

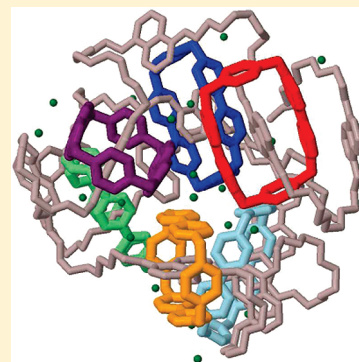
Coulombic Interactions and Crystal Packing Effects in the Folding of Donor–Acceptor Oligorotaxanes

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Supporting Information

ABSTRACT: The folding of a series of donor–acceptor oligorotaxanes is studied by means of molecular dynamics simulations. The oligorotaxanes consist of tetracationic cyclobis-(paraquat-*p*-phenylene) rings threaded onto oligomers of 1,5-dioxynaphthalene linked by polyethers. Minimum energy structures are isolated using simulated annealing from which insights into the interactions responsible for the folding are extracted. The folding in vacuum is primarily driven by Coulombic interactions between the ionic species. In turn, in a high dielectric medium, the folding is the result of a series of conflicting interactions primarily orchestrated by the rings. In both cases, folded globular structures result. The observed secondary structures extend a previously proposed pleated π -stacked model for the folding that has been, in fact, observed in crystal samples of a [3]Rotaxane, the smallest of the oligorotaxanes considered. Simulations using two different force fields in the crystal environment, in vacuum, and in explicit solvent indicate that the π -stacked conformation adopted by the [3]Rotaxane is stable due to crystal packing effects rather than intracomplex interactions. The π -stacked conformation is also shown to be thermodynamically improbable in longer oligomers.



I. INTRODUCTION

Rotaxanes are mechanically interlocked molecular complexes in which a macrocycle is threaded onto a linear molecule with stoppers at both ends. The efficient synthesis of rotaxanes relies on incorporating complementary sites in the molecules that form it, typically an electron rich and an electron deficient unit, that act together as a template for assembly through noncovalent interactions.^{1–3}

The inherent interest in the mechanical bond holding rotaxanes and related catenanes together, as well as their potential use in the design of materials with specific functionalities, has driven rapid progress in establishing synthetic strategies to build increasingly more complex versions of these molecules. These developments have fostered the design of rotaxane- or catenane-based chemically, electrochemically, or photopowered molecular devices,^{4,5} including shuttles,^{6,7} switches,^{8–10} valves,^{11,12} and molecular muscle-analogues.¹³ In turn, theoretical efforts have provided insight into the interactions responsible for the stability of simple rotaxane and catenanes,^{14–16} into the relative motion that the two interlocked macromolecules can perform,^{17–21} and into the unfolding of oligomeric versions of these molecules under stress.²²

A pair of complementary molecules often used in building rotaxanes consists of cyclobis(paraquat-*p*-phenylene) tetracationic cyclophanes (CBPQT⁴⁺) as the electron-deficient macrocycle and 1,5-dioxynaphthalene (DNP) units linked to polyethers as the electron rich docking station for the ring. The stability of the isolated [2]Rotaxanes formed by this pair—or closely related pairs—has been suggested^{14,15} as arising mainly from the π – π stacking interactions between the

naphthalene and the bipyridinium ions, and from the interaction of the oxygen atoms in the polyether with the positively charged macrocycle through ion–dipole and dipole–dipole interactions.

Recently, it has been proposed^{23,24} that this set of relatively weak noncovalent interactions can also lead to a well-defined pleated conformation in polyrotaxanes and oligorotaxanes in solution. NMR data that has been presented^{23,24} as suggestive of this model is typically obtained in low temperature (233–245 K) deuterated acetonitrile solutions. Figure 1 shows a schematic representation of the composition and proposed secondary structure of the oligorotaxanes.³⁴ In it, the CBPQT⁴⁺ rings in the oligomer π -stack perfectly with the undocked DNP units along the chain, forming a linear foldamer. This view is further supported by crystallographic evidence²³ that shows that a [3]Rotaxane can indeed adopt a perfectly π -stacked pleated conformation in the solid state (see Figure 2).

In this paper, we present an analysis of the folding of the oligorotaxanes using molecular dynamics (MD) techniques. We focus on the final secondary structure adopted by the oligorotaxanes rather than on the folding process. The *m*DNP–[*n*]Rotaxanes considered consist of (*n*–1) CBPQT⁴⁺ rings threaded onto a chain of *m* DNP units linked by tetraethyleneglycol (TEG) chains, with TEG chains at each end. A previous free energy analysis²² demonstrated that the folding of the oligorotaxanes is energetically driven. Minimum energy structures are thus useful and indicative of the native state. Here,

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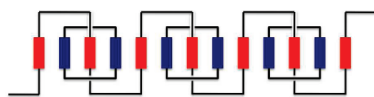


Figure 1. Schematic representation of the pleated conformation proposed in refs 23 and 24 for the oligorotaxanes. The paraquat units in the CBPQT⁴⁺ rings are represented in blue, the DNP units in the polymer thread in red, and the tetraethyleneglycol (or closely related polyether) chains in black.

