

Molecular mechanics study of hydrogen bonded self-assembled adenine monolayers on graphite

M. Edelwirth, J. Freund, S.J. Sowerby, W.M. Heckl *

*Institut für Kristallographie und Angewandte Mineralogie, Ludwig Maximilians Universität München, Theresienstr. 41,
80333 München, Germany*

Received 10 October 1997; accepted for publication 12 July 1998

Abstract

Molecular mechanics calculations using the Dreiding II force field were applied to self-assembled monolayer configurations of the nucleic acid base adenine adsorbed on graphite surfaces. Energy minimization calculations were used to refine the structures proposed by scanning tunneling microscopy (STM) studies and low energy electron diffraction (LEED), and allowed discrimination between competing models on the basis of final configurations and local minima convergence. This allowed the relative position of the adenine molecules within the unit cell of p2gg symmetry to be inferred. © 1998 Elsevier Science B.V. All rights reserved.

Keywords: Hydrogen bonds; MM simulators; Organic monolayers; Self-assembly

1. Introduction

An understanding of the properties of adsorbed supramolecular organic layers at the molecular level is of high interest in surface science and catalysis. Numerous applications in the fields of biotechnology and electronics could result from the concept of supramolecular chemistry [1,2].

Some types of molecules with special topology can serve as modules in two-dimensional hydrogen bonded networks. Best suited for such purposes are stiff planar molecules with both hydrogen-bond donor and acceptor moieties. Prominent representatives of this class of molecules are the nucleic acid bases which have biological function as a component of linear polymeric deoxyribose

nucleic acid (DNA) and ribose nucleic acid (RNA). Molecular recognition between complementary subunits within these polymers is involved in the process of hereditary as well as protein synthesis. The recognition processes observed in these systems involves hydrogen bond mediated complementary base pairing between adenine and the other base components within the same polymer or other polymer strands. The self-complementary interaction of adenines has been observed in nucleic acid molecules as well as in the solid state and similarly involves intermolecular hydrogen bonds [3].

Electrochemical investigations [4] using the hanging mercury drop electrode showed the formation of two-dimensional monolayers of the nucleic acid bases and it was proposed that they were stabilized by self-complementary intermolecular hydrogen bonds. These studies were recently fol-

* Corresponding author. Fax: +49 89 2394 4331;
e-mail: W.Heckl@lrz.uni-muenchen.de

lowed by real-space structure investigations on solid surfaces using electrochemical scanning tunneling microscopy (ECSTM) [5,6], STM in air [7,8] and in UHV [9].

The ECSTM and STM studies of the nucleic acid purine and pyrimidine monolayer systems have recently been reviewed and their spontaneous formation has been proposed to have a functional role in the origin of life [10].

Recently, complementary experimental techniques have been used to investigate ordered monolayers of the purine base adenine (6-amino-purine) (Fig. 1) on the basal graphite (0001) surface [9]. Combining real-space STM images and reciprocal space data from LEED we had proposed a monolayer unit cell of rectangular shape ($90 \pm 1^\circ$) with vectors $\mathbf{a} = 22 \pm 1 \text{ \AA}$ (parallel to a graphite lattice vector) and $\mathbf{b} = 8.5 \pm 0.5 \text{ \AA}$ with p2gg symmetry. The relative position of the adenine molecules within the unit cell could not, however, be determined by these methods. The symmetry constraints of the adsorbate suggested that the molecules assembled in the form of centrosymmetrical hydrogen-bonded dimers. It has been observed that this is also the favored configuration for homo base pairs in bulk crystals [11]. Since adenine molecules exhibit a considerable dipole moment, this configuration would result in a cancellation of the total electric field over the complete monolayer. Three different hydrogen bonded dimer arrangements with a two-fold symmetry center are possible (a–c in Fig. 2). This results in three competing structural possibilities.

