A Molecular Brake

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Both the arrest and the creation of movement are fundamental aspects of dynamics on macroscopic as well as microscopic levels. Brakes and motors dominate the operation of machines, be they those of daily life, such as vehicles and appliances, or those of living systems, like muscles and flagellae. On the molecular level motion is the norm; spontaneous free rotation around single bonds is thus the rule, not the exception. In machines of ordinary experience, such as automobiles, the brake is often as important as the accelerator. We now report the first molecular analog: a reversible molecular brake.

Figure 1 presents the concept in both general and specific terms. With the brake disengaged, the wheel—(a) represented as a three-toothed gear (**1**) and (b) constructed as a triptycene (**2**)[1] — spins rapidly. Engagement of the brake (**3** and **4**) slows or stops rotation. With the actual system, the brake is activated remotely (**2** → **4**) by addition of Hg^{2+} ion. In the absence of Hg^{2+} (or other metal ions), the triptycene wheel spins rapidly at 30 °C, as evidenced by the simplicity of the ^1H NMR spectrum of **2** (Figure 2b), wherein by virtue of C_3 symmetry arising from relatively rapid rotation, the 12 triptycene aromatic protons give rise to only four sets (asterisked) of resonances. Addition of $Hg(O_2CCF_3)_2$ to **2** results in profound changes in the 30 °C (and other) ^1H NMR spectrum (Figure 3a). Most noteworthy are the change in the extraordinary chemical shift of the B-ring methoxy in **2** (δ 2.11!)[2] to a normal δ 4.13 value (not shown) and the obvious broadening of the four resonances attributable to the hydrogens in the three benzo rings of the triptycene.

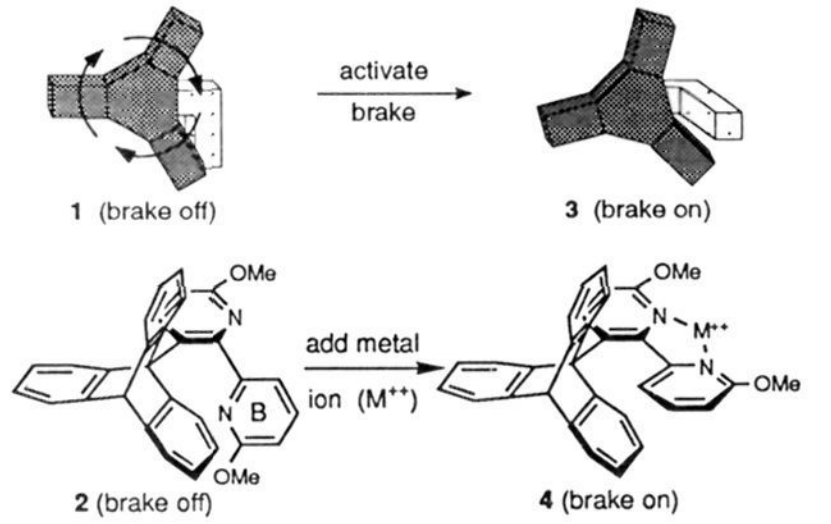

Figure 1. Conceptual and actual depiction of the operation of a molecular brake.

Variable-temperature ^1H NMR experiments[3] (see Figure 3) document the engagement of the brake. In particular, at −30 °C (contrast Figure 2), the three aromatic rings of the triptycene are no longer equivalent because of the arrest of rotation on the NMR time scale. That nonequivalency is most clearly seen (Figure 3d) in the two asterisked doublets at δ 7.67 and 7.53 (in a 2:1 ratio) due to the two H_a and one $H_{a'}$ protons (see structure inset in Figure 3) of the nonrotating (on the NMR time scale) form; the 2:1 ratio of the H_a to $H_{a'}$ resonances in Figure 3d indicates that engagement of the brake results in the plane of symmetry implied in **4**. By contrast, in the absence of metal, restricted rotation at low temperature (Figure 2e) renders all 12 triptycene protons nonequivalent. As the Figure 3d sample is warmed and the brake begins to slip, the H_a and $H_{a'}$ resonances coalesce (~21 °C), but the complex irreversibly decomposes (~70 °C) before the spectrum has sharpened sufficiently to indicate rapid rotation. Treatment[3] of the Hg^{2+} complex **4** with EDTA removes the Hg^{2+} and releases the brake, restoring **2**. Other temperature-dependent changes in the spectra in Figure 3 mirror those just described; peak assignments are corroborated by COSY[3] and various decoupling experiments.

