Discriminating Chiral Molecules of (*R*)-PPA and (*S*)-PPA in Aqueous Solution by ECSTM**

Qing-Min Xu, Dong Wang, Li-Jun Wan,*
Chen Wang, Chun-Li Bai,* Guo-Qiang Feng, and
Mei-Xiang Wang*

Chiral discrimination is one of the most attractive areas in chemistry because of the important applications of chiral molecules in catalysis and stereoselective synthesis. A feasible approach to chiral discrimination is the use of solid surfaces modified with chiral molecules.[1–4]. The scanning tunneling microscope (STM) is a powerful tool to reveal molecular structures on solid surfaces with atomic resolution in real space.[5–8] Recently, STM has been successfully applied to determine the conformation and chirality of individual molecules on metal and semiconductor surfaces under ambient and ultra-high vacuum (UHV) conditions.[9–15] Lopinski et al. determined the absolute configuration of isolated chiral centers of alkene molecules chemisorbed on Si(100) in UHV.[10] Böhringer et al. observed the chiral packing of 1-nitronaphthalene (NN) molecules on a reconstructed Au(111) surface and found a coverage-driving chiral phase transition at low-temperature.[11,12] Lorenzo et al. investigated the adsorption of tartaric acid molecules on a Cu(110) surface which result in formation of a chiral surface with the chiral channels by hydrogen-bonding interactions between the OH groups of the molecules.[14,15] Ohtani et al. took advantage of the self-assembling and covalent-binding properties of 1,1′-binaphthalene-2,2′-dithiol (BNSH) molecules and fabricated a self-assembled monolayer (SAM) on Au(111); the chirality of BNSH molecules in the SAM was revealed under ambient conditions.[13] However, most chiral molecules are in solution when chemical reactions take place. Therefore, imaging chiral molecules in solution is one of the most significant issues in discriminating chirality. This task represents a challenge to electrochemical STM (ECSTM).[5–8] ECSTM can work in solution without the use of UHV or low temperature and allows the observation of molecules without being hindered by limitations such as solubility and evaporative properties. The application of ECSTM to chiral discrimination may result in a simple and routine analytical method.

For the first time, we have demonstrated that chiral molecules can be discriminated in aqueous solution. The discrimination was carried out by using ECSTM in the adlayers of enantiomeric molecules ((*R*)- and (*S*)-2-phenylpropionamide (PPA; $C_9H_{11}ON$) on Cu(111) in 0.1M $HClO_4$. These compounds are used in the chemical and pharmaceutical industries. Scheme 1 shows their chemical structures generated by hyperchem software and optimized by an AM1 method to a root-mean-square value of less than 0.01 kcal Å^{-1}. The parameters for the molecules such as interatomic distances were estimated from the models. The chiral centers in the molecules are indicated by arrows. Cu(111) was used as a solid substrate for the molecular adsorption. Although fcc(111) is not a chiral surface, the chiral nature of the molecules makes the discrimination possible. The adsorption of (*R*)- and (*S*)-PPA molecules results in the same ordered structures with a (4 × 4) symmetry in the double-layer potential region. The structural details of the *R* and *S* molecules differ from each other because of chirality, although the applied potentials are the same. The chirality can clearly discriminated in high-resolution STM images (see below).

Scheme 1. Chemical structure of (*R*)- and (*S*)-2-phenylpropionamide molecules (hyperchem software).

Both (*R*)- and (*S*)-PPA molecules form well-ordered adlayers on the Cu(111) surface in solutions. Figure 1 shows a typical STM image of (*R*)-PPA on Cu(111). It can be seen that the molecules form a highly ordered adlayer and yield a completely different pattern from Cu(111)-(1 × 1). One direction of molecular rows, indicated by arrow A, runs along the Cu(111)-[1$\bar{1}$0] direction with a period of 0.96 ± 0.02 nm which corresponds to four times the Cu(111) lattice length. In direction B a period of 0.96 ± 0.02 nm (i.e. four times the Cu(111) lattice) is measured. The angle between A and B is 120° ± 2°. On the basis of intermolecular distance and orientation of molecular rows, a (4 × 4) structure for the adlayer can be determined. A unit cell is outlined in Figure 1 a.

