such as that offered in Fig. 6 provide one starting place for evaluation. Synthesis of optically enriched biaryl compounds using enantioselective catalysts and dynamic kinetic resolution should enable improved access to stereodefined atropisomeric materials. More broadly, the approach described herein may also stimulate related research involving selective reactions of other interconverting, axially chiral compounds, promoted by simple peptide-based catalysts.

References and Notes
30. Experimental procedures and compound characterization are available as supporting material on Science Online.
36. We are grateful to the National Institute of General Medical Sciences of the NIH for support (GM068649). Metrical parameters for the solid state structure of compound 3d are available free of charge from the Cambridge Crystallographic Data Centre under CCDC-773872.
37. Supporting Online Material
www.sciencemag.org/cgi/content/full/328/5983/1251/DC1 Materials and Methods
Figs. S1 to S4
Tables S1 to S10
References and Notes
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Operation Mechanism of a Molecular Machine Revealed Using Time-Resolved Vibrational Spectroscopy
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Rotaxanes comprise macrocycles that can shuttle between docking stations along an axle. We explored the nanosecond shuttling mechanism by reversing the relative binding affinities of two stations through ultraviolet-induced transient reduction. We monitored the ensuing changes in the CO-stretching bands of the two stations and the shuttling macrocycle by means of an infrared probing pulse. Because hydrogen-bond scission and formation at the initial and final stations CO-stretching bands of the two stations and the shuttling macrocycle by means of an infrared pump-probe experiments on a light-triggered rotaxane shuttle to unravel its operating mechanism. Rotaxanes consist of mechanically interlocked wheel- and axle-like components. Figure 1 shows the chemical structure of this type of molecular machine, together with its operation cycle, which we characterized previously with spectroelectrochemistry and transient ultraviolet-visible (UV-Vis) spectroscopy (3, 19). In the neutral molecule, the macrocycle is hydrogen-bonded predominantly (~99%) to the succinimide station (supec) (3, 19). After excitation of the naphthalimide station (ni) with a 355-nm light pulse, the rotaxane undergoes rapid (~1.6 ns) intersystem crossing to the triplet state (20). In this state, the ni station is reduced by an external electron donor to form a radical anion (ni−). The ni− station has a much greater affinity for the macrocycle than does the supec station [equilibrium constant (>1000) (3)]. Consequently, the macrocycle shuttles over the thread and forms hydrogen bonds to the ni− station. After slow (~100 µs) charge recombination between ni− and the radical cation of the electron donor, the macrocycle travels back over the thread and binds to the supec station, and the system is ready to shuttle again (3). In the following, rotaxanes with track length n are referred to as Cnp.

The vibrational absorption spectrum of the C12 rotaxane in its initial state is shown in Fig. 2A. All peaks in the rotaxane spectrum can be assigned by comparison with spectra of the constituent components (19). The symmetric and antisymmetric CO-stretch modes of the ni station are observed as peaks 1 and 7, respectively (the latter also contains a contribution from the CO-stretch vibration

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of the macrocycle), and the CO-stretch mode of the succ station is observed as peak 5.

In the time-resolved experiments, we trigger the rotaxane with a 4-ns, 355-nm pulse and observe the subsequent vibrational absorption change by means of a 100-fs mid-infrared (IR) probe pulse (21, 22). In Fig. 2, B and C, we show normalized (19, 21) UV-IR transient spectra of the C12 rotaxane at different delay times. The spectra at early delays (<120 ns) show how the triplet state evolves to the radical anion state (ni−). Subsequently, the spectrum evolves further as the macrocycle shuttles from the succ to the ni− station (Fig. 2C). For the assignment of the peaks in Fig. 2C we use steady-state spectra of the initial, charged, and final states (19). Peaks 2 and 3 (labeled ARRIVAL) are the CO-stretch modes of the ni− station when it is free and when it is hydrogen-bonded to the macrocycle, respectively. The temporal evolution of these peaks therefore directly mirrors the arrival of the macrocycle at the ni− station. Similarly, peaks 4 and 5 (labeled DEPARTURE) are the CO-stretch modes of the succ station when free and when hydrogen-bonded to the macrocycle. The behavior of these two peaks therefore mirrors the departure of the macrocycle from the succ station. Peak 6 is due to the CO-stretch mode of the macrocycle when its NH groups are hydrogen-bonded to the macrocycle, respectively. The corresponding absorption decrease of the CO-stretch mode of succ-bound macrocycles as they leave the succ station is superimposed on (temporally static) peak 7.

