

# Crystalline Molecular Machines: A Quest Toward Solid-State Dynamics and Function

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Received January 13, 2006

## ABSTRACT

Complex molecular machinery may be envisioned as densely packed, multicomponent, self-assembling systems built with high structural precision to control the dynamics of one or more internal degrees of freedom. With molecular gyroscopes as a test, we describe a general strategy to design crystals capable of supporting structurally programmed molecular motions, a practical approach to their synthesis, convenient strategies to characterize their solid-state dynamics, and potential applications based on polar structures responding collectively to external fields.

## 1. Machines

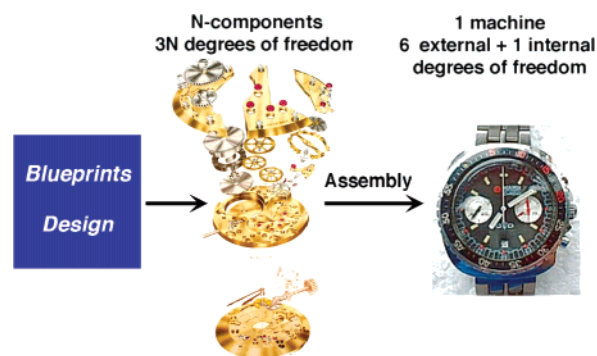
The word “machine” summons images of complex devices, rapid means of locomotion, fast computers, etc. It is often forgotten that machines begun at the dawn of mankind with the advent of mundane devices and tools designed to reduce the amount of work required to accomplish simple tasks. A dictionary states that a machine is “an assemblage of parts that transmit forces, motion, or energy from one to another in a predetermined manner”.<sup>1</sup> We are usually introduced to the field of mechanics by studying the relation between the gravity of earth, the mass of an object, and surprisingly simple arrangements of parts that make up pulleys, levers, inclined planes, wedges, and wheels and axles, known collectively as “simple machines”. Other complex machines are based on the transport and emission of

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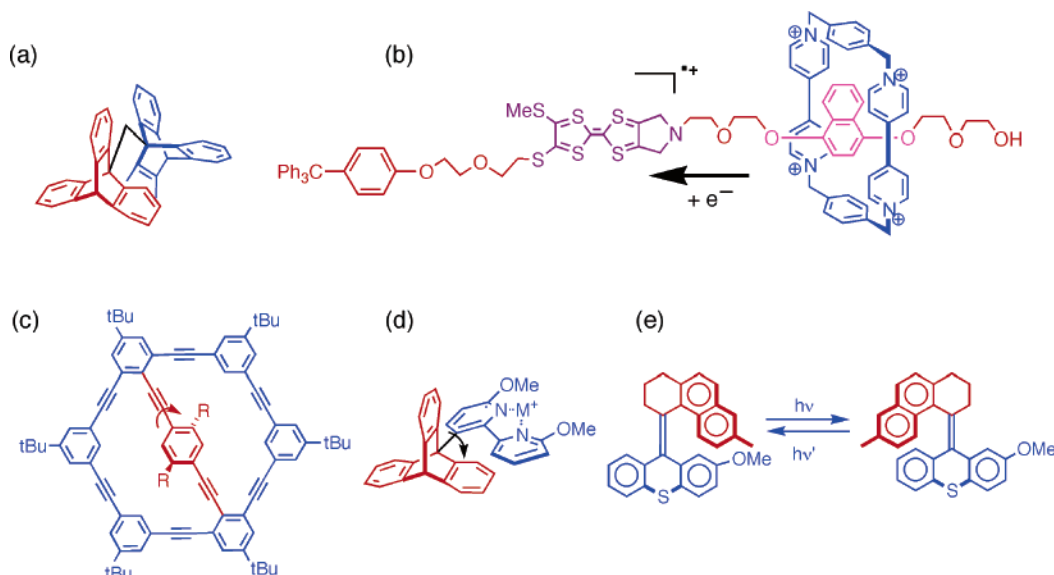
**FIGURE 1.** Blueprints contain all of the structural information needed to build and assemble the components of a mechanical wristwatch (figure adapted from ref 18a).

electrons and photons to process, store, or transfer information, rather than doing mechanical work. While the range of objects covered by the above definition is exceedingly broad, most machines are complex assemblies that act as a unit under the influence of a suitable stimulus.

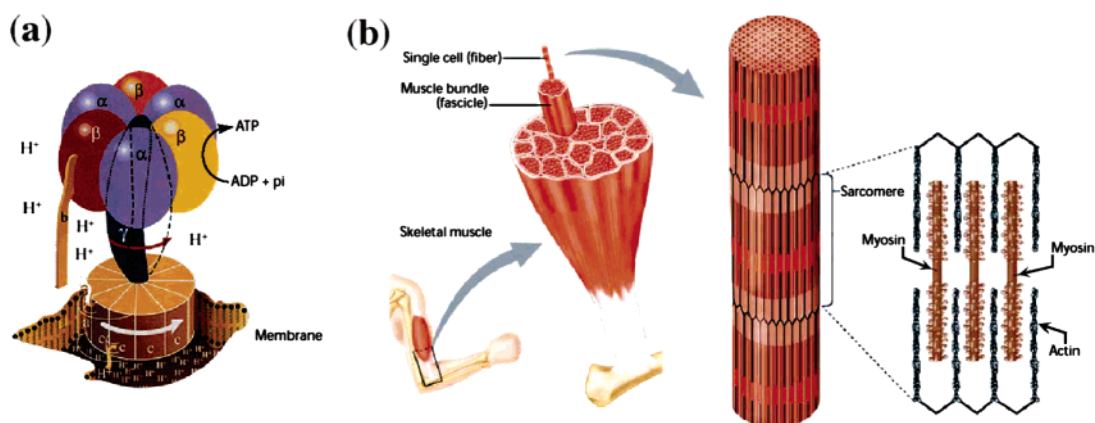
**Artificial Molecular Machines.**<sup>2</sup> With an intuition that arises from handling molecular models, chemists recognize that forces, motion, and energy can indeed be transferred within molecules or from one to another in a manner that depends upon the structure of the atomic assembly.<sup>3,4</sup> Inspired by the design of macroscopic machines, we postulate that the information required to fulfill specific functions may be formulated in terms of the structure-determined degrees of freedom surrendered by the components of the machine as compared to those gained by the assembly (Figure 1). The careful design depicted in the blueprints of a wristwatch contains all of the structural information needed to create the wheels, ratchets, pivots, shafts, screws, cocks, barrels, etc., as well as the information needed to put them together. While the  $N$ -rigid components have a total of  $6N$  degrees of freedom (assuming parts with arbitrary shapes), the end product is a single unit with 3 rotational and 3 translational whole-body degrees of freedom and as few as 1 internal degree of freedom that defines the function of the assembly. In the case of the wristwatch, many components move in precise, periodic motion, leading to the advance of a set of needles with a 1 Hz frequency when the spring is loaded.

