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Photoinduction of Fast, Reversible, Translational Motion in a Hydrogen-Bonded Molecular Shuttle

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Experimental Details for the Synthesis of Molecular Shuttle, 1

[2]-(1,4,7,14,17,20-hexaaza-2,6,15,19-tetraoxo-3,5,9,12,16,18,22,25-tetrabenzocyclohexacosane)-(N\textsuperscript{1} [12-[5,8-di(tert-butyl)-1,3-dioxo-1H-benzo[de]isoquinolin-2(3H)-yl)dodecyl]-N\textsuperscript{4}-(2,2-diphenylethyl)succinamide)-rotaxane (I).

The thread 2 (0.30 g, 0.39 mmol) and triethylamine (2 mL, 15.1 mmol) were dissolved in chloroform\textsuperscript{1} (50 mL), and stirred vigorously whilst solutions of the diamine (7.76 mmol) in chloroform\textsuperscript{1}(40 mL) and the diacid chloride (7.76 mmol) in chloroform\textsuperscript{1} (40 mL) were simultaneously added over a period of 4 hours using motor-driven syringe pumps. The resulting suspension was filtered and concentrated under reduced pressure to afford the crude product. This solution was passed through a pad of silica gel (CHCl\textsubscript{3}) to remove polar impurities to afford a mixture of thread 2 and rotaxane I. The rotaxane was then isolated by trituration with hot diethyl ether. Yield 0.30 g (59%); m.p. 223°C; \textsuperscript{1}H NMR (400 MHz, CD\textsubscript{3}CN at 56°C) \(\delta = 1.10\) (s, 4 H, NHCH\textsubscript{2}CH\textsubscript{2}NH), 1.20-1.45 (m, 18 H, CH\textsubscript{2}), 1.53 (s, 18 H, C(CH\textsubscript{3})\textsubscript{3}), 1.71 (m, \(J = 7.5\) Hz, 2 H, NCH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}), 2.96 (dd, \(J = 6.0\) Hz, \(J = 6.8\) Hz, 2 H, CONHCH\textsubscript{2}CH\textsubscript{2}), 3.70 (dd, \(J = 5.6\) Hz, \(J = 7.9\) Hz, 2 H, CHCH\textsubscript{2}NH), 4.09-4.16 (m, 3 H, CH+CH\textsubscript{2}CH\textsubscript{2}CH\textsubscript{2}N), 4.49 (m, \(J = 5.5\) Hz, \(J = 14.3\) Hz, 8 H, H\textsubscript{E+e}), 6.42 (br, 1 H, NHCH\textsubscript{2}CH\textsubscript{2}), 6.47 (br, 1 H, CHCH\textsubscript{2}NH), 7.12 (s, 8 H, H\textsubscript{F}), 7.20-7.35 (m, 10 H, Ph), 7.64 (t, \(J = 7.9\) Hz, 2 H, H\textsubscript{A}), 7.71 (t, \(J = 5.5\) Hz, 4 H, H\textsubscript{D}), 8.16 (dd, \(J = 1.8\) Hz, \(J = 7.9\) Hz, 4 H, H\textsubscript{B}), 8.34 (d, \(J = 1.8\) Hz, 2 H, ArH), 8.54 (t, \(J = 1.8\) Hz, 2 H, H\textsubscript{C}), 8.64 (d, \(J = 1.8\) Hz, 2 H, ArH); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta = 27.32, 27.54, 28.57, 29.64, .29.73, 29.82, 29.91, 30.01, 31.32, 31.61, 35.69, 40.28, 40.83, 44.09, 44.34, 44.64, 50.91, 122.52, 124.36, 125.27, 127.59, 128.23, 128.78, 129.31, 129.51, 129.62, 131.96, 132.31, 132.42, 134.27, 138.18, 141.89, 150.67, 165.11, 166.85, 173.17, 173.37; FAB-MS (mNBA matrix): m/z 1306 [(rotaxane+H)+]; 535 [(macrocycle+H)+]; anal. calcd for C\textsubscript{82}H\textsubscript{93}N\textsubscript{7}O\textsubscript{8}: C 75.49, H 7.18, N 7.52; found C 75.22, H 7.33, N 7.42.
Footnotes

(1) Chloroform was stabilized with amylenes, not ethanol.