The time evolution of the intensity of peaks 2, 3, 4, 5, and 6 is shown in Fig. 3. We find that the departure and arrival of the macrocycle can be well described with the same time constant. We performed a global least-squares fit to the data (21), in which the charging and shuttling are each described by a single rate constant. From the fit (see curves in Fig. 3) we obtain 〈kcharge〉 = 2.8 (±0.4) × 106 s−1, which corresponds to the charging lifetime of 35 ± 5 ns. We find that for the C12 rotaxane, 〈kcharge〉 = 1.30 (±0.03) × 106 s−1; this shuttling rate constant corresponds to a shuttling time of 0.77 ± 0.02 μs, in agreement with previous UV-Vis experiments (3).

The fact that the departure and arrival exhibit the same dynamics implies that during the shuttling process, an individual macrocycle spends only a short time on the thread relative to the average shuttling time of the ensemble. The observed average shuttling time is therefore not determined by the time the macrocycle spends on the CH2 chain, but rather by the time it takes for the macrocycle to escape from the initial station. The sequence of events in the shuttling of this rotaxane is thus as follows: occasional escape from the succ station, followed by a rapid motion over the thread, ending at either the ni− (where it can no longer escape because of the stronger hydrogen bonding) or the initial succ station (where it will wait until the next escape). Below, we investigate the two steps of this mechanism in more detail.

To quantify the energy barrier that the macrocycle must overcome to escape from the succ station, we measured the shuttling rate of a C9 rotaxane (23) over a temperature range of 45 K (21). The temperature increase due to the partial conversion of the pump energy into heat is negligible (21). The temperature dependence of kexp displays Arrhenius behavior, indicating that the escape from the succ station is effectively a single-barrier event and that the energy required by the macrocycle to cross it is provided by thermal fluctuations. We find that the data can be well described with the Eyring equation,

$$k_T = \frac{k_0 T}{h} \exp \left[ -\frac{(\Delta G^t)^2}{RT} \right]$$    \[(1)\]

where \(k_0\) is the Boltzmann factor, R is the gas constant, h is the Planck constant, \(\Delta G^t\) is the Gibbs free energy of activation, and T is the absolute temperature of the system. From a least-squares fit (fig. S5), we find that the enthalpy of activation \(\Delta H^t\) is 26 (±1) kJ mol−1 and the entropy of activation \(\Delta S^t\) is −32 (±3) J mol−1 K−1. The energy barrier \(\Delta H^t\) is consistent with the breaking of approximately four hydrogen bonds, assuming a binding energy of −7.5 (±0.8) kJ mol−1 per hydrogen bond (24).

The negative activation entropy suggests that some ordering of the system is required for escaping from the succ station. Folding of the thread onto itself can be excluded, as this should be evident in the ni− and/or ni+− CO-stretch response in the transient spectra (19). The ordering might involve a relative positioning of macrocycle and thread that is favorable for breaking the macrocycle-succ hydrogen bonds.

The next step in the shuttling process is the fast motion of the macrocycle over the thread, ending at either the succ station or the ni− station. To investigate the nature of this fast motion, we explored how changing the carbon-chain length affects the probability of the macrocycle ending at the ni− station. This probability is proportional to the observed shuttling rate, as the rate at which escape from the succ station occurs is independent of the carbon-chain length. The shuttling rates of rotaxanes with thread lengths \(n = 5, 9, 12, 16\) are shown in Fig. 4. The rate of shuttling was observed to decrease markedly with increasing thread length. We analyzed the data by modeling the motion of the macrocycle over the thread as a one-dimensional random walk. In the simplest version of this model, the C9 chain is modeled as a track of \(n\) local free-energy minima, between which the macrocycle makes random jumps, to end up at either the ni− or succ station. If we assume equal probabilities for the macrocycle to make one step toward

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**Fig. 1.** Chemical structures of the [2]rotaxane shuttle in the neutral, radical anion, and shuttled radical anion states. 1,4-Diazabicyclo[2.2.2]octane (DABCO) was used as the external electron donor. We studied derivatives with different track lengths \(n\). The labeled CO groups correspond to the labeled peaks in Fig. 2. Ph, phenyl; Bu, butyl.
either station, the probability of the macrocycle arriving at the ni\textsuperscript{−} station is given by

\[ P_s(n) = \frac{1}{n+1} \quad (2) \]

A least-squares fit of the rate data to this equation, with the proportionality factor between the observed rate constant and \( P_s(n) \) as the only fit parameter, is shown as the gray dashed curve in Fig. 4. Although the model reproduces the observed trend, the quantitative agreement is poor. Allowing for a certain number of CH\textsubscript{2} units to be occupied by the macrocycle (25) still results in a poor description of the data (21).

