

Redox-Controlled Molecular Flipper Based on a Chiral Cu Complex

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A molecular bipaddled flipper based on a tetradentate chiral Cu complex has been designed. The paddling motion of this unprecedented molecular-scale machine can be controlled by reversible oxidation of the metal center. Kinetic and computational (density functional theory) analyses provide a detailed picture of the flipper motion at the molecular scale, rationalize the switching role of the metal-ion oxidation state, and pose the basis for the fine-tuning of the dynamic motion of this new class of molecular-scale devices.

Molecular machines can transfer energy, motion, or forces at molecular scale, and their design constitutes a major goal in modern science and technology.¹ The design of these engines relies on the use of molecules that can undergo well-defined changes in shape in response to an external stimulus such as thermal, electrochemical, or photochemical excitation. Along this path, molecular rotors, gears, switches, shuttles, turnstiles, ratchets, brakes, and pedals have been designed over the last years and constitute the necessary basis for building more sophisticated multimolecular devices.^{1–3}

Because of basic thermodynamic considerations, molecular machines could only work under thermodynamic nonequilibrium conditions, a requisite not fulfilled by many of the earlier described molecular-scale devices. However, these molecules provide a useful nanotool kit to engineer complex machines built from organized gearing of different devices, capable of transferring the motion as a unit under the influence of an external equilibrium-breaking stimulus.^{1–3} Inspired by the work of Canary on Cu-based molecular switches⁴ and the well-established dynamic properties of copper(I) polyamine complexes,⁵ in this work we describe an unprecedented molecular flipper whose motion is based on the isomerization process of a transition-metal complex. This motion is established at the molecular scale by a combination of kinetic and computational methods. It is also shown that the flipper can be switched on/off by reversible oxidation of the metal center, which can be viewed as an electrochemical brake.⁶

To this end, Δ -[Cu^I((N_R,N_R,R,R)-L)]PF₆ (Δ -1PF₆) was isolated as the single product from the reaction of ((1*R*,2*R*)-L) and Cu^I(CH₃CN)₄PF₆ in CH₃CN (Supporting Information) and structurally characterized. The molecular structure of Δ -1PF₆⁷ (Scheme 1 and Figure 1) contains a Cu^I ion coordinated to the four N atoms of the ligand adopting a highly distorted tetrahedral geometry and a noncoordinating PF₆⁻ counterion balancing the charge. The complex contains a crystallographic 2-fold axis that passes through the Cu atom and bisects the cyclohexyl ring. This 2-fold symmetry results

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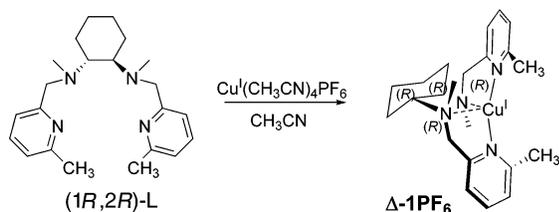
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Scheme 1



in a propeller-like structure in which the orientation of the rotation axis is determined by the chirality of the four stereogenic centers, adopting a Δ helicate chirality for the N_R, N_R, R, R isomer (Figure 1).

Time-dependent NMR analysis of Δ -1PF₆ in CD₂Cl₂ indicates that the complex undergoes a transformation into a new 2-fold symmetric species Λ -2PF₆. A final $K_{eq} = [\Lambda$ -2PF₆]/[Δ -1PF₆] = 1.3 at 298 K was measured at the end of the reaction ($\Delta G^\circ = -0.2$ kcal mol⁻¹), indicating a slight energetic preference for Λ -2PF₆ in solution. $K_{eq} = 1.3$ persists in the temperature range from 10 to 35 °C, but crystallization by ether diffusion leads to quantitative recovery of Δ -1PF₆.⁸ The structure of Λ -2PF₆ was established as Λ -[Cu^I((N_S,N_S,R,R)-L)]PF₆ by NMR spectroscopy and density functional theory (DFT) calculations (Supporting Information). Δ -1PF₆ and Λ -2PF₆ are related by inversion of the chirality of the aliphatic N atoms but most significantly by the opposite helicate chirality.