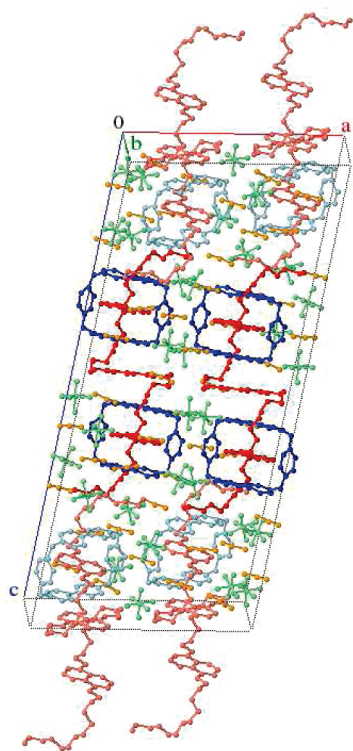


Figure 2. Experimental crystal structure for a 3DNP-[3]Rotaxane·8PF₆ system. The unit cell consists of 4 3DNP-[3]Rotaxane·8PF₆ complexes and 50 CH₃CN solvent molecules. In the figure, the CBPQT⁴⁺ rings are depicted in blue, the oligomeric thread in red, the PF₆[−] counterions in green, and the included solvent in orange. Note the perfectly π -stacked structure adopted by this [3]Rotaxane in the crystal environment. The crystal data was obtained from ref 23.

minimum energy structures for the oligorotaxanes are obtained using simulated annealing (SA) MD simulations. Insight into the interactions responsible for the folding is provided by determining the changes in the interaction energy occurring during the folding among the different functional groups composing the rotaxanes. Further, an analysis of the stability of the pleated π -stacked conformation is provided by following the dynamics of the [3]Rotaxane shown in Figure 2 in vacuum, in the crystal environment, and in explicit solvent using two different force fields.

As shown below, since the oligorotaxanes are polyelectrolytes, the interactions between the charged species actually dominate the folding in vacuum, with other noncovalent interactions playing a secondary role. Even when small oligorotaxanes do fold into regular structures, the final structure adopted does not pleat precisely as hypothesized in refs 23 and 24. Our MD study shows that the pleated conformation is also not stable in longer

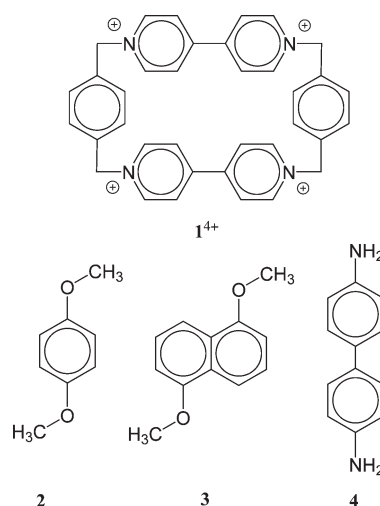


Figure 3. Components of the complexes in Table 1.

oligomers; these fold, instead, into globular structures. Further, the π -stacked pleated conformation of the [3]Rotaxane observed in solid state samples is shown to be stable due to the crystal packing effects rather than to the weak noncovalent intracomplex interactions known to be important in the stabilization of [2]Rotaxane systems.

The structure of this manuscript is as follows. In section II, the ability of the MM3 force field to describe the oligorotaxanes is tested. In section III, the folding of the oligorotaxanes both in vacuum and in a dielectric medium is presented. Section IV discusses possible crystal packing and explicit solvent effects on the stability of the π -stacked structure of the 3DNP-[3]Rotaxane. Our main findings are summarized in section V.

II. THE FORCE FIELD

Unless specified otherwise, the simulations reported below are done using Tinker 4.2²⁵ and the MM3 force field model. The MM3 force field^{26–28} contains explicit parameters for the pyridinium N⁺ ions (py) that form an integral part of the oligorotaxanes studied here.³⁵ As shown below, this force field is successful in reproducing the complexation energies of model rotaxanes, the crystal structure of the 3DNP-[3]Rotaxane·8PF₆ system, as well as the π - π stacking interactions believed to play an important role^{23,24} in the folding of the oligorotaxanes.

