

Manipulating Self-Assembly with Achiral Molecules: An STM Study of Chiral Segregation by Achiral Adsorbates

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The self-assembly of a mixture of hexadecanoic acid with racemic (*R*)/(*S*)-2-bromohexadecanoic acid has been investigated using scanning tunneling microscopy. When this mixture is physisorbed onto the basal plane of graphite, hexadecanoic acid controls the resultant two-dimensional structure. By self-assembling on a graphite substrate into two distinct domains exhibiting nonsuperimposable mirror image morphology, achiral hexadecanoic acid induces the segregation of 2-bromohexadecanoic acid into enantiomerically pure (*R* and *S*) domains. The 2-bromohexadecanoic acid molecules provide convenient markers to directly differentiate the 2D chiral domains of inherently achiral hexadecanoic acid. The pattern in which hexadecanoic acid assembles with enantiomerically pure 2-bromohexadecanoic acid is shown to be more energetically favorable than a monolayer in which the unsubstituted fatty acid is mixed with both chiral isomers of 2-bromohexadecanoic acid.

Introduction

The ability to distinguish between and separate chiral conformers has become an important necessity in today's chemical world since a molecule's chirality plays a significant role in its function. Optical spectroscopy was the technique first used by Louis Pasteur 150 years ago to separate enantiomers of sodium tartrate. Methods such as NMR,¹ circular dichroism,² polarimetry,³ and X-ray crystallography⁴ have since been added to the list of available technologies used to elucidate chiral configurations. The latest newcomer to this roster of techniques is the family of scanning probe microscopies, which includes scanning tunneling microscopy (STM)⁵ and atomic force microscopy (AFM).⁶ The advantage of STM and AFM over traditional analysis tools is that these high-resolution imaging methods allow for a determination of absolute chirality while obviating the need for a standard sample or a compound with known chirality.

Several chiral systems have already been explored with STM and AFM. Separation of achiral molecules into lattices with chiral packing⁷ and separation of chiral phases of chiral organic molecules in Langmuir–Blodgett films have been observed by AFM.⁸ Chiral liquid crystals have also been investigated with STM and found to form domains that exhibit two-dimensional chirality.⁹ Recently, supramolecular clusters of 1-nitronaphthalene on gold have been observed to aggregate in 2D domains that are mirror images of each other.¹⁰ In all these cases, the submolecular or even atomic resolution necessary to determine the absolute chirality for individual enantiomers was not achieved. Assignment of absolute chirality has, however, been accomplished within the past year in studies of (1) the resolution of racemic 2-bromohexadecanoic acid into enantiomerically pure domains physisorbed on a graphite surface,¹¹ (2) the determination of the configuration of chiral centers formed by the chemisorption of simple alkenes (propylene, *trans*-2-butene, *cis*-2-butene) on silicon¹² and (3) the adsorption of sterically hindered 1*S*(+)-3-carene onto silicon in an enantioselective reaction.¹³

These last few reports show that the chirality of individual molecules can be determined and investigated using scanning probe methodologies, and it is now appropriate to ask how the self-assembly of chiral molecules is affected by the presence of other nonchiral species. De Feyter et al.¹⁴ have studied monolayers of enantiomerically pure isophthalic acid derivatives coadsorbed onto a graphite surface with the achiral solvent, 1-heptanol. This work has shown that the orientation of the achiral solvent molecules expresses the chirality of the domains. The effect of a third element (a coadsorbate in the form of another solute), however, has not been previously studied. Introducing this factor into a system that already contains solvent and one adsorbate poses interesting and potentially useful complications for manipulating the intermolecular interactions involved and the resulting structure of the monolayer film. Such achiral coadsorbates show promise as powerful tools to segregate chiral molecules and control self-assembled monolayers.

In this paper we present an STM study at the liquid–solid interface of a mixture of hexadecanoic acid with racemic 2-bromohexadecanoic acid physisorbed onto a graphite surface. Through the use of STM chemical “marker” groups, these two solutes are found to coadsorb onto the surface, and the mixed monolayer film resolves into domains of hexadecanoic acid with either (*R*)- or (*S*)-2-bromohexadecanoic acid. Further analysis reveals that achiral hexadecanoic acid forms domains exhibiting nonsuperimposable mirror image morphology (enantiomorphous domains) on a graphite surface, similar to that observed for behenic acid,¹⁵ and these 2D chiral domains in fact effect enantiomeric resolution of 2-bromohexadecanoic acid in the self-assembled structure. Moreover, by varying the concentration of hexadecanoic acid, it may be possible to manipulate the self-assembly of 2-bromohexadecanoic acid on the surface.

Experimental Section

All the studies described were performed under ambient conditions using a Nanoscope III scanning tunneling microscope (Digital Instruments). The experiments were conducted at the

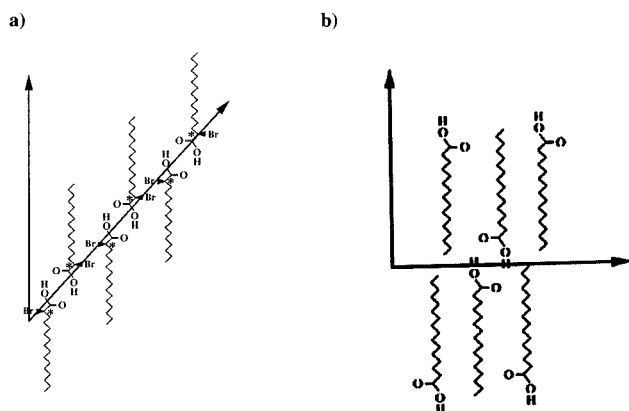


Figure 1. Schematic representations of different molecules self-assembled on a graphite surface. A representation of a domain of (*R*)-2-bromohexadecanoic acid on graphite is presented in (a). The self-assembly of 2-bromohexadecanoic acid produces separate chiral domains; the chiral carbons are marked by an asterisk. The molecular axis and the lamella form a 45° angle as depicted by the arrows. The two-dimensional structure formed by hexadecanoic acid in (b) shows interdigitating carboxylic acid groups. In contrast to (a), here the lamellar axis is perpendicular to the molecular axis.

liquid–solid interface by immersing an STM tip, mechanically cut from 0.25 mm diameter platinum/rhodium (87/13) wire (Omega), into a droplet of solution. The small (10 μ L) droplet of solution is applied directly to the surface of a freshly cleaved piece of highly oriented pyrolytic graphite, HOPG (Advanced Ceramics, ZYB grade).

