Can a synthetic thread act as an electrochemically switchable molecular device?†

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Here we report that at room temperature in acetonitrile after the reduction of the naphthalimide-site, a synthetic molecular thread undergoes a complete conformational change which makes possible an efficient conversion of chemical energy into mechanical work; such results point out the ability of the thread to act as a molecular device under electrochemical control.

During the past few decades science has been trying to mimic nature, in particular its ability to efficiently transform chemical, electrical or photochemical energy into controllable mechanical work. Inspired by biological systems such as ATP synthase or myosin, synthetic molecular motors (or molecular machines) represent a very active and promising area of chemical and physical investigation.[1] The perception of molecular motors as simple mechanical systems such as springs or levers may in fact oversimplify our mental representation of these systems. Actually, all the experimental measurements usually take place in solution, at room temperature, and involve flexible molecules with a large number of internal degrees of freedom undergoing typical thermal fluctuations. Consequently, the basic feature molecular motors should possess is the possibility, upon some sort of chemical or photochemical transformation, of producing mechanical work *via* a few (even a single) internal degrees of freedom associated with large amplitude motions.

Theoretical/computational investigation may be of great help for this purpose. In this respect, there are two conceptually distinct approaches to the problem. The first one, extensively used in the past few years, is aimed at searching for a simplified but rigorous physico-mathematical model of molecular motors.[2] The alternative one, pointing toward a more generalized description, is based on atomistic simulations using molecular dynamics (MD) or Monte Carlo (MC) simulations.[3] The latter approach, however, may sometimes be complicated by the presence of different electronic states, conceivably involved because of chemical and/or photochemical triggering. For this reason an explicit treatment of electronic degrees of freedom cannot be excluded by the theoretical model, hence requiring the use of mixed quantum mechanics/molecular mechanics (QM/MM) methods. In the past few years we have proposed[4] and extensively applied[5] a theoretical/computational methodology, a perturbed matrix method (PMM), whose main aim is the possibility of incorporating electronic degrees of freedom into an efficient MD sampling. The effects of the classical environment on a region where the electronic wavefunctions are explicitly taken into account are included in a perturbed electronic Hamiltonian which is diagonalized at each MD step.

In this communication, PMM has been applied for characterizing, at an atomistic level, the synthetic molecular system **1**, shown in Fig. 1, consisting in a succinimide (succ) site and a 3,6-di-*tert*-butyl-1,8-naphthalimide (ni) site, separated by a C_{12} alkyl spacer. Such a molecule has been used in molecular machine experiments[6] as a potential thread in a fast and reversible hydrogen-bonded molecular shuttle. In the original experimental design a benzylic amide macrocycle, initially bound to the succ site, upon photoreduction of **1** is reversibly shifted toward the ni-site where the negative charge is located (see for example, molecular orbitals in Fig. 4),[6] producing mechanical work. Modelling the overall process, taking place on the microsecond time scale, is, realistically, far beyond the possibilities of a rigorous theoretical and computational approach. However, inspired by the above experiment, we have investigated for the first time the possibility of using only **1**, upon reduction, as a potential molecular machine schematically acting as shown in Scheme 1.

We have performed two MD simulations of 20 ns of **1** and $\mathbf{1}^-$ at 298 K in the canonical (NVT) ensemble in acetonitrile dilute solution.[7] In order to validate our procedure we reproduced the UV spectrum of $\mathbf{1}^-$ theoretically, in the range 350–470 nm corresponding to ni site excitations, to be compared with the experimental spectrum reported in the literature by Brouwer *et al.*[6] PMM calculations[13] were used for this purpose and the results are reported in Fig. 2. Taking as reference the gas-phase condition we observe that, although the electrostatic field plays a key role in fine-tuning the spectroscopic response of ni, it basically does not alter the position of the maximum ($\lambda_{\max}$ = 414 nm at the TD-PW91/

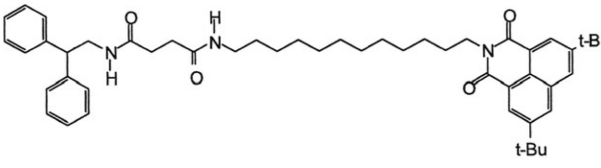

Fig. 1 Schematic view of **1**. The succ and ni sites are on the left and right side of the C_{12} alkyl spacer, respectively.

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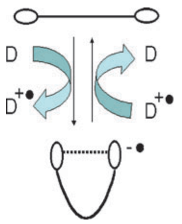
† Electronic supplementary information (ESI) available: Computational setup section, atomic point charges, molecular geometries, basic statistical mechanical relations for computing ΔA_{ox} and $\Delta A_{\mathrm{redox}}$. See DOI: 10.1039/b804031a



Scheme 1 D represents a generic electron donor/acceptor.