Here, we describe force-field calculations used to complement the structural data allowing discrimination between structure models on the

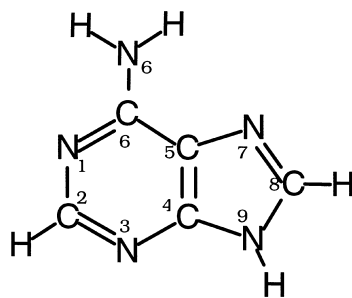


Fig. 1. Chemical structure of adenine.

basis of lattice–energy calculations. In spite of its simplicity this approach is flexible enough to reproduce the properties of organic and ionic solids [12] and surfaces [13]. This method has previously been used to calculate the structure and energy of physisorbed molecules on graphite substrates [14,15], and more recently, of PTCDA molecules on silver [16].

The organization of this paper is as follows: Section 2 contains a description of the computational methods which are used to model the molecule–molecule interactions and the molecule–substrate interaction. Section 3.2 describes the calculation of the stabilization energies of some centrosymmetrical adenine dimers in the gas phase. To check the reliability of the DREIDING II force field in modeling the lateral interactions in the molecular layer, these energies were compared with literature values obtained by nonempirical ab initio beyond Hartree–Fock computations. Section 3.3 contains the calculation of one molecule adsorbed on the graphite substrate. The competition between the Lennard–Jones interaction and the electrostatic interaction is analyzed and the calculated adsorption energy is compared with estimates received from thermal desorption spectroscopy (TDS) (a detailed study will be published elsewhere). Section 3.4 describes the calculation of the complete adenine unit cell on the graphite substrate, Section 3.5 compares the measured STM image with the model.

2. Computational methods

Owing to the system size and limitations in computational power, the only practical method to simulate organic adsorbates is often the molecular mechanics approximation (MM). The basic concept is the potential energy surface (PES). The PES describes the potential energy in terms of the molecular geometry which is defined – from a very simple point of view – by the positions of the atomic nuclei. Since the equilibrium structure of a solid and its surface corresponds to the minimum of the systems free energy F , the fundamental idea of the MM approximation is to find the minimum of the PES.

In MM force fields, both inter- and intramolecular interactions are represented by a set of pairwise additive two-center, three-center, four-center,... functions with the force centers placed on the atomic nuclei. The PES can be expressed as:

$$\text{PES} = E_{\text{mm}} + E_{\text{ms}} + E_{\text{m}}, \quad (1)$$

where E_{mm} is the energy of the lateral interaction within the molecule layer, E_{ms} is the interaction energy between adsorbed molecules and the substrate atoms and E_{m} is the intramolecular potential energy. E_{mm} , E_{ms} , and E_{m} are expressed as

$$E_{\text{mm}} = \sum_k^N \sum_i^{N_k} \sum_j \left\{ d_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - 2 \cdot \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] - \left[\frac{q_i q_j}{\epsilon \cdot r_{ij}} \right] + \sum_{l,m} \left\{ d_{lm}^h \left[5 \cdot \left(\frac{\sigma_{lm}^h}{r_{ij}} \right)^{12} - 6 \cdot \left(\frac{\sigma_{lm}^h}{r_{lm}} \right)^{10} \right] \cdot \cos^4 \theta \right\} \right\}, \quad (2)$$

$$E_{\text{ms}} = \sum_k^N \sum_i^{N_k} \sum_j \left\{ d_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - 2 \cdot \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right] - \frac{1}{2} \alpha_j \left[\left(\sum_i E_{X_i} \right)^2 + \left(\sum_i E_{Y_i} \right)^2 + \left(\sum_i E_{Z_i} \right)^2 \right] \right\}, \quad (3)$$

$$E_{\text{m}} = E_b + E_a + E_t + E_i, \quad (4)$$

where N is total number of molecules and N_k is the number of atoms in molecule k . The index j runs over all atoms which are not part of molecule k . r_{ij} is the distance between atom i and atom j . The first term in Eq. (2) describes both dispersion and repulsive interactions in form of the Lennard–Jones 12-6 potential. In the second term, non-bonded electrostatics are represented as simple coulombic interactions between point charges q_i placed on atomic centers i . These partial charges were obtained from fitting to semi-empirical computed molecular electrostatic potentials (ESP). In the last term of Eq. (2) hydrogen-bonding is explicitly described by the 12-10 potential. The sum is over all hydrogen-bonding donor and acceptor atoms with distance less than a predefined cut-off radius r_{cut} . θ is the angle between *acceptor–hydrogen–donor*.