Hexadecanoic acid ($\text{CH}_3(\text{CH}_2)_{14}\text{COOH}$) and a racemic mixture of 2-bromohexadecanoic acid ($\text{CH}_3(\text{CH}_2)_{13}\text{CHBrCOOH}$) were procured from Aldrich. These samples were dissolved in 1-phenyloctane (Aldrich) to produce saturated solutions of 2-bromohexadecanoic acid or hexadecanoic acid. The solutions were allowed to thermally equilibrate for approximately 24 h prior to scanning under the microscope. The 2-bromohexadecanoic acid solution and hexadecanoic acid solution were subsequently mixed in a 1:1 ratio by volume. Several samples of this mixture were prepared and studied to check for reproducibility of results.

All of the images displayed were obtained in the constant current mode of operation whereby the height of the STM tip relative to the surface is monitored via an electronic feedback loop and adjusted in order to maintain a fixed tunneling current set by the user. A zeroth order flattening procedure has been utilized to normalize the vertical offset produced in this operating mode. Typical tunneling parameters used in the experiments include a bias voltage of 1.5 V (sample negative) and a tunneling current of 250–400 pA. The resulting constant current images display relative topographic height where “bright” corresponds to topographically higher areas and “dark” corresponds to topographically lower regions.

Molecular models were created with the molecular modeling software package Biosym (InsightII, Molecular Simulations, Inc.) running on a Silicon Graphics workstation.

Results

Racemic 2-Bromohexadecanoic Acid. The self-assembly of 2-bromohexadecanoic acid ($\text{CH}_3(\text{CH}_2)_{13}\text{CHBrCOOH}$) onto a graphite surface has been previously studied via STM. Fang et al.¹¹ have demonstrated that this racemic mixture segregates into separate chiral (*R* and *S*) domains on a graphite surface. (Figures 2 and 3 in ref 11 display high-resolution images of segregated *R* and *S* domains.) Figure 1a schematically represents a portion of the domain formed by the *R* enantiomer with asterisks

marking the chiral center of each molecule. The molecular and lamellar axes form a 45° angle for this species (marked by arrows) when self-assembled on a graphite surface. STM images of 2-bromohexadecanoic acid reveal “dark” (topographically depressed) spots in the troughs that are assigned to the locations of individual carboxylic acid groups.¹¹ In accordance with previous studies,^{16,17} the carboxylic functional group at the end of each molecule appears “dark” (topographically depressed) with respect to the rest of the alkyl chain due to a decrease in tip height needed to maintain constant electron tunneling current at this specific location. In addition to these dark spots, the images reveal “bright” (topographically elevated) spots that have been attributed in Fang’s work¹¹ as well as other studies¹⁸ to the bromine functional group when it appears either at a nonterminal position along the hydrocarbon chain or at a terminal position in the gauche conformation. When a terminal bromine adopts the trans conformation at the end of a chain, it actually appears dark (topographically depressed) compared to the rest of the alkyl chain atoms.^{18,19} The use of these chemical markers (bromine atoms and carboxylic acid groups) along with high-resolution STM imaging has allowed the absolute chirality of individual molecules to be assigned directly.

Hexadecanoic Acid. As described previously,^{16,17,20} hexadecanoic acid ($\text{CH}_3(\text{CH}_2)_{13}\text{CH}_2\text{COOH}$), like other fatty acids, forms a well-ordered monolayer when physisorbed onto a graphite surface. A schematic of the self-assembly for this fatty acid, depicted in Figure 1b, shows a very different pattern than the two-dimensional structure formed by 2-bromohexadecanoic acid in Figure 1a and discussed in the previous section. Figure 1b reveals a classic interdigitating pattern commonly found among fatty acids. The fatty acids lie down “head-to-head” with a carboxyl group adjacent to another carboxyl group in order to facilitate hydrogen bonding between these end groups.

A corresponding $8.5 \times 8.5 \text{ nm}^2$ STM image of hexadecanoic acid in Figure 2a reveals organized lamellae separated by dark troughs where each lamella consists of individual molecules, and troughs are composed of dark, circular regions. Similar to the case for 2-bromohexadecanoic acid, the dark (topographically depressed) regions in the STM image are attributed to the hydrogen-bonding carboxylic groups that adopt the “head-to-head” formation depicted in Figure 1b. The length of one molecule, denoted by a black bar, is measured to be $2.16 \pm 0.04 \text{ nm}$ in reasonable agreement with the 2.25 nm length expected for a 16-carbon long, all trans carboxylic acid, lying flat on the basal plane of graphite. Finally, the lamellae form a right angle with the molecular axis, which is also marked by arrows in the schematic of Figure 1b.

Mixtures of 2-Bromohexadecanoic Acid and Hexadecanoic Acid. Mixtures of 2-bromohexadecanoic acid and hexadecanoic acid exhibit long-range order when physisorbed onto a graphite substrate. Multiple domains are formed extending in width from 30 nm to over 100 nm. Figure 2b shows a representative STM topograph of a 1:1 mixture of hexadecanoic acid with 2-bromohexadecanoic acid imaged at the phenyloctane-graphite interface. This image also depicts well-ordered lamella separated by dark troughs (labeled *T* in the figure), and individual molecules in the lamella are signified by a black or blue bar. (The significance of the black versus blue bar is explained below.) The length of a given molecule, $2.25 \pm 0.08 \text{ nm}$, corresponds to the expected 2.25 nm length of either a hexadecanoic acid or a 2-bromohexadecanoic acid molecule configured in an all-trans conformation lying flat on the surface. Further, the lamellae form a 90° angle with the molecular axis in this two-dimensional array.

