

Characterization of Organized Molecular Layers Including Amphiphilic Isothiuronium Derivatives

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Fluorescence-active long-chain amphiphiles with an isothiuronium segment that serves as an anion-binding moiety were newly synthesized. The monolayers on the surface of pure water (Milli-Q, pH 5.8) as well as of the aqueous subphases containing NaOAc or Na₂HPO₄ were studied from the standpoint of anion recognition for biologically important species in water. Surface pressure versus area per molecule (π -A) isotherms implied that the monolayers showed an expansion at low surface pressure region below 10 mN m⁻¹ by introducing the anions into the aqueous subphases. The organized molecular layers were deposited by a horizontal lifting method at about 24 mN m⁻¹, and were characterized by IR spectroscopy, X-ray diffraction, and atomic force microscopy. It is noteworthy that the formation of the stable organized molecular layers and the interaction with anions. However, fluorescence detection of the anions has not yet been successful using the organized film because it seems that the fluorescence of the film is not quenched by the binding of water molecule (or Br⁻ counter anion) at the isothiuronium moiety.

Key words: Isothiuronium, Organized Molecular Layer, Anion Recognition

1. INTRODUCTION

Recognizing and sensing anionic species in water¹ has recently emerged as a research target not only in supramolecular chemistry but also in analytical chemistry. Although several examples based on host/guest interaction between synthetic receptors and target anions have been reported so far², there has still been a challenge because water molecules surrounding the anion interfere with the desired host/guest association, resulting in the low affinity of receptors with anions in water. Therefore, the systems enable to overcome such a problem are desired. Here, employing a cationic isothiuronium group^{3,4} as anion-binding and hydrophilic group, we decided to newly synthesize isothiuronium amphiphiles with long alkyl-chains. This approach is mainly due to the fact that hydrogen bondings at the air-water interface are stronger than those in bulk water.⁵ Furthermore, the synthetic versatility of isothiuronium unit allowed us to make the related fluorescence-active amphiphiles by introducing naphthalene ring. In this paper, we report the synthesis of the desired amphiphiles **1** as well as the properties of the monolayers on the surface of pure water and of the aqueous subphases containing anion species. The cationic organized monolayers on solid substrates were also characterized by polarized IR spectroscopy, X-ray diffraction (XRD), and atomic force microscopy (AFM).

2. EXPERIMENTALS

2.1 Materials and methods

The starting materials, 3,5-dihydroxybenzyl alcohol (**2**) was purchased from Aldrich. Pure water (Milli-Q, 18 M Ω cm) was used in all experiments. Surface pressure versus area per molecule (π -A) isotherms were measured by Langmuir-type film balance (Lauda). The monolayers of the isothiuronium amphiphiles were spread from chloroform solution onto the pure water or the aqueous solution containing anions. The isothiuronium monolayers were transferred by a horizontal lifting method at 24 mN m⁻¹ and 10 °C. Out-of-plane and in-plane X-ray diffraction were measured by Rigaku Rad-B (Cu K α radiation, 40 kV, 30 mA), MXP-BX (40 kV, 40 mA), respectively. FT-IR spectra were measured by a polarized FTIR 660 (JASCO) with the incidence angle of 0° and 45°. AFM images of the films on mica were measured by a SPA 300 (spring constant is 0.09 N m⁻¹). Fluorescence spectra were recorded by a FP-6300 spectrophotometer (JASCO).

2.2 Synthesis of isothiuronium amphiphiles

The synthesis of **1a** and **1b** is outlined in Scheme 1. Alkylation of 3,5-dihydroxybenzyl alcohol (**2**) with 1-bromohexadecane or 1-bromooctadecane in DMF at 70 °C in the presence of K₂CO₃ afforded **3a** and **3b**, respectively, followed by bromination with PBr₃ in THF. Dialkylbenzylbromide (**4a**) or (**4b**) and 2-[(*N*-methylthioureido)methyl]naphthalene (**5**)^{4b} were stirred in EtOH at 60 °C to give **1a** and **1b**, respectively. The assignment of **1** was conducted by means of several spectral data.[†]

layers on silicon plate. The CH_2 symmetric and antisymmetric stretching vibration bands due to the hydrocarbon chains appeared at 2850 and 2919 cm^{-1} , respectively. Assuming an axial distribution of transition dipole moments, the tilt angle of amphiphiles for silicon plate can be estimated to be 51° .⁸

Figure 3 shows out-of plane and in-plane XRD patterns obtained for 16 layers of **1b**. The long spacing of **1b** in the film can be estimated to be 3.53 nm. From the Chem 3D modeling, the length of **1b** in the molecular long axis can be estimated to be 2.9 nm. Therefore the above value suggests the formation of a bilayer in the film. The in-plane XRD gave single diffraction ($d = 0.41$ nm), suggesting a hexagonal packing with 0.41 nm spacing among the hydrocarbon