The interaction between the adsorbed molecules

and the substrate is constructed following Steele's method (Eq. (3)) which showed the reliability of this approach to model the energetics of polar molecules physisorbed on graphite [14,15]. The index j runs over all substrate atoms. The Lennard–Jones potential describing the electrostatic interaction was reduced to the component involving the dipole moment of the molecules and the polarizability α_j of the substrate carbon atoms. E_{X_i} , E_{Y_i} , E_{Z_i} are the Cartesian components of the electric field at each substrate atom due to the sum of partial atomic charges of the adsorbed molecules. Both the response of the graphite and the magnitude of the molecular electric field are grouped together in one term.

The four parts in Eq. (4) are the bond, angle, torsion and inversion terms of the Dreiding II force field [17]. The parameters d_{ij} , σ_{ij} , d_{ij}^h , σ_{ij}^h were also taken from the Dreiding II force field. We used this force field because of the limited available experimental data on the adsorbate system. While specialized force fields are more accurate for predicting a limited number of structures (e.g. the AMBER 4.1 force field [18] best reproduces hydrogen-bonding energies of the adenine dimers [19]), Dreiding II is an "all-purpose" force field which gives reasonable predictions for a very large number of structures.

For the polarizability of carbon (α_j) the value $1.5 \times 10^{-24} \text{ cm}^3$ was used [20].

3. Model calculations and results

The dimer calculations and the cell minimization were performed with the modules "Minimizer" and "Crystal Packer" from the commercially available computer program CERIUS[2] running on an SGI Indigo[2] workstation. For the semi-empirical calculations, we used MOPAC 93 [21] ported to the SGI platform. The adsorption calculations of the single molecule were performed with a self-written code (running on a Pentium 166 MHz PC).

3.1. Esp and molecule geometry

Semi-empirical MNDO-AMJ [22] calculations were performed to derive the molecular ESP and

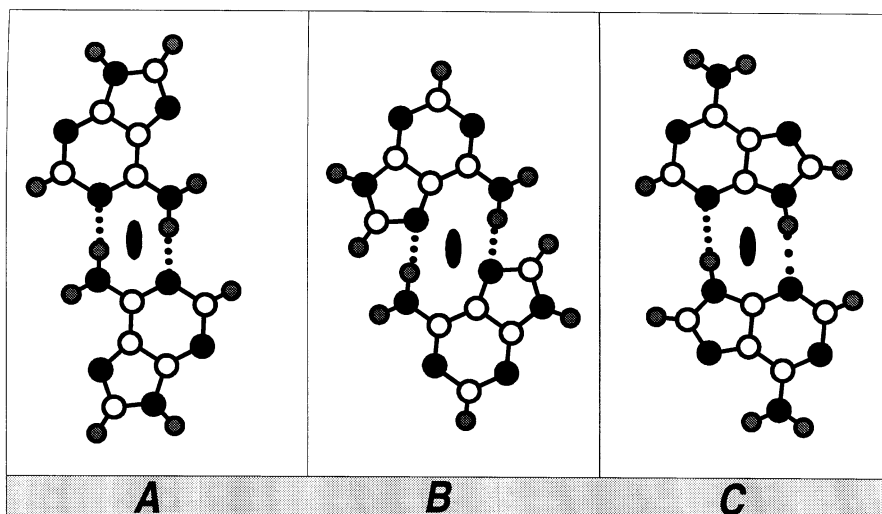


Fig. 2. The three possible hydrogen-bonded adenine dimers with a twofold symmetry center.

the geometry of the molecules. We favored AM1 over the newer generation of semi-empirical method PM3 [23] because it has been shown that AM1 gives better results (compared with *ab initio* RHF/6-31G* calculation) in predicting the ESP [24]. From the ESP, the partial atomic charges were calculated with the method of K. M. Merz and B. H. Besler [25]. The AM1 calculations resulted in a geometry which is in reasonable agreement with 2nd order Møller Plesset calculations (MP2)[26] (mean error in bond length 0.03 Å, mean error in bond angle less than 1.4°).

3.2. Adenine dimers

The stabilization energy of the three possible centrosymmetrical dimer arrangements and one nonsymmetrical dimer (dimer AA 2 [19]) are given in Table 1. The stabilization energy is defined as the difference between the energy of an adenine pair optimized in the particular structure and the sum of the energies of the optimized isolated adenine molecules.