We find that very good agreement is obtained by introducing a small bias in the probabilities of making a step in the forward or backward direction. Assuming a probability \( p \) of hopping forward (in the direction of the ni\textsuperscript{−} station), and \( 1 - p \) of hopping backward, the probability of arriving at the ni\textsuperscript{−} station becomes

\[ P_s(n) = \frac{1 - p}{1 - (1 - p)^{n+1}} \quad (3) \]

From a least-squares fit (with \( p \) and an overall scaling factor as the only fit parameters), we find that the best description of the data is obtained for \( p = 0.442 \pm 0.003 \) (red curve in Fig. 4). This value of \( p \) implies that the event of the macrocycle moving one step toward the ni\textsuperscript{−} station is slightly less probable than the event of it moving toward the succ station (\( 1 - p = 0.56 \)); that is, the random translational motion of the macrocycle along the track has a small bias toward the succ station. At present, we can only speculate as to the driving force behind this bias. An enthalpic driving force seems improbable in view of the short-range nature of the hydrogen-bond interactions that give rise to the overall }\Delta H of the shuttling. It is more likely that the bias is mainly of entropic origin. This could be the case if the thread conformation is on average slightly more favorable to macrocycle translation at the succ side than at the ni\textsuperscript{−} side. Interestingly, the overall motion of the macrocycle from succ to ni\textsuperscript{−} occurs against the bias (which is toward the succ station). This is possible only because there is a global free-energy minimum at the ni\textsuperscript{−} station.

Our findings can be summarized by combining Eqs. 1 and 3 to obtain an expression for the shuttling rate as a function of temperature and track length:

\[ k_s(T,n) \propto \frac{k_B T}{h} \exp \left[ -\frac{\Delta G_1^b}{RT} \right] P_s(n) \quad (4) \]

Each term describes one stage of the shuttling mechanism (Fig. 4, inset). The probability \( P_s(n) \) for the random walk to end at the final station is \( << 1 \) [for the shortest shuttle, \( P_s(5) = 0.09 \); for the longest, \( P_s(16) = 0.005 \)], so that many escapes (tens to hundreds) of the macrocycle from the initial station are required before a successful shuttling event occurs. This leads to a certain amount of randomness in the timing of the arrival of the shuttle.

A more detailed understanding of the bias against shuttling requires an exploration of the rotaxane’s free-energy landscape using molecular dynamics simulations. Because shuttling is such a rare event, this will require state-of-the-art simulation methods, and we hope that our results will stimulate work in this direction. On a more fundamental level, it is noteworthy that the
The Thermodynamics of the Elusive HO$_3$ Radical

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The role of HO$_3$ as a temporary reservoir of atmospheric OH radicals remains an open question largely because of the considerable uncertainty in the value of the dissociation energy of the HO–O$_2$ bond ($D_{0}$) or, equivalently, the standard enthalpy of formation of HO$_3$ ($\Delta H^\circ$). Using a supersonic flow apparatus, we have observed by means of laser-induced fluorescence the decay of OH radicals in the presence of O$_2$ at temperatures between 55.7 and 110.8 kelvin (K). Between 87.4 and 99.8 K, the OH concentration approached a nonzero value at long times, allowing equilibrium constants for the reaction with O$_2$ to be calculated. Using expressions for the equilibrium constant from classical and statistical thermodynamics, and values of partition functions and standard entropies calculated from spectroscopic data, we derived values of $D_{0} = (12.3 \pm 0.3)$ kilojoules per mole and $\Delta H^\circ$ (298 K) = (19.3 ± 0.5) kilojoules per mole. The atmospheric implications of HO$_3$ formation are therefore very slight.

The weakly bound HO$_3$ radical has been postulated as a transient intermediate in three processes of importance in the Earth’s atmosphere (Scheme 1, reactions R1 to R3). Sridharan et al. (1) showed that when $^{18}$O was used as the atomic reactant in the rapid reaction R1 with HO$_2$, the hydroxyl product was exclusively $^{16}$OH, suggesting that the reaction occurred not through H-atom abstraction but rather via transient formation of HO$_2$O$^{16}$O. Vibrationally excited OH formed in reaction R2 is the source of the Meinel bands emitted from the upper atmosphere (2). The reaction leads to high yields of the OH product in the highest energetically accessible vibrational levels $v = 7$ to $9$ ($3$, $4$), indicating energy release on a highly attractive potential energy surface (5), which would be the form expected if HO$_3$ is weakly bound relative to OH + O$_2$ (4). A third process—the relaxation of the OH product in the highest energetically accessible vibrational levels $v = 7$ to $9$ ($3$, $4$), indicating energy release on a highly attractive potential energy surface (5), which would be the form expected if HO$_3$ is weakly bound relative to OH + O$_2$ (4). A third process—a third process—a third process—a third process.