The adlayer structure of (*S*)-PPA molecules on Cu(111) in 0.1M $HClO_4$ is the same as that of (*R*)-PPA molecules in a (4 × 4) symmetry array (Figure 2; a unit cell is also outlined in the image. The directions C and D are along the close-packed Cu(iii) lattice and make an angle of 120 ± 2°).

The results described above show that the adlayer symmetry is independent of the chirality. To understand the electrochemical behaviors of (*R*)- and (*S*)-PPA on Cu(111) in 0.1M $HClO_4$ solution, a bare Cu(111) electrode was initially examined by cyclic voltammetry in 0.1M $HClO_4$ for comparison with published data.[16] After the examination, the electrode was transferred into saturated 0.1M $HClO_4$ solutions of (*R*)- and (*S*)-PPA. The overall shape of the cyclic voltammograms of (*R*)- and (*S*)-PPA (not shown) is almost the same as that of bare Cu(111). The adsorption of the two molecules results in the formation of a featureless double-layer region which can be detected as a small electric charge in the cyclic voltammograms. This effect indicates the molecular adsorption onto Cu(111) in 0.1M $HClO_4$. After recording the

---

[*] Prof. Dr. L.-J. Wan, Prof. Dr. C.-L. Bai, Prof. Dr. M.-X. Wang,
Dr. Q.-M. Xu, D. Wang, Prof. Dr. C. Wang, G.-Q. Feng
Institute of Chemistry
The Chinese Academy of Sciences
Beijing 100080 (China)
Fax: (+86) 10-62558934
E-mail: wanlijun@infoc3.icas.ac.cn
clbai@infoc3.icas.ac.cn

[**] This work was supported by National Natural Science Foundation of China (Nos. 20025308 and 20177025), the National Key Project on Basic Research (Grant G2000077501), and The Chinese Academy of Sciences. PPA = 2-phenylpropionamide, ECSTM = electrochemical scanning tunneling microscopy.

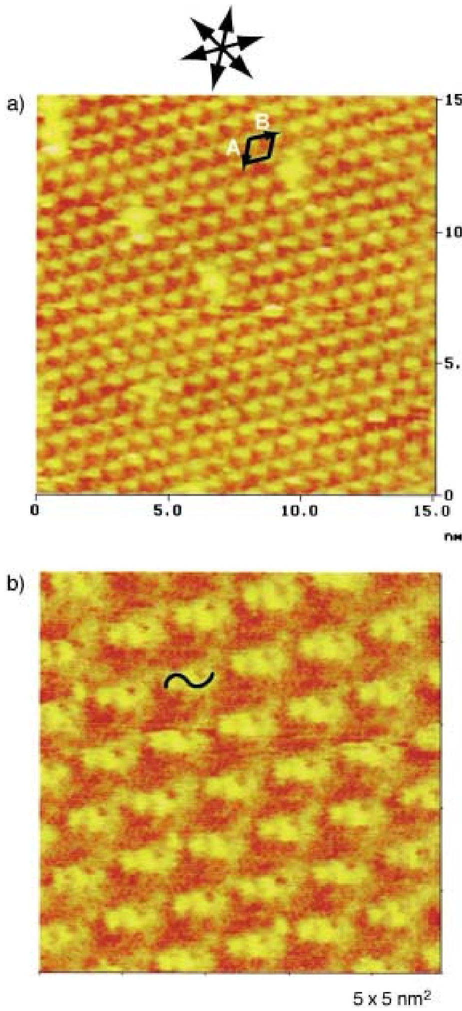

Figure 1. a) In situ STM images of (*R*)-PPA molecules on Cu(111) in 0.1M $HClO_4$. The image was recorded at 0 V. b) Expansion of (a), ~ indicates the shape of an (*R*)-PPA molecule.

