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published in

*NIC Symposium 2008*,  
G. Münster, D. Wolf, M. Kremer (Editors),  
John von Neumann Institute for Computing, Jülich,  
NIC Series, Vol. **39**, ISBN 978-3-9810843-5-1, pp. 109-116, 2008.

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# Supramolecular Chemistry from Supercomputers

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We present the results of a computational study of different supramolecular systems which are assumed to enable the access to molecular machines. Mainly we treat systems which are involved in the formation of rotaxanes. Rotaxanes constitute a class of supramolecular complexes consisting of two mechanically linked components, a macrocyclic wheel and a linear molecule (axle). A study of the dynamical properties of a tetralactam macrocycle shows its ability to adapt to potential guest molecules. A constrained simulation of the dethreading of a pseudorotaxane demonstrates that the breaking and formation of hydrogen bonds is essential for this process. An analysis of different binding situations for the pseudorotaxane indicates that dispersion interaction may also play a role in this context. In addition we can show that it should be possible to distinguish different binding situations of pseudorotaxane complexes by means of IR spectroscopy. We show that hydrogen bonds are also responsible for the observed self organization of TLM on the Au(111) surface. Finally we present first results of the investigation of peptide hydrogen bonds on the Ag(111) surface.

## 1 Introduction

Supramolecular chemistry comprises chemical processes of large molecules often interacting via many, comparatively weak, non bonding contacts. An important and generic process in supramolecular chemistry is molecular recognition in host-guest complexes, which is for instance, the basis of protein-substrate interactions in biochemistry. A few examples for supramolecular systems are rotaxanes, catenanes, molecular knots, calixarenes, and molecular tweezers.<sup>1</sup>

Here we present a computational study of supramolecular systems which contain a tetralactam macrocycle (TLM) as central motif, see Fig. 1. The TLM can act as receptor for p-benzoquinone<sup>2</sup> and is widely used for the synthesis of catenanes and rotaxanes.<sup>3</sup> In addition it can act as a sensor for the detection of trans-2-hexenal and acrylamide.<sup>4</sup> The special features of the TLM are its ability to build up a multiplicity of different hydrogen bonds (The TLM has four amide groups which can act either as hydrogen bond donor or as acceptor.) and its comparative rigid cavity. It is assumed that the interaction between the TLM host and the guest can be controlled by external influences. This enables the access to molecular machines.

One example for these systems are rotaxanes. Rotaxanes constitute a class of supramolecular complexes consisting of two mechanically linked components which are referred to as axle, and wheel. Sterically demanding functional groups at the ends of the axle prevent a dethreading. In this work we investigated so-called pseudorotaxanes where the wheel is threaded on an axle omitting appropriate stopper groups. The resulting complex is linked via non-covalent interactions like hydrogen bonds.

Furthermore we studied in cooperation with the experimental group of M. Sokolowski the adsorption of hydrogen bond templated supramolecular systems. The adsorption of building blocks of molecular machines is interesting since it constitutes a first step towards the design of 2D functional arrays of these molecules. We show that a hydrogen bond mediated template effect can lead to the formation of ordered 2D structures of larger and non planar molecules on surfaces. Hereby a specific functionalization of surfaces is possible.

This article is organized as follows: We start with a short description of the methodology we use for the investigation of large supramolecular systems which is followed by a short summary of the investigation of the dynamical properties of the TLM and of the dethreading process of a pseudorotaxane complex. Next we show the results of an energetic and vibrational analysis of different binding situations of the pseudorotaxane system. Finally we present the hydrogen bond mediated self assembly of the TLM on the Au(111) surface and the adsorption of formamide polymers on the Ag(111) surface.

## 2 Methodology

Density functional theory (DFT)<sup>5</sup> is nowadays the most-widely used electronic structure method. Since DFT combines reasonable accuracy in different chemical environments with minimal computational effort we chose this method for the investigation of large supramolecular systems. The calculations presented in this article are in large part performed with plane wave DFT codes, namely the Car-Parrinello Molecular Dynamics code (CPMD)<sup>6</sup> and the VASP code<sup>7</sup> which are well suited for an efficient parallelization. The numerical effort of applying a DFT plane wave code mainly consists of basic linear algebra subprograms (BLAS) and fast Fourier transform (FFT) operations. The former ones generally require quite little communication. However the latter one requires more complicated communication patterns since in larger systems the data on which the FFT is performed needs to be distributed on the processors. Combined with a suitable grouping of the FFT's one can achieve good scaling up to tens of thousands of processors.

