Modeling of a Rotaxane-based Molecular Device

Xiange Zheng and Karl Sohlberg
Department of Chemistry, Drexel University, Philadelphia, PA 19104

ABSTRACT

A computational procedure is presented for investigating photo-induced switchable rotaxanes and demonstrated for a known system. This procedure starts with the generation of more than $10^4$ chemically reasonable rotaxane conformations based on an empirical intramolecular potential energy function. Single-point energy calculations at the semi-empirical (AM1) level are carried out for each structure in the singlet (ground), triplet, and anionic doublet states. The structural features are assigned and then correlated with energy for each state. What emerges is a profile of the structure-energy relationship that captures the salient features of the system that endow it with device-like character. Full geometry optimization of a subset of co-conformations (~1%) demonstrates that the procedure based on single-point calculations is sufficient to obtain a profile of the relationship of structural features to energy that is consistent with experiments, at greatly reduced computational cost.

INTRODUCTION

The design, synthesis and characterization of stimuli-responsive molecular devices and machines presents a great challenge. The chemistry of macromolecular systems, especially rotaxanes, has been of considerable interest in recent years[1-5] in part because they hold promise for the fabrication of prototype molecular devices. A rotaxane is an assembly of mechanically interlocked molecules in which a dumbbell-shaped component is encycled by one (or more) chemically independent cyclic component(s).

To facilitate the systematic design and refinement of functional molecular devices, it would be desirable to have available robust and validated modeling techniques. Such molecular device systems present a formidable challenge to computational chemistry owing to the large size of the molecules involved. Nevertheless, some pioneering modeling studies have been reported[5-7]. Here we demonstrate, on an experimentally realized example, a procedure for modeling rotaxane-based molecular devices that captures the features critical to their device-like character. Specifically, the modeling procedure predicts the spontaneous shuttling of the ring relative to the shaft in a switchable rotaxane, herein for a system with redox-dependant bi-stability. The overall procedure accurately captures the structural and switching characteristics of the physical system, ergo: the method shows promise to serve as a tool for molecular-device “design engineering”.

COMPUTATION METHOD

Initial rotaxane structure generation was performed with a graphical-user-interface molecular editor[8]. Starting structures for conformational searching were generated by stepwise translation and rotation of the crown component about the shaft component in the initial rotaxane structure. The SCAN module in the Tinker molecular mechanics (MM) software[9] was employed for the conformational searching over the full torsional space with the OPLS-AA[10] force-field parameter set. Semi-empirical single point calculations and geometry optimizations
were performed with the AM1[11, 12] method using the GAMESS program[13]. Previous success in treating inclusion phenomena with semi-empirical methods[5, 14, 15] and in modeling intermolecular hydrogen bonding[16] supports the choice of semi-empirical calculations for treating rotaxane systems.

RESULTS

The rotaxane studied here was reported by Brower et al. [2] and consists of two components, one is a peptide shaft with succinamide and naphthalimide groups serving as two stoppers at the two ends of a fully-anti (CH$_2$)$_{12}$ linear chain, which threads through the other component, a macrocyclic crown. The structure of the rotaxane is shown in figure 1. As demonstrated experimentally[2], the succinamide (succ) station is a better macrocyclic ring binding site than the naphthalimide (ni) station in the neutral ground state. The H-bond-accepting affinity of naphthalimide is greatly enhanced when the shaft is reduced to the anionic state (doublet), which enables the shuttling of the macrocyclic ring down the shaft, from its succ station to the reduced ni station where ring binding is preferred in the reduced state. A successful modeling procedure should capture this switching behavior, and we will show how computations indeed illustrate this bistability.

Each of 10118 associated structures identified by conformational searching was assigned by its gross structural features (coiled or extended), and by the position of the ring component along the shaft (succ and ni). The distances from the centroid of crown component to the left most atom (C$_8$ in figure 1, succ station) and the right most atom (N$_{43}$, ni station) on the shaft component are designated to be $R_{succ}$ and $R_{ni}$ respectively. Single point calculations were carried out in the singlet (ground), triplet, and anionic doublet states for each structure.

Based on the single point calculations, in the singlet ground state, the number (presented in figure 2 (a)) and percentage (2 (c)) of extended conformations are predominantly higher than those of coiled conformations, especially in the low energy regime, which shows that low energy conformations are preferentially extended rather than coiled in the singlet state. Further evidence of the energetic preference for extended structures in the singlet state comes from analysis of the moment of inertia tensor $I$, and the radius of gyration $K$, which depends on the largest eigenvalue.