Compared with the *ab initio* results, the stabilization energies are systematically overestimated by the Dreiding II force field. However, the relative strength of the different dimers is predicted in reasonable agreement with the MP2 calculations.

Table 1

Stabilization energy in kcal/mol		
Adenine dimer	Dreiding 11	(MP2)16-31G*(0.25) ^a
Model A	14.8	11.5
Model B	11.7	10.0(9.8) ^b
Model C	14.4	–
AA2 ^a	12.6	11.0

^aRef. [19]

^bRef. [29]

3.3. One molecule adsorbed on graphite

The structure and partial charges from Section 3.1 were taken for the single adsorbed molecule. Following the method of Hammond et al. [15], a lattice of 30 × 30 atoms × 3 layers was used for the graphite substrate. The carbon bond length in each layer is 1.42 Å, and the layer distance is 3.35 Å. Both molecule and substrate were considered as rigid units. For the minimization calculation of the PES, the positions of the substrate carbon atoms were fixed. The adenosine molecule was allowed to move independently in all six degrees of freedom. For minimization, the built-in function “FindMinimum” of the Mathematica 3.0 package was used. Starting from several initial geometric configurations, the same end position

given in Fig. 3 was reached every time. The adenine molecule lies flat on the graphite substrate. The distance between graphite surface and molecule is 3.40 Å. This is also the mean stacking distance found for bases in DNA molecules. By Atomic Force Microscopy (AFM) Tao and Shi [27] estimated the thickness of an adenine monolayer on graphite in NaCl Solution as 3 Å. The rings of the adenine molecule are roughly above the centers of the hexagons on the first graphite plane and the amino group is centered above a graphite hexagon. In this geometry, the molecule stacks above the surface similar to the graphite planes.

The adsorption energy was calculated at -21.0 kcal/mol. This agreed reasonably well with the estimated value of 23.2 kcal/mol obtained from TDS [28]. Since the corrugation of the adsorption potential is rather small (approximately 0.8 kcal/mol), the uncertainty in the preferred adsorption site was considerable. These results also imply that at room temperature the single adenine molecules have only small diffusion barriers to lateral movement. This allows for the observed growth of large (up to several hundred nanometers) two-dimensional adenine crystals. The ratio of the total magnitude of the electrostatic to the Lennard–Jones potentials is between 0.1×10^{-3}

and 0.3×10^{-3} . This shows that the Lennard–Jones component plays the dominant role in the molecule–substrate interaction suggesting that the electrostatic energy between adenine molecules and graphite can be neglected in further calculations.