## 3 Results

### 3.1 Dynamical Properties of Macrocycles

We started our study with a detailed investigation of the isolated tetralactam macrocycle TLM, see Fig. 1. For this purpose we performed a Car-Parrinello molecular dynamics simulation with a time step of 0.12 fs. From the total trajectory of 1.5 ps we harvested every third time step the Wannier functions. During the simulation we observe a conformational changing from the so called 4-out-0-in conformation to the 3-out-1-in conformation (out: C=O (hydrogen bond acceptor) pointing away from cavity, N-H (hydrogen bond donor) pointing inside the cavity; in: C=O pointing inside cavity). This observed conformational flexibility of the otherwise rigid TLM is connected with a changing of the TLM ability to build up hydrogen bonds to guest molecules. This demonstrates that the TLM can easily adapt its properties to potential guests.

Since Diederich and coworkers have pointed out the importance of inter- and intramolecular multipole interactions in supramolecular chemistry<sup>8</sup> we turn our attention to changes of the total dipole moment during the simulation. In Fig. 1 we show the dipole

along the time step. We observe in the right graph that the dipole drops until the 750th time step is reached. After this the dipole moment suddenly rises. This change of dipole moments could influence the intra-supermolecule dynamics of wheel and axle in a rotaxane and thus the potential motion of a rotaxane.

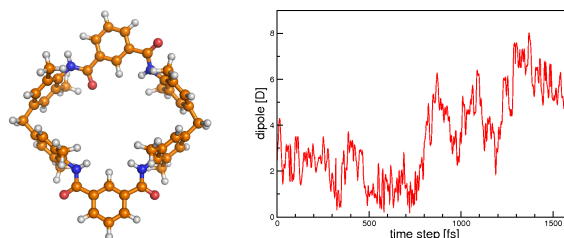


Figure 1. Left: The tetralactam macrocycle (TLM), right: dipole of the TLM during the CPMD simulation.

### 3.2 Dethreading of a Pseudorotaxane

The aim of our study is to get a deeper insight in the mechanism of the threading and dethreading process of rotaxanes. This knowledge will be useful for the realization of rotaxane based molecular machines. The system under examination is a pseudorotaxane system where a secondary amide axle builds up three hydrogen bonds to TLM, see Fig. 2. We performed constrained CPMD simulations with a time step of 0.12 fs where we used the GROWTH algorithm to enforce the dethreading of the axle. Hereby we enlarged the distance between selected axle and wheel atoms by 0.001 a.u. per time step.

We start the simulation at the most stable conformation of the pseudorotaxane where the axle builds up all together three hydrogen bonds to the wheel. We observe during the simulation the breaking and formation of hydrogen bonds. This process ends in a situation where the axle is connected to the wheel via a single hydrogen bond. This hydrogen bond is retained during the further dethreading process: The corresponding TLM amide group performs a rotation from an *in* to an *out* conformation. This leads to an arrangement where the axle is situated above the macrocycle and not inside the cavity. Although this constrained dethreading is connected with an unphysical deformation of the components one can see that the breaking and formation of hydrogen bonds is essential for this process. In particular one can assume that the first step of the threading process is the formation of a single hydrogen bond outside the cavity.

### 3.3 Energetic and Vibrational Analysis of Pseudorotaxanes

The results of the constrained dethreading process encouraged us to investigate the different binding situations for the pseudorotaxane in more detail. We performed an energetic and vibrational analysis of complexes which differ in the wheel conformation and in the hydrogen bonding pattern provided by the mutual interactions between the wheel and the axle.<sup>9</sup> We studied a complex where the maximum of three hydrogen bonds is formed (**1a**, see Fig. 2), a complex where the wheel and the axle are connected via a twofold hydrogen