We first assess the ability of this MM3 force field to reproduce the complexation energies of model rotaxanes. The molecular complexes under consideration are formed by the host paraquat ring **1** and the guest systems **2–4** shown in Figure 3. The complexation energy is defined as the energy of the host–guest complex minus the energy of the isolated components. Table 1 compares results obtained using the MM3 force field with the *ab initio* results reported in ref 14 which explicitly include electronic correlation effects. The MM3 XYZ coordinates for these complexes are included in the Supporting Information. The data reported in ref 14 uses B3LYP/6-31G(d,p) for geometry optimization and a counterpoise corrected MP2/6-31G(d,p) method to obtain the total energy. As shown, the MM3 force field reproduces remarkably well the *ab initio* results for the complexation energies of the model rotaxanes.³⁶

As an additional test to the MM3 force field, we performed a full crystal energy minimization for the 3DNP-[3]Rotaxane·8PF₆ system shown in Figure 2 starting from the experimentally

Table 1. Complexation Energies ΔE of the Host–Guest Complexes in Figure 3^a

complex	ΔE (kcal/mol)	
	MM3	ab initio
1·2	−25.6	−24.2
1·3	−31.6	−31.6
1·4	−34.0	−36.0

^a The table compares the complexation energies predicted by the MM3 force field with the counterpoise corrected MP2/6-31G(d,p) *ab initio* results reported in ref 14.

Table 2. Experimental and Fully Optimized Crystal Parameters for the [3]Rotaxane·8PF₆ System Shown in Figure 2^a

	<i>a</i>	<i>b</i>	<i>c</i>	α	β	γ
experimental	23.20	14.92	51.04	90.0	100.2	90.0
MM3 optimized	23.25	14.70	51.52	90.0	98.2	90.0

^a The edge distances *a*, *b*, and *c* are reported in Å, and the crystal angles α , β , and γ , in degrees. The angle α is that between the *b* and *c* axes, β between *a* and *c*, and γ between *a* and *b*.

determined crystal structure. In it, both the molecular conformation and the cell parameters were allowed to vary. An Ewald summation was employed in the computation of the electrostatic interactions of this periodic system. The additional parameters needed for the description of the PF₆[−] counterions were taken from ref 29. The resulting crystal structure parameters before and after the minimization are shown in Table 2. There is a variation of just 2° in the β angle, changes of less than 1% in the lattice parameters, and an average root-mean-square variation in the molecular structure (including counterions, hydrogen atoms, and solvent molecules) of just 1.1 Å. That is, the minimum energy structure determined by the force field essentially coincides with the experimentally determined crystal structure, further indicating that the force field employed adequately represents the system.

Further note that the MM3 force field also well reproduces π – π stacking interactions. For instance, the MM3 binding energy (equilibrium distance) of a benzene dimer in a sandwich configuration is 2.4 kcal/mol (3.6 Å). This compares reasonably well with the fully correlated *ab initio* results reported in ref 30 of 1.8 kcal/mol (3.7 Å).

III. FOLDING OF THE OLIGOROTAXANES

A. Simulated Annealing. Minimum energy structures for the oligorotaxanes were isolated by means of simulated annealing (SA) molecular dynamics (MD) simulations. In them, the system is first thermalized at a given temperature and subsequently slowly cooled down toward 0 K. The thermalization and cooling processes were simulated in a NVT ensemble with a Nosé–Hoover chain as the thermostat. The propagation was done using a modified Beeman algorithm with a 1 fs integration time step. The system was first allowed to equilibrate at a selected temperature for 1000 ps and subsequently cooled down to 0 K in 100, 1000, or 10000 ps using a linear temperature ramp. A broad sampling of the configurational space was further enforced by employing two different initial temperatures of 300 and 500 K and two largely different initial geometries: fully extended and model folded oligomers. The model

Table 3. Difference in the MM3 Energy (in kcal/mol) between the Extended and Fully Relaxed Conformations of the Oligorotaxanes

system	3DNP–[3]- Rotaxane	6DNP–[4]- Rotaxane	12DNP–[7]- Rotaxane
vacuum	−122.8	−230.4	−528.8
dielectric	−62.4	−126.4	−279.2

folded conformations approximately mimic the model for the folding of polyrotaxanes in Figure 1.

In building the initial structures for the *m*DNP–[*n*]Rotaxanes, it was supposed that the paraquat rings initially dock in every other DNP unit along the thread. This supposition is consistent with the ring distribution expected for the polyrotaxane studied in ref 24. Note, however, that, since ring migration from one docking station to another one is a process that is slow with respect to the simulation time considered here, the final structure selected by the SA procedure will often have the same ring distribution that was chosen for the initial state. Further note that while the SA procedure generally leads to very low energy structures, there is no way to ascertain that these structures actually correspond to the global minimum, unless, of course, the full potential energy surface of the molecule is characterized.

