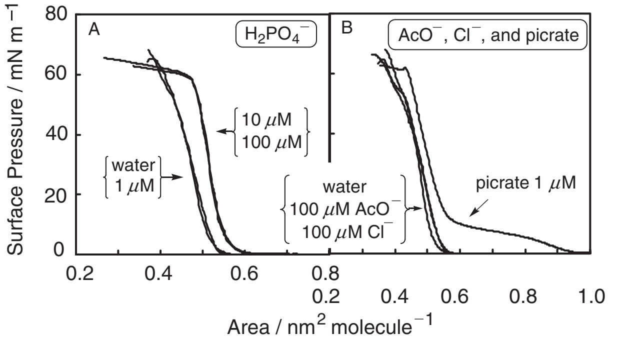


Figure 1. (A) π-A Isotherms of the monolayers of **1** on the subphase of water and in the presence of varying concentrations of NaH_2PO_4 at 20 °C; (B) π-A Isotherms of the monolayers of **1** on the subphase of water, 100 μM of NaOAc and NaCl, and 1 μM of potassium picrate.

for 30-layers on CaF_2 plate. The polarized transmission measurements for the inclined CaF_2 plate can evaluate the tilt angle of alkyl chains from the dichroic ratio of the band.[9] The CH_2 symmetric and antisymmetric stretching vibration bands due to the hydrocarbon chains appeared at 2850 and 2917 cm^{-1}, respectively. These wavenumbers indicate that the alkyl-chains are mostly in a *trans*-zigzag conformation involving a certain number of *gauche* states.[10] Assuming a uniaxial distribution of transition dipole moments, the tilt angle of the alkyl chains from the normal line of the CaF_2 plate can be estimated to be ca. 10°. Out-of plane XRD patterns obtained for 30-layers of the monolayer of **1** showed that the long spacing of the film is 3.2 nm. This value is similar to that estimated from Chem 3D modeling (not containing counter anion). The in-plane XRD (Bruker AXS, MXP-BX) gave single diffraction ($d = 0.41$ nm), suggesting a hexagonal packing with 0.41 nm spacing among the hydrocarbon chains.[11] The polarized IR and XRD profiles indicate the presence of a highly ordered layer structure (Figure 2).

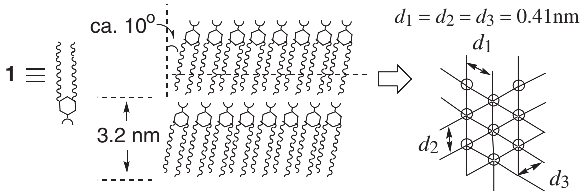


Figure 2. Schematic representation of the film of **1** (〰: alkyl chain, ⚲: *S*-benzyl-*N*,*N′*-dimethylisothiouronium segment).

Since significant interaction of the monolayer of **1** and picrate was observed in the π-A isotherm experiment (Figure 1B), we tried to read out selective $H_2PO_4^-$-binding using LB films fabricated from the monolayer under competitive conditions for anions with picrate indicator. The 30-layer LB films were prepared in the presence of picrate (1 μM) deposited on the quart plate; the color was light yellow. The UV–vis spectra were then recorded, showing an absorption band at 365 nm. This implies that the prepared LB film contained the picrate. When similar films were prepared with picrate and $H_2PO_4^-$ in the subphase, the absorption intensity at 365 nm significantly decreased with increasing amounts of $H_2PO_4^-$ as a result of competitive binding between picrate and the anion at the air-water interface. Subsequently there is almost no absorption of the films in the presence of 20 equiv. of $H_2PO_4^-$. In contrast, AcO^- and Cl^- scarcely induced any change in the absorption spectra. The intensity change at 365 nm with 50 μM of $H_2PO_4^-$ is larger than those with other anions under similar conditions by a factor of 8 for AcO^- and 25 for Cl^-, respectively (Figure 3). Clear selectivity was therefore observed, being consistent with the results of the π-A isotherm experiments (Figure 1). Although in this approach we used 30-layer LB films because of the low color value of picrate, the obtained result is promising for the design of new types of sensor films, since recognition and sensing of anion species in water has still been a challenge[12] due to the fact that the water molecules surrounding the anion (e.g. phosphates) interfere with the desired host/guest interactions.

In conclusion, we have shown that an organized film composed of an isothiouronium-derived amphiphile exhibits significant $H_2PO_4^-$-selectivity on the surface of aqueous subphases containing anion species, and we can read out the anion through a competitive assay with picrate. This provides a promising way to design new types of film-based sensor systems for detecting anions in water. Further investigation is underway involving the exploration of a more powerful indicator than picrate.

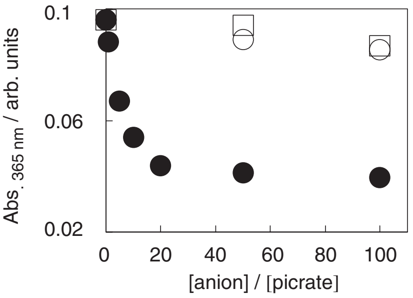


Figure 3. Absorbance at 365 nm of the film of **1** deposited from different concentrations of anions in the presence of 1 μM of picrate at 24 $mN\,m^{-1}$ and 20 °C: (●) NaH_2PO_4, (○) NaOAc, (□) NaCl.

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