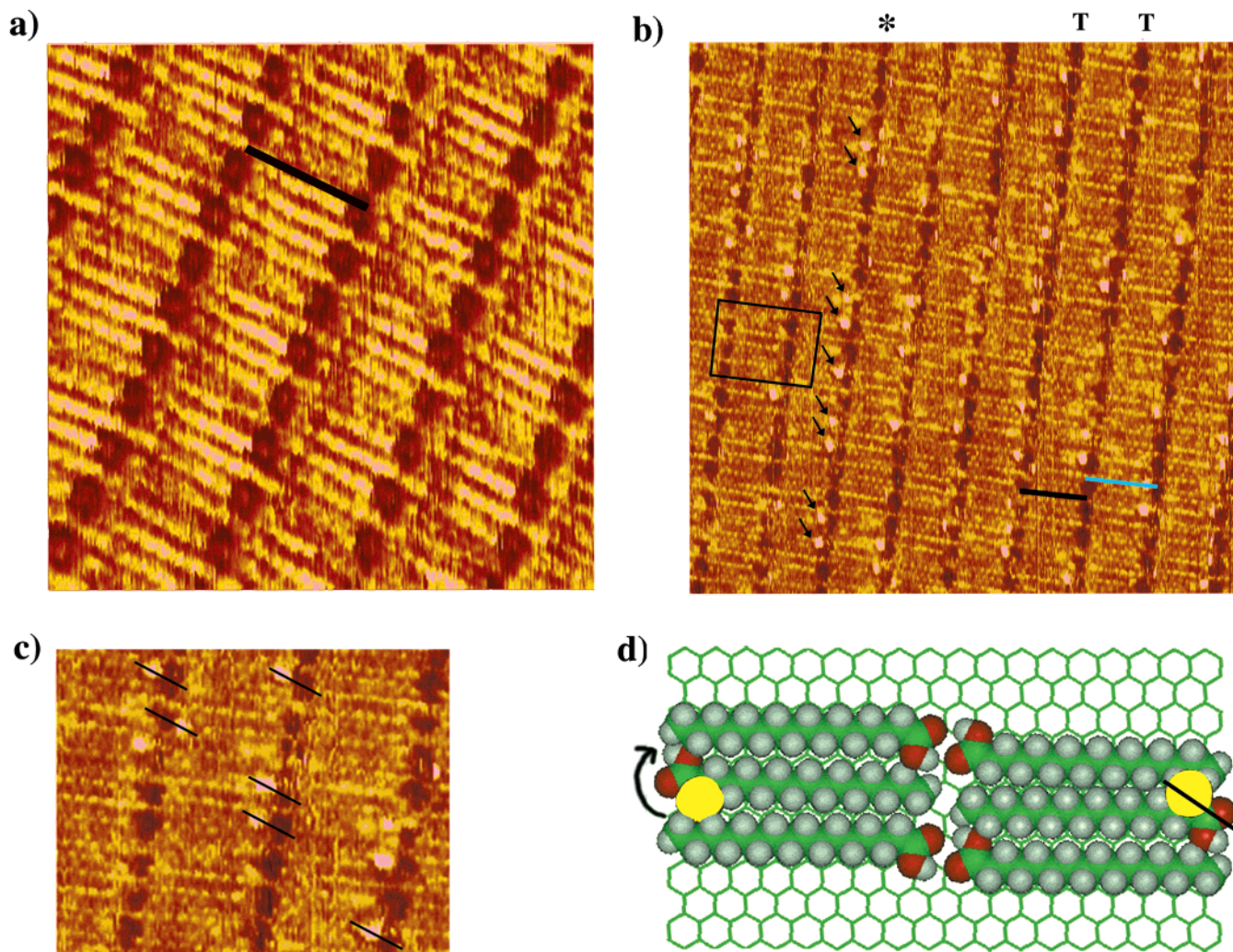


Figure 2. (a) An STM constant-current topograph of a hexadecanoic acid monolayer physisorbed onto a graphite surface taken at 1.5 V (sample negative) and 300 pA. This 8.5 nm \times 8.5 nm image shows well-ordered lamellae separated by troughs, and a black bar represents a single molecule. These troughs consist of individual hydrogen-bonding carboxylic acid groups, which are identified as the dark circles. (b) through (d) show constant-current STM topographs of a 1:1 mixture by volume of 2-bromohexadecanoic acid to hexadecanoic acid physisorbed onto a graphite surface, imaged at 1.5 V (sample negative) and 300 pA. (b) 19 nm \times 19 nm image displays hexadecanoic acid molecules (marked by a black bar) and an occasional (*R*)-2-bromohexadecanoic acid molecule (marked by a blue bar), both of which are configured in the all-trans conformation. A trough is signified by a "T" and reveals dark regions that are attributed to the locations of hydrogen-bonding carboxyl groups accompanied sporadically by bright, topographical protrusions attributed to bromine atoms. All of the bromine atoms in the starred trough are signified by small arrows. The squared off region displays a small area where the interdigitation pattern, common to fatty acids, is apparent. The lamella axis is perpendicular to the molecular axis. An enlarged portion of (b) shown in (c) reveals a consistent orientation of bromine atoms relative to carboxyl groups; either the bromine lies above and to the left or below and to the right of the carboxylic group. Black lines superimposed onto some individual carboxyl/bromine combinations mark this orientation. The carboxyl-bromine-remainder of alkyl chain orientation is used to identify the 2-bromohexadecanoic acid molecules in the domain as *R* chiral conformers of the molecule. A top view of a model of hexadecanoic acid interspersed by (*R*)-2-bromohexadecanoic acid physisorbed onto the graphite surface is shown in (d). The black line superimposed on one of the bromine/carboxyl combinations mimics the arrangement found in the STM image (c). An arrow marking the clockwise direction of the bromine-carboxyl group-alkyl group orientation classifies the brominated molecules as the *R* conformer.

Troughs consisting of two different elements are evident in this constant-current topograph. The majority of each trough is composed of dark, circular groups that are located at the end of each molecule, while a small portion of every trough has bright spots accompanying these dark regions (see arrows in starred trough of Figure 2b). As described previously, the dark areas can be associated with the hydrogen-bonding carboxyl functional group. The bright spots (topographical protrusions) correspond to bromine atoms as observed for other bromines located at a nonterminal position along the hydrocarbon chain.¹¹ These chemical marker groups, therefore, allow for a straightforward differentiation between molecules of hexadecanoic acid and those of 2-bromohexadecanoic acid present in this self-assembled, chemically mixed monolayer. In Figure 2b an indi-

vidual hexadecanoic acid molecule is marked by a black bar, whereas a single 2-bromohexadecanoic acid molecule with its bright bromine feature is signified by a blue bar. All of the carboxyl groups in Figure 2 form an interdigitating pattern similar to the one reported for pure hexadecanoic acid (Figure 2a). In the section of the mixed monolayer bound by a box in Figure 2b, this interdigitating pattern is more readily observed. As demonstrated by a random array of bright, topographical protrusions visible in this image, the 2-bromohexadecanoic acid molecules are sporadically located throughout the two-dimensional structure. For example, the "starred" trough in Figure 2b shows that of the approximately 50 individual molecules present in this particular row, only 9 are 2-bromohexadecanoic acid molecules. Each of the 9 "bright" bromines

has been marked by a small arrow. The observation that a 1:1 ratio by volume in solution yields a significantly different ratio on the surface (in the sampled lamella above, the ratio of 2-bromohexadecanoic acid: hexadecanoic acid is roughly 1:5) suggests that the equilibrium between the adsorbed molecules on the surface and those in solution favors hexadecanoic acid and not 2-bromohexadecanoic acid, analogous to mixtures of alkanes and alcohols where the alcohol has a higher affinity for the surface in a 1:1 mixture.²¹ Hexadecanoic acid molecules dominate the monolayer while some 2-bromohexadecanoic acid molecules are able to squeeze into the dominant ordering structure of the nonbrominated moiety.