6-311++G(d,p) level, mainly a $^2\pi \rightarrow \pi^*$ character). The spectrum, *i.e.*, the absorption maximum and the shape of the signal derived from an overlap of two different electronic excitations is in excellent agreement with the experimental one (the maximum characteristic of ni in acetonitrile dilute solution is located at 415 nm, and the full width at half maximum (FWHM) is about 30 nm[6]) hence proving the good quality of the computational setup.

In order to analyze the mechanical properties of our system, we selected an internal degree of freedom as an indicator of the geometrical deformations of **1** upon reduction. The obvious choice was to follow the distance between the succ and ni geometrical centres, hereafter termed as $R_{\mathrm{s-n}}$. Conformational Helmholtz free energy (ΔA_{c}) was calculated as a function of $R_{\mathrm{s-n}}$ by using eqn (1):

$$\Delta A_{\mathrm{c}} = -k_{\mathrm{B}}T\ln\frac{\boldsymbol{\rho}(R_{\mathrm{s-n}})}{\boldsymbol{\rho}(R^*_{\mathrm{s-n}})} \qquad (1)$$

where $\boldsymbol{\rho}(R_{\mathrm{s-n}})$ represents the probability density of finding succ and ni geometrical centres at a distance $R_{\mathrm{s-n}}$ and $R^*_{\mathrm{s-n}}$ indicates the most probable value (defined as the equilibrium distance).

The resulting free energy curves for **1** and $\mathbf{1}^-$, reported in Fig. 3, and the structures corresponding to the free energy minima, also reported in Fig. 3, clearly indicate an elongation-like conformational transition of **1** upon redox reaction (note that we chose the $\mathbf{1}^-$ minimum as the reference free energy value, *i.e.*, the zero in the figure scale). In the current case, MD simulations suggest that the solution reaction guideline is essentially a simple and fast one step process in which the naphthalimide radical anion attacks the neutral succinimide substrate forming a strong hydrogen bonding network. It is interesting to note that $\mathbf{1}^-$ is characterized by a highly reduced conformational space, *i.e.* deep free energy minimum (see Fig. 3). On the other hand, the accessible conformational space of the oxidized species being larger than $\mathbf{1}^-$, characterizes the **1** molecular system as basically in an elongated configuration ($R^*_{\mathrm{s-n}} = 18.0 \pm 2.5$ Å at thermal energy). It must be also noted that the free energy curve of **1** was obtained *via* $\Delta A_{\mathbf{1}}(R_{\mathrm{s-n}}) = \Delta A_{\mathrm{ox}} + \Delta A_{\mathrm{c},\mathbf{1}}(R_{\mathrm{s-n}})$ where ΔA_{ox} corresponds to the vertical oxidation free energy indicated as a red dashed arrow in Fig. 3 and $\Delta A_{\mathrm{c},\mathbf{1}}(R_{\mathrm{s-n}})$ is the conformational free energy of the oxidized species.

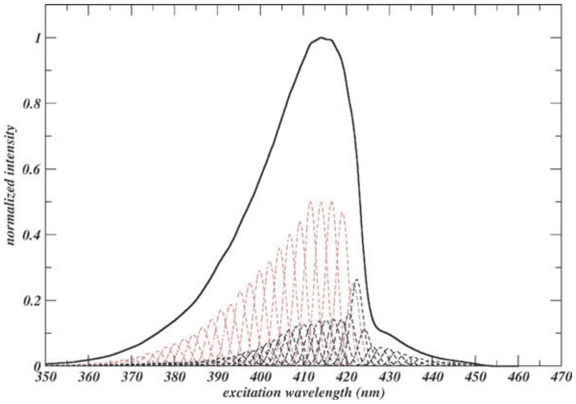


Fig. 2 Calculated (solid line), at the PMM/PW91/6-311++G(d,p) level of theory from an MD simulation in acetonitrile, UV spectrum of the $\mathbf{1}^-$ molecular system, in the range between 350–470 nm, generated by convoluting the PMM calculated spectra for the ground → 10th (black dashed lines) and ground → 11th (brown dashed lines) perturbed electronic transition (excluding quantum vibrational effects) with a Gaussian broadening function having a standard deviation of 3 nm; the experimental absorption maximum was found to be at 415 nm (see ref. 6).