The circular dichroism (CD) spectrum of a freshly prepared solution of Δ -1PF₆ in CH₂Cl₂ displays negative curves with large amplitudes at 268 nm ($\Delta\epsilon = -11.5$ M⁻¹ cm⁻¹) and 350 nm ($\Delta\epsilon = -4.4$ M⁻¹ cm⁻¹) and a prominent positive curve at 290 nm ($\Delta\epsilon = 8.7$ M⁻¹ cm⁻¹). The Δ -1PF₆ to Λ -2PF₆ isomerization reaction was monitored by CD (Figure 2), showing a quenching of the differential absorption at 268, 290, and 350 nm. Kinetic traces of the CD data were fitted to a reversible single-exponential process, where the two reversal reactions (k_1 and k_{-1}) are unimolecular. Isomerization rate constants in CH₂Cl₂ at 298 K are $k_1 = 2.8 (\pm 0.1) \times 10^{-4}$ s⁻¹ and $k_{-1} = 2.1 (\pm 0.1) \times 10^{-4}$ s⁻¹, and they are

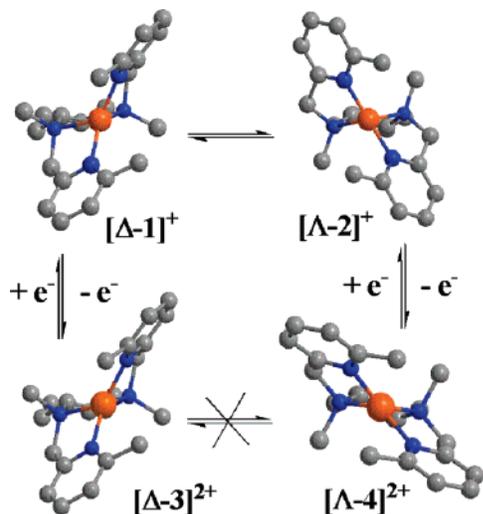


Figure 1. Crystal structure (Mercury diagram) of [Δ -1]⁺ (top left) and DFT structures of [Λ -2]⁺ (top right), [Δ -3]²⁺ (bottom left), and [Λ -4]²⁺ (bottom right).

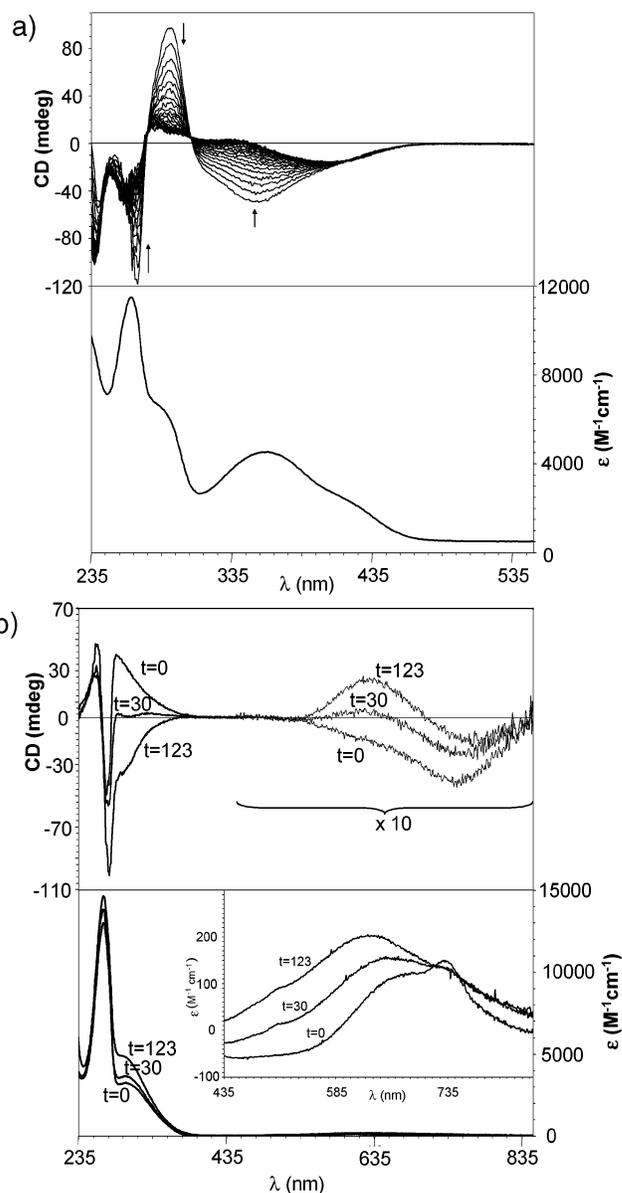


Figure 2. (a) Top: CD monitoring of the Δ -1PF₆/ Λ -2PF₆ isomerization reaction in CH₂Cl₂ ([I]₀ = 0.34 mM, path length = 1 cm, spectrum interval = 5 min). Bottom: corresponding UV-vis spectra. (b) Top: CD spectra of the oxidized Δ -1PF₆/ Λ -2PF₆ couple with AgBF₄ at different isomerization times (min) yielding [Δ -3]²⁺ at $t = 0$ min and mixtures of [Δ -3]²⁺ and [Λ -4]²⁺ at $t > 0$ min. Bottom: corresponding UV-vis spectra.