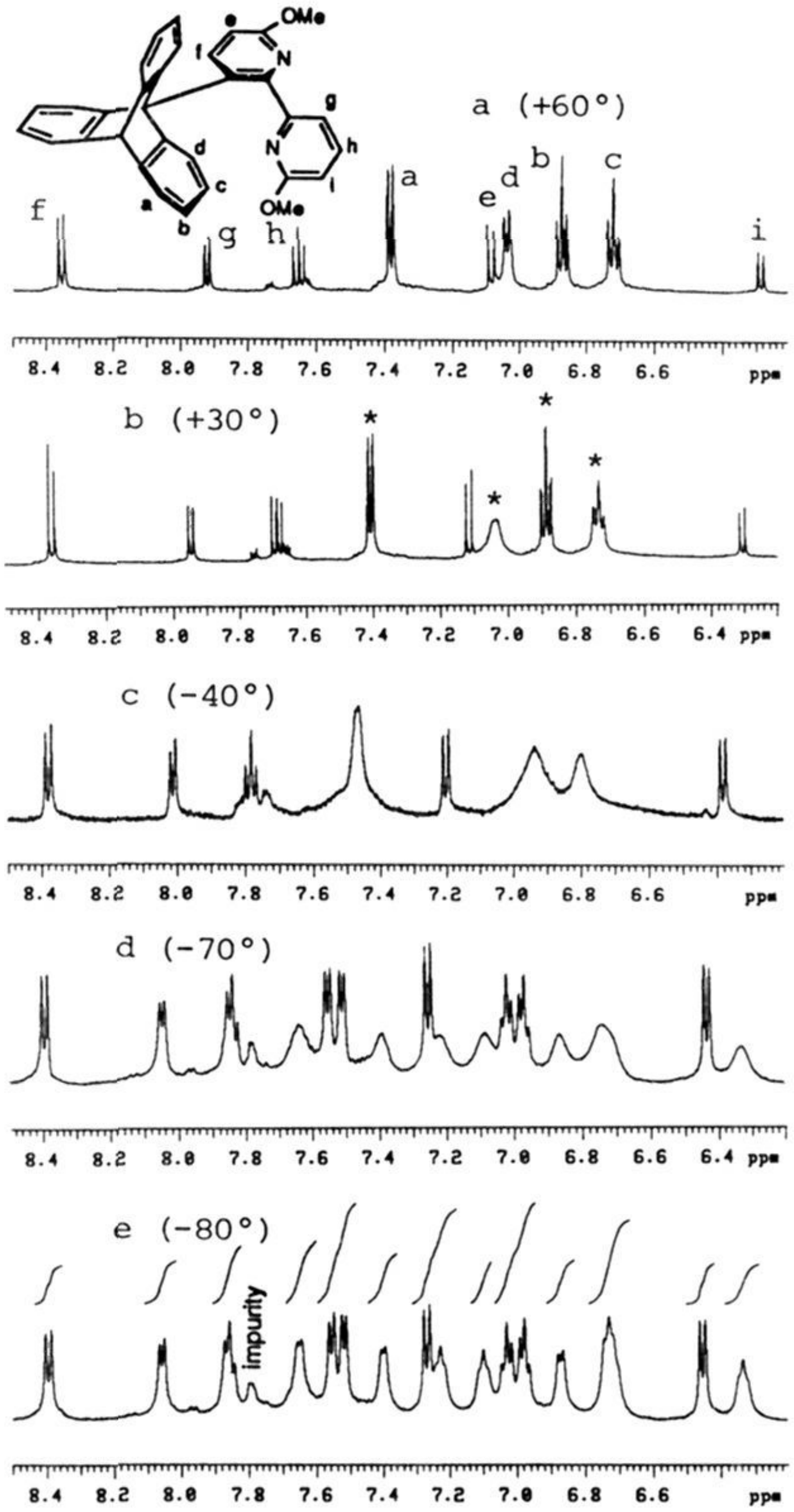

Figure 2. Aromatic region of the 500-MHz ^1H NMR spectrum (acetone-d_6) of **2** at various temperatures. Note that at 30 °C, the asterisked peaks for the 12 triptycene aromatic protons appear as four sets of resonances, indicating equivalence (due to relatively rapid rotation). At −40 °C, peak broadening reflects slowed rotation, but even at −70 °C (2 days), the broadened peaks indicate that rotation has not stopped on the NMR time scale.

