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Chiral Self-Assembled Monolayers

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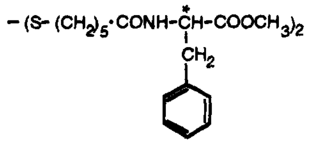
We report here on the electrochemical differentiation between the organization of a racemic and pure enantiomeric self-assembled monolayers. Until now, chirality in monolayers has been studied primarily in Langmuir films,[1−4] i.e., when formed at the liquid−air interface. The extensive work in this field by Arnett and his co-workers has been well documented[2] and describes the various techniques employed in determining the differences in the organization of the pure enantiomers versus the racemic mixture of the monolayers. These differences could be detected only when a high degree of organization was obtained, which required atomically flat surfaces such as liquids. On the other hand, two-dimensional chiral recognition has been investigated and applied in fields such as chromatographic separations,[5] asymmetric electrochemistry[6] and photochemistry of adsorbates on surfaces.[7]

The organization of thiol-based self-assembled monolayers, SAMs, in particular on gold(111), has been the subject of numerous studies.[8−10] Nevertheless, our attempts to detect chiral effects on gold(111) failed. Although these surfaces exhibit large flat terraces,[11] they are far from being atomically flat in large areas as used in macroelectrodes, i.e., millimeter size.

Recently, we applied ω-mercapto carboxylic acid monolayers on mercury thin films as a means of designing an extremely sensitive electrode for cadmium ions.[12] We showed that, besides higher sensitivity being obtained than with gold substrates, the excess of surface coverage of the thiols could easily be determined on thin mercury films. Mercury provides an atomically flat surface where chiral effects should be electrochemically detectable.

Two basic concepts guided us in designing the chiral molecule to be self-assembled: (i) The length of the hydrocarbon chain is a compromise between the quest for organization (requires long alkyl chains) and a reasonable rate of electron transfer (prefers short chains). (ii) On the other hand, the functional groups attached to the stereogenic center, i.e., to the chiral carbon, should facilitate nonidentical attractive and repulsive forces between pairs of the same chirality, as opposed to enantiomers. As a result, a carbomethoxy phenylalanine derivative of 6-mercaptohexanoic acid (**I**) was synthesized.[13]


(I)

The organization of SAMs based on I was studied[14] on a hanging mercury drop electrode (HMDE). The HMDE was modified in a stirred acidic THF solution (0.1 M $HClO_4$ and 2.0 mM of I in THF) for 30 min.[15] Disulfides are rapidly and irreversibly adsorbed on Hg (eq 1). The adsorbed disulfides react further with the surface (eq 2) to form mercuric salt.[16]

$$\mathrm{RSSR} \rightarrow \mathrm{RSSR}_{(\mathrm{ads})} \qquad (1)$$

$$\mathrm{RSSR}_{(\mathrm{ads})} + \mathrm{Hg} \rightarrow \mathrm{Hg(SR)}_{2(\mathrm{ads})} \qquad (2)$$

Figure 1 shows the cyclic voltammetry of a HMDE modified with *d*-, *l*-, and the *dl*-monolayers.[17] A reduction wave, which is attributed to the reduction of the thiol−mercury complex, is observed at −0.33 V vs Ag/AgCl (eq 3). Previous studies[18] carried out on other thiols and disulfides with a DME as well as with a HMDE showed similar waves. The almost complete absence of an anodic wave (Figure 1) is due to the desorption of the reduced species.

$$\mathrm{Hg(SR)}_{2(\mathrm{ads})} + 2\mathrm{e}^- + 2\mathrm{H}^+ \rightarrow \mathrm{Hg} + 2\mathrm{RSH} \qquad (3)$$

Since the reduction process was performed in disulfide-free solutions, the area under the reduction wave is proportional to the disulfide adsorbed onto the surface, i.e., to the excess of surface coverage. It is apparent that the excess of surface coverage of the racemic monolayer, Γ_{dl}, is higher than those of the pure enantiomers. Specifically, Γ_{dl} equals (0.963 ± 0.033) $\mathrm{nmol{\cdot}cm^{-2}}$, whereas Γ_d and Γ_l equal (0.840 ± 0.019) and (0.843 ± 0.024) $\mathrm{nmol{\cdot}cm^{-2}}$, respectively.[19] It should be noted that these results represent an average of several experiments. Moreover, the racemic solution was prepared by mixing the two pure enantiomeric solutions. These results suggest that while both enantiomers self-assemble likewise, the racemic monolayer is more densely packed. Kakiuchi and Senda,[20] who studied the adsorption of phenylalanine on Hg, also reported that the racemate showed a higher surface activity, i.e., surface excess,

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(1) (a) Stallberg-Stenhagen, S.; Stenhagen, E. *Ark. Kemi, Mineral. Geol.* **1945**, *18*, 1−8. (b) Lundquist, M. *Ark. Kemi* **1961**, *17*, 183−195.