The individual molecules within a lamella also exhibit a Moire pattern, which results from an incommensurate registry between the molecules and the graphite surface. This variation in image contrast across the lamella has been reported for other unsubstituted and substituted carboxylic acids (including 2-bromohexadecanoic acid) adsorbed onto graphite.^{16,17} This phenomenon within the lamellae occurs because of the bulkiness of both the bromine and carboxyl group and the carboxyl group's strong preference to hydrogen bond. These factors combine to push neighboring molecules away from each other and subsequently prevent them from fitting commensurately into the graphite lattice. Attempts to obtain a quantitative measure of the periodicity of the Moire pattern in these mixtures have been inconclusive due to the sporadic intrusion of 2-bromohexadecanoic acid into the self-assembled monolayer film.

The relative orientation of the bromine atoms to the carboxylic acid groups remains consistent throughout the STM images of a single domain. Figure 2c presents a magnified portion of the constant current topograph shown in Figure 2b where the bromine/carboxyl combination is more readily apparent. All of the bromine atoms lie either above and to the left of the carboxyl group or below and to the right of the carboxyl group. Black lines have been superimposed on some of the individual carboxyl/bromine combinations to denote this arrangement in Figure 2c. A different marker group positioning is found in the 13 nm \times 13 nm STM image of Figure 3a where this bromine/carboxyl group orientation is the mirror image of that presented in Figure 2b. Again, a black bar identifies a hexadecanoic acid molecule, and a blue bar marks a 2-bromohexadecanoic acid molecule. Figure 3b provides an enlarged view of Figure 3a where each bromine lies either above and to the right or below and to the left of its respective carboxyl group, as noted by the superimposed black lines.

Figures 2d and 3c provide molecular models based on a general portion of the self-assembled monolayer; these models are not meant to represent a specific region in the STM images previously described. The interdigitating pattern has been accurately depicted, and the orientation of carboxyl groups with their accompanying bromines (Figures 2c and 3b) are accordingly reflected in the respective models. A black line superimposed on a carboxylic/bromine combination in Figure 2d shows a bromine atom above and to the left of its carboxyl group, similar to the pattern found in the corresponding STM image in Figure 2c. A similar comparison arises in Figure 3c where the model's Br/COOH arrangement, highlighted by a black line, mimics the orientation found in the corresponding STM image (Figure 3b).

Comparison of the relative orientations of three of the four dissimilar groups on the chiral carbon center—the bromine, carboxyl group and the remainder of the alkyl chain—allows for a determination of the absolute chirality of the 2-bromohexadecanoic molecules in the entire physisorbed assembly. The

models in Figures 2d and 3c demonstrate that the position of the bromine atom necessarily dictates the orientation of the remainder of the alkyl chain since the bromine atom is located at the alpha position relative to the carboxylic acid. For instance, if the bromine lies to the left of the carboxylic acid group, the alkyl chain also lies to the left of this end group as is the case for the molecule signified by the blue bar in Figure 2b. A clockwise bromine-carboxyl group-alkyl chain orientation defines the *R* conformer of 2-bromohexadecanoic whereas the counterclockwise direction corresponds to the *S* conformer. On the basis of the model in Figure 2d where the arrow shows a clockwise direction for these three groups at the chiral carbon, the brominated molecules in Figure 2c can be assigned exclusively as the *R* conformer of 2-bromohexadecanoic acid. Likewise, the molecular models in Figure 3c depict a counterclockwise orientation for the three chemical functionalities, and so the chiral molecules in Figure 3 are uniquely identified as the *S* conformer of 2-bromohexadecanoic acid. Finally, note that unlike the 45° angle between the lamella direction and molecular axis present in pure 2-bromohexadecanoic acid from Fang's work¹¹ and from Figure 1a, our images display a 90° angle between these two axes for both hexadecanoic acid with (*R*)-2-bromohexadecanoic acid and hexadecanoic acid with (*S*)-2-bromohexadecanoic acid. Recall that pure hexadecanoic acid self-assembles with a 90° lamellar-molecular axis angle (Figures 1b and 2a). As discussed below, the 45° structure shown in Figure 1a is driven by favorable Br—Br attractive interactions. These are effectively shut down in mixtures where the probability that two molecules containing Br will be found adjacent to each other is low.

Discussion

Two phenomena clearly stand out in the STM images described in the previous section. First, the ability to effect a specific self-assembly of 2-bromohexadecanoic acid by introducing hexadecanoic acid into the solution has been demonstrated in Figures 2 and 3. The element of control for this feature is the "forced" opening of the angle between the molecular axis and the lamellar direction from 45° to 90° in the mixed self-assembly. Second, racemic 2-bromohexadecanoic acid coadsorbed with hexadecanoic acid segregates into separate chiral domains when the solution is applied to a graphite surface. This phenomenon is attributed to a curious effect of the two-dimensional graphite surface on one element in the mixture, the achiral hexadecanoic acid molecules. In fact, physisorption of hexadecanoic acid on a graphite surface causes it to separate into two distinct domains that exhibit nonsuperimposable mirror image morphology (enantiomorphous domains), a general feature observed for fatty acids possessing an even number of carbon atoms.¹⁵ As discussed below, these enantiomorphous domains necessarily lead to a resolution of (*R*)/(*S*) 2-bromohexadecanoic acid in the self-assembled monolayer when the mixture is physisorbed onto a graphite surface. Finally, molecular models can be used to show that domains of hexadecanoic acid containing either exclusively (*R*)-2-bromohexadecanoic acid or (*S*)-2-bromohexadecanoic acid are energetically more favorable than monolayers where the two enantiomers are mixed together with the unsubstituted acid.

Controlling Self-Assembly. By introducing a cosolute in the form of hexadecanoic acid into a solution of 2-bromohexadecanoic acid, the self-assembly of 2-bromohexadecanoic acid onto a graphite surface has been manipulated. In its "natural" state, the bromine-substituted carboxylic acid forms a two-dimensional structure with a 45° angle between the lamellar and molecular