concentration-independent in the 0.1–1 mM range, thus confirming their unimolecular nature. Eyring plots for k_1 and

- (7) Crystal data for Δ -1PF₆: Bruker CCD diffractometer, C₂₂H₃₂CuF₆N₄P, fw = 561.03, 0.4 × 0.1 × 0.05 mm, orthorhombic, space group P2₁2₁2, $a = 16.921(3)$ Å, $b = 34.176(6)$ Å, $c = 8.4534(15)$ Å, $\alpha = 90^\circ$, $\beta = 90^\circ$, $\gamma = 90^\circ$, $V = 4888.4(15)$ Å³, $D_c = 1.525$ g cm⁻³, $Z = 4$, monochromated Mo K α radiation, φ and ω scan methods, $T = 100(2)$ K, $\mu = 1.023$ mm⁻¹, 76 923 reflections collected, 11 939 independent reflections ($R_{int} = 0.0480$), GOF = 1.065, $R [I > 2\sigma(I)] = 0.0415$, wR = 0.1013 (refined against $|F^2|$).
- (8) A number of attempts have been made to obtain crystallographic characterization of Λ -2X (X = CF₃SO₃, PF₆, BF₄, SbF₆, and ClO₄), but in all cases, Δ -1X is the single product isolated.
- (9) Zn reduction is slow and affords isomeric Δ -1PF₆/ Λ -2PF₆ mixtures. Ag^I oxidation results in Ag precipitation, and no Zn^{II} complexes were formed upon reaction with metallic Zn, as ascertained by NMR spectroscopy.
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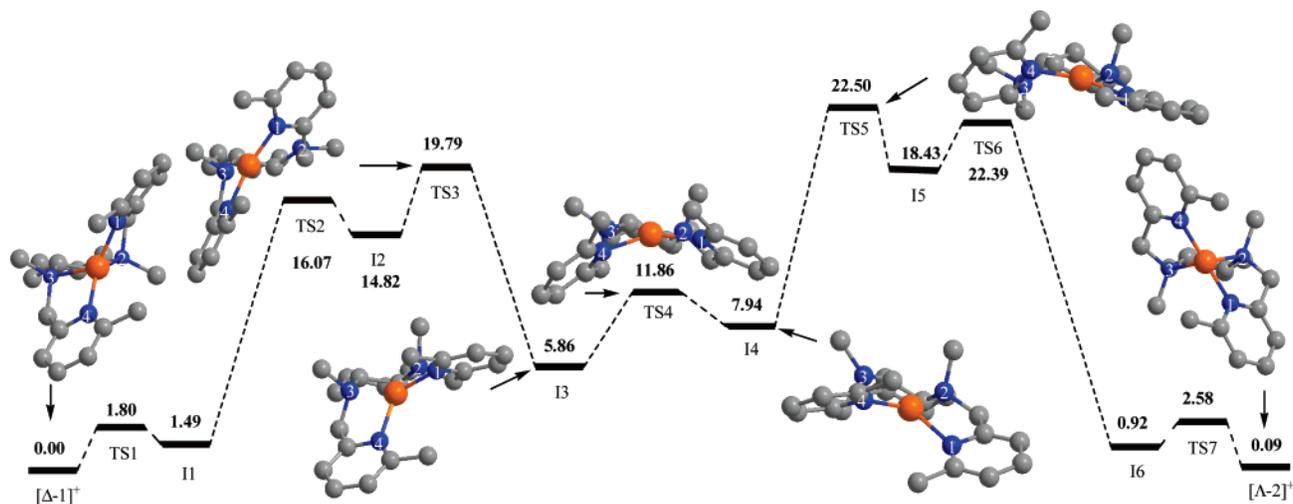


Figure 3. Calculated reaction pathway of the $[\Delta-1]^+ \rightarrow [\Lambda-2]^+$ isomerization with B3LYP/6-311G(d,p) Gibbs free energies at 298.15 K (kcal mol⁻¹).

k_{-1} in the 10–35 °C temperature range provide enthalpy and entropy activation parameters (Table S1 in the Supporting Information). Thermal excitation has a profound effect on the isomerization rate, indicating that the enthalpic contribution accounts for the most important part of the activation barrier.

