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# Enantioselective Adsorption of Phenylalanine onto Self-Assembled Monolayers of 1,1′-Binaphthalene-2,2′-dithiol on Gold

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Chiral recognition is an important subject in the fields of medical and pharmaceutical technologies. For chiral discrimination at a solid surface modified with a chiral component such as an enantioselective heterogeneous catalyst, supramolecular assemblies of the modifier are expected to induce enantioselectivity, as suggested for tartaric acid adsorbed on Cu(110).[1] Recently, a self-assembled monolayer (SAM) of an atropisomeric compound, 1,1′-binaphthalene-2,2′-dithiol (BNSH), was reported to consist of a well-ordered two-dimensional arrangement on a gold (111) single-crystal surface.[2] A honeycomblike structure consisting of screw-like units, each of which is composed of three BNSH molecules, was observed by scanning tunneling microscopy. The two-dimensional molecular arrangements in (*R*)- and (*S*)-BNSH SAM are mirror images with respect to each other. Because such a specific "screw" structure with a supramolecular size is considered to be desirable for catching and discriminating guest organic molecules, SAMs of BNSH are expected to be useful for fabricating sensors for chiral discrimination. Indeed, modification with binaphthyl-derivatives was reported to induce enantioselectivity in electron transfer at ZnO-nanocrystallite surfaces.[3] We report here the enantioselective adsorption of chiral amino acid, D- and L-phenylalanine (Phe), onto (*R*)- and (*S*)-BNSH SAM, which was monitored by using a quartz crystal microbalance (QCM). Although QCM is known to be suitable for evaluating enantioselective adsorption,[4] the work reported here represents the first investigation on the application of monolayer-modified chiral surfaces prepared via self-assembling and covalent binding.

The gold substrate employed (200 nm in thickness) was prepared by vapor deposition on a quartz crystal (AT-cut, 9 MHz) with 15-nm-thick titanium as an adhesive layer. After flame annealing, the substrate was immersed into an ethanolic solution of BNSH to prepare the BNSH-modified QCM substrate. To avoid influences of any other molecules and ions, QCM measurements were performed in Milli-Q water, with the injection of 125-mM Phe solution to make the final concentration equal to 1 mM. D-Phe, 99+% (98% ee/GLC, Aldrich) and L-Phe, 99% (98% ee/GLC, Aldrich) were used as received. Injection was carried out at the front part of QCM after the frequency became stable within ±0.1 Hz over a period of 10−20 min. The temperature was kept at ca. 25 °C by placing the detection cell in a heat-insulated case covered with polyurethane foam.

Because the Au(111) single-crystal surface is a requisite for the fabrication of the above-mentioned two-dimensional chiral arrangement of BNSH,[2] it was confirmed by cyclic voltammetry (CV) in 0.1 M $H_2SO_4$ that (111)-orientation was dominant[5] for the surface of vapor-deposited gold. To confirm the formation of the SAM, reductive desorption behavior[6] was examined for the BNSH-modified gold in 0.5 M KOH.[2] Similarities in potential and shape of desorption peak were observed between cyclic voltammograms for single-crystal and vapor-deposited gold. The amount of self-assembled molecules on vapor-deposited gold estimated from the electric charge for the reductive desorption was $\sim 8 \times 10^{13}$ molecules $cm^{-2}$, which corresponds to the coverage of 80% of that on a single-crystal gold.[7] In addition, the peak potential, the peak shape, and the electric charge for the reductive desorption were quite similar for (*R*)- and (*S*)-BNSH, suggesting the formation of SAMs of the same quality for both enantiomers.

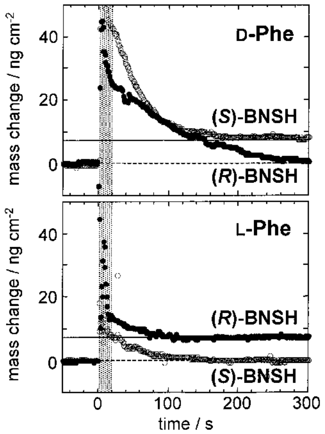

***Figure 1.*** Responses of BNSH-modified QCM specimen observed after injection of D- (top) and L-Phe (bottom). Filled and open symbols indicate responses on (*R*)- and (*S*)-BNSH, respectively. Solid lines indicate the mass change expected for the adsorption of Phe to BNSH screw (see text).

As shown in Figure 1, the mode of mass change[8] with time was found to depend on the chirality of BNSH for D- and L-Phe. With D-Phe, a steep increase followed by a gradual decrease (*relaxation*) of surface mass was observed. An increase in steady-state surface mass of $\sim$8 ng $cm^{-2}$ was observed after a 100-s decay for (*S*)-BNSH, whereas for (*R*)-BNSH the surface mass returned to the initial value after decay for over 200 s. With L-Phe, on the other hand, initial responses were found to be smaller than those observed with D-Phe. An increase in steady-state surface mass of .$\sim$8 ng $cm^{-2}$ was found within 100 s for (*R*)-BNSH, whereas the surface mass returned to the initial value after a 150-s decay for (*S*)-BNSH. The spikes and the unstable response during the 20 s after the injection (hatched region in Figure 1) are not due to the adsorption process but to the agitation in the QCM cell, because a similar

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***Table 1.*** QCM Response Parameters Characterizing Enantioselectivity of (*R*)- and (*S*)-BNSH SAM for D- and L-Phe Molecules

| | BNSH | $m_{\mathrm{stable}}$ (ng cm$^{-2}$)$^a$ | $\tau$ (s)$^a$ |
|---|---|---|---|
| D-Phe | (*R*) | 0−1 | 90−120 |
| | (*S*) | 6−8 | 35−55 |
| L-Phe | (*R*) | 7−8 | 25−30 |
| | (*S*) | 0−1 | 45−65 |

[a] To see reproducible characteristic tendency of each Phe−BNSH set, the equation, $\Delta m = C \exp(-t/\tau) + m_{\mathrm{stable}}$, was used to determine the parameters by fitting the QCM response for each Phe−BNSH combination. The fitting was carried out for the responses observed after 20-s agitation.

response was observed after the injection of Milli-Q water. The mass changes in the steady state clearly showed enantioselectivity.