(2) For solubility reasons the spectrum was acquired above room temperature.
X-Ray Crystal Structure of a Model Rotaxane with the Succinamide Hydrogen Bonding Motif.
Cyclic voltammetry of the Thread (2, dashed line) and Shuttle (1, solid line) showing Electrochemical-induced Shuttling in DMF.

The effect of rotaxane formation on the redox properties of the naphthalimide moiety in DMF at 298K is shown above (1.0 mM substrate concentration, 0.05 M tetrabuthylammonium hexafluorophosphate (TBAH) DMF solutions. T = 25 °C, scan rate = 1.0 V/s, working electrode: platinum wire. A silver wire was used as quasi-reference electrode in a single compartment cell. Potentials were measured with respect ferrocene as internal standard). The one-electron reversible reduction observed in 2, with \( E_{1/2} = -1.61 \) V, corresponds to the conversion of naphthalimide to its radical anion. Significantly in 1, (i) the corresponding process (peak I) is shifted to less negative potentials, (ii) peak I lacks its reversible anodic counterpart (i.e. an oxidation peak within 60 mV), while (iii) an oxidation peak (A) is observed at much less negative potentials (\( \Delta E_p = 480 \) mV). Peak A is also irreversible, as observed in successive scans (not shown above), performed without renewal of the diffusion.
layer, where the CV pattern consistently remains the same. This behavior suggests the conversion of pristine \textbf{I}, after reduction \textbf{I}, to a novel species, which is oxidised in \textbf{A}, and that, after the oxidation, regenerates \textbf{I} (i.e. a \textit{square mechanism}). As expected for this mechanism, a change of scan rate results in a shift of both peaks \textbf{I} and \textbf{A}: as the scan rate is increased (between 20 mV/s and 2 kV/s), peak \textbf{I} becomes more negative (slope: ca. 30 mV/decade), and, at the same time, peak \textbf{A} becomes more positive (slope: ca. 60 mV/decade). At any scan rate (up to 10 kV/s), neither \textbf{I} nor \textbf{A} showed their respective reversible partner, suggesting that the follow-up reactions, responsible for the irreversible CV behavior, are very fast.

Hydrogen bonding of the benzylic amide macrocycle to the reduced naphthalimide moiety explains the features of the CV curve. After reduction, the macrocycle shuttles from the succinamide station to the naphthalimide group. Hydrogen-bonding stabilizes the radical anion resulting in the observed shift in the reoxidation peak. On the other hand, reoxidation regenerates the starting conditions and macrocycle therefore shuttles back to its original position.

The thermodynamic cycle from the CV studies is (energies in kcal/mol):

\[
\begin{align*}
\text{(i) } & \quad G = 0 \\
\text{(ii) } & \quad G = 0 \\
\text{\quad } & \quad G = -4.3 \\
\text{\quad } & \quad G = 0 \\
\text{(iii) } & \quad G = -4.3 \\
\text{(iv) } & \quad G = 0 \\
\end{align*}
\]

\[\begin{align*}
^{2}G & = -6.9 \\
^{2}G & = +11.2 \\
^{2}G & = -6.9
\end{align*}\]

The ••G between (i) and (ii) is arbitrarily set to 0; the energy needed to oxidize (“oxidation potential”) for \textbf{n} when rotaxanated (iii) \rightarrow (iv) is 11.2 kcal/mol larger (more positive) than
the energy needed to oxidize $n_i^-$ when it is “free”. Thus, the sum of the $\Delta G$’s along the horizontal arrows is $-11.2$ kcal/mol.
The intensity of the naphthalimide radical anion absorption peak (~416 nm) of 1 before and following the laser pulse at time = zero. The nonexponential decay of the signal is typical of a bimolecular recombination reaction. Rate (k) = 9 \times 10^9 \text{ M}^{-1}\text{s}^{-1}. Under the experimental conditions used, after 100 \mu s >70% of the rotaxanes have been reoxidized (i.e. the macrocycle has shuttled back to the succinamide site).
Determination of the Quantum Yield of Light-induced Shuttling in Molecular Shuttle 1.