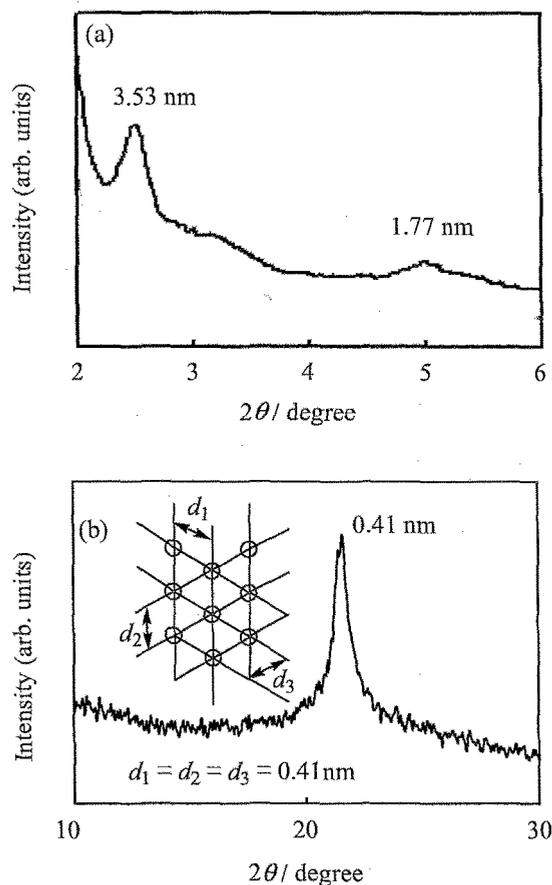


Fig. 3. XRD patterns for **1b** deposited on glass plate at 24 mN m^{-1} and 10°C by a horizontal lifting method; (a) out-of plane XRD, (b) in-plane XRD.

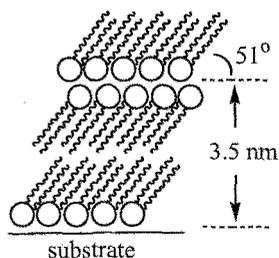


Fig. 4. Schematic representation of **1b** film (wavy: alkyl-chain, \bigcirc : naphthalene-isothiuronium moiety).

chains. The XRD profiles indicate the presence of a highly ordered layer structure (Fig. 4).

To obtain the information of the surface structure of the **1b**-organized layer, AFM experiments were carried out. Figure 5 shows the AFM images of one and two-layer films of **1b** deposited on mica. The thickness of the one-layer film was estimated to be 1.8 nm, and that of the two-layer film was 3.6 nm. The thickness of the films corresponds to the results of XRD and Chem 3D modeling.

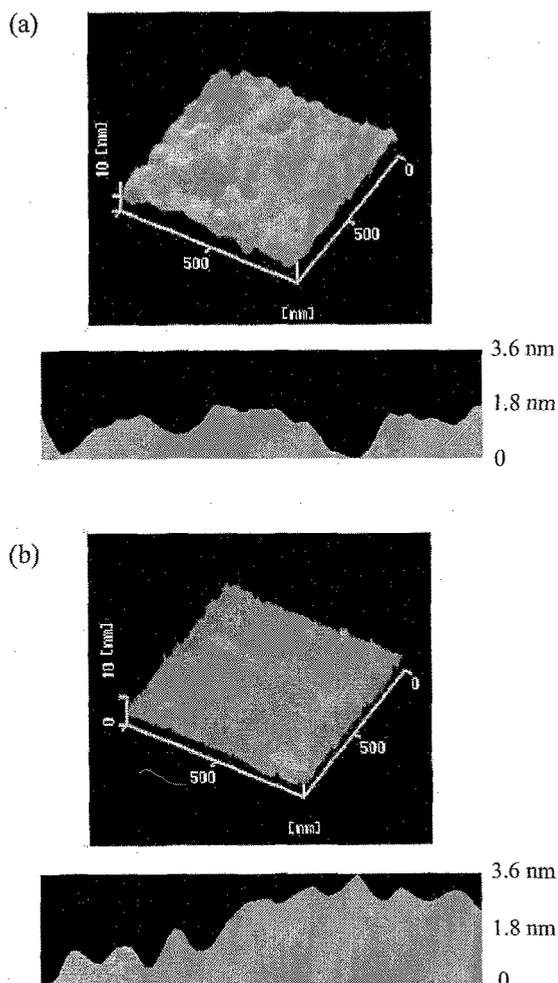


Fig. 5. AFM images of (a) one-layer and (b) two-layer films of **1b**.

