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Molecular Spur Gears Comprising Triptycene Rotators and Bibenzimidazole-Based Stators

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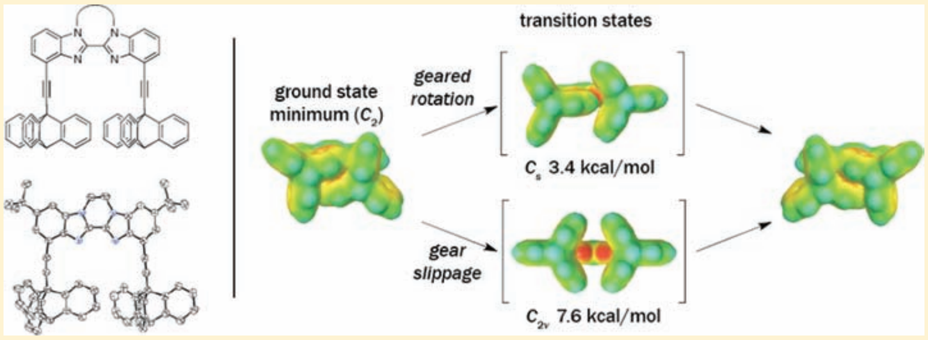
Supporting Information



ABSTRACT: Dynamic gearing of molecular spur gears, the most common type of mechanical gear, is elucidated. Molecular design and conformational analysis show that derivatives of 4,4-bis(triptycen-9-ylethynyl)bibenzimidazole represent suitable constructs to investigate gearing behavior of collateral triptycene (Tp) groups. To test this design, DFT calculations (B97-D/Def2-TZVP) were employed and the results suggest that these molecules undergo geared rotation preferentially to gear slippage. Synthesis of derivatives was carried out, providing a series of molecular spur gears, including the first desymmetrized spur gear molecules, which were subsequently subjected to stereochemical analysis.

INTRODUCTION

The hard-sphere model of a molecule evokes an image of a mechanical object,[1] within which the molecular rotator[2−4] is a fundamental mechanical component. Coupling two or more molecular rotators, such that their motions are correlated, corresponds to gearing, a principal mechanical mechanism. At the molecular level, dynamic gearing[5] has been demonstrated in bevel gears comprising intermeshed triptycene (Tp) groups.[6] To date, no extensive investigations into the function of molecular representations of spur gears (Figure 1) have been reported, though these are the most common gear arrangements found in macroscopic machinery. This report presents the stereochemical analysis, design, calculations, syntheses, and dynamic NMR studies of molecular spur gears.


bevel gear spur gear

Figure 1. Macroscopic bevel and spur gears. Photographs courtesy of Emerson Power Transmission Corp. (www.emerson-ept.com).

Inspired by Ōki's investigations into the rotational barriers of 9-substituted derivatives of Tp,[7] Mislow and Iwamura independently synthesized and studied the stereochemical consequences[8] (vide infra) of dynamic gearing in derivatives of di(triptycen-9-yl)methane (**1**)[9] and di(triptycene-9-yl) ether (**2**),[10] respectively. The energy barriers for correlated disrotation (geared rotation) in derivatives of **1** and **2** have been calculated to be 1−2 kcal/mol; correlated conrotation of the Tp groups, the process of gear slippage, requires highly strained transition structures whose activation energies have been experimentally determined to lie in the range of 32−45 kcal/mol.[11] Analogs of **1** and **2** include isostructural derivatives **3**,[12] in which the Tp groups are linked by a variety of atoms or groups, and a tightly intermeshed vinylene-linked system **4**.[13] A molecular gear that incorporates a clutch function by silane−silicate interconversion **5** has recently been synthesized and studied.[14]

Molecules with three secured rotator components have been synthesized in linear (**6**)[15] or cyclic (**7**, **8**)[16] arrangements, the former exhibit smooth rotation (E_a < 2 kcal/mol) as a correlated triplet, whereas the parity requirement of disrotatory motion locks the latter in a frustrated state (E_a of rotation = 20 kcal/mol). Each of these arrangements has stereochemical consequences: system **6** is dynamic and exhibits phase isomerism;[17] **7** is static and achiral (C_{3h}) whereas **8** is static and chiral (C_3).