The observed QCM responses of the Au(111) surface modified with (*R*)- and (*S*)-BNSH for Phe molecules with the same chirality can be classified into two categories, one exhibiting a long relaxation time for recovery to the initial value (type A) and the other exhibiting a short relaxation time with an increase in steady-state surface mass of .$\sim$8 ng cm$^{-2}$ (type B).[9] Combinations of D-Phe/(*R*)-BNSH and L-Phe/(*S*)-BNSH show type-A response, while those of L-Phe/(*R*)-BNSH and D-Phe/(*S*)-BNSH show type-B response (Table 1). The observed surface-mass increase agrees with a mass of 7.3 ng cm$^{-2}$, which is expected from the assumption that one Phe molecule is adsorbed on a "screw" composed of three BNSH molecules (solid lines in Figure 1).

The above-mentioned relaxation behavior is considered to reflect the interaction between BNSH SAM and Phe molecules. The monolayer of BNSH provides a hydrophobic surface for the adsorption of the aromatic amino acid, Phe, because the BNSH-modified surface contains many naphthalene rings. In addition, the "screw" is assumed to play a role as a space for chiral recognition. The relaxation behavior can be explained by the balance between adsorption and desorption processes. As a concentrated Phe solution of 125 mM is injected at the front of the QCM specimen surface, Phe molecules approach BNSH SAM first because of the high concentration gradient and the hydrophobic interaction. Subsequently, desorption and diffusion of excess Phe molecules into the bulk Milli-Q water are assumed to take place because the final concentration is as low as 1 mM. If steric matching is not accomplished between the BNSH screw and the Phe molecule, BNSH SAM does not provide specific adsorption sites and behaves only as a hydrophobic surface. In this case, all Phe molecules are expected to behave uniformly (*a* in Figure 2A), and the time dependence can be explained by a one-component gradual desorption model. On the other hand, if the screw structure behaves as a specific adsorption site, Phe molecules stabilized by the screw are considered not to desorb (*b* in Figure 2B). Those stabilized molecules inhibit the approach of additional Phe molecules to BNSH SAM because of steric hindrance and the lack of an adsorption site (*c* in Figure 2B). In this case, the time dependence can be explained by a two-component model. The one- and two-component models can account for the type-A and -B responses, respectively. The observed responses can be recognized to be enantioselective even though D-Phe induces larger initial response than L-Phe after the injection. The reason D-Phe induces a larger initial response than does L-Phe, independently of the chirality of BNSH molecule, is not completely understood at present. One probable reason was thought to be that the initial response is affected by an impurity or impurities. However, the reagents purified by using ion-exchange resin also showed essentially the same responses as those shown in Figure 1.

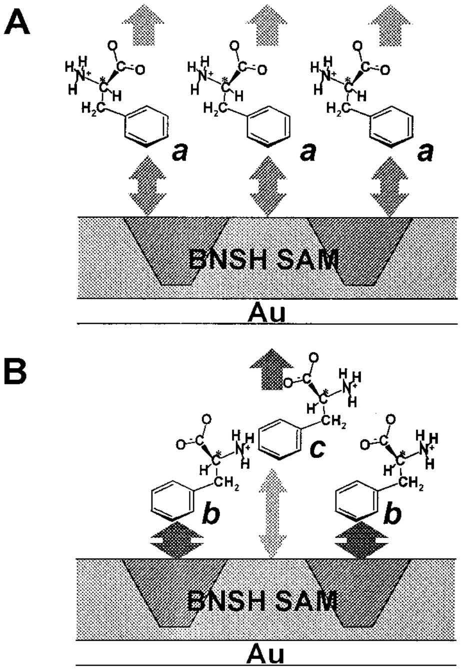

***Figure 2.*** Schematic models for (A) one- and (B) two-component relaxation. Trapezoids indicate screw-like structures of BNSH with chirality (see text).

With a less (111)-dominant gold film[10] as a substrate, on which an imperfect two-dimensional chiral arrangement was expected, little enantioselectivity was observed.[11] Apparently, the chirality of the screw-like structures in BNSH SAM plays an important role in the enantioselectivity of Phe molecules rather than that of BNSH molecule itself.

In conclusion, SAM of BNSH with two-dimensional chirality[2] was found to be applicable to chiral discrimination of Phe. Applications to other analytes are under investigation.

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(7) The lower coverage may be due to the intrinsic characteristics of vapor-deposited gold films, i.e., they possess smaller regions of (111) terraces and a higher density of steps than a Au(111) single crystal. The BNSH-SAM formation requires close matching to the arrangement of surface gold atoms.
(8) A frequency change of 1 Hz corresponds to 5.45 ng cm$^{-2}$ according to Sauerbrey's equation, see: Sauerbrey, G. Z. *Z. Phys.* **1959**, *155*, 206.
(9) The length of relaxation period refers to the relative length between (*R*)- and (*S*)-BNSH films for each enantiomer of Phe.
(10) This type of gold substrate was prepared by vapor deposition at a high deposition rate, and the degree of (111) orientation of gold crystallites was examined by using CV and X-ray diffraction techniques.
(11) It should be noted that D-Phe still showed a large initial response, independently of the chirality of BNSH molecule.

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