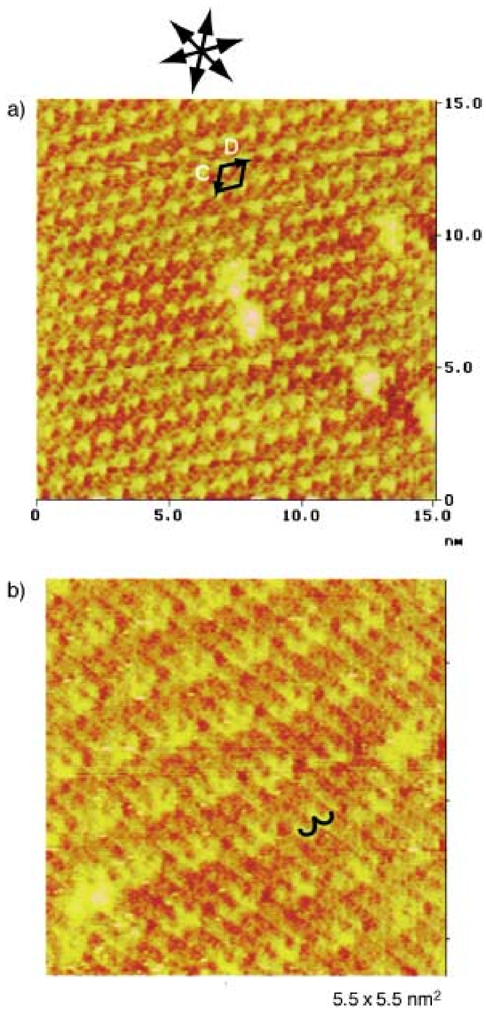

Figure 2. a) In situ STM images of (*S*)-PPA molecules on Cu(111) in 0.1M $HClO_4$. b) Expansion of (a) ω indicates the shape of an (*S*)-2-PPA molecule. Images acquired at 0 V by using the same imaging conditions as for Figure 1.

images shown in Figure 1 and Figure 2 at 0 V, the electrode potential was stepped from −0.2 to 0.2 V in increments of 10 mV. A set of STM images of the two molecular adlayers was acquired at different potentials during the potential steps. Similar images with the same molecular features were consistently observed. The structures of both (*R*)- and (*S*)-PPA adlayers were stable in the potential region from −0.2 to 0.2 V, which indicates the same adsorption behavior of the chiral molecules at the liquid/solid interface.

However, the structural details of the two molecules can be seen by the comparison of Figure 1b and 2b. Instead of a "~" shape in Figure 1b for each (*R*)-PPA molecule, the (*S*)-PPA molecules appear in the "ω" shape shown in Figure 2b. We have tried to rotate and translate Figure 1b and 2b, but the molecular images can not be superimposed. The existence of the mirror-images indicates that the adsorbed molecules preserve their chiral nature and create 2D chiral surface on the Cu(111) surface.

The adsorbed molecules consist of a phenyl ring, methyl, and $CONH_2$ groups. The chiral feature of the molecules arise from the arrangement of methyl and $CONH_2$ groups. To reveal the internal molecular structure in the 2D chiral surfaces, higher-resolution STM images were acquired under carefully adjusted experimental conditions with minimal drift. Figure 3a shows one of the highest resolution images recorded on the (*R*)-PPA adlayer. Each molecule appears as three bright spots and a "Y" shape tail. According to the previous results, the three bright spots are attributed to a phenyl ring lying flat on a threefold hollow site of the Cu(111) lattice.[17,18] The tail is attributed to methyl and $CONH_2$ groups of the chiral center. Based on the chemical structure and measured distance, M and N shown in Figure 3a correspond to the methyl and $CONH_2$ groups, respectively; a structural model for the (*R*)-PPA SAM is proposed in Figure 3b. In the model, the (*R*)-PPA SAM has a (4 × 4) structure. The phenyl rings are parallel to the Cu(111) surface and positioned in hollow sites. The amino, carbonyl and methyl groups occupy two-bridge sites.

It is intriguing to see the chirality in (*S*)-PPA adlayer. Figure 4a is one of the higher-resolution images recorded on the (*S*)-PPA adlayer. Although a great effort was made to acquire a high quality image, it was found that the image of (*S*)-PPA is not as good as that for (*R*)-PPA. This is attributed to the adsorption geometry. However, the image features for