While macroscopic machines are based on Newtonian mechanics and deterministic theories, molecular machines must be based on quantum mechanics and statistical theories. Conceptually, one may start with different types of atoms linked together to form components of increasing complexity. Their internal dynamics would be determined by degrees of freedom brought about by covalent, supramolecular, or mechanical bonds, and their trajectories for motion would be determined by the topography of their energy landscape. The earliest ex-

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**FIGURE 2.** Molecular structures that undergo conformational motions and/or structural changes in solution that are reminiscent of those observed in macroscopic machines.



**FIGURE 3.** (a) Representation of ATP synthase as a molecular machine with an autonomous function, consisting of several parts (proteins  $\alpha$ – $\epsilon$  and a–c) supported in a cell membrane. Arrows in the figure indicate its rotary motion, the translocation of protons across the membrane, and the synthesis of ATP from ADP +  $P_i$ . (b) Sketch of a skeletal muscle as a molecular machine with a collective function illustrating the hierarchical levels of structure [adapted from (a) <http://www.nobel.se/chemistry/laureates/1997/illpres/boyer-walker.html> and (b) <http://www.bmb.psu.edu/courses/bisci004a/>].<sup>18</sup>

amples of artificial “molecular machines” were designed to illustrate the relation between the molecular structure and internal dynamics under thermal equilibrium.<sup>4</sup> Two well-known examples are Mislow and Iwamura’s “molecular bevel gears” (Figure 2a)<sup>5</sup> and Moore’s “molecular turnstiles” (Figure 2c),<sup>6</sup> both of which have motions reminiscent of their macroscopic namesakes when the proper frames of reference are considered. For example, the motion of a molecular bevel gear requires a frame of reference where the central  $-\text{CH}_2-$  is static, while the two triptycenes rotate in a correlated fashion. Similarly, a molecular turnstile can be recognized in a frame of reference that considers the peripheral ring of *meta*-phenylenes, static as the central ring rotates. After many such “molecular devices” were described,<sup>7</sup> chemists recognized the need to consider “assemblies designed to perform mechanical-like movements (output) as a consequence of appropriate external stimuli (input)”.<sup>8</sup> Increasing levels of sophistication led to Stoddart’s “shuttles”

(Figure 2b),<sup>9</sup> Kelly’s “brakes” (Figure 2d),<sup>10</sup> and Feringa’s photochemically driven “motors” (Figure 2e),<sup>11</sup> among many others.<sup>12</sup> Other molecules with translations and rotations controlled by red–ox processes, added ions, or electronic excitation have been designed.<sup>13,14</sup>

#### Autonomous and Collective Molecular Machines.

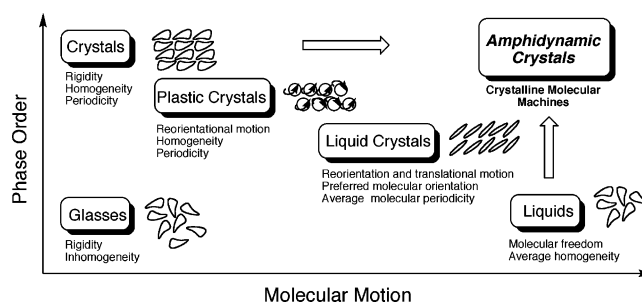
While searching for insight into complex molecular-level phenomena, one may obtain valuable clues from biological systems.<sup>15</sup> Because it pertains to the design and scale of action of molecular machines, one can identify two general strategies based on the number of molecular units required for their function: (a) autonomous molecular (supramolecular) machines that act as single units and (b) collective molecular machines that base their function on the cooperative action of many close-packed repeating units. An inspiring example of the first class is ATP synthase, often described as a protomotive, membrane-bound, three-stage rotary motor (Figure 3a).<sup>16</sup> An example of the second category is the skeletal muscle,<sup>17</sup> with a

function that derives from the collective dynamics of actin, myosin, and a few other proteins spontaneously self-assembled into a highly hierarchical macroscopic structure. As shown in Figure 3b, polymeric filaments of actin and myosin organize into contractile units known as sarcomers, arrays of which constitute the fibers that bundle together in fascicles that constitute the muscle. To do work, muscles contract as a result of collective changes that occur along their volume at the molecular level. Although the detailed mechanism of function is beyond the scope of this Account, the sliding filament model explains contraction as the result of actin and myosin filaments sliding past each other because of binding interactions and conformational motions coupled to ATP hydrolysis.<sup>17,18</sup> The significance of this mechanism is that *macroscopic function is traced to the collective effects of many molecular units experiencing relatively simple chemical phenomena.*