3.4. Lattice calculations

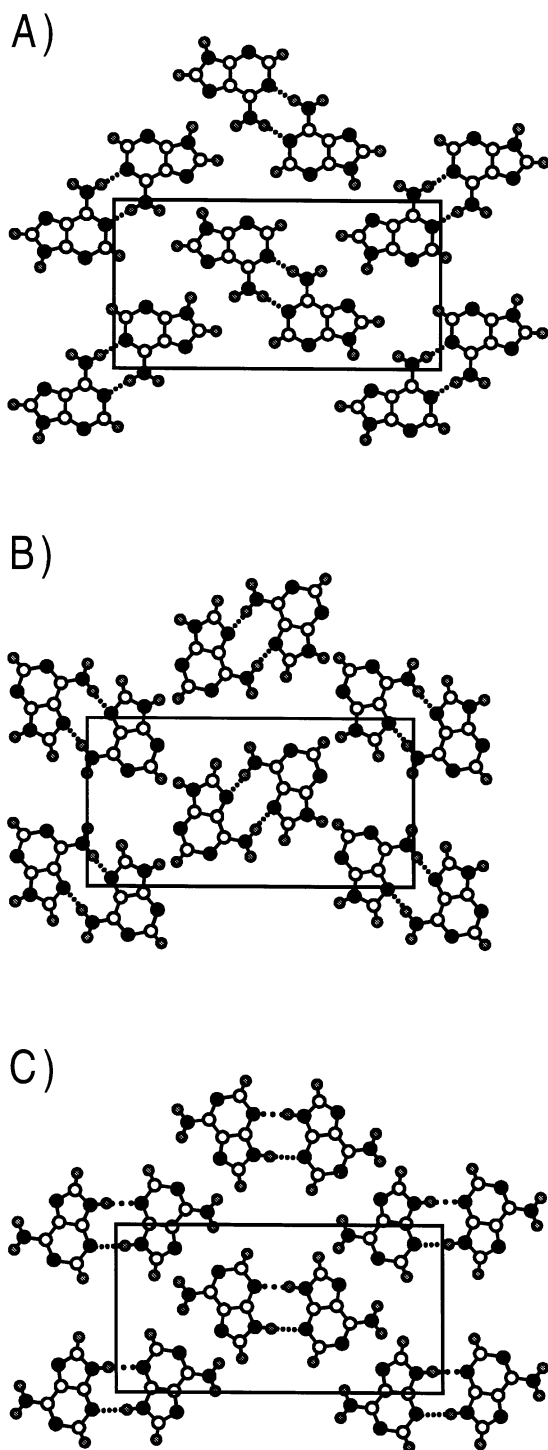
The graphite substrate was represented by a four-layer slab. Four adenine molecules were set in the model cell. The lateral cell dimensions of the model surface were those of the experimentally determined adsorbate cell. To simulate an infinite 2D surface, 3D-periodic boundary conditions on a model cell of P1 symmetry were applied. To avoid errors in the lattice calculation due to the unphysical periodic replicas of the system perpendicular to the surface (c -dimension), the length of the c -axis was set to 120 Å. This value was obtained by making the lattice energy a function of c and looking for convergence. For each of the three possible dimer configurations, an adsorbate model was constructed (see Fig. 4) and placed manually on the substrate model surface. There are two reasons for performing the calculations on all three structures: (a) numerical convergence is sterically hindered in the fixed unit cell; and (b) in contrast to molecular dynamics computations (MD) the MM approach gives only reasonable results starting with a initial structure near the real minimum.

For all three cases, the two-fold axis of the first dimer was centered on the origin of the unit cell. Thus the second dimer was centered on $a/2 + b/2$. The angles in the plane parallel to the substrate surface are set in a way to build a closely packed adsorbate structure. Due to the results of Section 3.3, flat lying molecules were assumed. The geometry obtained from semiempirical calculations was used as the initial structure for the adenine molecules. Partial atomic charges were assigned to the molecules by the semi-empirical ESP calculations. For the minimization, both model cell dimensions and positions of the substrate carbon atoms were kept fixed.

The lattice minimization was performed in two steps. In the first step, the molecules were assumed to be rigid. During the minimization, all transla-



Fig. 3. Top view of the minimized structure of one single adenine molecule on a 3-layer graphite slab. Only the first graphite layer is shown. The molecule lies flat above the graphite surface.



tional and rotational degrees of freedom of the molecules were varied in the search for energy minima. The modified Newton search algorithm method was used. The termination criterion was an overall energy gradient smaller than 10^{-5} kcal/(mol Å).

From all three calculations, only the one with dimer model C reached the termination criterion. Both model A and model B failed to reach a gradient better than 0.2 kcal/(mol Å). Also, this model resulted in the lowest energy configuration (even though the energy difference between the competing structure models was approximately between 8 and 14%). Whereas the final arrangements of both structure models A and B break the observed p2gg symmetry, the end configuration of model C obeys the two orthogonal glide symmetry planes observed by LEED. The molecules, however, are slightly tilted out of the graphite plane. This is the structural model previously proposed [9].

In the present work, a second refinement step was added to the calculation in which the assumption of molecular rigidity of the adsorbate molecules was removed. With Eq. (4) the conformations of the molecules in the crystal field were taken into account. During minimization, all atoms of the molecules were allowed to move in three dimensions. Every 20 cycles, the partial charges were re-calculated from the semi-empirical ESP in the actual molecule configuration. The results from the calculation with rigid molecules were used as starting configuration.