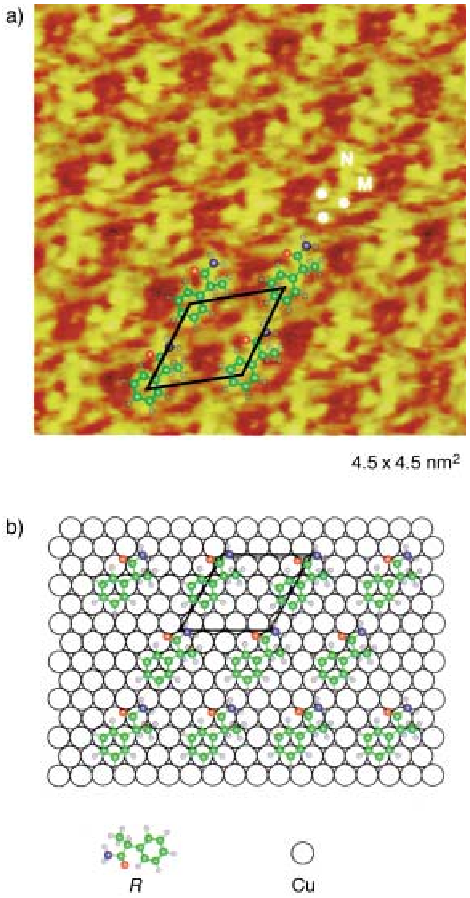

Figure 3. a) High resolution STM image of (R)-PPA molecules on Cu(111) in 0.1M $HClO_4$. b) A proposed model of (R)-PPA molecules with a structure of (4 × 4) symmetry.

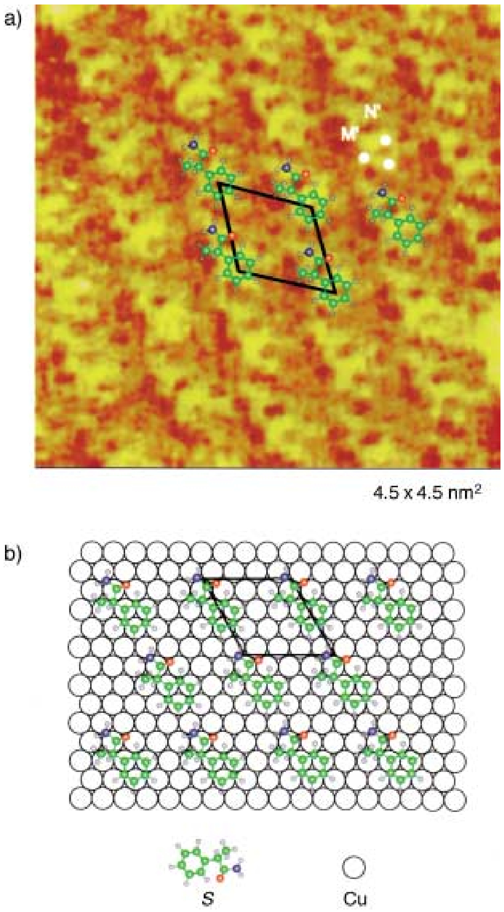

Figure 4. a) High resolution STM image of (S)-2-PPA molecules on Cu(111) in 0.1M $HClO_4$. b) A proposed model of (S)-PPA molecules with a structure of (4 × 4) symmetry.

an (S)-PPA molecule can still be seen in Figure 4a. The structural details are almost the same as those shown in Figure 3a, and include a three-spot phenyl ring and a “Y” shape tail. M′ and N′ indicate the methyl and $CONH_2$ groups. The molecular chirality is directly expressed in the STM image. The distances between the center of the amino group and the chiral center, and between the center of the methyl group and the chiral center, are measured to be around 0.23 nm and 0.15 nm, respectively, close to the distances in the molecule and equal to those distances in Figure 3a. A structural model for the (S)-PPA adlayer is illustrated in Figure 4b. Compared with the two structures of (R)-PPA and (S)-PPA in Figure 3 and 4, the chirality is clearly seen from the arrangement of the methyl and $CONH_2$ groups. The present results demonstrate that chirality can be discriminated by ECSTM. However, the substrate material plays an important role in molecule adsorption. Different structures could be obtained on different substrate materials and crystallographic surfaces. In electrolyte solution, protonation of the molecule will vary with solution pH value. Therefore, to generalize the observations on a substrate such as Cu(111), a systemic study of chirality on other substrates such as Au(111), Pt(hkl), and HOPG in various solutions is necessary. A more detailed study is now in progress.