## 2. Crystalline Molecular Machines

With the goal of emulating some of the mechanical functions and high packing densities of macroscopic machines and skeletal muscles with artificial molecular systems, we recently started a research program to design and construct crystalline molecular machines.<sup>19</sup> Our studies complement recent work on molecular machines built on self-assembled monolayers and bound to nanoporous materials.<sup>20,21</sup> We envision crystalline, multicomponent molecular arrays, acting in concert, transferring forces, motion, and energy from one molecule to another along the crystal lattice. Ideally, molecular components will act as gears, pivots, axles, etc., and communicate their state of motion and orientations through steric contacts, electrostatic interactions, or magnetic forces. Similar to biological systems, crystalline molecular machines could be driven by chemical reactions caused by light, charge transport, and diffusing reagents,<sup>22,23</sup> or one may envision crystals with a few mobile components collectively responding to the presence of external electric and/or magnetic fields, as described recently for one- and two-dimensional structures by the groups of Ratner, Michl, and Price.<sup>24–26</sup>

**Amphidynamic Crystals.** To control their dynamics, crystalline molecular machines will require self-assembling constituents with precise alignment, orientation, and intermolecular distances. In search of a relation between molecular structure, solid-state dynamics, and phase order, we consider the phase-order–molecular-dynamics diagram shown in Figure 4.<sup>19</sup> With a measure of molecular dynamics in the horizontal axis and order in the vertical, we note that molecular crystals and isotropic liquids represent the extremes of the top-left to bottom-right diagonal, where a molecular mobility is acquired at the expense of the phase order. Conventional crystals of molecules with arbitrary shapes have the highest degree of order, but their molecular motility is limited to normal modes and lattice vibrations.<sup>27</sup> Along the diagonal, molecules in plastic crystals retain their position in the lattice

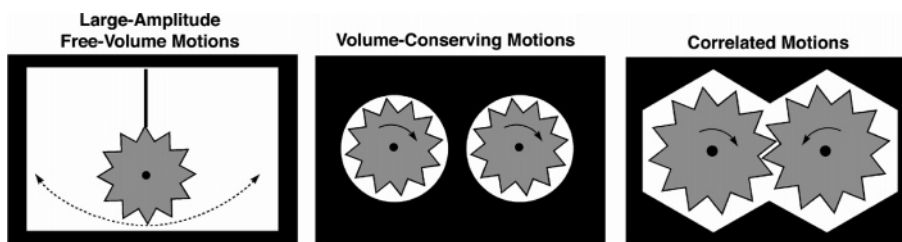


**FIGURE 4.** Phase-order–molecular-motion diagram illustrating possible forms of condensed phase matter (adapted from ref 19).

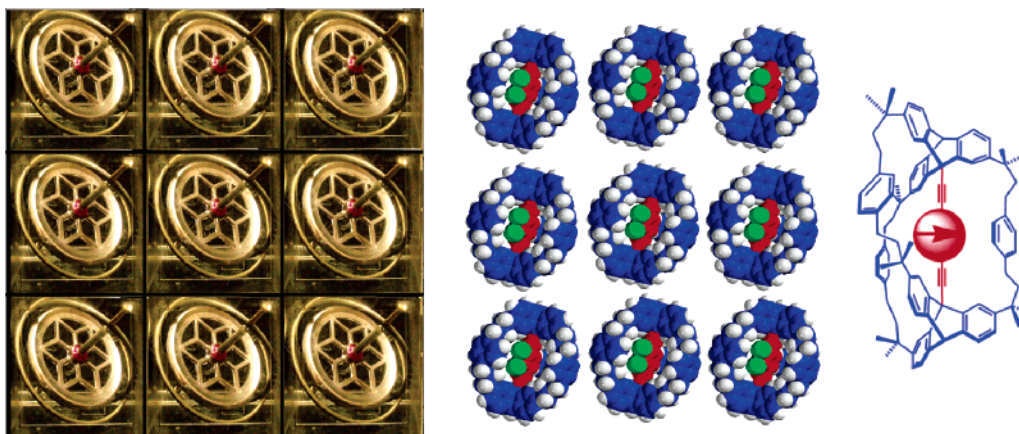
but undergo rapid whole-body rotations.<sup>28,29</sup> Liquid crystals have preferred molecular orientations but experience rapid rotational and translational motion.<sup>30</sup> It is interesting to point out that the formation of plastic- and liquid-crystal phases is determined by the molecular structure. Liquid-crystal-forming structures have rigid cores with floppy long chains, and plastic crystals have spherical or cylindrical shapes. One may expect that the high mobility and order desired for crystalline molecular machines will also require specific molecular structures with components forming an extended rigid network with the desired periodicity and symmetry acting as stators, linked to the dynamic components by covalent, supramolecular, or mechanical bonds. Notably, the combination of opposites within a given structure tends to result in properties that are not observed in either component, as illustrated by amphiphiles (hydrophilicity/hydrophobicity), amphoteres (acidic/basic), and others. With the suffix “amphi” meaning “both sides”, we refer to the structures on the upper right portion of Figure 4 as “*amphidynamic crystals*”.

## 3. Amphidynamic Crystals: Free Volume, Volume-Conserving Processes, and Correlated Motions

The first step for the construction of crystalline molecular machines is to develop strategies to engineer amphidynamic crystals with controllable molecular dynamics. To accomplish that, one may emulate the structural attributes that make the function of automobile engines, typewriters, mechanical clocks, and other tightly packed objects possible. Among these, we have identified the implementation of (1) *free volume*, (2) *volume-conserving processes*, and (3) *correlated motions*. As illustrated in Figure 5 with an object undergoing “pendular” displacements, free volume is required for large amplitude motions mapping out trajectories that depart from the shape of the moving object. Volume-conserving motions are those that occur without disturbing the local environment, such as the toothed wheel rotation in the center of Figure 5. Finally, correlated motions require the greatest structural and dynamic complexity with matching rates, symmetries, and phases for the concerted displacement of various components. A deep understanding of correlated motions at the molecular and supramolecular level will be required for the construction of complex, highest density molecular machines.



**FIGURE 5.** Representations of the general requirements to have mobile components in high-density media.



**FIGURE 6.** Gyroscopes possess an ideal structure for the construction of amphidynamic crystals with stator, axle, and rotator that can be emulated at the molecular level.