The quantum yield of radical ion formation ($\Phi_{ri}$) was determined by measuring the absorption of the naphthalimide radical ($A_{ri}$) directly after the laser pulse and comparing this to the absorption maximum of triplet benzophenone in benzene ($A_{BP}$), generated by excitation with an equally intense laser pulse. Since both the molar absorption coefficient of n$i·$ ($\varepsilon_{ni} = 23550$ M$^{-1}$cm$^{-1}$)[S. Van Dijk et al., J. Am. Chem. Soc. 118, 8425-8432 (1996)] and $^3$BP* ($\varepsilon_{BP} = 7220$ M$^{-1}$cm$^{-1}$)[I. Carmichael, et al., J. Phys. Chem. Ref. Data 15, 1-250 (1986)] at their maximum are known, $\Phi_{ri}$ can be calculated using,

$$\Phi_{ri} = \frac{1 - T_{BP}^x A_{ni}/\varepsilon_{ni}}{1 - T_{ni}^x A_{BP}/\varepsilon_{BP}}$$

Where $T_{BP}^x$ and $T_{ni}^x$ are the ground state transmittance of BP and $ni$ at the excitation wavelength (355 nm). For a $5 \times 10^{-5}$ M solution of 1 in MeCN in the presence of 10 mM DABCO, this yielded a quantum yield of radical anions of 0.20. This value is dependent of donor concentration, but can serve as a typical value of $\Phi_{ri}$ and can be used to estimate the efficiency of the switching process.

Knowing the yield of radical anions, the percentage of this that shuttles needs to be determined in order to obtain an estimate of the efficiency of the complete switching process. The naphthalimide radical anion in the rotaxane is formed when it resides mainly in the succ-$i$-$1·$ co-conformation. Shuttling of the macrocycle to form the $ni$-$1·$ co-conformation ($k_{shift}$) then competes with back electron transfer to donor radical cations ($k_{bet}$). These processes are a combination of first and second order reactions, hence the kinetic scheme cannot be solved analytically. Therefore, to determine the yield of $ni$-$1·$, a numerical solution was sought using Chemical Kinetics Simulator,[W. Hinsberg, et al. (IBM, Almaden Research Center, 1996)] a computer program that uses a stochastic method, based on reaction probabilities, to calculate the time history of a chemical system using the reaction’s mechanism and the initial conditions specified.

As shown in the figure below, shuttling is fast compared to recombination of the radical anion. The quantum yield of shuttling ($\Phi_{shift}$) is given by the ratio between the area under the $ni$-$1·$ decay curve and the total decay area. Using the experimentally found rates in MeCN, $\Phi_{shift} = 0.999$ is found. Thus the efficiency of the overall switching process is only limited by the yield of radical anions, $\Phi_{ri} = 0.20$. The only previously reported example of a quantum yield of light-induced shuttling is 0.03 [Amaroli et al, J Am Chem Soc, 121, 4397 (1999)]
(1) succ-1$^- \rightarrow$ ni-1$^-$
(2) succ-1$^- + D^+ \rightarrow$ succ-1 + D
(3) ni-1$^- + D^+ \rightarrow$ ni-1 + D

$k_{\text{in}} = 1.35 \times 10^6 \text{ s}^{-1}$
$k_{\text{out}} = 9 \times 10^7 \text{ M} \text{s}^{-1}$
$k_{\text{out}} = 9 \times 10^7 \text{ M} \text{s}^{-1}$

$[\text{succ-1}^-] = [\text{D}^+] = 1.5 \times 10^4 \text{ M}$

Simulation of the shuttling process in reduced 1, using the kinetic scheme and reaction conditions shown below the graph. The calculated radical anion decay (continuous) is the sum of the contributions of succ-$1^-$ (dotted) and ni-$1^-$ (dashed) co-conformers.
Evidence for Shuttling as opposed to Folding mechanism

A combination of arguments shows that the observed effects in the transient absorption spectrum of 1⁺ (shown as Fig 4b and 5a in the manuscript) cannot be due to a simple folding mechanism without macrocycle shuttling occurring (Scheme I).

(i) If only one or two intercomponent hydrogen bonds produce the shifts seen in the CV and absorption spectra of 1, a similar process could take place in the thread (2) using the succinamide amide groups as hydrogen bond donors, but it evidently does not (See Fig. 4a, 5b).