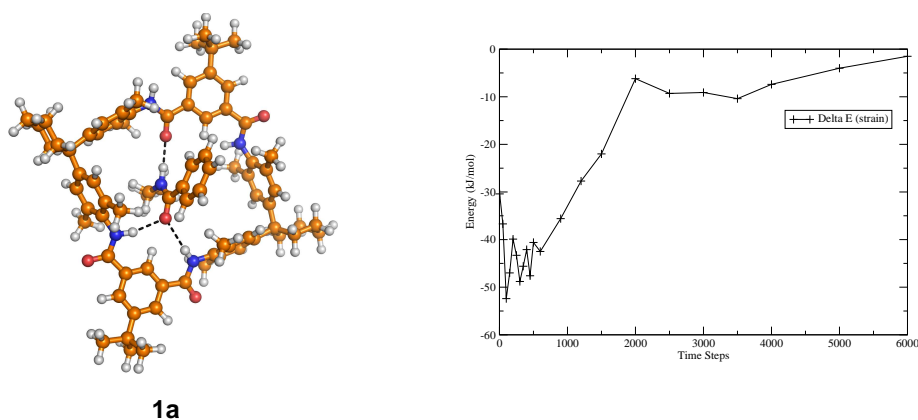


Figure 2. Left: pseudorotaxane complex **1a** with three hydrogen bonds. Right: Interaction energy in kJ/mol during the constrained dethreading (single point calculation of snapshots).

bond (**1b**) and two complexes with only a single hydrogen bond, see Fig 3. For the latter we distinguish between the situation where the axle is placed inside the cavity (**1c**), and the situation where the axle is outside the cavity (**1d**). These chosen minimum structures may serve as different steps of the dethreading event of the pseudorotaxane.

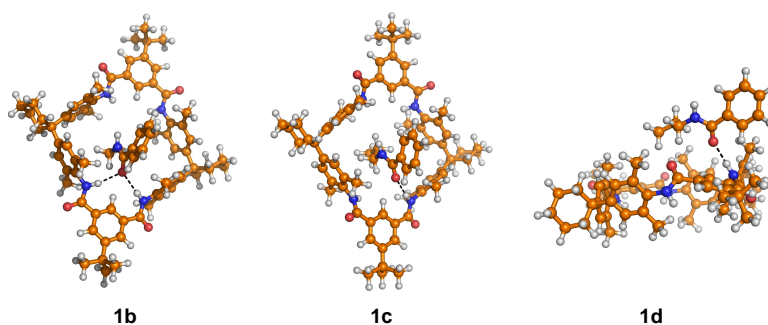


Figure 3. Left: system **1b** (twofold hydrogen bridge), middle: system **1c** (single hydrogen bridge, inside the cavity), right: system **1d** (single hydrogen bridge, outside the cavity)

The interaction energies of these systems are calculated with different density functional methods (BP, BLYP, B3LYP, BHLYP, BLYP-D, and B2-PLYP) as well as with the SCS-MP2 and MP2 method, see table 1. The B2-PLYP and the SCS-MP2 calculations are performed at truncated geometries where the TLM t-butyl and cyclohexyl groups are replaced by hydrogen atoms. This approach enables for the first time a quantitative estimation of the role of dispersion interaction for the formation of such systems.

The most stable structure in these isolated system considerations is one with three hydrogen bonds between axle and wheel. For almost all methods the next stable compound is represented by the structure with the twofold hydrogen bond. This complex is predicted

	BP86	BLYP	B3LYP	BHLYP	BLYP-D	B2-PLYP	SCS-MP2	MP2
<b>1a</b>	-47	-42	-58	-75	-132	-86	-102	-122
<b>1b</b>	-21	-16	-31	-46	-103	-59	-80	-98
<b>1c</b>	-12	-9	-21	-34	-87	-48	-66	-84
<b>1d</b>	-22	-20	-27	-35	-59	-40	-46	-54

Table 1. Interaction energies (in kJ/mol) for the investigated pseudorotaxanes **1a** – **1d**.

to be about 30 kJ/mol above the most stable structure considering all studied functionals. For almost all employed functionals the structure with the axle inside the wheel and one single hydrogen bond lies approximately another 10 kJ/mol above the second most stable structure. The comparison of the two single hydrogen bonded system **1c** and **1d** shows that **1d** is more stable for the standard density functionals with a poor description of dispersion interaction whereas **1c** is more stable for the methods where dispersion interaction is considered in a better way.