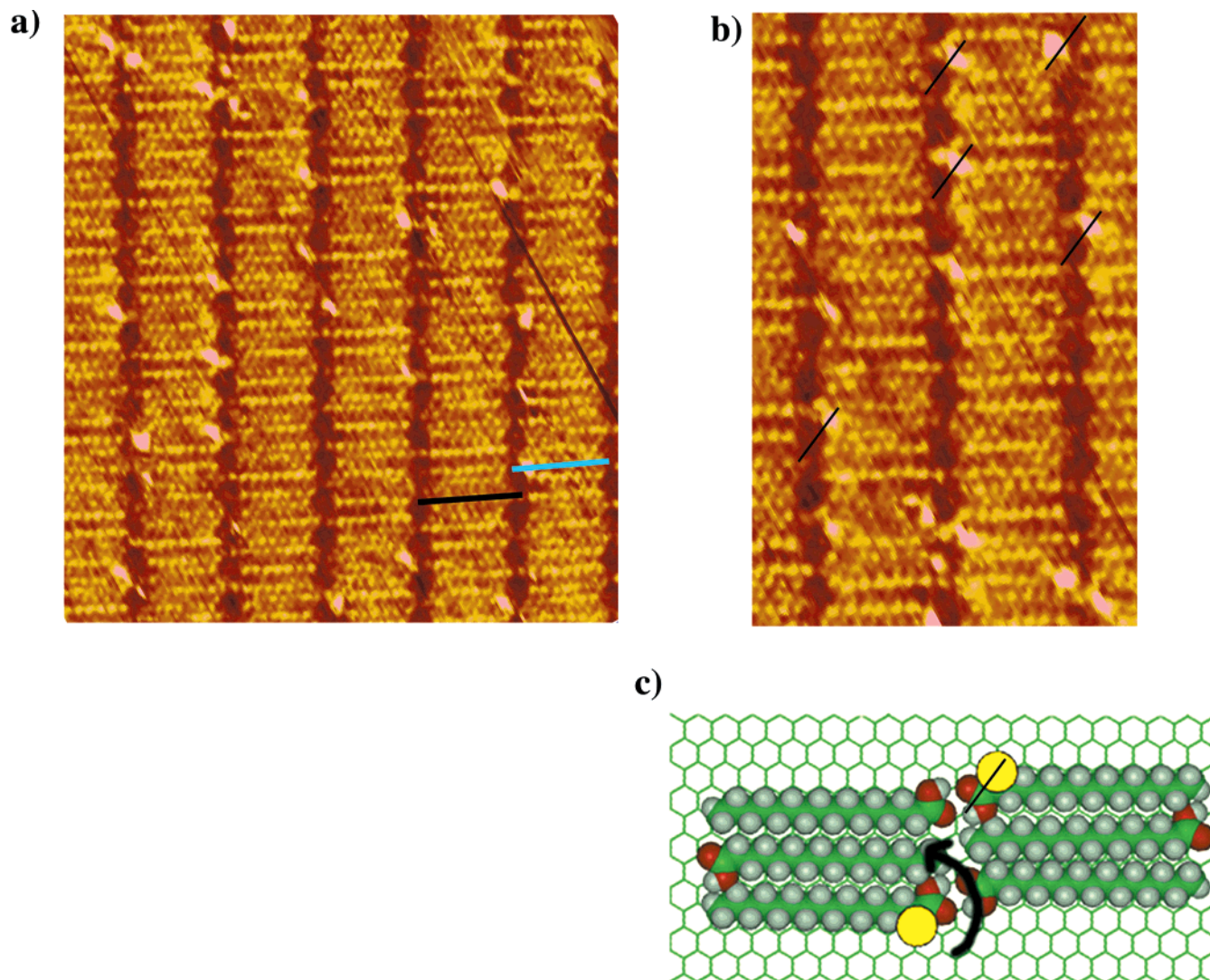


Figure 3. Constant current STM images of a domain of hexadecanoic acid interspersed with (*S*)-2-bromohexadecanoic acid. A 13 nm \times 13 nm topograph taken at 300 pA and 1.5 V (sample negative) is shown in (a) where a solid black bar depicts hexadecanoic acid and a blue bar depicts 2-bromohexadecanoic acid. The bromine/carboxyl orientation is the mirror image of that presented in Figure 2b–d. An enlarged portion of (a) is presented in (b) where the bromine atom lies above and to the right or below and to the left of the carboxyl group. This orientation is highlighted by the superimposed black lines. The orientation of the bromine, carboxyl, and alkyl chain on the chiral carbon is used to identify the 2-bromohexadecanoic acid molecules in this domain as the *S* chiral conformers of the molecule. A top view of a model of hexadecanoic acid interspersed by (*S*)-2-bromohexadecanoic acid on the graphite surface is shown in (c). The black line superimposed on a bromine/carboxylic combination shows the same pattern depicted in the STM image (b). An arrow demonstrating the counterclockwise direction of the bromine-carboxyl group-alkyl group orientation identifies the brominated molecules as the *S* conformer.

axes (Figure 1a). This configuration has been previously analyzed and is attributed to a self-assembly process in which two different types of intermolecular interactions are maximized.¹¹ Specifically, by organizing in this pattern on the surface, the carboxylic acid groups are allowed to hydrogen-bond, and the bromine atoms may favorably interact by lying adjacent to one another. Recent studies on other bromine-substituted, long-chain hydrocarbons atoms have attributed this preferred orientation of bromines to van der Waals-like interactions between the bromine atoms.^{11,18}

The presence of hexadecanoic acid molecules in the 2-bromohexadecanoic solution significantly changes the intermolecular interactions involved in self-assembly, thereby affecting the resulting monolayer formed at the phenyloctane–graphite interface. Hydrogen bonding remains a significant force as both the hexadecanoic acid and 2-bromohexadecanoic acid molecules contain the carboxylic acid functional groups. However, the bromine atoms play a lesser role in governing the 2-D structures in the mixed species domains since hexadecanoic acid mol-

ecules, which dominate the interfacial layer, do not contain any bromines. The resultant self-assembly reflects the interplay between these two different intermolecular forces. The template for the interfacial domain is set by the hexadecanoic acid molecules. The STM topographs of Figures 2b and 3a reveal a pattern that is remarkably similar to that of pure hexadecanoic acid (Figure 2a): the carboxylic acid groups are present in an interdigitating pattern and the angle between the molecular axis and lamellar direction is 90°. The hydrogen-bonding hexadecanoic acid molecules therefore determine the self-assembly framework to which the 2-bromohexadecanoic acid molecules are forced to conform. Instead of maximizing their bromine–bromine interactions and lying down in their “natural” self-assembled configuration, involving a 45° angle between the molecular and lamellar axes, 2-bromohexadecanoic acid adopts the 90° conformation precisely because the bromine/bromine attraction is frustrated.