**Supramolecular Assemblies and Crystal Design.** One may visualize methyl, *tert*-butyl, adamantyl, phenyl, triptycyl, and other well-defined rigid groups as the mobile components of crystalline assemblies. In addition to designing and synthesizing molecules with the desired components, one will have to engineer their self-assembly with the picometric precision required for their motion to occur in concert. While some success may be expected with strong directional interactions such as hydrogen bonds and coordination chemistry,<sup>31</sup> robust strategies for crystal design are not currently available.<sup>32</sup> However, it is well-known that simple van der Waals interactions between molecules shaped as discs, spheres, and rods often lead to predictable packing motifs.<sup>33</sup> In search of molecular systems that can satisfy these requirements, we have considered simple machines that can be emulated at the molecular level with readily accessible structures. As a starting point, we have centered much of our attention on structures with shapes and functions analogous to those of macroscopic gyroscopes.

#### 4. Molecular Gyroscopes

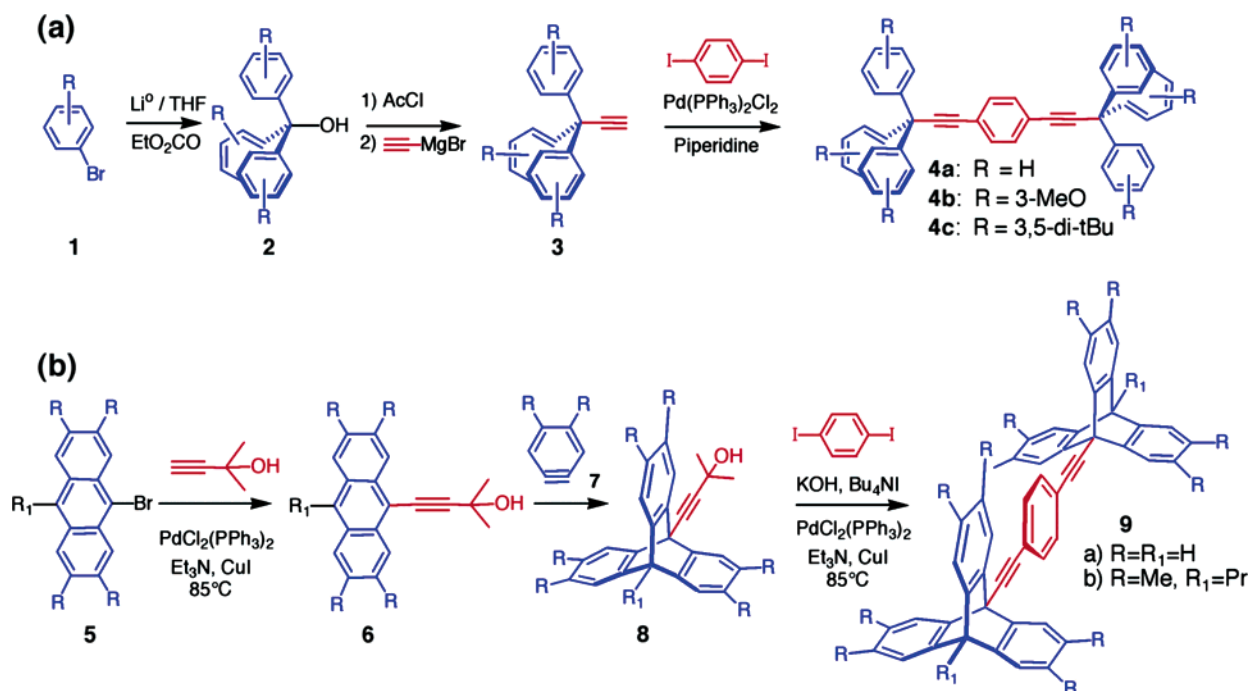
A simple gyroscope is a device with 1 degree of freedom consisting of a spinning mass or *rotator*<sup>7</sup> with its spinning axis positioned through the center of the mass and mounted within a rigid frame or stator. When mounted on gimbals, gyroscopes have up to 3 degrees of freedom and form the basis of inertial navigation systems used in airplanes and satellites. As illustrated in Figure 6, macroscopic gyroscopes require free volume about their rotators, and their stators are designed to function in densely packed instrument consoles. To emulate the structure of

a gyroscope at the molecular level, one must identify a rotator with bonds coaxially aligned with the center of mass to supply the rotary axis and the point of attachment to the stator (Figure 6). The stator can be made up by the rest of the molecule, with a design that shields the rotator from contacts with adjacent molecules in the lattice.

As illustrated in Figure 6, a simple design entails the use of a *para*-phenylene connected by alkynes at the 1,4 positions to triarylmethyl (trityl) or triptycyl groups.<sup>34</sup> Phenylene rotators are synthetically accessible and possess the correct symmetry for attachment of a molecular axle along their center of mass. Alkynes are ideal axes because the intrinsic barriers for rotation of groups directly linked to them are very low.<sup>35</sup> To complete the required elements, an encapsulating stator must provide the free volume needed to render phenylene rotation, a sterically unhindered process. On our way toward the synthesis of triply bridged molecular gyroscopes such as that in Figure 6, we begun with structures having open topologies based on triphenylmethyl (trityl) and triptycyl stators (Scheme 1). Both trityl and triptycyl groups are relatively large, form a cavity to shield the rotator, and can be modified to fine-tune crystal packing. Synthetic strategies to close the topology of the frame should be accessible, and a rigid, rodlike shape should favor the parallel alignment of the long molecular axes in the crystal.<sup>33</sup>

As shown in Scheme 1a, molecular gyroscopes with trityl frames and phenylene rotators are constructed from aryl halides **1** and 1,4-diiodobenzene. Trityl alcohols **2** can be converted into trityl acetylenes **3**, which are subsequently assembled into the desired molecular gyroscopes **4** by a Pd(0)-coupling reaction.<sup>36</sup> The R groups in Scheme