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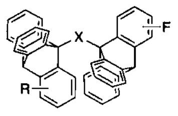

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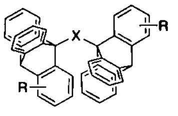
2 X = O



X = S, CHOH, CO, SiH_2, NH
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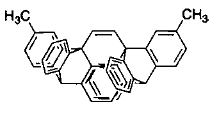

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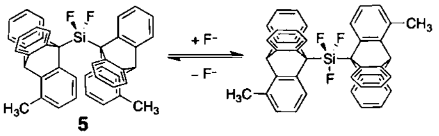

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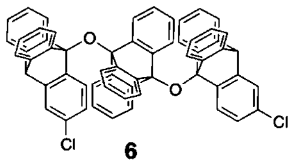

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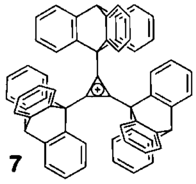

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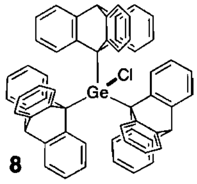

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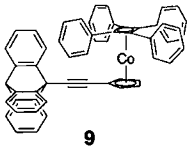
Several gear-like constructs have been reported without stereochemical investigations of labeled derivatives. Representatives of this type include a metallocene-based gearing prototype **9**[18] with a 3 × 4 gearing ratio and di(triptyceno) crown ethers **10a** and **10b**, whose shapes resemble spur gears.[19]



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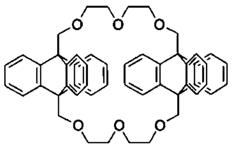
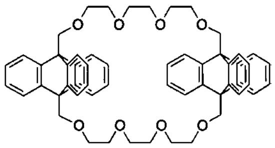


10a



10b

Given the development of molecular gears and the general interest in molecular machines, it would be useful to have some parameters that characterize gearing efficiency. *Gearing fidelity* (F_{gear}) and *gearing temperature* (T_{gear}) are terms to address this issue.[20] The expression $F_{gear} = k_{geared\ rotation}/k_{gear\ slippage}$ provides a measure of gearing fidelity at a given temperature (298 K, for example) as the average number of geared rotations per gear slip. Gearing temperature is the temperature below which the rate of gear slippage remains slower than a certain value (1 s^{-1} when not otherwise stated) and is expressed as $T_{gear}^{\#}$ where # is the log of the number of slips/second (0 when not otherwise stated).

In molecules **1**–**6**, the efficiency of gearing is outstanding, giving high values of F_{gear} and T_{gear}; if 2 kcal/mol were the barrier to geared rotation and 35 kcal/mol the barrier to gear slippage, F_{gear} would be on the order of 10^{23} and T_{gear} would be 584 K. Because a small difference in $\Delta G^{\ddagger}_{geared\ rotation}$ and $\Delta G^{\ddagger}_{gear\ slippage}$ has a significant effect on the rates of the processes, systems whose barriers to geared rotation are only a few kcal/mol lower in energy than their barriers to gear slippage can still function as efficient gears.

Up to this point, all detailed studies of molecular gear constructs have focused on bevel gears. A precise depiction of a molecule as a machine requires that it not only structurally resembles, but also functionally act as, a mechanical component; from this perspective, no investigations of molecular spur gears have yet been reported. Before discussing the details of our study, let us discuss the conformational analysis necessary to motivate such molecular designs.

■ CONFORMATIONAL ANALYSIS AND MOLECULAR DESIGN

Design of molecular gears requires a detailed understanding of conformational analysis and steric shape. Simple valence bond graphs attract one to notions of gearing that are immediately seen as untenable from a space-filling representation.[21] For example, in 1,9-dimethyltriptycene (**11**) (Figure 2), the energy minimum ground state was originally assumed[22] to be a gear-meshed C_s conformation in which the methyl groups undergo correlated rotation, but was later calculated[23] to prefer a buttressed, gear-clashed C_s conformation that does not exhibit correlated rotation of the methyl groups. These studies demonstrate that the geometry of a methyl group closely resembles a triangle-based pyramid (tetrahedron); its effective steric size is conformation-dependent and cannot be best represented simply by its hydrodynamic radius.[24]

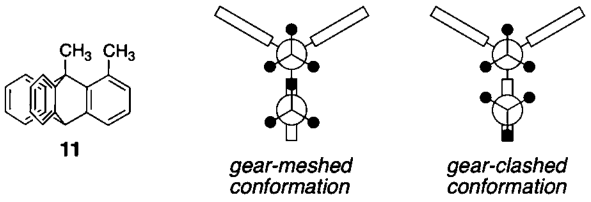


Figure 2. Gear-meshed and gear-clashed conformations of 1,9-dimethyltriptycene.