3.3 Fluorescence study

As the next stage, our attention has been devoted to investigate if the solid-supported organized film could act as a fluorescent sensor. The 10 layers LB films of **1b** were prepared in the absence and presence of NaOAc ($1 \times 10^{-5} \text{ M}$) deposited on quartz plate, the fluorescence spectra being recorded at an excitation wavelength of 290 nm (Fig. 6). It seems that the fluorescence of **1b** film fabricated from the monolayer on pure water is not quenched by the built-in isothiuronium group (Fig. 6(a)), being unexpected data because the prototypical naphthalene-isothiuronium dyad (**6**) showed almost no fluorescence spectra in CH_3CN based on a photoinduced

electron transfer (PET) process from the excited naphthalene to the isothiouonium group (Inset data of Fig. 6).^{4b} As a result, AcO⁻-induced fluorescent response of **1b** monolayer could not be obtained as shown in Fig. 6. This finding is attributable to the plausible phenomenon that water molecule (or Br⁻ counter anion) tightly binds to the isothiouonium of **1b** when the organized layer is fabricated from the corresponding monolayers. To obtain more detailed information, the continuous investigation is now underway with different counter anion of **1b**.

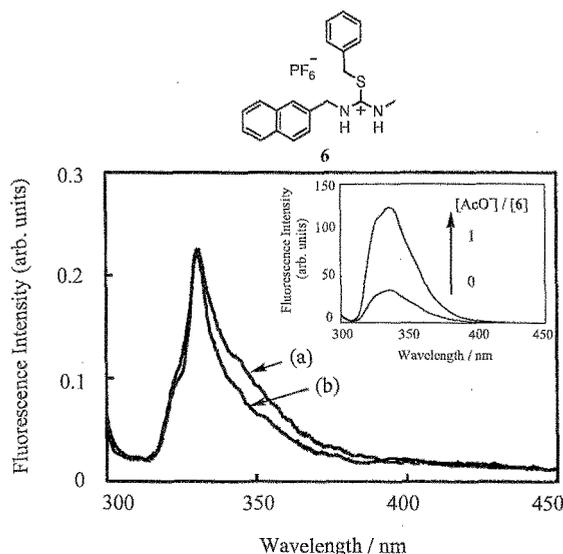


Fig. 6. Fluorescence spectra of **1b** film deposited on quartz plate in (a) pure water and (b) NaOAc (1×10^{-5} M) solution excited at 290 nm. Inset: Fluorescence spectra of **6** (2×10^{-5} M) in CH_3CN excited at 270 nm upon addition of AcO⁻ as a (*n*-Bu)₄N salt.

4. CONCLUSION

As our ongoing program to develop new chemosensors for the detection of anions in water, we have synthesized fluorescence-active isothiouonium amphiphiles **1a** and **1b**, the monolayers being well fabricated. The π -A isotherms using **1b** monolayer indicate significant interactions of anions at the air-water interface. The organized molecular films of **1b** can be also prepared and has periodic arrangements with hexagonal packing. It is noteworthy that the formation of the stable organized molecular layers and the interaction with anions. However, fluorescence detection of anions has not yet been successful using the organized films because it seems that the fluorescence of **1b** is not quenched by the binding of water molecule (or Br⁻ counter anion) at the isothiouonium moiety.

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Notes and references

‡2-[(*S*-3,5-Dihexadecyloxybenzyl-*N*'-methyl-*N*-isothiouonio)methyl]naphthalene bromide (**1a**) has ¹H NMR (400 MHz, CDCl_3 : $\text{CD}_3\text{OD} = 4 : 1$ (v/v), TMS), δ

7.85-7.81 (m, 3H), 7.68 (s, 1H), 7.53-7.49 (m, 2H), 7.36 (br s, 1H), 6.47 (s, 2H), 6.40 (t, $J = 2.0$ Hz, 1H), 4.80 (s, 2H), 4.39 (s, 2H), 3.86 (t, $J = 6.1$ Hz, 4H), 3.14 (s, 3H), 1.74-1.69 (m, 4H), 1.43-1.27 (m, 52H), and 0.88 (t, $J = 6.8$ Hz, 6H); FAB-MS, m/z 802 [M-Br]⁺; Anal. Calcd for $\text{C}_{52}\text{H}_{85}\text{BrN}_2\text{O}_2\text{S}_2$: C, 70.79; H, 9.71; N, 3.18. Found: C, 70.88; H, 9.63; N, 3.09.