(2) Rose, P. L.; Harvey, N. G.; Arnett, E. M. *Adv. Phys. Org. Chem.* **1993**, *28*, 45−138 and references therein.

(3) (a) Qian, P.; Matsuda, M.; Miyashita, T. *J. Am. Chem. Soc.* **1993**, *115*, 5624−5628. (b) Selinger, J. V.; Wang, Z.-G.; Bruinsma, R. F.; Knobler, C. M. *Phys. Rev. Lett.* **1993**, *70*, 1139−1142. (c) Weis, R. M.; McConnell, H. M. *Nature* **1984**, *310*, 47−49.

(4) (a) Stine, K. J.; Uang, Y.-J.; Dingman, S. D. *Langmuir* **1993**, *9*, 2112−2118. (b) Bouloussa, O.; Dupeyrat, M. *Biochim. Biophys. Acta* **1988**, *938*, 395−402.

(5) (a) Pirkle, W. H.; Reno, D. S. *J. Am. Chem. Soc.* **1987**, *109*, 7189−7190. (b) Pirkle, W. H.; Chang, J.-P.; Burke, J. A., III. *J. Chromatogr.* **1992**, *598*, 1−6.

(6) For example: (a) Watkins, B. F.; Behling, J. R.; Kariv, E.; Miller, L. L. *J. Am. Chem. Soc.* **1975**, *97*, 3549−3550. (b) Chia, V. K. F.; Soriaga, M. P.; Hubbard, A. T.; Anderson, S. E. *J. Phys. Chem.* **1983**, *87*, 232−235. (c) Mariani, R. D.; Abruna, H. D. *J. Electrochem. Soc.* **1989**, *136*, 113−119. (d) Yamagishi, A.; Aramata, A. *J. Chem. Soc., Chem. Commun.* **1984**, 452−453.

(7) Avnir, D.; Wellner, E.; Ottolenghi, M. *J. Am. Chem. Soc.* **1989**, *111*, 2001−2003.

(8) Ulman, A. *Ultrathin Organic Films*; Academic Press: New York, 1991.

(9) For example: (a) Nuzzo, R. G.; Fusco, F. A.; Allara, D. L. *J. Am. Chem. Soc.* **1987**, *109*, 2358−2368. (b) Bain, C. D.; Whitesides, G. M. *Angew. Chem.* **1989**, *101*, 522−528. (c) Sabatani, E.; Rubinstein, I.; Maoz, R.; Sagiv, J. *J. Electroanal. Chem.* **1987**, *219*, 365−371.

(10) (a) Widrig, C. A.; Alves, C. A.; Porter, M. D. *J. Am. Chem. Soc.* **1991**, *113*, 2805−2810. (b) Kim, Y.-T.; McCarley, R. L.; Bard, A. J. *J. Phys. Chem.* **1992**, *96*, 7416−7421.

(11) (a) Golan, Y.; Margulis, L.; Rubinstein, I. *Surf. Sci.* **1992**, *264*, 312−326. (b) Alves, C. A.; Smith E. L.; Porter, M. D. *J. Am. Chem. Soc.* **1992**, *114*, 1222−1227.

(12) Turyan, I.; Mandler, D. *Anal. Chem.* **1994**, *66*, 58−63.

(13) The chiral monolayers were synthesized by the amidation of $[S(CH_2)_5CO_2H]_2$ with phenylalanine methyl ester. The details of the synthesis will be published elsewhere. Microanalysis (%). Found$_l$/found$_d$/calcd: C, 62.43/62.56/62.34; H, 7.25/7.38/7.14; N, 4.64/4.54/4.54. ^1H NMR (ppm, in $CDCl_3$): s (OCH_3) 3.54, q (CH) 4.70, d (NH) 5.76, t (CH_2-φ) 2.94, t (CH_2S) 2.94, t (CH_2CO) 2.00, m ($(CH_2)_3$) ≈1.3, m (C_6H_5) ≈7.0. The specific rotation for both enantiomers was $[\alpha]^{22}{}_{\mathrm{D}} = \pm 6.6$ (in ethanol).