The SA simulations were performed both in vacuum and in a continuum strong dielectric medium. In both cases, electrically neutral structures were employed, with Cl[−] ions acting as counterions for the tetracationic paraquat rings. Note that if counterions are not included in the vacuum simulations the cyclophane units repel each other and no folding occurs. In the continuum dielectric case, the overall dielectric constant in the force field was set to that of water at room temperature (78.3). This is to be compared with the MM3 dielectric constant for vacuum of 1.5.³¹ By changing the dielectric constant, the ion–ion, dipole–ion, and dipole–dipole interactions in the force field are scaled accordingly. However, the van der Waals, bond and torsional interactions remain intact and thereby assume a more prominent role in the dynamics. Last, a flat-walled harmonic box centered at the oligomer's center of mass was employed to prevent a large separation of the chloride ions from the main molecular backbone upon increasing the dielectric constant.

The net change in the total energy of the complexes during the folding is shown in Table 3. These values reflect the difference in the total energy of the molecule from its fully extended form (linear chain) to the lowest-energy folded structure determined by the SA procedure. The XYZ coordinates of the final isolated structures are included in the Supporting Information. Quantitative insight into what drives the folding from an energetic perspective is obtained by partitioning the oligorotaxane into structural groups and determining the changes in the interaction energy among the different groups during the folding. The selected partitioning, even when clearly not unique, reflects the different chemical components of the oligorotaxanes (naphthalenes, ether chains, cyclophane rings, and Cl[−] counterions) and, importantly, is such that the sum of the intra- and intergroup interactions yields the total energy of the full molecule. We will refer to the resulting changes in the interaction among the groups as the *differential interaction map*.

B. Folding in Vacuum. Consider first the folding in vacuum of the 3DNP–[3]Rotaxane, the simplest oligorotaxane studied here. Figure 4 shows the initial extended and fully relaxed folded conformation for this oligorotaxane, as well as the differential

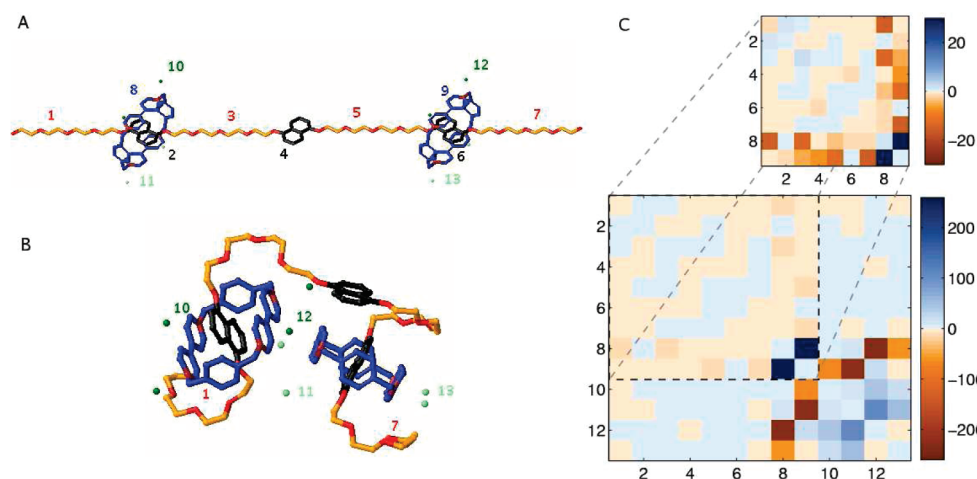


Figure 4. 3DNP-[3]Rotaxane in vacuum: minimum energy structure and interactions responsible for the folding. (A) Initial extended conformation; (B) final structure isolated by the SA procedure. The plots in part C depict changes in the interaction energy (in kcal/mol) among the different components of the molecule when the system goes from the extended to the folded conformation. The axes label chemical units along the oligomer in the numbering sequence shown in part A. The color convention adopted in parts A and B is the following: oxygen atoms are depicted in red, the naphthalene units in black, and the polyether chains in orange. The CBPQT⁴⁺ rings are depicted in blue with the pyridinium N⁺ ions in brown. The isolated atoms correspond to the chloride counterions.

interaction map. The most prominent changes in the interaction map occur among the ionic species which play a determining role in the folding. Note that while the interaction between the paraquat rings is largely repulsive, this is compensated by the attractive interactions between the chloride ions and the paraquat rings. This leads to an effective counterion-mediated net attraction among the rings which accounts for roughly half the total folding energy (-55.8 kcal/mol of the total -122.8 kcal/mol). The remaining -67 kcal/mol arises from attractive interactions between the paraquat rings and the polyether chains through ion-dipole interactions and, to a lesser extent, from the interactions between the naphthalene 4 and the cyclophanes.

This emerging hierarchy of interactions determining the folding in vacuum (ionic > paraquat-polyether > paraquat-naphthalene interactions) is also manifest in the folding of 6DNP-[4]Rotaxane, and leads to the highly structured conformations shown in Figure 5. In this case also, purely ionic interactions account for roughly half the folding energy. Note that this interaction hierarchy does not necessarily lead to a dominant minimum-energy structure for the oligorotaxanes. For instance, Figure 5 shows two qualitatively different folded conformations for the 6DNP-[4]Rotaxane isolated by the SA procedure with total energies differing just by 0.2 kcal/mol. The regularity in the primary structure together with the fact that Coulombic interactions are not directional lead to degeneracies at very low energies.