Again, only model C retained the symmetry conditions and reached the energy gradient criterion. But this time, the molecules ordered flat above the graphite surface (distance 3.4 Å). The end geometry of the single molecules was approximately the same as the starting configuration. The mean differences of the intermolecular bond lengths and angles (in comparison with the starting configuration) were 0.034 Å and 3.5°, respectively. Although this is only a slight change in the molecu-

Fig. 4. The three p2gg unit cells for each possible adenine dimer from Fig. 2. (a) unit cell with dimer A. (b) unit cell with dimer B. (c) unit cell with dimer C. (Drawings not to scale.)

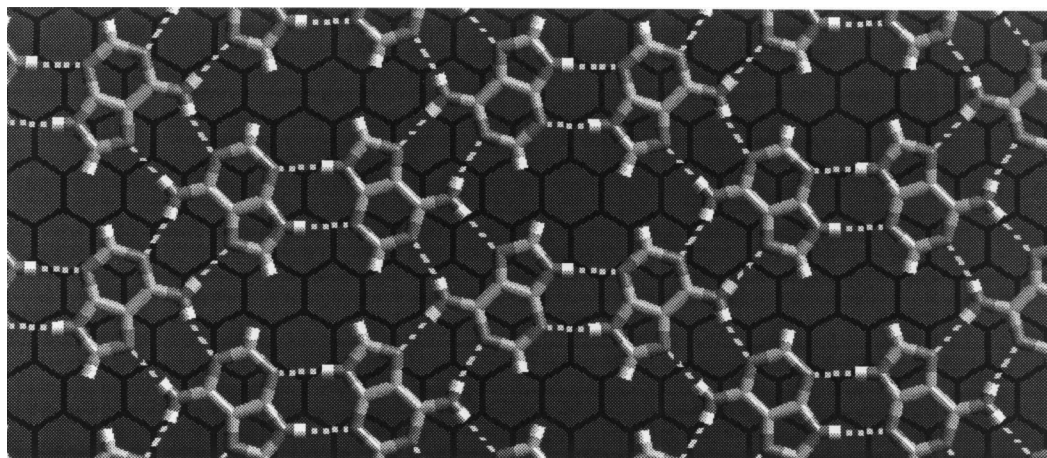


Fig. 5. Final model of the adenine crystal together with the topmost graphite layer. The hydrogen-bonds are represented by the dashed lines.

lar conformation, the origin of the previously proposed tilting of the molecules could be a numerical artefact due to the neglect of the crystal field induced change in molecular conformation. However, it cannot be excluded that the tilted grouping of the molecules is also a possible stable polymorphic modification. In Fig. 5 the final arrangement is given, regarded as the correct model that can be superimposed on the STM image. The total lattice energies are given in Table 2. Because the preservation of the $p2gg$ symmetry occurs only in model C and because the energy gradient in the minimum is 4 orders of magnitude better than it is for models A and B, we suppose that the obtained result is not in the range of systematic or static errors. The energy difference between model C (flat) and model A and B are approximately 21 and 29% and therefore significant. A further verification of this model can be obtained by kinematic simulation of the LEED pattern. In [9] we have shown that model C yields

good qualitative correspondence with the experimentally observed intensities.

3.5. Comparison with experiment

The molecules are assembled in a dense, hydrogen-bonded network with all six geometrical possible hydrogen bonds realized. All hydrogen bonds have a length of $2.94 \pm 0.2 \text{ \AA}$, which is well within the range of $\text{NH} \cdots \text{H}$ bonds ($2.75\text{--}3.15 \text{ \AA}$) found in bulk structures of the bases [3]. The molecules are on different positions relative to the substrate atoms (see Fig. 5). The amino groups of two molecules are nearly centered above a graphite hexagon. The amino groups of the other molecules lie roughly on a “bridge” position. This can be verified in the STM image (Fig. 6) where α denotes the centered side and β the bridge side. We suggest, that this is the reason for the observed pattern with periodic brightness in the STM contrast. It has been proposed that hydrogen bonding in some classes of biological molecules with continuous periodic structures sometimes displays the property of cooperativity [11]. This suggests that cooperativity effects, mainly leading to either polarizability or charge transfer, may have a strong influence on the STM contrast at these locations. Both quantum chemical and experimental investigations of these

Table 2

Total lattice energy of the minimum configuration (kcal/mol)