Enantiomorphous Domains of Hexadecanoic Acid on a Graphite Surface. Free hexadecanoic acid is an achiral

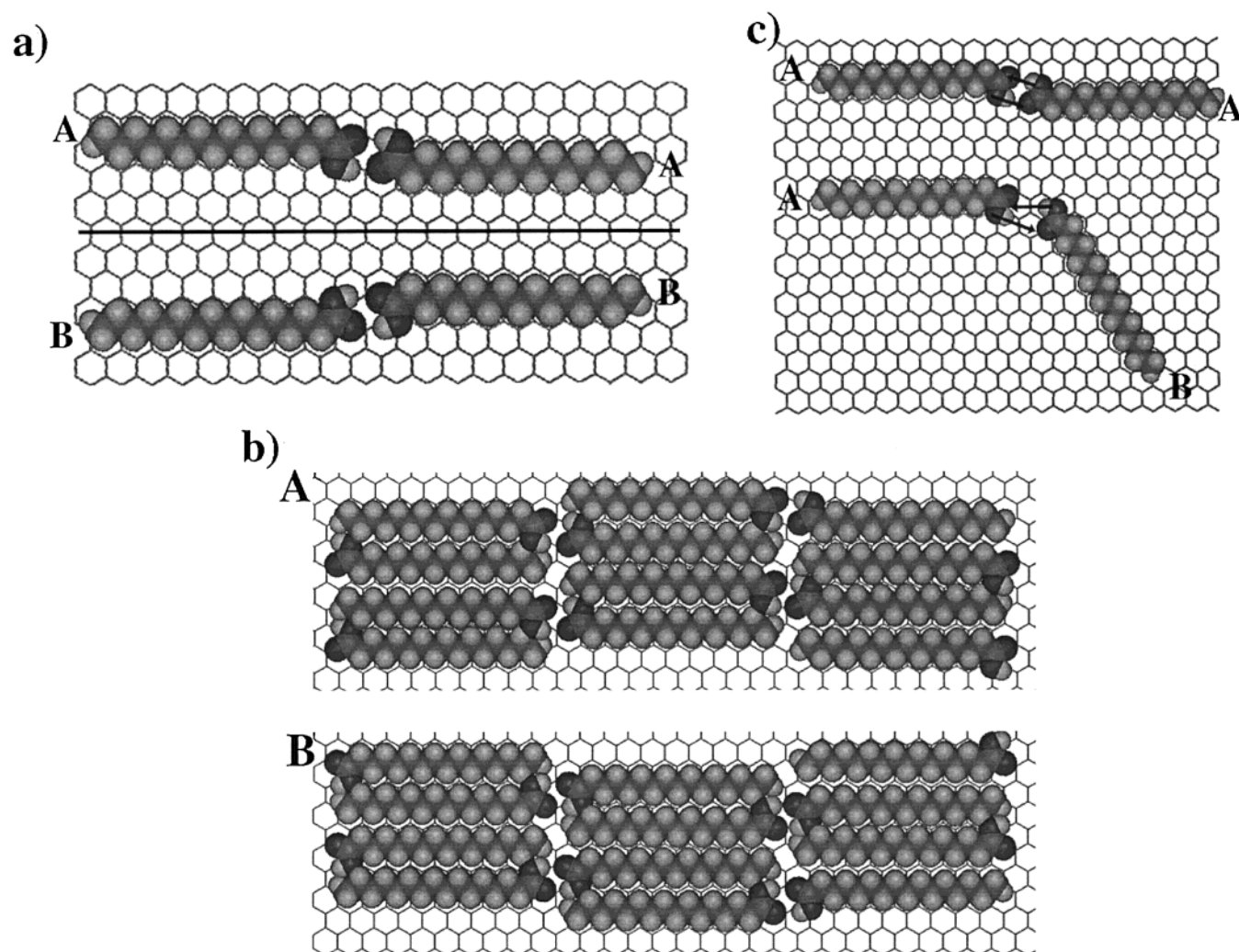


Figure 4. A series of models showing different self-assembly patterns for hexadecanoic acid on a graphite surface. The two-dimensional chiral nature of achiral hexadecanoic acid physisorbed onto a graphite surface is shown in (a). The pair of molecules on top have been arbitrarily labeled as “A” while the orientation on the bottom is “B”. The “B” molecules on graphite are a mirror image of the “A” molecules on the surface, reflected through the mirror plane indicated by a black bar. Hexadecanoic acid self-assembles into the two distinct enantiomorphous domains (possessing mirror image morphology) depicted in (b). The top panel in (b) shows an array of molecules in the “A” arrangement while the bottom panel in (b) shows the resultant self-assembly of molecules in the “B” orientation. A possible self-assembly that mixes an “A” molecule with a “B” molecule is depicted in the bottom pair of molecules in (c). A herringbone pattern such as the one depicted in (c) is not observed in the STM images and the hydroxyl oxygen–hydrogen–carbonyl oxygen arrangement is less than optimal for hydrogen-bonding. The top pair of “A” molecules hydrogen-bonded together in an optimal manner is included for comparison.

molecule that is always superimposable with its mirror image in three dimensions. This property changes dramatically when hexadecanoic acid is adsorbed onto a graphite surface, for now the molecule is fixed in a plane instead of being able to rotate freely in three dimensions.¹⁵ As discussed above, two hexadecanoic acid molecules will adsorb onto a graphite surface in a manner that allows the carboxylic acid functional groups to hydrogen bond together; Figure 4a depicts two such molecules whose conformations have been labeled “A”. When this pair is reflected through a mirror plane demarcated by the black line, the resultant molecules on graphite adopt the configuration labeled “B”, which (in the restricted two-dimensional world of the interface) is a nonsuperimposable mirror image of the “A” molecules on the surface. The surface ultimately drives hexadecanoic acid to self-assemble in two distinct enantiomorphous domains that now possess 2D chirality, as defined in ref 9. Such 2D chiral films are generally formed on a graphite surface for fatty acids with an even number of carbon atoms, but not for fatty acids with an odd number of carbon atoms.¹⁵ Two-dimensional arrays arising from the assembly of molecules

configured in the “A” or “B” arrangements are presented in Figure 4b. Achiral molecules forming enantiomorphous domains on the surface have been previously observed for discotic liquid crystals studied by STM,²² for a liquid crystal phase of achiral molecules investigated via optical microscopy,²³ for calcium arachidate assembled on mica probed by AFM,⁷ and for adenine molecules adsorbed onto molybdenum disulfide observed via STM.²⁴

Mixing the two enantiomorphous conformations of hexadecanoic acid physisorbed onto graphite yields energetically unfavorable results. A possible self-assembly pattern that does this is depicted by the bottom pair of molecules in Figure 4c, where a hexadecanoic acid molecule in the “A” configuration is hydrogen bonded with a hexadecanoic acid molecule arranged in the “B” configuration. The molecule in the “B” orientation has been rotated by 180° about the bond between the carbon of the carboxyl group and the alpha carbon, creating the rotator phase of this molecule, to accommodate hydrogen bonding. (Compare the position of the alpha hydrogen here with those of the other “B” molecules in Figure 4a.) However, this