The synthesis of **2**, despite the molecule's apparent complexity, is quite straightforward (Scheme 1),[3] thanks to the enlistment of

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[1] For the use of triptycenes as gears see, inter alia (a) Guenzi, A.; Johnson, C. A.; Cozzi, F.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1438. (b) Kawada, Y.; Iwamura, H. *J. Am. Chem. Soc.* **1983**, *105*, 1449. Kawada, Y.; Sakai, H.; Oguri, M.; Koga, G. *Tetrahedron Lett.* **1994**, *35*, 135. (c) Nakamura, M.; Oki, M. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2106. Oki, M.; Takuchi, Y.; Toyota, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2616. (d) Yamamoto, G. *Tetrahedron* **1990**, *46*, 2761.

[2] The B-ring methoxy group is evidently (see models) in the shielding zone of the triptycene benzo rings; the B-ring methoxy group in **9** is similarly shielded (δ 2.00).[3]

[3] See supplementary material for specifics.

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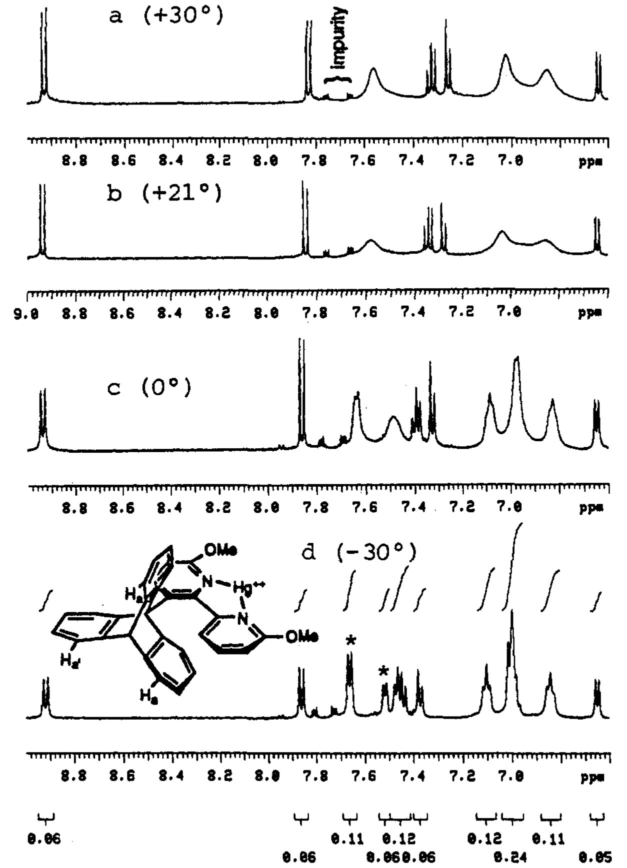
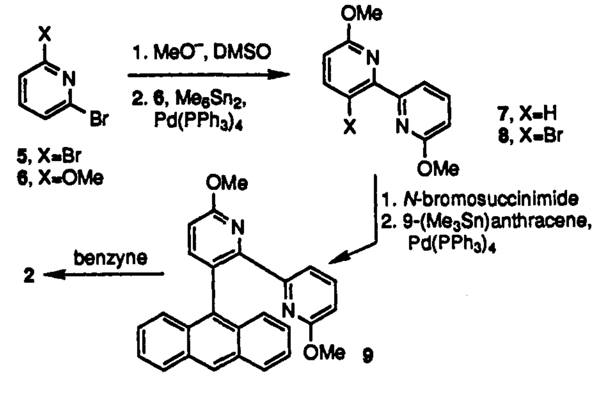


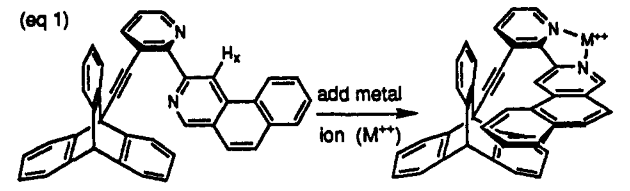
Figure 3. Aromatic region of the 500-MHz ^{1}H NMR spectrum (acetone-d_6) of **4** (M = Hg^{2+}). Contrast the broad peaks at 30 °C with the sharp peaks at 30 °C in Figure 2b and the sharp peaks at –30 °C in this figure (indicating frozen rotation) with the broad peaks at –40 °C and –70 °C in Figure 2. Heating of the complex (**4**, M = Hg^{2+}) led to irreversible decomposition at ~70 °C before the spectrum had sharpened to reflect rapid triptycene rotation.