With the caveat in mind that any serious discussion of molecular gearing warrants a rigorous geometric analysis, let us consider a framework that holds two identical three-bladed rotators, with hydrodynamic radii of r, in a collateral arrangement. Depending on the nature of the blades, the rotators could be approximated by several models: one extreme could render the rotators as three-toothed propellers of negligible thickness, a moderate estimation could approximate the components as triangular prisms, and the other extreme case, where the rotators' steric bulk is well approximated by its hydrodynamic radius, may be represented by cylinders (Figure 3). Positioning these models in gearing (C_2 and C_s) and gear-clashed (C_{2v} and C_{2v}*) orientations,[25] with respect to the molecular framework, and examining their minimum interaxle distances establish their effective steric size.

In any imaginable orientation, the cylinders' minimum interaxle distance is $2r$. In contrast, the minimum axle–axle distances of the propeller or triangular prism approximations depend on their conformations: $0.86r$ (C_2), r (C_s), and r (C_{2v}) for the propeller and $1.15r$ (C_2), $3r/2$ (C_s), and r (C_{2v}) for the triangular prism.

Assuming a hard-surface model, full rotation can only occur in the absence of surface clashing. This condition can be met by increasing the interaxle distance to a point where one

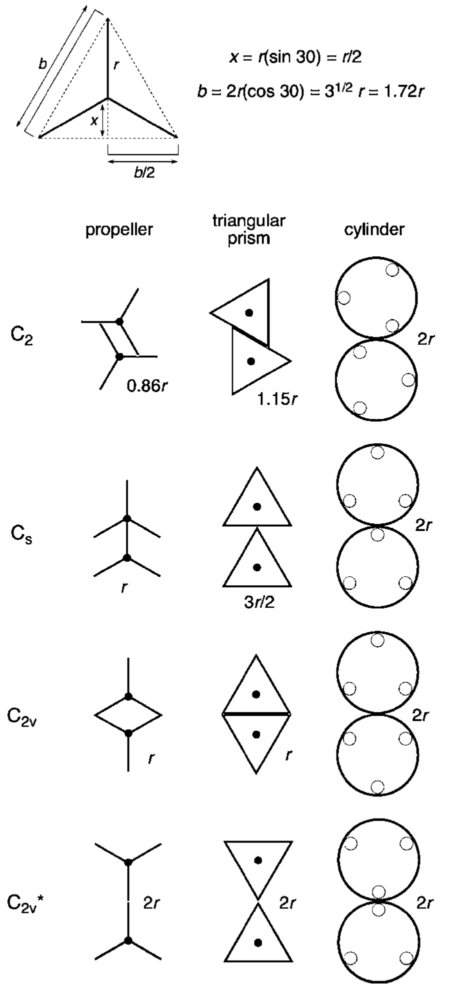


Figure 3. Geometrical analysis of two three-bladed rotators, approximated as propellers, triangular prisms, and cylinders, in C_2, C_s, C_{2v}, and C_{2v}* orientations. The distance from the axle to the blade is r, and the minimum distance between axles is given as a function of r.

rotator can rotate by 2π without clashing with its static partner, as is the case for the C_s structure in rotators resembling triangular prisms. Alternatively, clashing can be avoided by correlated motion of both rotators (gearing) or by gear slippage.

Assuming there is a spring-like tension holding the rotators together, then Hooke's law indicates that the relative interaxle distance r is a measure of potential energy. From this assumption, the relative potential energy of each conformer can be assessed from its interaxle distance. In a system with cylinders, all orientations have the same energy and the groups rotate freely and independently of one another. In the case of triangular prisms, the C_{2v} orientation is predicted to be the lowest energy conformation. In the propeller system, the C_2 orientation would suffer the least repulsion due to steric exclusion, whereas C_s and C_{2v} orientations are higher in energy but not distinguished.

Adding a thickness to the blades requires a larger separation for C_s orientations compared to C_{2v} orientations. Thus, the conclusion from the simple mechanical model would then be that C_s orientations would suffer more steric repulsion due to exclusion than C_{2v} orientations at close distances.

A macro-mechanical analysis considers gears to be hard shapes that fit together with shape complementarity defined by steric exclusion.[26] An equivalent molecular model would consider then only steric exclusion when the conformational energy is assessed.

In molecular systems, the thickness of the gear blade might be estimated by the rough van der Waals surface. Bringing the Tp groups in these C_2, C_s, and C_{2v} orientations together as closely as their van der Waals surfaces[27] reveals that the minimum axle–axle distances are 7.0, 8.1, and 7.2 Å, respectively (Figure 4). Thus, the C_s conformation is required to have a longer axle–axle distance than the C_{2v} conformation by almost 1 Å. In this molecular model, forcing the rotators closer together would increase the energy required for geared rotation more than for gear slippage. Focusing only on van der Waals repulsion by exclusion leaves little hope for this design to result in an effective gear system.