2-[(*S*-3,5-Dioctadecyloxybenzyl-*N*'-methyl-*N*-isothiouonio)methyl]naphthalene bromide (**1b**) has ¹H NMR (400 MHz, CDCl_3 : $\text{CD}_3\text{OD} = 4 : 1$ (v/v), TMS), δ 7.85-7.81 (m, 3H), 7.68 (s, 1H), 7.53-7.49 (m, 2H), 7.35 (br s, 1H), 6.47 (s, 2H), 6.40 (t, $J = 2.1$ Hz, 1H), 4.79 (s, 2H), 4.37 (s, 2H), 3.86 (t, $J = 6.2$ Hz, 4H), 3.13 (s, 3H), 1.76-1.69 (m, 4H), 1.43-1.26 (m, 60H), and 0.88 (t, $J = 6.8$ Hz, 6H); FAB-MS, m/z 858 [M-Br]⁺; Anal. Calcd for $\text{C}_{56}\text{H}_{93}\text{BrN}_2\text{O}_2\text{S}_2$: C, 71.68; H, 9.99; N, 2.98. Found: C, 71.87; H, 10.25; N, 2.70.

[1] For current reports, see: (a) D. H. Lee, J. H. Im, S. U. Son, Y. K. Chung, and J.-I. Hong, *J. Am. Chem. Soc.*, **125**, 7752-7753 (2003). (b) H. A. Ho, and M. Leclerc, *J. Am. Chem. Soc.*, **125**, 4412-4413 (2003). (c) M. S. Han, and D. H. Kim, *Angew. Chem. Int. Ed.*, **41**, 3809-3811 (2002). (d) L. Fabbrizzi, N. Marcotte, F. Stomeo, and A. Taglietti, *Angew. Chem. Int. Ed.*, **41**, 3811-3814 (2002). (e) S. Mizukami, T. Nagano, Y. Urano, A. Odani, and K. Kikuchi, *J. Am. Chem. Soc.*, **124**, 3920-3925 (2002). (f) M. Robitzner, C. Sirlin, N. Kyritsakas, and M. Pfeiffer, *Eur. J. Inorg. Chem.*, 2312-2319 (2002).

[2] For reviews for anion receptors, see: (a) Edited by P. A. Gale, *Coord. Chem. Rev.*, **240**, 1-226 (2003). (b) P. D. Beer, and P. A. Gale, *Angew. Chem. Int. Ed.*, **40**, 486-516 (2001). (c) P. D. Beer, *Acc. Chem. Res.*, **31**, 71-80 (1998). (d) F. P. Schmidtchen, and M. Berger, *Chem. Rev.*, **97**, 1609-1646 (1997).

[3] J. March, "Advanced Organic Chemistry", John Wiley & Sons, New York (1985) pp. 360.

[4] Isothiouonium derivatives as anion-binding sites: (a) Y. Kato, S. Nishizawa and N. Teramae, *Org. Lett.*, **4**, 4407-4410 (2002). (b) Y. Kubo, S. Ishihara, M. Tsukahara and S. Tokita, *J. Chem. Soc., Perkin Trans. 2*, 1455-1460 (2002). (c) S. Nishizawa, Y.-Y. Cui, M. Minagawa, K. Morita, Y. Kato, S. Taniguchi, R. Kato and N. Teramae, *J. Chem. Soc., Perkin Trans. 2*, 866-870 (2002). (d) S. Sasaki, A. Hashizume, S. Ozawa, D. Citterio, N. Iwasawa and K. Suzuki, *Chem. Lett.*, **30**, 382-383 (2001). (e) W.-S. Yeo and J.-I. Hong, *Tetrahedron Lett.*, **39**, 8137-8140 (1998). (f) W.-S. Yeo and J.-I. Hong, *Tetrahedron Lett.*, **39**, 3769-3772 (1998).

[5] K. Ariga and T. Kunitake, *Acc. Chem. Res.*, **31**, 371-378 (1998).

[6] D. D. Perrin, *Pure Appl. Chem.*, **20**, 133-236 (1969); S. Nishizawa, and N. Teramae, *Anal. Sci.*, **13**, Suppl., 485-488 (1997).

[7] For fluorescent LB film sensors: see, (a) Y. Zheng, J. Orbulescu, X. Ji, F. M. Andreopoulos, S. M. Pham, and R. M. Leblanc, *J. Am. Chem. Soc.*, **125**, 2680-2686 (2003). (b) P. Kele, J. Orbulescu, T. L. Calhoun, R. E. Gawley, and R. M. Leblanc, *Langmuir*, **18**, 8523-8526 (2002).

[8] H. Akutsu, Y. Kyougoku, H. Nakahara and K. Fukuda, *Chem. Phys. Lipids*, **15**, 222-242 (1975).