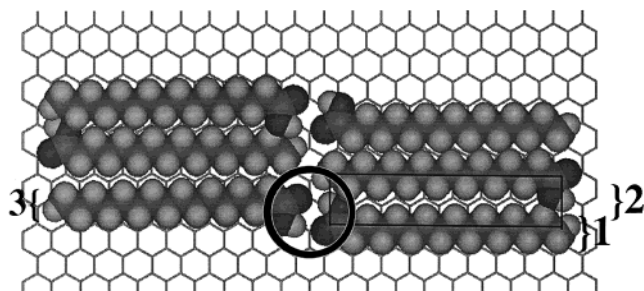


Figure 5. Model of several hexadecanoic acid molecules in the “A” orientation of Figure 4 adsorbed onto a graphite surface. The black circle represents the dark, circular, topographically depressed region in the STM image that signifies the position of the hydrogen-bonded carboxyl functional groups (Figure 2a). This dark region in the STM topograph is fairly large and therefore provides inconclusive evidence as to which molecules are hydrogen-bonded together. The model clearly shows molecule 1 hydrogen-bonding with molecule 3. However, the resolution in the STM topographs does not distinguish molecule 1 bonding with molecule 3 from a hypothetical molecule 2, located within the black rectangle, bonding with molecule 3 (note that the black circle is large and overlaps with both the end of the alkyl chain of molecule 2 and to a lesser extent, the “up” hydrogens at the alpha positions of molecules 1 and 3). Molecules 1 and 3 are in the “A” configuration whereas molecules 2 and 3 can be mistakenly interpreted as arranged in the “B” conformation. The 2D chiral domains from Figure 4 are therefore difficult, if not impossible, to directly distinguish via STM.

configuration yields unfavorable angles for hydrogen-bonding. Hydrogen bonding between any two carboxyl groups is optimized by a 180° angle between the OH group of one molecule and the carbonyl oxygen of a second molecule as is the case for the top pair of “A” hydrogen-bonded molecules in Figure 4c. The three atoms of the hydrogen bond—hydroxyl oxygen, hydrogen, and carbonyl oxygen—should optimally lie along one line as depicted by arrows extending from the oxygen of the hydroxyl group in one molecule to the carbonyl oxygen of the second molecule. “A” bonding with “B” as shown in the bottom pair of Figure 4c does not allow for a 180° angle between the carbonyl and hydroxyl groups. Lines originating at the oxygen (of the hydroxyl functionality) in both molecules do not provide a linear hydroxyl oxygen—hydrogen—carbonyl oxygen configuration. A shift of the position of one of the chains to optimize the hydrogen bonding would necessarily result in an incommensurate packing arrangement with the graphite surface. The orientations depicted in Figure 4, where the “A” and “B” configurations of hexadecanoic acid mix, are therefore less energetically favorable as models for the self-assembly of hexadecanoic acid on a graphite surface. Instead, self-assembly involving the segregation of the two enantiomorphous domains is the most favorable configuration.

The two enantiomorphous domains of hexadecanoic acid on a graphite surface are difficult to directly distinguish via STM. 2D chiral domains have been indirectly observed for behenic acid.¹⁵ The difficulty lies in the extremely high-resolution that would be needed for the tip not only to “see” the individual hydrogens along the hydrocarbon backbone but also to identify which hydrocarbon backbone belongs to which carboxyl group. Figure 5 shows several hexadecanoic acid molecules self-assembled on a graphite surface in the “A” configuration. The dark chemical marker groups in the STM image, represented by a black circle in the model in Figure 5, signify the position of the carboxyl functional groups. These groups are fairly large (Figure 2a) and appear in the STM image as dark, circular regions. Though the molecular models clearly reveal that the carboxyl groups of molecules 1 and 3 are indeed hydrogen-bonded together, the STM image by itself (Figure 2a) cannot

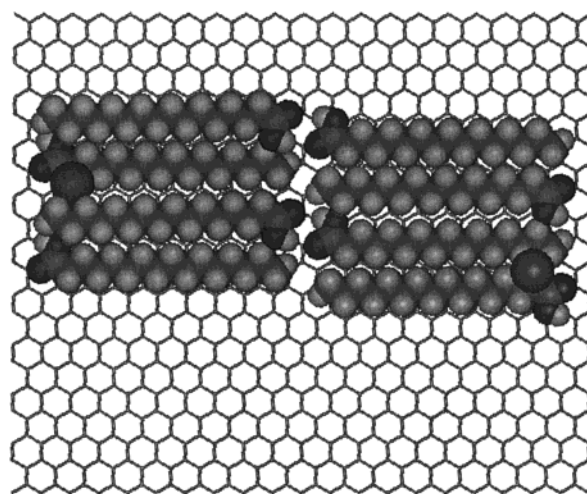


Figure 6. Top view of a model of hexadecanoic acid molecules assembled on a graphite lattice. All the hydrogens that are “up” at the alpha position, if substituted by a bromine, yield the *R* conformer of 2-bromohexadecanoic acid. Two of the molecules have thus been substituted and portray *R* enantiomers. This shows that this particular self-assembled configuration of hexadecanoic acid molecules permits the coexistence of only one chiral configuration.

be used to directly identify the hydrogen-bonded molecular pair. For instance, the resolution in the STM topographs does not permit hydrogen bonding between molecule 1 and a hypothetical molecule 2 (enclosed in the black rectangle) to be distinguished from hydrogen-bonding between molecules 1 and 3. The section of the STM image that appears topographically depressed (i.e., the dark region) extends slightly beyond the strict borders of the hydrogen bond (note the overlap of the black circle with both the CH_3 tail of molecule 2 and, to a lesser extent, the “up” hydrogen at the alpha positions of molecules 1 and 3 in Figure 5) thereby blurring the hydrogen-bonded carboxylic groups. There is a significant difference between molecule 1 bonding with 3 and molecule 2 bonding with 3 in that the former denotes an “A” configuration of hexadecanoic acid molecules (Figure 4a) while the latter would mistakenly indicate “B” orientations of the molecules. The models differentiate between domains of hexadecanoic acid molecules self-assembled in either the “A” or “B” configuration, while the STM images do not clearly show this distinction for individual molecules.