(14) Simultaneous experiments that were conducted on thin mercury films electrodeposited on glassy carbon electrodes gave similar results.

(15) After a HMDE was modified it was carefully washed with water before it was transferred into the aqueous solution, e.g., 0.01 M $HClO_4$, in which it was examined.

(16) (a) Miller, I. R.; Teva, J. *J. Electroanal. Chem.* **1972**, *36*, 157−166. (b) Florence, T. M. *J. Electroanal. Chem.* **1979**, *97*, 219−236. (c) O'Shea, T. J.; Lunte, S. M. *Anal. Chem.* **1993**, *65*, 247−250.

(17) *d*- and *l*-monolayers refer to monolayers derived from *d*- and *l*-phenylalanine, respectively.

(18) (a) Kolthoff, I. M.; Barnum, C. *J. Am. Chem. Soc.* **1940**, *62*, 3061−3065. (b) Stankovich, M. T.; Bard, A. J. *J. Electroanal. Chem.* **1977**, *75*, 487−505.

(19) The excess of surface coverage was calculated on the basis of the geometrical area of the HMDE, i.e., 0.0099 cm^2.

(20) Kakiuchi, T.; Senda, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 535−539.

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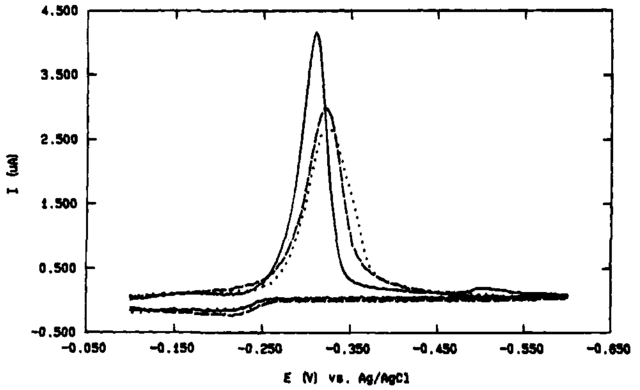

Figure 1. Cyclic voltammetry of a HMDE in a disulfide-free solution consisting of 0.01 M $HClO_4$ after modification with pure enantiomers: *d* (— — —), *l* (•••), and racemic mixture (—), scan rate 100 mV•s^{-1}.

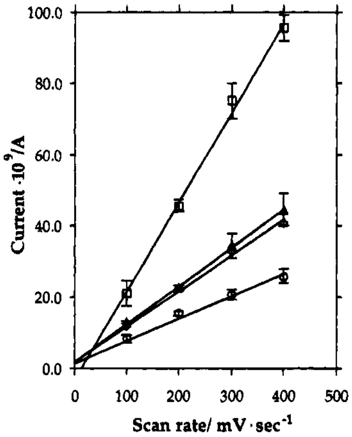

Figure 2. Dependence of non-faradaic charging currents as a function of the scan rate for a bare HMDE (□) and for mercury drops modified with pure enantiomers: *d* (△), *l* (◇) and racemic mixture (○).

than the enantiomers. Nevertheless, the organization of racemic mixtures is sometimes less condensed than the pure enantiomers, as has been observed by us, for example, in monolayers of chiral homocystine.[21]

The adsorption of one of the enantiomers was followed as a function of time. The isotherm reveals that an organized monolayer is formed within a relatively short time, i.e., 30 min. Hence, the differences observed between the racemate and the enantiomers (formed as a result of immersing the surfaces for 30 min in the disulfide solutions) evidently originate from their final organization on the mercury surface.

Differences in surface organization should influence the double layer and thus might be detected by other measurements as well. Figure 2 shows the dependence of the non-faradaic charging current as a function of the scan rate for a bare HMDE and for mercury drops modified with homo- and heterochiral monolayers.[22] The slope of the linear curves equals the double-layer differential capacitance. It can be seen that while electrodes covered with molecules of the same chirality resulted in similar differential capacitance, C_d and C_l equaling (9.64 ± 2.41) and (10.80 ± 2.16) μF•cm^{-2}, respectively, the differential capacitance of a HMDE modified with the racemate is noticeably lower, i.e., $C_{dl} = 5.19 \pm 1.04$ μF•cm^{-2}. This is consistent with the above observation. A more densely packed film is expected to decrease the dielectric constant of the double layer, thus decreasing its capacitance.[23]

A more organized and densely packed array should also affect electron transfer to outer-sphere redox couples.[24] Figure 3 shows the cyclic voltammetry of $Ru(NH_3)_6^{3+}$ on a bare HMDE and at modified surfaces. It is evident that the rate of electron transfer of the redox couple is substantially decreased by the presence of a monolayer. However, while pure enantiomers exhibit almost identical voltammograms, the rate of electron transfer of $Ru(NH_3)_6^{3+/2+}$ is substantially decreased on HMDE modified with the heterochiral monolayer relative to the homochiral systems.