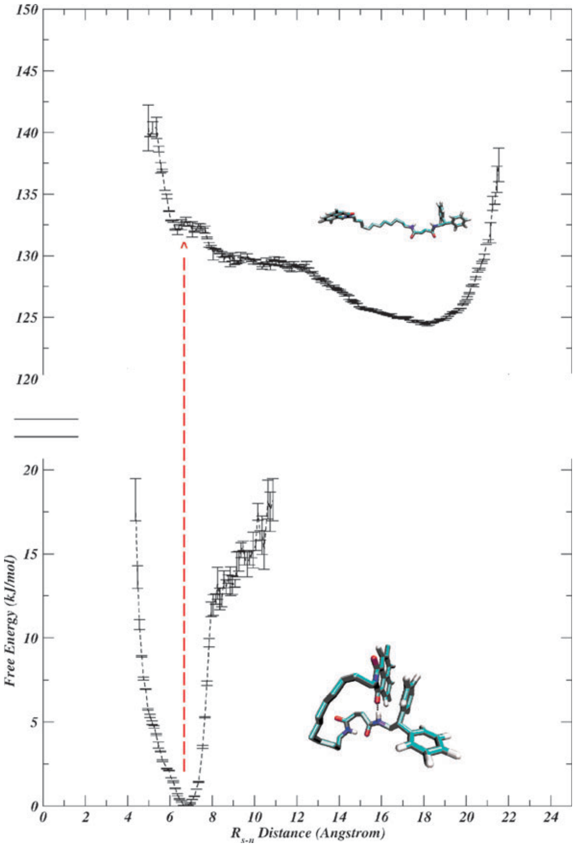


Fig. 3 298 K Helmholtz free energy as a function of $R_{\mathrm{s-n}}$ from eqn (1), see the ESI.† Structures schematically reported show the representative configurations of the two absolute free energy minima as obtained by means of classical MD sampling in dilute acetonitrile solution. ΔA_{ox} (red dashed arrow) indicates the reversible work for (vertically) removing an electron from $\mathbf{1}^-$ confined in its free energy minimum. It is worth noting that free energy profiles are calculated at the equilibrium conditions.

By means of PMM, with the same theoretical level as adopted for the UV spectrum, we evaluated the perturbed ground state electronic energy of $\mathbf{1}^-$ ($U_{\mathbf{1}-}$) and **1** ($U_{\mathbf{1}}$) within the $\mathbf{1}^-$ free energy minimum ensemble. The obtained perturbed electronic energies were then used for calculating ΔA_{ox},

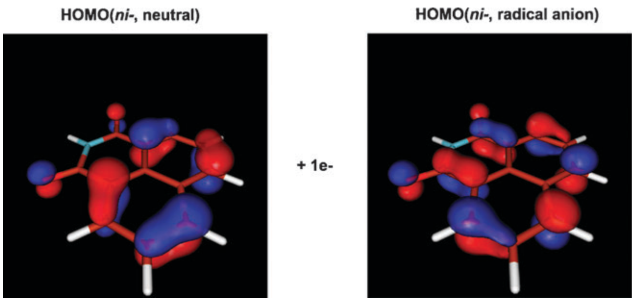


Fig. 4 Highest occupied molecular orbital, HOMO, for a neutral and radical anion 1,8-naphthalimide site at the PW91/6-311++G(d,p) level of theory, respectively; isodensity surfaces equal to 0.1 e Å^{-3}.

providing a value of 136.0 kJ mol^{-1}.† The overall free energy associated with the oxidation of **1**$^-$ ($\Delta A_{\mathrm{redox}}$) was finally calculated by using ΔA_{ox}, $\Delta A_{\mathrm{c},\mathbf{1}}(R_{\mathrm{s-n}})$ and $\Delta A_{\mathrm{c},\mathbf{1}^-}(R_{\mathrm{s-n}})$ in combination with basic statistical mechanics relations,† obtaining a value of 124.4 kJ mol^{-1} (in analogy with previous definitions, $\Delta A_{\mathrm{c},\mathbf{1}^-}(R_{\mathrm{s-n}})$ represents the conformational free energy of **1**$^-$). Such a value was then used to estimate the actual redox potential, *i.e.* reversible work of reduction, with respect to a ferrocenium/ferrocene (Fc$^+$/Fc) couple[15] to be compared with available cyclic voltammetry measurements. The obtained value of −1.71 V, in excellent agreement with experimental data (−1.70 V) for unbound ni in CH_3CN,[16] further confirms the reliability and accuracy of the overall theoretical and computational procedure and quantitatively shows the efficiency of the **1**/**1**$^-$ system to act as a sort of molecular machine of potential great interest in nanotechnology.

Summarizing, here we report results of a statistical mechanics based approach, showing that a recently proposed synthetic molecular thread for hydrogen-bonded molecular shuttles may efficiently convert chemical into mechanical energy. The evidenced intimate correlation between the oxidation state and the conformational transitions points out the subtle coupling between chemical/electronic states (see Fig. 4) and conformational fluctuations. Finally, our theoretical/computational study shows for the first time that the succ–[C_{12} alkyl spacer]–ni system might be an interesting example of an electrochemically switchable molecular device that undergoes a reversible conformational change in response to external stimuli (*i.e.*, oxidation–reduction of the 3,6-di-*tert*-butyl-1,8-naphthalimide station, ni).

However, it must be also remarked that dynamical and dissipative processes, occurring upon electron transfer from the donor to the acceptor, should be included to characterize the kinetics of the process. In this study we do not address such an issue as we describe the thermodynamics of the electrochemical–mechanical switching. Moreover, our data suggest that during the proposed[6] shuttling process of the benzylic amide macrocycle, the succ–[C_{12} alkyl spacer]–ni molecular thread conformational transition may also be somewhat involved in the mechanism determining the spectroscopic transitions experimentally observed.[6]

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