Note that the perfectly π -stacked conformations are highly energetic with respect to the native states isolated here. To evidence this point, simulations were performed in which the structure of a single 3DNP-[3]Rotaxane chain in the pleated conformation was left intact (the structure was taken from the MM3 optimized crystal structure) and the positions of Cl⁻ counterions were optimized using SA. The resulting structure (included in the Supporting Information) is 91 kcal/mol higher in energy than the one shown in Figure 4B because the perfectly π -stacked conformation does not minimize the Coulombic interactions among the ionic species.

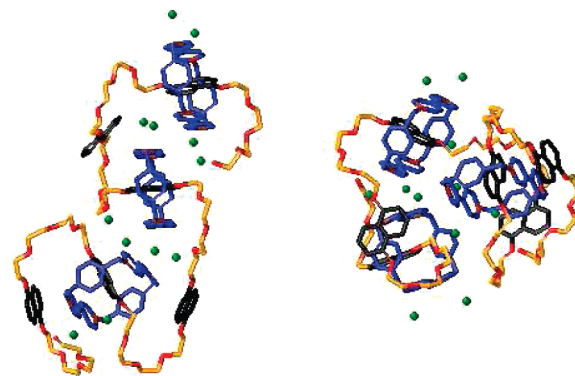


Figure 5. Minimum energy structures for the 6DNP-[4]rotaxane in vacuum. These two qualitatively different folded conformations differ in energy by just 0.2 kcal/mol, with the globular conformation being slightly higher in energy. The color convention adopted is described in Figure 4.

C. Folding in a High Dielectric Medium. We now focus on the folding problem in a high dielectric medium. The folding energy in this case is considerably smaller—roughly half—than that observed in vacuum (cf. Table 3), since ion-ion, ion-dipole, and dipole-dipole interactions are now weaker, and the strong counterion-induced net attraction among paraquat rings observed in vacuum is no longer present. Figure 6 shows the final structure obtained through the SA procedure for the 3DNP-[3]Rotaxane and the resulting differential interaction map. The 3DNP-[3]Rotaxane folds into a globular structure analogous to that observed in vacuum (cf. Figure 4). While the CBPQT⁴⁺ rings play an orchestrating role in the folding through interactions with the different components of the thread, there are a wealth of secondary interactions that collectively play an important role. Note that here the naphthalene-paraquat interactions are as important in the folding as the polyether-cyclophane interactions, contrary to what was observed in vacuum in which the polyethers played a more important role.

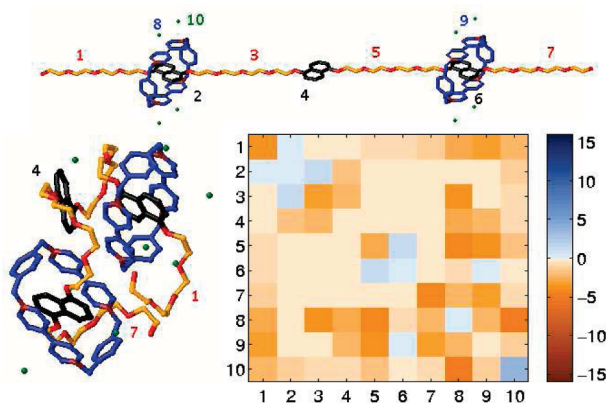


Figure 6. 3DNP-[3]Rotaxane in a high dielectric medium: minimum energy structure and differential interaction map (in kcal/mol). The distribution and meaning of the different panels is the same as in Figure 4. Note that all the chloride ions are included in group 10.

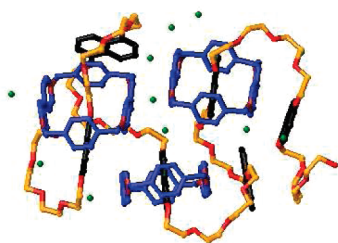


Figure 7. Minimum energy structure isolated by the SA procedure for a 6DNP-[4]Rotaxane in a high dielectric medium. The color convention adopted is described in Figure 4.

Further, a reduction in the torsional energy of the ether chains also plays a stabilizing role here, while in vacuum the energy of the polyethers actually increased upon relaxation due to penalizing intragroup dipole-dipole interactions. The interactions responsible for the folding in a high dielectric medium also lead to a relatively regular structure in the folding of the 6DNP-[4]Rotaxane (see Figure 7).