Scheme 1



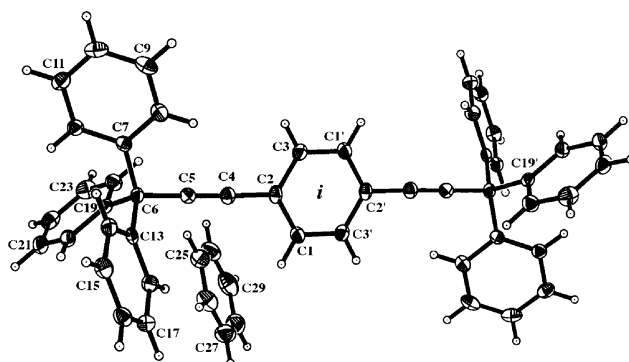
1 provide steric shielding in the final structures. They may be bulky groups or chains that bridge one end of the molecule to the other, such as the structure in Figure 6. The unsubstituted molecular gyroscope **4a** (R=H) was prepared as a model, not expecting that it would exhibit efficient phenylene rotation in crystals. Although the required 1,4-diethynylphenylene rotator was present, we suspected that the space around the center of the molecule would be filled by adjacent molecules, resulting in prohibitively high phenylene rotation barriers. Remarkably, the rotary dynamics of the phenylene group in **4a** turned out to be very efficient, as determined by variable-temperature (VT)  $^{13}\text{C}$  CP/MAS NMR and quadrupolar echo  $^2\text{H}$  NMR line-shape analysis (see below).

Crystals of molecular gyroscope **4a** from benzene formed a clathrate, and crystals from  $\text{CH}_2\text{Cl}_2$  formed a solvent-free structure.<sup>37</sup> Both occur in the space group  $P\bar{1}$  with coincident crystallographic and molecular inversion centers with trityl groups of opposite chiral propeller configurations. Analysis of the packing structures confirmed that molecules align parallel to each other by taking advantage of aromatic edge–face interactions, which in the benzene clathrate take the form of a 6-fold trityl embrace. Thermal and spectroscopic analyses showed that the benzene clathrate converts to the solvent-free structure between 80 and 100 °C. The solvent-free crystal showed excellent thermal stability and a mp = 316 °C.<sup>37</sup>

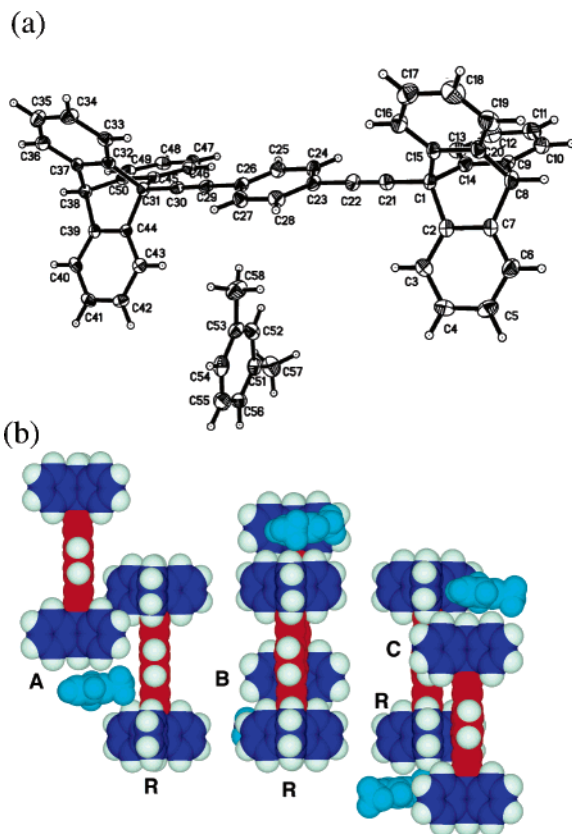
In contrast to the maneuverable trityl system, molecular gyroscopes with triptycyl groups are more challenging to prepare and handle. The simplest one, with a triptycene stator and a phenylene rotator, was prepared in four steps from 9-bromoanthracene **5** (Scheme 1b, R=R<sub>1</sub>=H).<sup>38</sup> Modifications to the triptycyl stators require substituted anthracenes and anthranilic acids, for which we have developed highly convergent strategies. The parent tripty-

cene-based molecular gyroscope was highly insoluble and crystallized with one molecule of *meta*-xylene per molecular gyroscope (Figure 8). Thermal analysis showed the loss of *meta*-xylene upon heating above 120 °C and decomposition without melting at ca. 400 °C. Molecules crystallized with the two triptycyls in an eclipsed conformation and interdigitated with edge–face and face–face contacts. Just as in the trityl-based compound (Figure 7), parallel alignment of molecules was successfully programmed into the crystal. The *meta*-xylenes in the lattice are wedged as spacers between the head and tail of adjacent molecular gyroscopes (Figure 8). Not surprisingly, the closely packed structure creates no free volume, and the lack of rotational and torsional degrees of freedom prevents any serendipitous correlated motion.

**Phenylene Rotation in Crystalline Molecular Gyroscopes.** With modest expectations and mainly to compare the performance of future generations of molecular gyroscopes, we examined the solid-state dynamics of compound **4a** (Scheme 1) in its benzene clathrate and solvent-free forms by VT CP/MAS  $^{13}\text{C}$  NMR and quadrupolar



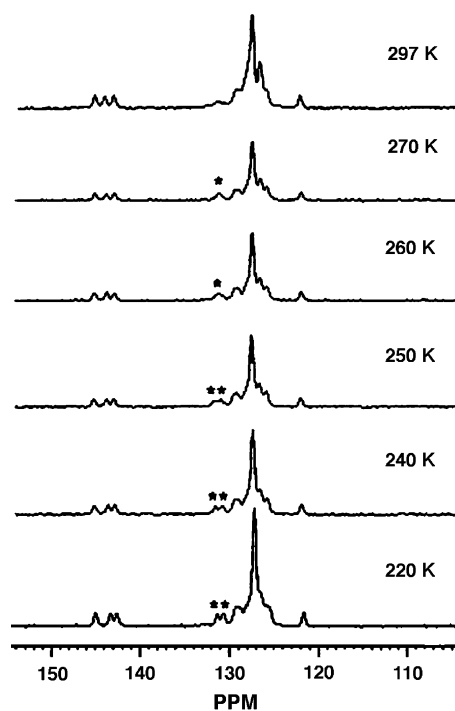
**FIGURE 7.** ORTEP diagram of molecular gyroscope **4a** illustrating its relation with a benzene molecule in the lattice.