![Figure 1](image-url)  
**Figure 1**  Initial structure of the rotaxane complex. 1a (left panel) shows the complex with the shaft component threaded through the crown component. 1b (right panel) shows the crown component only. Atoms within the regions C$1$–C$56$ and C$22$–C$35$ (except for H atoms) were used to define the crown centroid.
of the moment of inertia tensor and therefore reflects to some extent the shape of the corresponding molecule. Figure 3 presents the moving average radius of gyration ($\kappa$, of the shaft only) versus energy based on single point energy calculations. A lower $\kappa$ value betrays the appearance of some coiled structures. In the low energy regime, doublet species have lower $\kappa$ values than singlet species, which indicates that low energy structures tend to be more extended in the ground singlet state than in the doublet state. As energy increases, the $\kappa$ values decrease rapidly for singlet species while the curve is more flat for doublet species, which reveals the preference for extended structures in low energy regime for the singlet species and a greater coiling tendency for the doublet species. The qualitative distribution for neutral triplet systems (not shown) is similar to that in the singlet state.

As discussed above, based on single point calculations it may be concluded that the rotaxane prefers conformations with an extended shaft component at low energy in the singlet and triplet states, but displays some coiling tendency in the doublet state. Constructing the profile of energy versus structure in this manner is dramatically less expensive computationally than carrying out full structural optimizations for each trial structure. We propose that as long as the trial structures generated from the systematic conformational search are “chemically reasonable,” the use of single point calculations will produce a structure versus energy profile that is qualitatively consistent with what would be obtained if each structure were fully optimized. To test this proposal numerically, geometrical optimizations were carried out for a subset of co-conformations (one every 100 over the full energy range, totally 101 co-conformations, plus 15 selected low energy co-conformations), including calculations for their ground (singlet), excited (triplet), and anionic (doublet) states. Figure 2 shows the number (2 (b)) and percentage (2 (d)) of different structural features (extended or coiled) versus energy for the singlet species based on the optimizations. The results are qualitatively the same as from the single point calculations, shown in 2(a) and 2(c). The same is true for the triplet and doublet states (not shown). The shaft component tends to be extended at low energy in the singlet state, in agreement with what was concluded from single point calculations.

Figure 4 shows the profile of the system energy versus position of the ring along the shaft based on single point calculations. The change in binding preference with electronic state is clearly evident. The lowest energy conformations locate in the 18.0–24.0 Å region for the doublet, which represents the $ni$-station, while they are in the 3.5–6.5 Å region for the singlet and
triplet states, which indicates that the succ-co-conformations predominate in the latter two states. Low energy co-conformations tend to adopt structures with the crown component binding at the succ station in neutral singlet and triplet systems, and on the ni station in anionic doublet systems, in agreement with experimental observations[2].

The energy barrier ($\epsilon_{\text{act}}$) for switching to a ni doublet structure from the succ doublet structure, at the value of $R_{\text{succ}}$ corresponding to the minimum energy succ triplet, which was demonstrated as an intermediate for the formation of the doublet from the singlet upon photoexcitation[2], is $\approx 11$ kcal/mol. (From the lowest energy succ doublet structure, $\epsilon_{\text{act}}$ is $\approx 16$ kcal/mol.) The relatively large barrier, in combination with the significant structural difference between the representative succ-singlet and ni-doublet co-conformers is consistent with the barrier reported by Brouwer et al.[2](10.2±0.7 kcal/mol) and with the observed long time scale for switching (about 1 µs)[2].
A computational study was carried out for a rotaxane with photo-induced redox bi-stability that has been previously demonstrated experimentally[2]. Based on calculations of single point energy and radius of gyration for 10118 rotaxane structures, succ co-conformations predominate in the low energy regime for singlet and triplet species, with preference for the shaft component being extended. Doublet species prefer to take-on ni- co-conformations in low energy structures, with coiled and extended conformations being competitive for the shaft component. We obtained effectively the same results by geometrical optimizations of a subset of co-conformations. These results are in agreement with previous experimental observations[2]. Therefore, we believe that the structure versus energy profile produced in the less expensive way, by using systematic conformational searching followed by semi-empirical single point energy calculations, and correlating the structural features to energy, is consistent with what would be obtained if each structure were fully optimized, as long as the trial structures generated from the systematic conformational search are “chemically reasonable”.

**Figure 4** Binding preference for all three states versus energy, where RE is the relative energy of the corresponding conformation, which is referenced to the energy of the lowest energy conformation of the doublet. The lower (upper) curves corresponds to the lowest energy points, RE_{min}, (Boltzmann average energies, RE_{bz}) in 60 energy windows of 0.5 angstrom width for each of the three states. Here RE_{min-sgl} and RE_{bz-sgl} are for the singlet, RE_{min-dbl} and RE_{bz-dbl} are for the doublet, and RE_{min-tpl} and RE_{bz-tpl} are for the triplet respectively. The area between the RE_{min} and RE_{bz} curves is shaded for each state to highlight the difference. $\varepsilon_{act}=11$ kcal/mol.
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REFERENCES