D. Folding of Longer Oligomers. We now study the folding dynamics of a 12DNP-[7]Rotaxane, and assess the plausibility of the pleated conformation proposed in ref 24 for the polyrotaxanes. This extended system is sufficiently large to provide reasonable insight into how a polyrotaxane will actually fold. For this, we follow the constant temperature dynamics (300 K) of the oligorotaxane, both in vacuum and in a high dielectric medium, starting from both fully extended and pleated initial structures. The degree of folding of the oligomer is followed by monitoring the radius of gyration, defined as $R_g^2 = (1/M) \sum_k m_k (\mathbf{r}_k - \mathbf{R}_c)^2$, where M is the total mass, m_k and $\mathbf{r}_k$ the mass and position of the k th atom, and $\mathbf{R}_c$ the position of the center of mass. The folding of the main molecular backbone is highlighted by neglecting any contributions to R_g^2 coming from the Cl^- counterions. Figure 8 shows representative results. Irrespective of the initial conformation chosen or the dielectric constant employed, the 12DNP-[7]Rotaxane folds into a globular structure with $R_g^2 \sim 140 \text{ \AA}^2$. The pleated conformations collapse under thermal evolution, and the long-range order and symmetry suggested in ref 24 are not observed.

Figure 9 shows the minimum energy structure isolated by the SA procedure. At 0 K, the system adopts a globular structure with

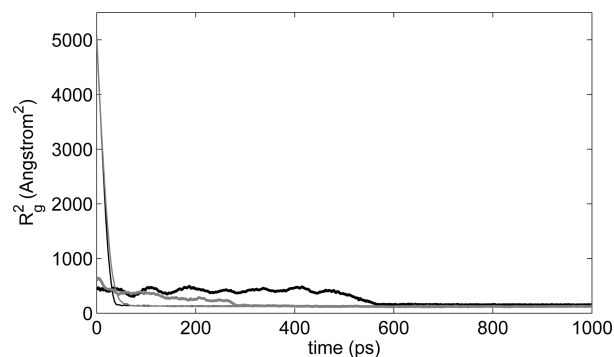


Figure 8. Evolution of the radius of gyration R_g^2 for the 12DNP-[7]Rotaxane at 300 K. The simulations start from either fully extended (thin lines) or model-folded (thick lines) conformations, and the dynamics is followed in vacuum (black lines) or in a high dielectric medium (gray lines).

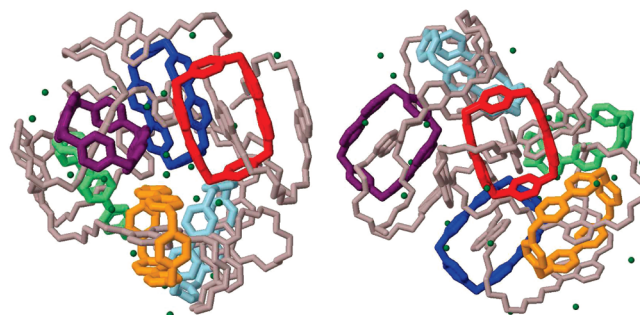


Figure 9. The minimum energy structures of 12DNP-[7]Rotaxane in both vacuum (left) and in a high dielectric medium (right) are globular. For clarity, the oligomer thread is shown in gray, and the CBPQT^{4+} units in different colors.

no long-range order. Such a structure maximizes favorable interactions among the different components of the complex. Even when the orchestrating role of the CBPQT^{4+} rings in the folding is apparent in the final structure, there is no evidence that these interactions will actually lead to stable π -stacked pleated conformations. Further, the experimental evidence presented in ref 24 is qualitatively consistent with the globular structures with no apparent long-range order obtained through the SA procedure.

IV. CRYSTAL PACKING EFFECTS

The simulations presented above indicate that perfectly π -stacked conformations of isolated oligorotaxanes do not correspond to the energy minimum, nor are they thermodynamically probable. Such observation, however, seems to be at odds with the fact that in the solid state the 3DNP-[3]Rotaxane does assemble into a perfectly π -stacked conformation (see Figure 2). How do we reconcile these confronting observations?

Clearly, one possibility is that the force field employed does not properly describe the secondary structure of the oligorotaxanes. After all, in MM3, the positive charges on the CBPQT^{4+} rings are localized on the N^+ atoms of the pyridine units, while electronic structure computations³² indicate that these charges are actually diffuse along the ring. It may be argued that the observed collapse of the pleated conformation is because the force field does not mimic correctly the charge distribution of