**FIGURE 8.** (a) ORTEP diagram of the triptycyl molecular gyroscope and the incorporated *meta*-xylene molecule. (b) Views of close-packing interactions highlighting the interdigitation between a reference molecule R and its closest neighbors A–C.

polar echo  $^2\text{H}$  NMR line-shape analysis.<sup>34,37</sup> We selected these techniques based on their complementary dynamic ranges and relative simplicity. Assuming favorable chemical-shift differences between exchanging carbons ( $\Delta\delta \sim 0.5\text{--}5$  ppm),  $^{13}\text{C}$  NMR measured at 75 MHz provides dynamic information in a range of rate constants from  $\sim 100$  to  $2000\text{ s}^{-1}$  and activation energies within  $\sim 10\text{--}20$  kcal/mol. Line-shape analyses of quadrupolar echo  $^2\text{H}$  NMR with samples having a deuterated rotator provide information on the nature of the motion for rate constants of ca.  $10^3\text{--}10^8\text{ s}^{-1}$ . Characteristic changes in spectral line shapes make it possible to differentiate between the exchange processes involving jumps of  $180^\circ$ ,  $120^\circ$ , and  $60^\circ$ , continuous rotation, and more complex motions.<sup>39</sup>

Starting with VT CPMAS  $^{13}\text{C}$  NMR, we assigned signals corresponding to benzene molecules, trityl, and phenylene groups by measurements with samples deuterated at each of those groups.<sup>34</sup> Signals corresponding to the crystallographically and magnetically nonequivalent phenylene carbons C1 and C3 (Figure 7) were analyzed as a function of temperature to determine their rate of exchange by phenylene rotation (Figure 9). It should be mentioned that chemical exchange in phenylenes requires angular displacements of  $180^\circ$ , often referred to as 2-fold flipping or 2-fold jumping motions. It should also be noted that NMR experiments cannot distinguish between continuous rotation in the same direction and random displacements in either direction. A singlet at 132 ppm assigned to both

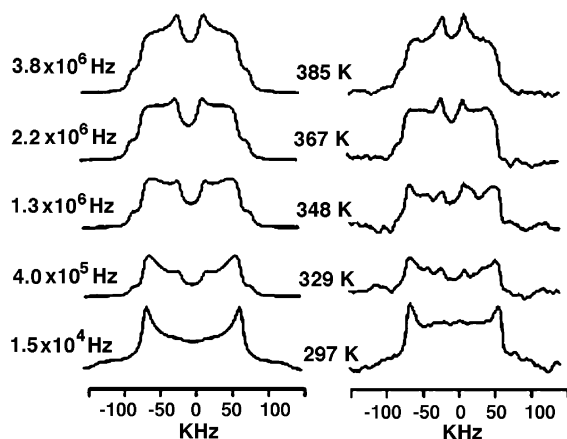


**FIGURE 9.** VT CPMAS  $^{13}\text{C}$  NMR spectra of the benzene clathrate of trityl gyroscope **4a** (R=H) showing the coalescence of the phenylene rotator signals (\*).

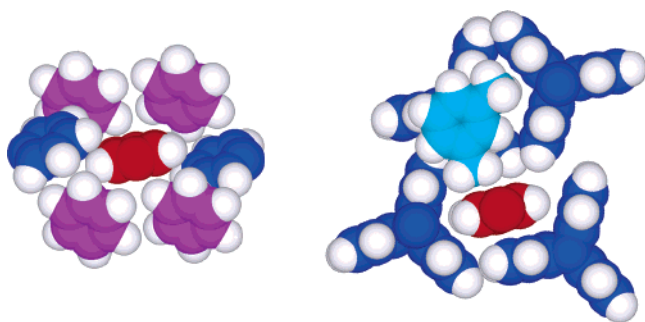
C1 and C3 at room temperature splits into two signals passing through a coalescence point at ca. 255 K. From a  $\Delta\delta$  of 60 Hz, one can estimate a time constant for exchange of 7.7 ms and a remarkably low solid-state barrier of 12.8 kcal/mol. In agreement with the VT  $^{13}\text{C}$  NMR results,  $^2\text{H}$  NMR measurements revealed that phenylene rotation occurs in the slow-exchange limit ( $k < 10^4\text{ s}^{-1}$ ) at temperatures where the clathrate is stable ( $T < 333\text{ K}$ ).  $^2\text{H}$  NMR measurements also indicated that benzene molecules rotate by  $60^\circ$  jumps with rates exceeding  $10^8\text{ s}^{-1}$ , even at 200 K, as previously shown in crystals of benzene<sup>40</sup> and in inclusion compounds.<sup>41</sup>

Taking advantage of the high thermal stability of the solvent-free sample, we decided to analyze the rotation of the phenylene group in compound **4a** by  $^2\text{H}$  NMR at high temperatures. As expected, the line shape of the powder pattern was sensitive to changes in temperature between 297 and 385 K (Figure 10). Suitable line-shape simulations were obtained with a model involving symmetric  $180^\circ$  phenylene flipping motion with rate constants of  $10^3\text{--}10^7\text{ s}^{-1}$ . An Arrhenius plot of these data revealed a barrier of 14.6 kcal/mol for phenylene rotation, which is ca. 1.8 kcal/mol higher than that of the benzene clathrate.<sup>34,37</sup> However, subsequent VT  $^{13}\text{C}$  CPMAS studies with solvent-free samples of labeled **4a** between 215 and 275 K indicated a barrier of ca. 11.3 kcal/mol,<sup>42</sup> suggesting either a relatively large experimental error or that the rotational barrier of this compound is temperature-dependent.