It attracts attention that the calculated interaction energy for the three systems with the axle inside the wheel is functional dependent. The trend for the pure density functionals (BP to BHLYP) corresponds to their expected description of hydrogen bonds: BP and BLYP tend to underestimate, BHLYP to overestimate hydrogen bonds. It is assumed that B3LYP provides good results for hydrogen bonds. A large increase of the interaction energy is observed for the other methods. The interaction energy compared to the B3LYP results increases about -28 kJ/mol for B2-PLYP, about -46 kJ/mol for SCS-MP2, about -65 kJ/mol for MP2, and about -71 kJ/mol for BLYP-D. These results indicate that the influence of dispersion interaction is unexpectedly large. Therefore one can assume that the first step of the threading process is the formation of a hydrogen bond outside the cavity. The driving power for the continuing threading process is the formation of further hydrogen bonds inside the cavity and the dispersion interaction which is also largest inside the cavity. However one should keep in mind that the dispersion interaction of solvent molecules which are not treated in this work is expected to be of the same order of magnitude as the dispersion interaction of the axle.

The vibrational analysis of the pseudorotaxane complexes demonstrates that it should be possible to distinguish the treated hydrogen bonding situations by means of IR spectroscopy.<sup>9</sup> In particular the N-H stretching modes of the wheel might act as indicator for the binding situation of the axle, since a large difference in the shifts is predicted if we compare the situation where the axle is bound inside the wheel cavity to the situation where the axle is bound outside the cavity. In the latter case we observe by far the largest red shift. The different hydrogen bonding situations for the cases where the axle is positioned inside the cavity can be distinguished on the basis of the carbonyl C=O stretching modes which show also a red shift if they are involved in hydrogen bonds. This red shift corresponds to the hydrogen bonding situation of the carbonyl group. The red shift is larger for a twofold hydrogen bonded C=O group than for a single hydrogen bonded group.

### 3.4 Adsorption of TLM on the Au(111) Surface

In cooperation with the experimental group of M. Sokolowski we investigated the template driven self organization of TLM on the Au(111) surface.<sup>10</sup> From scanning tunneling microscopy and our calculations two structural different phases with fully flat lying macrocycles were identified. The inert Au(111) surface acts only as a two dimensional template. The intermolecular ordering of the macrocycles results from hydrogen bonds between amide groups of next neighbour macrocycles. The so called  $\alpha$  phase, which is apparently the thermodynamically more stable phase at room temperature (Fig. 4) consists of linear chains of stacked TLM molecules.

From DFT calculations we find that two hydrogen bonds between amide groups are formed between each pair of overlapping molecules. In addition  $\pi - \pi$ -stacking interaction can stabilize the chain formation, since the distance between two overlapping benzene rings is only around 3.7 Å. The structure of the  $\beta$  phase is assumed as linear aggregates of three TLM molecules, see Fig. 4. Again the formation of linear hydrogen bonds is the central structural motive in this phase. Both, the  $\alpha$  phase and the  $\beta$  phase feature the maximum possible number of hydrogen bonds.

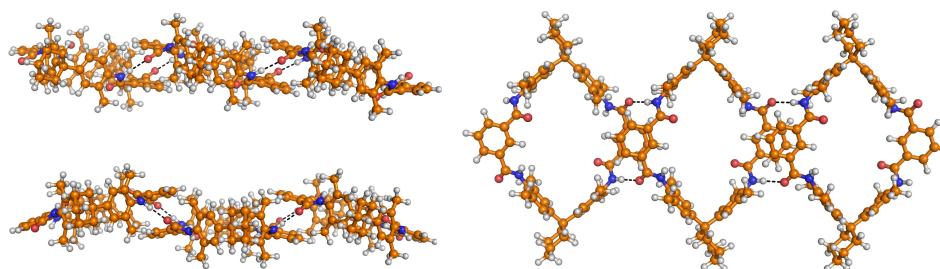


Figure 4. Calculated structure models for the  $\alpha$  (left upper and right structure) and  $\beta$  (left lower structure) phase of TLM.

### 3.5 Adsorption of Formamide Polymers on Ag(111)

In a further project we investigate the influence of surfaces on peptide hydrogen bond templated systems. For this purpose we studied the adsorption of formamide monomers and of formamide polymers in which each formamide molecule builds up to four hydrogen bonds to its neighbours. If these chains are placed on the Ag(111) surface we expect template induced chirality.