Model A	Model B	Model C (tilted)	Model C (flat)
120.0	113.6	129.5	146.2

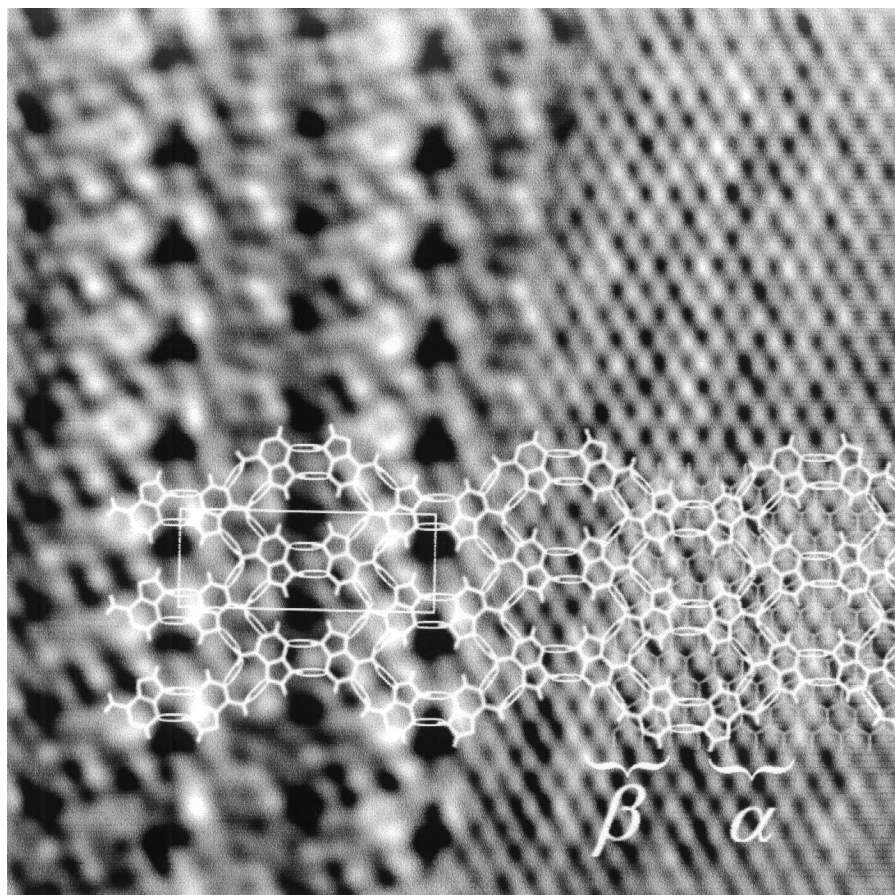


Fig. 6. STM image of a monolayer of adenine prepared on graphite by evaporation of an aqueous solution of adenine on a heated graphite (0001) surface. By decreasing the tunneling resistance in the middle of the image while scanning it was possible to visualize directly the underlying graphite lattice. The estimated molecule positions, the hydrogen bonds and the unit cell are indicated. Because of the different positions (α and β) of the molecules relative to the substrate atoms the image displays a moiré pattern. The STM image has been lowpass filtered in the Fourier space (size of the imaged area: $73.5 \times 73.5 \text{ \AA}^2$, $U_{T(\text{left})} = 0.8 \text{ V}$ (molecule layer), $U_{T(\text{right})} = 0.02 \text{ V}$ (graphite), $I = 100 \text{ pA}$, constant current mode, the scanning direction was approximately normal to the line.

polarizability effects are in progress and will be published elsewhere.

4. Conclusion

We have shown that molecular mechanics calculations can significantly contribute to the structure determination of molecular adsorbates studied by STM and LEED. This holds especially for the hydrogen-bonded systems of DNA bases where in many cases only a full LEED analysis or STM images where submolecular details can reliably be

assigned to the molecules could unambiguously lead to the correct structural model. The method can therefore complement incomplete structural data but needs extensive experimental input.

Acknowledgements

The authors would like to thank Dr S. Thomlinson from Molecular Simulations Inc. for his generosity in allowing us to test the CERIUS software. Financial support through Deutsche Forschungsgemeinschaft (He 1617/6-1) is gratefully

acknowledged. S.J. Sowerby thanks the Alexander von Humboldt Forschung–Stipendium for a post-doctoral research fellowship.

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