**Stator Effects.** Following our somewhat unexpected observations on the relatively fast dynamics of trityl derivative **4a**,  $^{13}\text{C}$  CPMAS NMR analysis of the parent triptycyl compound **9a** indicated that its phenylene group



**FIGURE 10.** Solid-state  $^2\text{H}$  NMR spectra obtained from quadrupolar echo experiments (right) and simulated spectra using a 2-fold flipping model at the rate shown (left).



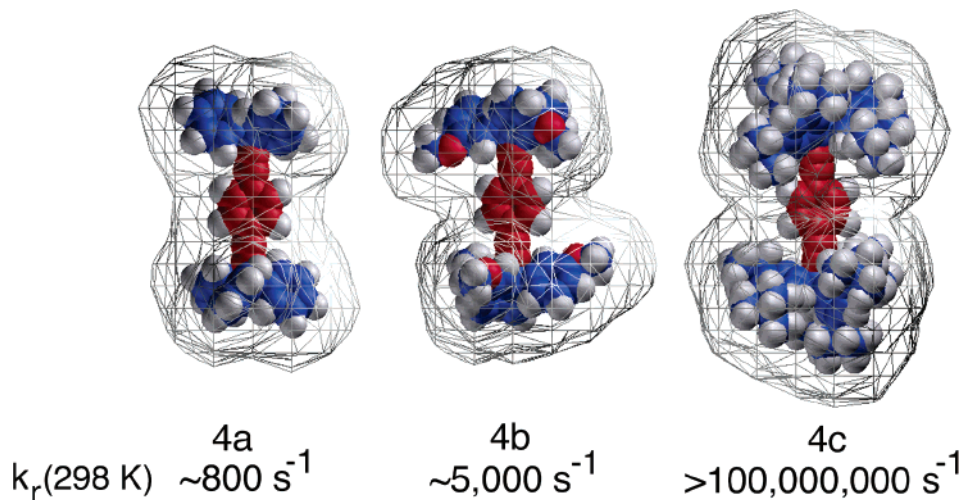
**FIGURE 11.** Views of the environment around the phenylene group in crystals of **4a** (left) and **9a** (right) down the phenylene 1,4 axis. Phenylenes are shown in red; benzene is shown in purple; *meta*-xylene is shown in light blue; and fragments from neighboring molecules are shown in blue.

is static in the solid state. Surprisingly, a closer look at the packing environment around the phenylene rotators of **4a** and **9a** reveals similarly crowded structures about the rotator (Figure 11). A simple comparison of their packing coefficients, defined by Kitaigorodski as the volume of the molecules in the unit cell relative to the volume of the unit cell,<sup>32</sup> shows that **9a** is indeed more dense than **4a**. While the packing coefficient derived for the structure of **9a** is 0.85, the packing coefficients of **4a** in its benzene clathrate and solvent-free forms are 0.72 and 0.74, respectively. In addition, while the phenylene rotator of benzene-containing crystals of **4a** is surrounded by four rapidly rotating benzene molecules (shown in purple) and two phenylene groups from adjacent molecular gyroscopes (in blue), the phenylene rotator of **9b** is surrounded by four static triptycenes from neighboring molecular gyroscopes (in blue) and one molecule of *meta*-xylene (light blue). An additional difference between phenylene rotators in crystals of **4a** and **9a** may derive from the relative mobility of their closest neighboring groups, which may facilitate correlated motions. It is likely that a small displacement of the rapidly rotating benzene molecules and the torsionally mobile phenyl groups from adjacent molecules in crystals of **4a** may allow for periodic variations in the cavity size to couple with (or determine) the rotary motion of the phenylene groups. In contrast,

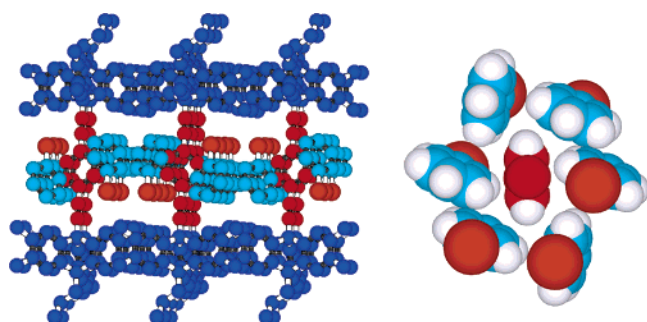
with much fewer degrees of freedom, molecules of **9a** form crystals with a more static environment and fewer opportunities for correlated motions and rotation of its phenylene.

Knowing that the theoretical limit for phenylene rotation estimated from its moment of inertia along the 1,4 axis falls in the terahertz regime ( $\sim 10^{12} \text{ s}^{-1}$ ),<sup>43</sup> we began to analyze the rotational dynamics of molecular gyroscopes with substituted trityl groups such as **4b** and **4c** with *meta*-methoxy<sup>44</sup> and 2,5-di-*tert*-butyl<sup>36</sup> substituents (Scheme 1a and Figure 12). Although the hexamethoxy derivative **4b** was shown to be highly polymorphic, we selected a well-characterized benzene clathrate to investigate its rotational dynamics by CPMAS  $^{13}\text{C}$  NMR and the line shape of the  $^2\text{H}$  NMR spectra. As expected for a better shielding and/or increased degrees of freedom resulting from the methoxy substituents of **4b**, we determined a lower energy barrier (11.7 kcal/mol) and faster rotation rates than those calculated for the benzene clathrate of **4a**. By the same token, the heavily substituted structure of **4c** resulted in ambient-temperature exchange rates that are greater than the upper limit of the  $^2\text{H}$  NMR line-shape analysis method ( $> 100 \text{ MHz}$ ). Unfortunately, X-ray diffraction quality crystals of **4c** obtained from  $\text{CH}_2\text{Cl}_2$  were very fragile and lost their integrity upon cooling, preventing us from obtaining an activation energy. Notably, the estimated packing coefficients of **4b** and **4c** were 0.68 and 0.66, suggesting that bulkier substituents in this series do help the formation of more open structures.