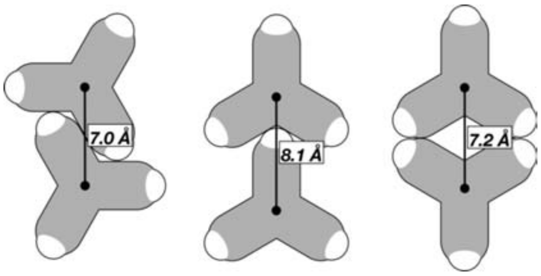
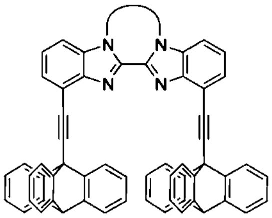


Figure 4. Space-filling representations of Tp groups in C_2 (left), C_s (center), and C_{2v} (right) conformations, indicating the minimum axle–axle distances.

Fortunately, molecular interactions are more varied than simple hard sphere repulsion. Attractive dispersive terms, along with various electrostatic terms, enrich the analysis and offer the possibility that gearing mechanisms can prevail; for example, van der Waals face-to-face and edge-to-face π–π interactions may stabilize the C_2 and C_s conformations and H–H repulsions or a pocket of vacuum between the Tp groups may destabilize the C_{2v} conformation. If such were the case, geared rotation could be preferred over gear slippage, albeit unlikely to reach the robust character seen in bevel gears **1**–**6**. Properly addressing such scenarios exceeds the abilities of simple qualitative models and commitment to full quantum mechanical (QM) analysis is thus called for (see below).

Despite the need for rigorous QM computations to assign an accurate energy ranking of the conformations, the basic conformational analysis sets rough target dimensions that should allow the Tp groups to interconvert between C_2 and C_s conformations with minimal strain. The stator must project the two axles in parallel and separate them by an appropriate distance that allows for interaction of the rotators. Our recent work on 1,1′-bridged derivatives of 4,4′-disubstituted 2,2′-bibenzimidazole (BBI)[28] provides synthetic access to a stator framework that meets these requirements. Substituents at the 4- and 4′-positions extend in parallel at a distance of roughly 8 Å,[29] accommodating a C_s conformation. Acetylene groups extend linearly and provide a sufficient distance between the stator and rotator, and their flexibility was expected to allow for a favorable C_2 conformation to be reached with minimal strain. The combination of these rotator, axle and stator components, leads to the generic structure **12**.



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The final aspect of the design concerns the location and type of labeling groups that must be added to the rotators to provide desymmetrized derivatives, potentially giving rise to phase isomers. Dynamic gearing of molecular rotators can be established by the observation of phase isomers in desymmetrized derivatives under conditions at which, on the time scale of observation, gear slippage is slow. In three-bladed gears, with one blade labeled, three phase isomers are expected: two enantiomers and one meso isomer (Figure 5).[30] The phase isomers exist as gearing circuits comprising six energy minimum conformations that, in the absence of gear slippage, may interconvert only through the individual phases of the circuit. Barriers to gear slippage can be calculated by determining the rates at which the phase isomers interconvert.

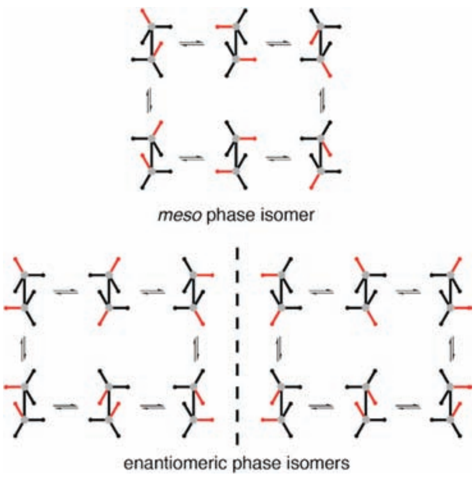
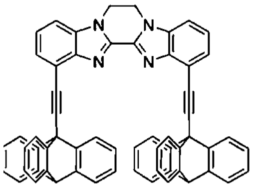


Figure 5. Schematic representation of phase isomers. Benzene rings containing substituents are red.