(ii) Electrochemical reduction of 1 shows the hydrogen bond stabilization of the ni⁺ station is very large, 0.48 V, \textit{i.e.} 11.2 kcalmol⁻¹, the equivalent of three or four strong hydrogen bonds (OCNH...O=CNR hydrogen bond strengths are in the range 2-5 kcalmol⁻¹ (ref 12 in manuscript)).

Three H-bonds to a ni⁻ unit cause a stabilization of ∼0.2 V in host-guest complexes of the type shown on the left [\textit{JACS} 1997, \textbf{119}, 10863 and \textit{JACS} 1996, \textbf{118}, 3976] \textit{cf} the 0.48 V stabilization.
seen in rotaxane 1. Although the arylamide H-bond donors in the host-guest complexes are slightly weaker H-bond donors than the alkylamides of the macrocycle in 1, at least three (and most probably four) strong hydrogen bonds must be responsible for the 0.48 V stabilization seen in 1.

(iii) Extensive molecular modeling studies (Amber forcefield) show that folded co-conformers (such as those shown in Scheme I) can only be hydrogen bonded by one or two hydrogen bonds from the macrocycle to the ni•• unit because of geometrical constraints. (Even then, molecular dynamics simulations shows that this is an unfavorable geometry and the macrocycle shuttles down the thread to form multipoint H-bonds to the ni-station)

(iv) the same CV and photoreduction optical responses occur with a modified version of 1 where the succinamide amide groups are both methylated (3), demonstrating that all the hydrogen bonds to the ni•• station in the photoreduced rotaxane must come from the macrocycle not the succinamide unit.

Again the only way three or four strong H-bonds can be formed between the ni-station and macrocycle is for shuttling to occur.

(v) a shorter (C₂ instead of C₁₂ spacer, i.e. 4) version of 1 which certainly cannot form three or four H-bonds from the macrocycle to the ni station by folding also shows the same optical shifts and CV behavior as 1, but over a much shorter timescale (reflecting the shorter distance required for the macrocycle to shuttle).
(vi) the dynamics of the solvent effect observed for 1 and 3 (4 is too fast to measure in all solvents), i.e. that polar solvents increase the speed of the process (see Fig. 6a), indicates that breaking of hydrogen bonds is the rate-limiting step, not the formation of hydrogen bonds which one might expect in a folding mechanism.

(vii) it is known that alkyl chains fold some two orders of magnitude faster than the dynamics observed here [J Phys Chem B, 1999, 103, 9356] plus (viii) folding a long alkyl chain is entropically unfavorable and cyclic hydrogen bonding arrangements are known to be unfavorable for large rings of the type that would be formed here if folding was occurring [JACS, 1991, 113, 1164].

(ix) the energy barrier determined for the photo-shuttling process ($\Delta G^\ddagger = 10.2\pm0.7$ kcal/mol at 298K) is consistent with the known energy barrier for shuttling between two degenerate stations in similar molecular shuttles (refs 4,15 in manuscript).

(x) given that folding cannot account for the multipoint hydrogen bonding that stabilizes the reduced $ni$ unit in 1, then the only alternative process occurring in these molecules must be shuttling. Naturally, we do not exclude the possibility that in some of these systems to some degree the succinamide groups might fold and hydrogen bond to the macrocycle on the $ni^*$ station (e.g. co-conformer "folded" $ni^*$-1), but we have no evidence to support it (and it cannot occur in rotaxane 3, for example).
Correlation between shift in $\lambda_{\text{max}}$ and rate of photoinduced shuttling

Following Scheme 2, when the rotaxane is reduced a new equilibrium, characterized by the equilibrium constant ($K_{\text{red}}$), has to set in with a typical time constant $\tau_{\text{shift}}$. The populations $p(t)$ of free and complexed naphthalimide radical anion (Equation 1) are a function of $\tau_{\text{shift}}$ and the new equilibrium constant $K_{\text{red}}$ as long as the radical anions recombine much more slowly than $\tau_{\text{shift}}$ and the difference for the recombination rate between complexed and free radical anions is negligible.