In summary, the chirality of (R)-PPA and (S)-PPA molecules has been observed on Cu(111) in solution by using ECSTM. Although the two molecules adsorb on Cu(111) in the same (4 × 4) symmetry, the molecular arrangements are different to each other. The chirality of the two molecules, which arises from the orientation of the methyl and $CONH_2$ groups, can be directly seen in higher-resolution STM images. The principle used here may be relevant for the development of a simple method for discriminating chiral molecules in aqueous solution.

Experimental Section

A commercial Cu(111) single-crystal disk with a diameter of 10 mm (from MaTeck) was used as a working electrode for in situ electrochemical STM observation. A well-defined single-crystal surface was prepared as described in the literature.[16] A solution of 0.1M $HClO_4$ was prepared by diluting ultrapure $HClO_4$ (Cica-Merck, Kanto Chemicals) with ultrapure Millipore water. Solutions of 0.1 mM synthesized (R)- and (S)-2-phenylpropionamide were prepared with ultrapure Millipore water. The home-made electrochemical cell contained a reversible hydrogen electrode (RHE) in 0.1M $HClO_4$ and a Pt counter electrode. All electrode potentials are reported with respect to the RHE.

Received: April 17, 2002
Revised: June 3, 2002 [Z19102]

---

[1] H. U. Blaser, M. Muller in *Heterogeneous Catalysis and Fine Chemicals II, Vol. 59* (Ed: M. Guisnet) Elsevier Science Publishers B. V., Amsterdam, **1991**, pp. 73.

[2] H. U. Blaser, *Tetrahedron: Asymmetry* **1991**, *2*, 843–866.

[3] B. F. Watkins, J. R. Behling, E. Kariv, L. L. Miller, *J. Am. Chem. Soc.* **1975**, *97*, 3549 – 3550.
[4] T. Komori, T. Nonaka, *J. Am. Chem. Soc.* **1984**, *106*, 2656 – 2659.
[5] D. M. Kolb, *Angew. Chem.* **2001**, *113*, 1198 – 1220; *Angew. Chem. Int. Ed.* **2001**, *40*, 1162 – 1181.
[6] Th. Dretschkow, A. S. Dakkouri, Th. Wandlowski, *Langmuir* **1997**, *13*, 2843 – 2856.
[7] T. P. Moffat in *Electroanalytical Chemistry, Vol. 21* (Eds.: A. J. Bard, I. Rubinstein), Marcel Dekker, New York, **1999**, pp. 211.
[8] K. Itaya, *Prog. Surf. Sci.* **1998**, *58*, 121 – 248.
[9] a)T. A. Jung, R. R. Schlitter, J. K. Gimzewski, *Nature* **1997**, *386*, 696 – 698; b)M. Schunack, E. Lægsgaard, I. Stensgaard, I. Johannsen, F. Besenbacher, *Angew. Chem.* **2001**, *113*, 2693—2696; *Angew. Chem. Int. Ed.* **2001**, *40*, 2623—2626.
[10] G. P. Lopinski, D. J. Moffatt, D. D. M. Wayner, R. A. Wolkow, *Nature*, **1998**, *392*, 909—911.
[11] M. Böhringer, W. D. Schneider, R. Berndt, *Angew. Chem.* **2000**, *112*, 821 – 825; *Angew. Chem. Int. Ed.* **2000**, *39*, 792 – 795.
[12] M. Böhringer, K. Morgenstern, W. D. Schneider, M. Wühn, C. Wöll, R. Berndt, *Surf. Sci.* **2000**, *444*, 199 – 210.
[13] B. Ohtani, A. Shintani, K. Uosaki, *J. Am. Chem. Soc.* **1999**, *121*, 6515 – 6516.
[14] M. O. Lorenzo, C. J. Baddeley, C. Muryn, R. Raval, *Nature* **2000**, *404*, 376 – 378.
[15] M. O. Lorenzo, S. Haq, T. Bertrams, P. Murray, R. Raval, C. J. Baddeley, *J. Phys. Chem. B* **1999**, *103*, 10661 – 10669.
[16] L.-J. Wan, K. Itaya, *Langmuir* **1997**, *13*, 7173 – 7179.
[17] P. S. Weiss, D. M. Eigler, *Phys. Rev. Lett.* 1993, *71*, 3139 – 3142.
[18] P. Sautet, *Chem. Rev.* **1997**, *97*, 1097 – 1116.