The results with **4c** suggested that, in addition to facilitating very rapid motion, ideal stators should guide the formation of robust crystal lattices. After a close analysis of the packing interactions in the crystal structure of compound **9a**, we speculated that alkyl substitution at the peripheral positions of the triptycyl frames would prevent interdigitation between close-neighboring molecules.<sup>45</sup> This was confirmed with crystals of the dodecamethyl derivative **9b** obtained from bromobenzene, which were shown to form a solvent clathrate with phenylene rotators and solvent molecules arranged in layers (Figure 13). Notably, an estimated packing coefficient of 0.62 for **9b** is lower than those of **4a–4c**, and inspection of the local environment around the rotator indicates a highly symmetric cavity with a potential for correlated motions between the bromobenzene molecules and the molecular rotator. Satisfyingly, recent analysis of single crystals of **9b- $d_4$**  by  $^2\text{H}$  NMR at ambient temperature revealed a line shape that approaches the continuous motion of a free rotator, rather than the characteristic  $180^\circ$  jumps observed with other samples.<sup>46</sup> In fact, crystals of **9b** had to be cooled to  $-90^\circ\text{C}$  for the rotator to enter the intermediate regime of the  $^2\text{H}$  NMR experiment ( $k \approx 10^8 \text{ s}^{-1}$ ), and an activation barrier of only 4.3 kcal/mol was determined from measurements between  $-80$  and  $-130 \text{ K}$ . Notably, the barrier of **9b** is only 1.3 kcal/mol higher than the barrier of 3.0 kcal/mol for the rotation of the two methyl groups in ethane in the gas phase! The favorable dynamics of compound **9b** clearly suggest the feasibility of engineering crystalline free-rotors. We believe that this feat



**FIGURE 12.** (a) Space-filling structures of molecular gyroscopes **4a–4c** with a 4 Å solvent-accessible surface and rates of rotation at 298 K.



**FIGURE 13.** (Left) Packing diagram of molecular gyroscope **9b** (hydrogen atoms removed) illustrating its layered structure and the location of bromobenzene (in light blue and orange) around the rotator (in red). (Right) Environment around the phenylene rotator.

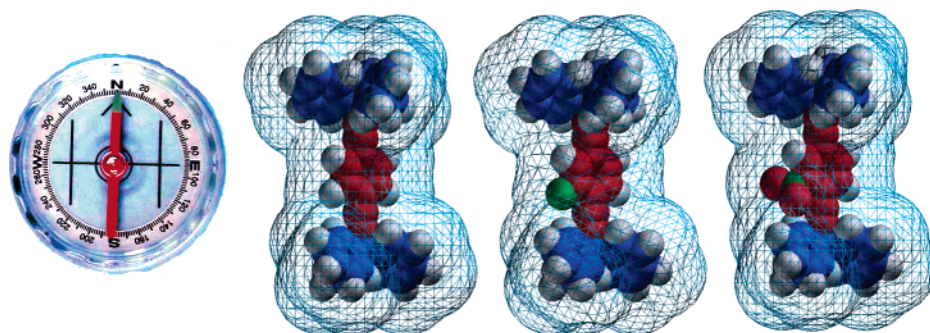
may be accomplished with structures having closed topologies such as that shown in Figure 6, by using volume-conserving rotators with more cylindrical shapes and higher rotational symmetry<sup>47</sup> or by taking advantage of very open, low-density structures based on metal organic frameworks.<sup>48</sup>

## 5. Future Work: Molecular Compasses and Barrierless Rotators

Although still at a very early stage, we have made progress in the formulation, design, and preparation of crystalline molecular machines. On the basis of the premise that the

molecular structure should contain most of the information required to determine the dynamics of crystalline solids, we propose that motion in close-packed molecular systems will rely on the design of (1) free volume, (2) volume-conserving motions, and/or (3) correlated motions. Our design is currently focused on achieving low-rotational barriers by using groups that isolate the central rotator and the exploration of compounds with polar rotary groups. In that regard, we recently begun work on structures with permanent magnetic and electric dipoles,<sup>49</sup> which we refer to as *molecular compasses*. As a starting point, we simply modified molecular gyroscope **4a** with fluoro-, amino-, *o*-diamino-, *p*-amino-nitro-, nitro-, and cyano- groups attached to the phenylene rotator (Figure 14).

It is expected that molecular compasses packed within interacting distances will exhibit a host of interesting properties, including spontaneous polarization and collective response to external electric, magnetic, or electromagnetic fields. We recently showed that these interactions can be measured by dielectric spectroscopy, where the rotary motion of the dipoles is interfaced with an oscillating AC field.<sup>50</sup> The potential of controlling and modulating bulk macroscopic polarization combined with the promising photophysical properties of diethynyl arenes<sup>51</sup> suggests that molecular compasses may be very attractive materials for a wide range of material applica-



**FIGURE 14.** Analogies between a macroscopic compass and molecules with reorienting dipoles of different magnitude (i.e.,  $-H, \mu = 0$ ;  $-F, \mu = 1.49$ ;  $-NO_2, \mu = 4.74$  D).



tions based on dielectric and optical phenomena.<sup>52</sup> We believe that the construction of solids designed to support the correlated motion of several molecular components will be accomplished in a short time.

We thank the National Science Foundation for support and Marcia Levitus, Zaira Dominguez, Carlos Sanrame, Hung Dang, Christopher Mortko, Steve Karlen, and Peter Jarowski for numerous contributions.

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AR0680217