Resolution of (*R*)/(*S*)-2-Bromohexadecanoic Acid. The 2D chiral assembly of hexadecanoic acid molecular pairs on a graphite surface described in Figure 4 drives the mixture of 2-bromohexadecanoic acid and hexadecanoic acid to segregate into enantiomerically pure domains on the graphite surface. Figure 2b shows an image of hexadecanoic acid with exclusively (*R*)-2-bromohexadecanoic acid while Figure 3a reveals a monolayer of hexadecanoic acid with uniquely (*S*)-2-bromohexadecanoic acid. The self-assembly of hexadecanoic acid into two distinct domains exhibiting 2D chirality constrains only one of the two chiral isomers of 2-bromohexadecanoic acid to coexist with the unsubstituted fatty acid provided that the hexadecanoic acid in the mixture orders in the same way as pure hexadecanoic acid. The STM images of Figures 2 and 3 do indeed suggest that the mixed monolayer assembles in a two-dimensional array similar to that seen for pure hexadecanoic acid where interdigitating carboxyl groups and a 90° lamellar-molecular axis angle have been observed. Figure 6 depicts a molecular model for several hexadecanoic acid molecules in the “A” configuration with hydrogens that are “up” at the alpha position. If bromine atoms are substituted for these alpha hydrogens, only the *R* enantiomer of 2-bromohexadecanoic acid is produced on the

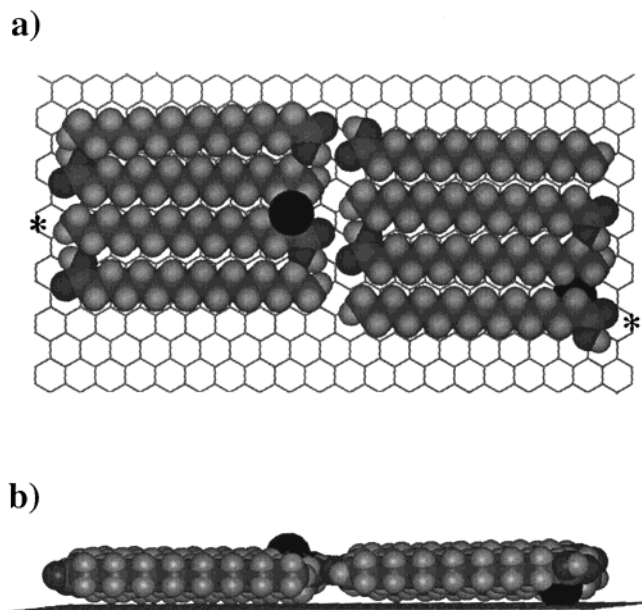


Figure 7. A top (a) and side (b) view of a possible model for a domain consisting of *both* (*R*) and (*S*)-2-bromohexadecanoic acid mixed with hexadecanoic acid molecules physisorbed on a graphite surface. Hexadecanoic acid molecules are arranged in their more classic interdigitating pattern with a sample brominated molecule on the left and on the right (the black ball signifies the position of the bromine). Asterisks in (a) mark the substituted fatty acids. The conformer on the left-hand side of the figure is identified as *R* while the one on the right is the *S* conformer. The *R* enantiomer has a bromine protruding up and away from the graphite substrate, while the (*S*)-2-bromohexadecanoic acid has the bromine pushing into the graphite. This configuration is energetically unfavorable and therefore also rejected as a model for the mixed monolayer.

surface. Two of the molecules in the model have been thus substituted with a bromine at this position and portray *R* enantiomers. Thus, (*R*)-2-bromohexadecanoic acid molecules can only physisorb from the mixture into a domain with hexadecanoic acid molecules that are arranged in the “A” configuration if the overall interfacial assembly is to remain unchanged in these “A” domains. However, hexadecanoic acid molecules can also self-assemble at the interface in the “B” conformation of Figure 4 to permit the second hydrogen at the alpha position to be exposed (this is the hydrogen pointing down into the surface in the “A” configuration of hexadecanoic acid in Figure 4a). Bromine substitution of this hydrogen results in the *S* conformer of 2-bromohexadecanoic acid.

A possible way of combining the *R* and *S* enantiomers of 2-bromohexadecanoic acid within a hexadecanoic acid domain is depicted in Figure 7 with models for both a top (a) and side view (b). Eight hexadecanoic acid molecules are arranged on the surface in the classic interdigitating pattern with one molecule on each side of the central trough being substituted with a bromine at the alpha position. Each substituted molecule is marked by an asterisk in Figure 7a. The brominated molecule on the left represents an *R* enantiomer whose bromine atom (colored in black) protrudes up and away from the graphite surface. The substituted hexadecanoic acid on the right is an *S* enantiomer with the bromine (colored in black) pointing down toward the graphite surface. To fit into the hexadecanoic acid two-dimensional lattice in this orientation, the *S* conformer directs the bromine into the graphite, and (because of the large size of the bromine atom) the rest of the molecule is tilted away from the substrate. This configuration is not energetically favorable because it reduces the attractive interactions between the surface and the hydrogen atoms in the adsorbed molecule

along the whole length of hexadecanoic acid. Eventually, such conformations must result in the 2-bromohexadecanoic acid molecules desorbing back into solution. The more energetically favorable self-assemblies where chiral segregation takes place are more stable and are those “seen” by the STM.

Finally, enantiomerically resolved 2-bromohexadecanoic acid provides a convenient marker to directly distinguish between the two enantiomorphous domains of hexadecanoic acid molecules depicted in Figure 4. Atomically resolved STM images provide a knowledge of the absolute chirality of 2-bromohexadecanoic acid on a graphite surface. Since (*R*)-2-bromohexadecanoic acid preferentially self-assembles with hexadecanoic acid in the “A” configuration from Figure 4, and (*S*)-2-bromohexadecanoic acid preferentially self-assembles with “B” hexadecanoic acid, the resolution of the chirality of 2-bromohexadecanoic acid provides an instantaneous method to deduce the ordering of the hexadecanoic acid domains present on the graphite surface. Therefore, a mixture of 2-bromohexadecanoic acid with hexadecanoic acid molecules not only resolves into enantiomerically pure 2-bromohexadecanoic acid domains, but also directly distinguishes the 2D chiral domains of hexadecanoic acid formed at the liquid–solid interface.

Conclusion

The self-assembly of a mixture of hexadecanoic acid with racemic 2-bromohexadecanoic acid has been investigated using scanning tunneling microscopy. Hexadecanoic acid has the ability to control the two-dimensional structure formed at the interface by creating a template that sets the angle between the molecular and lamellar axes in the mixed monolayer. Further, inherently achiral hexadecanoic acid self-assembles on the graphite surface into two distinct, although almost indistinguishable domains that exhibit mirror image morphology, similar to that observed for other even-numbered fatty acids.¹⁵ This property leads to resolution of (*R*)/(*S*)- 2-bromohexadecanoic acid into enantiomerically pure (*R* and *S*) domains when physisorbed onto a graphite surface from the mixture. This pattern on the surface is shown to be more energetically favorable than a monolayer in which the unsubstituted fatty acid is mixed with both chiral isomers of 2-bromohexadecanoic acid. In addition, 2-bromohexadecanoic acid can in turn be used to directly determine the specific two-dimensional chiral configuration of hexadecanoic acid within the monolayer. Achiral molecules such as hexadecanoic acid are thus shown to have remarkable potential as tools to manipulate self-assembly and more specifically, to induce enantiomeric resolution of racemic mixtures such as 2-bromohexadecanoic acid.

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