Scheme 1[3]



two palladium-catalyzed biaryl coupling reactions.[4] The two methoxy groups are included largely for synthetic purposes: in the absence of either (or both), the yield of the benzyne reaction is extremely low (<1%).[5,6]

It is perhaps instructive to consider **10**, which was our first attempt at achieving a molecular brake (eq 1).[7] Space-filling models indicated that coordination of the bipyridine unit in **10** by a metal would activate the brake (eq 1). Reaction of **10** with $Zn(OTf)_2$, $Hg(O_2CCF_3)_2$, and $Pd(O_2CCF_3)_2$ leads to enormous changes in the ^{1}H NMR spectra consistent with the formation of complexes **11**-**13** (for example, the resonance for H_x is shifted ~1.7 ppm downfield, consistent with H_x being forced into the deshielding region of the triple bond), but no peak broadening (let alone cessation of free rotation) was observed, even at temperatures as low as –120 °C. Replacing the relatively weak nitrogen–metal coordination bonds with covalent bonds (→**14**) by reaction[8] of **10** with $BrCH_2CH_2Br$ also did not detectably hinder rotation of the triptycene. We believe that in **11**-**14**, the intended brake acts more like a playing card fastened to a wheel of a child's bicycle, being continually dislodged by each passing spoke. The conversion of **2** to **4** (M = Hg^{2+}) is exoergic by several kilocalories per mole ($K_{assoc} \geq 1.5 \times 10^5$ M^{-1}).[3,9] It is noteworthy that unlike the case with **10**, it is impossible to construct CPK models of **2**. If one regards the bipyridine bonds in **2** and **10** as fulcrums, then the acetylene unit's extension of the lever arm in **10** provides greater leverage for the spinning triptycene to overcome the binding interaction and dislodge the brake in **10** compared to in **2**.[10]



10 (brake off)

(brake on)
11, M = Zn; **12**, M = Hg
13, M = Pd;
14, "M" = $-CH_2CH_2-$

In summary, we report the first example of a molecular brake. The brake operates by coordination of a metal at a *remote* site, which brings about a conformational change that reversibly halts rotation of a molecular-scale gear.

Acknowledgment. We thank innumerable colleagues (both faculty and students) in the department for helpful suggestions, assistance, and encouragement. A.G. thanks NATO for a postdoctoral fellowship.

Supplementary Material Available: Experimental information and spectroscopic data for compounds described and studies reported (50 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(4) For recent reviews, see: Bringmann, G.; Walter, R.; Weirich, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 977. Knight, D. W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3 (Pattenden, G., Ed.), p 481. Among publications from this laboratory utilizing Pd-catalyzed biaryl couplings, see: Kelly, T. R.; Xu, W.; Ma, Z.; Li, Q.; Bhushan, V. *J. Am. Chem. Soc.* **1993**, *115*, 5843. Kelly, T. R.; Bridger, G. J.; Zhao, C. *J. Am. Chem. Soc.* **1990**, *112*, 8024. Kelly, T. R.; Jagoe, C. T.; Gu, Z. *Tetrahedron Lett.* **1991**, *32*, 4263.

(5) It has been observed by others[6] that anthracenes bearing an electron-withdrawing group in the 9-position are poor substrates for cycloaddition with benzyne. The identification (and realization) of **2** as a viable synthetic target reflects the ability of the methoxy groups to counterbalance the electron-withdrawing properties of unsubstituted pyridine rings.

(6) Kornfeld, E. C.; Barney, P.; Blankley, J.; Faul, W. *J. Med. Chem.* **1965**, *8*, 342.

(7) This effort was undertaken as a group project. The synthesis[3] of **10** was achieved in 13 days.

(8) Analogous quaternizations of 2,2'-bipyridine with $BrCH_2CH_2Br$ to give the herbicide diquat have been examined extensively (Cf. Homer, R. F.; Tomlinson, T. E. *J. Chem. Soc.* **1960**, 2498).

(9) For literature values see, inter alia: Smith, R. M.; Martell, A. E. *Critical Stability Constants*; Plenum Press: New York, 1975; Vol. 2, p 236.

(10) A reviewer suggests that the reason the brake fails in **10** is because the barrier to rotation is reduced by excessive steric congestion (cf. Yamamoto, G.; Oki, M. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3550). In our view, the examination of CPK molecular models does not bear out that explanation.