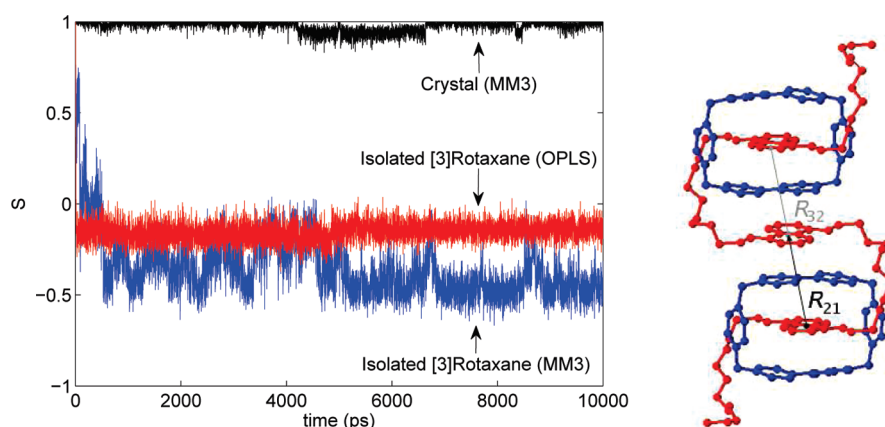


Figure 10. Crystal packing effects on the structure of the [3]Rotaxane · 8PF₆. The left panel shows the evolution of the degree of stacking $S = \hat{\mathbf{R}}_{21} \cdot \hat{\mathbf{R}}_{32}$ for the 3DNP–[3]Rotaxane either isolated or in its full crystal environment. The isolated dynamics was followed using the MM3 and OPLS force fields. The right panel depicts the distance vectors $\mathbf{R}_{21}$ and $\mathbf{R}_{32}$ connecting the center of masses of the naphthalene units in the complex and used in the definition of S .

the complexes. A second possibility is that the pleated conformation is stabilized by the crystal environment, since the oligorotaxanes are polyelectrolytes and the crystal environment provides an ionic medium that is expected to have substantial effects on the selected geometry.

To test these possibilities, we followed the dynamics of the full 3DNP–[3]Rotaxane · 8PF₆ crystal (300 K, NVT ensemble, Ewald summation, Nosé–Hoover thermostat, 1 fs integration time step) including both the PF₆[−] counterions and the trapped solvent using MM3, starting from the experimentally determined crystal structure. The crystal environment was simulated by following the dynamics of the unit cell in Figure 2 with periodic boundary conditions. If the force field is inadequate, one would expect the experimental crystal structure to be unstable under thermal motion. By contrast, if the pleated conformation is stabilized by the crystal environment, one would expect the π -stacked conformation to be stable only in the crystal. As a simple measure of π -stacking, we followed the dynamics of $S = \hat{\mathbf{R}}_{21} \cdot \hat{\mathbf{R}}_{32}$, where $\hat{\mathbf{R}}_{ij} = \mathbf{R}_{ij}/|\mathbf{R}_{ij}|$ is a unit vector pointing along $\mathbf{R}_{ij}$, the distance vector between the center of masses of naphthalene units i and j . Here, labels 1 and 3 denote the outer naphthalenes of the 3DNP–[3]Rotaxane, while label 2 corresponds to the middle one (see Figure 10). In a perfectly π -stacked system, $S = 1$ and a decrease in S indicates deviations from this conformation. Figure 10 shows the evolution of S in the full crystal and for a single 3DNP–[3]Rotaxane plus counterions in vacuum starting from the conformation adopted in the crystal. While in the full crystal S is stable and close to 1 at all times, once the crystal environment is removed, the π -stacked structure collapses into structures that are reminiscent to the ones isolated by the SA procedure. This collapse of the π -stacked structure is also observed when the unit cell is allowed to evolve without periodic boundary conditions.

To determine if the collapse of the pleated structure for the 3DNP–[3]Rotaxane upon removal of the crystal environment is an artifact of the force field employed, we also followed the dynamics of a single chain in vacuum using an alternative force field that explicitly takes into account that the charges on the CBPQT⁴⁺ rings are diffuse. Specifically, we employed the OPLS-AA force field³³ with atomic partial charges obtained from a Mulliken population analysis obtained at a B3LYP/DZP level calculated at the experimentally determined pleated conformation for the 3DNP–[3]Rotaxane. These partial charges are

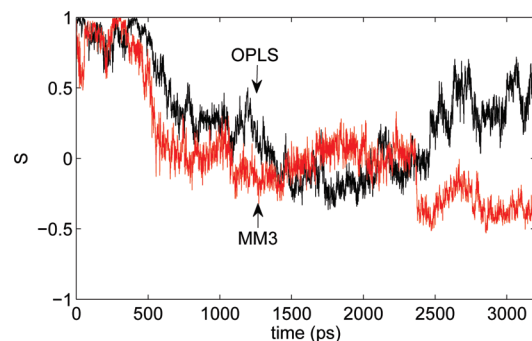


Figure 11. Evolution of the degree of stacking S for the 3DNP–[3]Rotaxane immersed in explicit solvent (CH₃CN) starting from the geometry observed in the crystal sample. The quantity S is defined in Figure 10. Note that the π -stacked structure as described by the MM3 and OPLS force fields collapses for isolated chains in explicit solvent.

included in the Supporting Information. A similar procedure to assign partial charges to Rotaxanes has been used before.²⁰ As shown in Figure 10, in this model, the π -stacked pleated conformation for isolated 3DNP–[3]Rotaxanes is also not stable. Further, the minimum energy structure predicted by this force field is qualitatively similar to the one isolated using the MM3 force field.