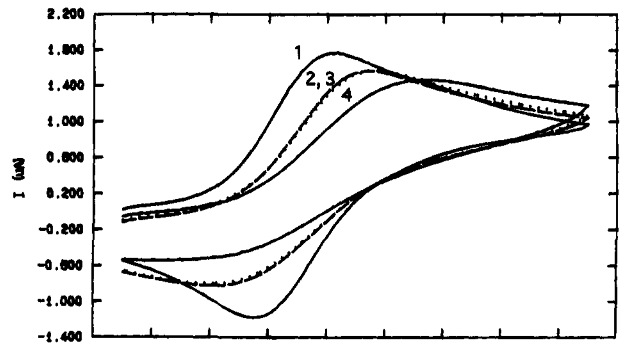

Figure 3. Cyclic voltammetry of 1 mM $Ru(NH_3)_6^{3+}$ in 0.1 M acetate buffer (pH 6.0) on a bare HMDE (1) and on mercury drops modified with pure enantiomers: *d* (2), *l* (3), and racemic mixture (4), scan rate 100 mV•s^{-1}.

Obviously, the differences observed in the excess of surface coverage, the differential capacitance, and the rate of electron transfer of $Ru(NH_3)_6^{3+}$ between the heterochiral and the homochiral monolayers must be rationalized on the basis of their organization on the surface. The fact that the racemate of **I** is more densely packed than the pure enantiomers suggests that the racemate is not separated into domains of pure enantiomers as was recently suggested for amphiphilic chiral monolayers.[25] Since SAMs on Hg have barely been studied,[26] we cannot, at this stage, suggest a clear and comprehensive description of the structure of the homo- and heterochiral systems that can provide an explanation for the difference in their organization. Nevertheless, at least two logical comments can be made. We have studied also monolayers of homologous alkanethiols and ω-mercapto carboxylic acids by the same approaches as mentioned above. From these results, it is clear that the alkyl chains do not tend to orient horizontally on the surface. Secondly, it is conceivable that the packing of the layer will be primarily governed by the stereogenic groups due to their bulkiness and as a result of the liquid, i.e., mercury, substrate, which does not limit the lateral diffusion of the adsorbed molecules. Therefore, we conclude that the differences detected between the organization of the homo- and heterochiral systems are indeed a result of different interactions between the stereogenic centers.

Further experiments that aim to highlight more specifically the relationship between the structure and the organization in chiral self-assembled monolayers are currently being undertaken.

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[21] The excess of surface coverage of SAMs of homocystine has been determined on a HMDE and will be published elsewhere.

[22] The non-faradaic charging current was measured (at $E = -0.15$ V) from the cyclic voltammetry recorded from −0.1 to −0.2 V vs Ag/AgCl in 0.1 M acetate buffer (pH 6.0).

[23] Miller, C.; Cuedent, P.; Grätzel, M. *J. Phys. Chem.* **1991**, *95*, 877–886.

[24] (a) Amatore, C.; Saveant, J. M.; Tessier, D. *J. Electroanal. Chem.* **1983**, *147*, 39–51. (b) Sabatani, E.; Rubinstein, I. *J. Phys. Chem.* **1987**, *91*, 6663–6669. (c) Chidsey, C. E. D.; Loiacono, D. N. *Langmuir* **1990**, *6*, 682–691. (d) Finklea, H. O.; Avery, S.; Lynch, M.; Furtsch, T. *Langmuir* **1987**, *3*, 409–413.

[25] Eckhardt, C. J.; Peachey, N. M.; Swanson, D. R.; Takacs, J. M.; Khan, M. A.; Gong, X.; Kim, J.-H.; Wang, J.; Uphaus, R. A. *Nature* **1993**, *362*, 614–616.

[26] (a) Li, T. T.-T.; Weaver, M. J. *J. Am. Chem. Soc.* **1984**, *106*, 6107–6108. (b) Demoz, A.; Harrison, D. J. *Langmuir* **1993**, *9*, 1046–1050.