Thermotropic Liquid Crystals from Planar Chiral Compounds: Optically Active Mesogenic [2.2]Paracyclophane Derivatives**

Elena L. Popova, Valeria I. Rozenberg,
Zoya A. Starikova, Susanne Keuker-Baumann,
Heinz-Siegfried Kitzerow, and Henning Hopf*

Chiral liquid-crystalline (LC) compounds constitute a central topic of present-day research on liquid crystals. For example, not only are the well-established applications of thermochromic materials as well as twisted nematic (TN) and supertwisted nematic (STN) displays based on chirality, but so are ferro-, ferri-, and antiferroelectric, second-harmonic generation, polymer-stabilized cholesteric texture (PSCT) displays and certain photonic crystals. Thus, new chiral structures are continuously proposed that provide new insights and promising applications.[1]

The way in which chirality is introduced into the mesogenic molecule is one of the crucial factors in determining the properties of the resultant LC material. The importance of the position of the stereogenic unit relative to the liquid-crystalline core is underlined by the fact that it forms the basis for a classification system for chiral LC compounds.[2] Most chiral mesogenic compounds are classified as Type I or Type II liquid crystals. In the former case chirality is introduced through an asymmetric carbon atom located in a terminal alkyl chain, whereas in the latter it is enclosed between two liquid-crystalline core units. These LC compounds have been well-studied and widely used. In Type III liquid crystals, the chiral unit is incorporated into the rigid core itself, and is thus particularly applicable to planar and axially chiral compounds. Although properties which are important for practical application have been predicted for materials of this type (for example, shortening of helical pitch length, increase in sponataneous polarization of a chiral dopant, as well as interesting optical effects[3]), planar, chiral liquid-crystalline compounds still remain relatively unexplored.

The molecular complexity of the structural unit necessary to generate an axis or a plane of chirality often creates serious obstacles to achieving stable mesomorphic properties. Only a few examples of planar and axially chiral mesogens have so far been reported. These include: cyclohexylideneethanone[4] and allene derivatives,[5] chiral biphenyls,[6] and iron-tricarbonyl–butadiene complexes.[7] Additionally, the first 1,3-unsymmetrically disubstituted optically active LC ferrocene derivative has recently been reported.[8] However, in most of these cases the mesophases only had a narrow temperature interval and several of the compounds obtained appear to be chemically or photochemically unstable. Moreover, the difficulties of synthesis and optical resolution associated with these derivatives are probably the reason for the lack of systematic studies on the physical properties of planar and axially chiral compounds as well as of their practical application.

In our opinion, the ease of functionalization, ready optical resolution, and high configurational stability of paracyclophane (PC) derivatives[9] make these bridged aromatic compounds unique candidates for chiral LC materials.

In our first attempt to investigate the ability of the PC unit to promote mesomorphism we used several racemic derivatives.[10] As shown by these exploratory investigations, the mesogenic potential of the PC core depends on the number and position of substituents in the PC moiety: of the structures investigated, *para*-substituted PC derivatives had superior mesogenic properties with a broad interval of either nematic or smectic A (SmA) phases. Herein we describe the first family of optically active mesogenic compounds containing a PC unit. Several synthetic problems had to be solved to prepare the required chiral PC precursors.

As mentioned above, *para*-substitution of the PC moiety was shown to best induce mesomorphism,[10] but known examples of specific *para*-PC derivatives are still scarce and a

---

[*] Prof. Dr. H. Hopf, Dr. E. L. Popova
Institut für Organische Chemie
Technische Universität Braunschweig
Hagenring 30, 38106 Braunschweig (Germany)
Fax: (+49) 531-391-5388
E-mail: h.hopf@tu-bs.de

Prof. Dr. V. I. Rozenberg, Z. A. Starikova
A. N. Nesmeyanov Institute of Organoelement Compounds
Russian Academy of Sciences
Vavilova 28, 117813 Moscow (Russia)

S. Keuker-Baumann, Prof. Dr. H.-S. Kitzerow
Fachbereich Chemie
Universität Paderborn
Warburger Strasse 100, 33098 Paderborn (Germany)

[**] This work was supported by the Fonds der Chemischen Industrie. We thank Mrs. Petra Holba-Schulz for recording the 2D ^{1}H NMR spectra.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.