$$
\begin{align*}
    p_{\text{complex}}(t) &= \frac{K_{\text{red}}}{1 + K_{\text{red}}} \left( 1 - e^{-t/\tau_{\text{shift}}} \right) \\
    p_{\text{free}}(t) &= \frac{1}{1 + K_{\text{red}}} \left( 1 + K_{\text{red}} e^{-t/\tau_{\text{shift}}} \right)
\end{align*}
$$

(Eq 1)

If we call the functions describing the two absorption spectra $s_{\text{complex}}(\lambda)$ and $s_{\text{free}}(\lambda)$, the complete translational process is described as:

$$
T(\lambda,t) = s_{\text{free}}(\lambda)p_{\text{free}}(t) + s_{\text{complex}}(\lambda)p_{\text{complex}}(t)
$$

(Eq 2)
Unfortunately, the transient absorption spectra are too complicated to obtain the spectra and time profiles directly, using e.g. Singular Value Decomposition or global fitting. Instead, we decided to look at one parameter of the absorption spectra, which is easily obtained experimentally: the absorption maximum of the radical anion ($\lambda_{max}$).

The task now is to obtain this parameter out of $T(\lambda,t)$ as a function of time. In order to do so we have to simplify the problem. The absorption spectra of complexed and free naphthalimide radical anion can be described by a gaussian function, called $g(\lambda)$. This is a reasonable approximation as can be seen in Figure 1. We furthermore assume that $g_{free}(\lambda)$ and $g_{complex}(\lambda)$ have the same fwhm and molar absorption, so they differ only in the location of their maximum.

![Figure 1](image1.png)

**Figure 1.** A trace from a typical transient absorption spectrum, showing the characteristic naphthalimide radical anion absorption peak (dotted), together with a gaussian fit (continuous line).

To determine the maximum of a linear combination of two displaced gaussians is not trivial, but we need only to consider the situation where the two bands coalesce. Coalescence will occur when the displacement $|\Delta \lambda|$ is smaller than $2\sigma$, as is shown in Figure 2. In our case, the fwhm of the radical anion absorption is approximately 25 nm, which corresponds to $\sigma \approx 11$ nm. A typical shift of the absorption maximum is 5 nm, which is well under $2\sigma$, so we only need to consider the coalescent case.

![Figure 2](image2.png)

**Figure 2.** An example, showing that two gaussian curves of equal width and height
will coalesce when they are displaced by less than $2\sigma$

We now need to find the maximum of a linear combination $\Psi$ of these two displaced gaussians (Equation 3).

$$\Psi(\lambda,t) = c_1(t)g(\lambda) + c_2(t)g(\lambda - \Delta\lambda)$$

(Eq 3)

The derivative, however, is a complicated function, which is not easily solved to find the maximum. Therefore, a simulation was done: $c_1$ and $c_2$ were varied linearly as:

$$c_1 = t$$
$$c_2 = 1 - t \quad 0 \leq t \leq 1$$

(Eq 4)

Then, on each $t$, the peak maximum was determined. This was repeated for several displacements $\Delta\lambda$ (Figure 3).

Figure 3. *The variation of the peak maximum, when $t$ is varied linearly (Equation 4) for different ratios $\Delta\lambda / \sigma$*

As is evident from Figure 3, the peak maximum does not vary linearly with $t$. The deviation from linearity however becomes negligible when the ratio $\Delta\lambda / \sigma$ decreases. In our experiments $\Delta\lambda / \sigma < 0.5$, so the approximation that the peak maximum varies linearly with $t$ is justified.

Indeed, if we substitute $c_1$ and $c_2$ for the more realistic time profiles from Equation 1, and use experimental values for $\Delta\lambda$ and $\sigma$, we observe a curve for the change in the peak maximum that is almost indistinguishable from the shift profile $p_{\text{complex}}$ (Figure 4). So as long as $\Delta\lambda / \sigma$ is small, the change in the peak maximum represents the change in relative population of free naphthalimide radical anion.
Figure 4. The populations $p$ of free (continuous) and complexed (dashed) compound as function of time (Equation 1) against the left axis for different values of $K_{red}$. The corresponding shift of the absorption maximum (circles) is plotted against the right axis. Parameters: fwhm = 25 nm, $\Delta \lambda = 6$ nm, $\tau_{shift}$.