As an additional test of the stability of the π -stacked pleated conformation, we followed the dynamics of a 3DNP–[3]Rotaxane in explicit solvent (CH₃CN) starting from the crystal structure geometry using MM3 and the OPLS force fields (PF₆[−] counterions, 300 K, NVT ensemble, Ewald summation, Nosé–Hoover thermostat, 1 fs integration time step, $40 \times 40 \times 40$ Å³ box size, solvent density 0.786 g/cm³). The evolution of the degree of stacking S is shown in Figure 11. As shown, even when explicit solvent effects are taken into account, the pleated π -stack structure still collapses into a globular structure, confirming that the pleated structure should not be expected in solution either.

Qualitative arguments that have been presented^{23,24} to discuss the folding in solution of the oligorotaxanes based on NMR measurements should be interpreted with care. NMR signals typically yield *average* information about the local chemical

environment. The symmetries and couplings observed in the NMR are thus averages over a series of conformations that are adopted by the molecule during the NMR signal and, hence, proper assignments require detailed modeling of the NMR.

Summarizing, the results indicate that the stability of the π -stacked pleated conformation observed in crystal samples of the 3DNP–[3]Rotaxane is really due to crystal packing effects rather than to interactions within each complex. The structure observed in crystals is qualitatively different from the one expected in solution because of the organized ionic and solvent environment that the crystal provides which is absent in the solvent. The native conformation for the isolated or solution-phase 3DNP–[3]Rotaxane is globular instead of π -stacked essentially because the folding is largely influenced by Coulombic interactions among charged species and Coulomb forces are nondirectional.

V. CONCLUSIONS

We have isolated minimum energy structures for a series of donor–acceptor oligorotaxanes by means of simulated annealing molecular dynamics simulations both in vacuum and in a high dielectric medium. The simulations indicate that, while small oligomers can fold into regular structures, larger oligomers tend to globular structures with local order only. The folding in vacuum is primarily driven by Coulombic interactions among the charged species, namely, the CBPQT⁴⁺ rings and the counterions. In fact, the presence of counterions leads to an effective attraction between the paraquat rings that accounts for roughly half the folding energy. In turn, in a high dielectric medium, the ions no longer assume such a prominent role and the final structures arise from a series of conflicting interactions primarily orchestrated by the cyclophanes. In both media and for all oligomers, the simulations show that the pleated π -stacked conformation previously proposed^{23,24} for the folding of this class of molecules is not the minimum energy structure and is thermodynamically improbable.

In addition, it was demonstrated that the pleated π -stacked conformation observed in crystal samples for the 3DNP–[3]Rotaxane is stabilized largely by the crystal environment rather than by interactions within each Rotaxane. This was shown using two quite different force fields, and by following the dynamics in the crystal environment, in vacuum, and in explicit solvent. These results constitute a clear example in which the structure observed in crystals is qualitatively different from the one expected in solution because of the organized ionic and solvent environment that the crystal provides which is absent in the solvent.

■ ASSOCIATED CONTENT

S Supporting Information. XYZ coordinates for (i) the molecules in Table 1, (ii) the isolated minimum energy structures of the *m*DNP–[*n*]Rotaxanes in vacuum and in a high dielectric medium, and (iii) the 3DNP–[3]Rotaxane in the experimentally determined crystal structure with SA optimized counterion positions. The computed B3LYP/DZP Mulliken charges obtained in the crystal geometry are also included. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (34) To be precise, we actually deal with pseudorotaxanes that lack the steric blocking units at the chain termini that force the cyclophanes to remain attached to the oligomeric chain. For simplicity, we will use the term rotaxane.
- (35) Some additional parameters need to be supplied to the MM3 force field to perform the simulations. The required parameters are for the (i) $C(sp^3)-N^+(py)$ out-of-plane bending, (ii) $N^+(py)-C(sp^3)-C(sp^2)$ angle bending, and (iii) $N^+(py)-C(sp^3)-C(sp^2)-C(sp^2)$ and $C(sp^2)-C(sp^3)-N^+(py)-C(sp^2)$ torsional contributions. The employed parameters were taken from those of analogous systems already contained in the force field. Specifically, for (i), the values for the analogous $H-N^+(py)$ case were employed; for (ii) and (iii), the values for the analogous benzene case were employed instead. Note that these parameters do not appreciably influence the interactions determining the complexation energies and the secondary structure of the oligorotaxanes.
- (36) In MM3, π -conjugated atoms receive special treatment. For these atoms, a self-consistent field molecular orbital calculation (SCF-MO) is set up to scale bond and torsion parameters. We have observed that the π -system SCF-MO procedure has little bearing on the complexation energies and, for this reason, is not employed in this work.