We observe a pronounced difference between the adsorption of formamide monomers which corresponds to a low coverage situation and the adsorption of formamide polymers: The adsorption of a monomer leads to a structure where the carbonyl group points downwards to the surface. The calculated adsorption energy is  $-25$  kJ/mol. In contrast the formamide molecules of the adsorbed polymers, which resemble the most stable configuration in the gas phase, are lying flat on the surface. For this system we get significantly larger  $R_{\text{OAg}}$  distances and we calculate smaller adsorption energies ( $-3$  to  $-8$  kJ/mol per molecule). However, due to the maximum number of intermolecular hydrogen bonds

this arrangement is energetically favored compared to independently adsorbed monomers. The total stabilization energy due to adsorption and hydrogen bonds is  $-85$  kJ/mol for the dimer,  $-216$  kJ/mol for the tetramer, and  $-333$  kJ/mol for the hexamer. The total interaction energy per molecule increases from  $-43$  kJ/mol (dimer) to  $-54$  kJ/mol (tetramer) to  $-56$  kJ/mol (hexamer) to  $-58$  kJ/mol for the adsorption of an infinite chain of formamide molecules which was also investigated.

A more detailed analysis shows that the formation of hydrogen bonds has an effect on the adsorption energy: The adsorption energy of the polymer is significantly lower than the sum of the adsorption energies of the corresponding monomers. From this follows that the interaction between the formamide and the Ag is weakened by the formation of hydrogen bonds parallel to the surface. It appears that first and foremost the outer oxygens which build up only one single hydrogen bond to their neighbours are responsible for the stabilization due to adsorption. This assumption is confirmed by the fact that we observe shorter  $R_{OAg}$  distances for these atoms.

We studied also the vertical adsorption of a formamide dimer where both carbonyl groups point downwards to the surface. This leads to the formation of a hydrogen bond of one carbonyl group to the adjacent formamide molecule. The calculated stabilization energy (adsorption and hydrogen bonds) for this system is  $-74$  kJ/mol,  $10$  kJ/mol less than for the flat system. Interestingly we observe for this vertical adsorption the opposite trend to the flat adsorption: The adsorption energy increases due to the formation of a vertical hydrogen bond. Our preliminary conclusion is that the formation of peptide hydrogen bonds parallel to the surface leads to a decrease of adsorption energy whereas the formation of hydrogen bonds vertical to the surface increases the adsorption energy.

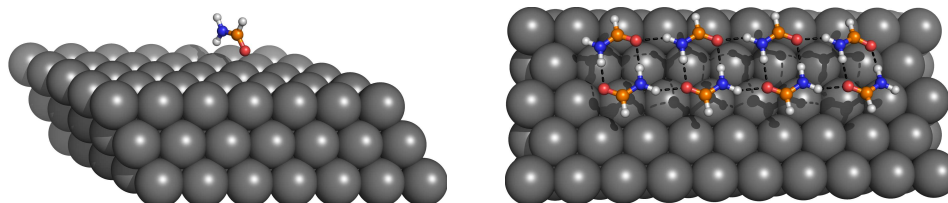


Figure 5. Adsorption on the Ag(111) surface, left: vertical adsorption of formamid monomer, right: flat adsorption of formamid oktamer

## 4 Computational Performance

Before starting our calculations we measured the scaling of the computing time when changing the accuracy and/or the number of processors incorporated in a job. Our test system for the CPMD simulations was the dethreading process of the pseudorotaxane system **1a**. The results of these calculations are shown in Fig. 6. We observe very good scaling.



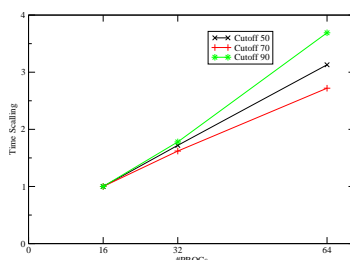


Figure 6. Scaling of the wall clock time for the CPMD simulations of pseudorotaxane **1a**

## Acknowledgments

We are grateful for computing time at the NIC in Jülich. Furthermore we acknowledge the financial support from the collaborative research center SFB 624 “Templates” at the University of Bonn, and from the ERA project “Modular Approach to Multi-responsive Surfactant/Peptide (SP) and Surfactant/Peptide/Nanoparticle (SPN) Hybrid Materials”. We thank our experimental collaborators I. Kossev and M. Sokolowski.

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