The mechanical motion undergone by Δ -1PF₆ and Λ -2PF₆ could be switched on/off by reversible metal oxidation. Cyclic voltammetry in CH₂Cl₂ indicates that Δ -1PF₆ and Λ -2PF₆ could be electrochemically oxidized ($E_{1/2} = 0.59$ V vs SSCE, $I_{ap}/I_{cp} \sim 1$) to the corresponding Cu^{II} complexes. Alternatively, Δ -1PF₆ and Λ -2PF₆ can be reversibly oxidized and reduced chemically with Ag⁺ and Zn,⁹ respectively. An oxidation experiment of species Δ -1PF₆ with AgBF₄ was performed at different times of the isomerization process and the CD of the resulting Cu^{II} species registered (Figure 2). The registered spectra progressively change depending on the degree of $[\Delta-1]^+ / [\Lambda-2]^+$ isomerization. However, no further changes were observed after oxidation over more than 1 week, thus indicating that the paddling motion has been stopped.

To give a detailed molecular picture of the isomerization process, the system was studied by means of DFT. The gas-phase geometries, energies, and vibrational frequencies of $[\Delta-1]^+$, $[\Lambda-2]^+$, and several intermediates and transition states labeled in Figure 3 were computed using the B3LYP¹⁰ functional. We use the 6-31G(d,p) basis set to determine the geometries and vibrational frequencies, whereas the energies were obtained by carrying out single-point 6-311G(d,p) calculations at the 6-31G(d,p) geometries. The $[\Delta-1]^+ / [\Lambda-2]^+$ isomerization has a complex mechanism with six intermediates and seven transition states (see the Supporting Information for details). There is a good agreement between the experimental crystal structure of Δ -1PF₆ and the corresponding B3LYP geometry of $[\Delta-1]^+$. The steps of the isomerization mechanism can be split into three main stages. The first stage ends in I3 and involves the rotation of the N²CH₃ group from a CH₃N²–N³CH₃ trans-like orientation to a cis-like orientation. This rotation also implies the transformation of one N_R to N_S. The second stage finishes at I4, and the most important feature is the paddling

movement of the two pyridylmethyl groups. Finally the last stage involves the rotation of the other N³CH₃ group and the transformation of the second N_R to N_S. TS3 and TS4 give the limiting steps of the first and second stages, respectively. However, the limiting step of the $[\Delta-1]^+ / [\Lambda-2]^+$ isomerization is given by TS5 of the third stage, which has a free energy of 22.50 kcal mol⁻¹ above $[\Delta-1]^+$. The computationally determined free energy barrier is in good agreement with the experimental data of $\Delta G_1^{\ddagger\circ}$ and $\Delta G_{-1}^{\ddagger\circ}$ presented in Table S1 in the Supporting Information. DFT analysis also provides an explanation for the role of the oxidation state of the metal in controlling the motion. The theoretically computed $[\Delta-3]^{2+} / [\Lambda-4]^{2+}$ isomerization has the same three stages as the $[\Delta-1]^+ / [\Lambda-2]^+$ isomerization, and also the limiting step is given by TS5', which is 36.19 and 37.60 kcal mol⁻¹ higher than $[\Delta-3]^{2+}$ and $[\Lambda-4]^{2+}$, respectively. It is clear that $\Delta G_1^{\ddagger\circ}$ and $\Delta G_{-1}^{\ddagger\circ}$ for these processes are prohibitively high for a normal solution-phase thermal reaction (Figure 1).

In conclusion, in this work we have described at the molecular scale the mechanical motion exhibited by $[\Delta-1]^+ / [\Lambda-2]^+$ isomerization. The transition metal integrated into this device acts as a redox switch that permits one to start/stop the motion at will. The well-defined molecular paddling motion as well as its redox control adds to the currently available nanotool box, makes these molecules suitable components for yet-to-build molecular machines, and could be particularly useful in acting as a brake of the machine.

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Supporting Information Available: Full details of the synthetic procedures, spectroscopic characterization of products, kinetic analysis, DFT-optimized coordinates of all minima and transition states located, and X-ray crystallographic data (CIF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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