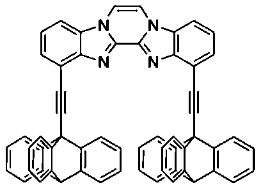
Introduction of labeling groups at the 4-positions of the Tp groups avoids steric hindrances between the two Tp rotators and between the rotators and the stator. In the enantiomeric phase isomers, the labeling groups come in close contact in three of the conformations; in the meso phase isomer, they remain distant from one another, a difference that was expected to induce chemical shift differences between the meso and enantiomeric phase isomers in NMR spectroscopy. Trifluoromethyl (CF_3) groups were chosen, as they permit ^{19}F-NMR experiments and were expected to enhance the chemical shift differences between phase isomers in ^{1}H NMR spectra. Methyl groups were also chosen, as the behavior of the ^{1}H NMR signal of this methyl group could indicate the presence of phase isomers at low temperatures.

■ RESULTS AND DISCUSSION

Calculations. Dispersion-enabled DFT, B97-D/Def2-TZVP, was applied to spur gear molecules **12a** and **12b**, which differ in the saturation of the pyrazine ring at the center of the stator.



12a



12b

Molecular geometries were fully optimized in C_2, C_s, and C_{2v} conformations from which their relative energies, including effects of zero point energy, were calculated (Figure 6). For both **12a** and **12b**, the C_2[31] conformation is the lowest energy ground state minimum. Hessian analysis confirms the C_s conformation as a transition structure for geared rotation and the C_{2v} conformation as a transition state to gear slippage, for **12b**. In **12a**, the C_s and C_{2v} conformations each exhibit two imaginary frequencies, one matching the motion and magnitude of the frequencies in the analogous structures of **12b**, and a much higher mode arising from out-of-plane twisting of the ethylene bridges. This result derives from the central 2,3-dihyropyrazine moiety's preference to avoid the eclipsed conformation and adopt a twisted/staggered conformation.[32] The planarity of this ring, as required by symmetry in the C_s and C_{2v} conformations, thereby uniformly raises the energies of these conformations to

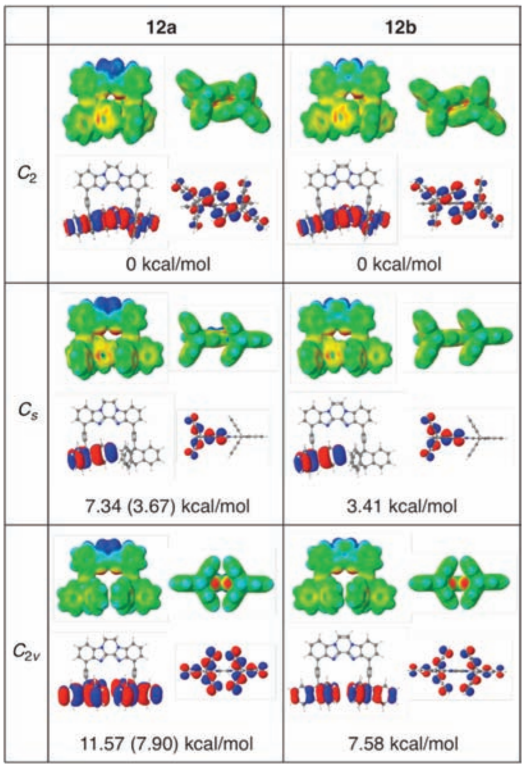
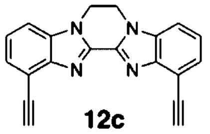


Figure 6. B97-D/Def2-TZVP calculated C_2, C_s, and C_{2v} structures and energetics of **12a** and **12b** rendered as electrostatic potential maps (top, contour level = 0.005) and HOMOs (bottom, contour level = 0.02) in each case. Energies relative to the respective C_2 conformations are given beneath the structures. Values in parentheses indicate the estimated energies for the transition state structures for gearing (C_s) and gear slippage (C_{2v}) in **12a**, calculated by subtracting the energetic cost of planarity in the stator/axle unit (see text).

levels that are higher than those of the genuine transition states. Analysis of molecule **12c** indicated that in the absence of gear interactions the twisted/staggered C_2 conformation is 3.67 kcal/mol lower in energy than the C_{2v} structure. Subtraction of this value from the energies of the C_s and C_{2v} conformations of **12a** provides an estimated value for the energies of the genuine transition state conformations (shown in parentheses in Figure 6). Hessian analysis of **12c** in the C_{2v} conformation showed a single imaginary mode essentially identical in motion and frequency to the higher mode found for **12a**. The high consistency among these computed structures (**12a**−**c**) provides greater confidence in the accuracy of the gearing model and analysis.



12c

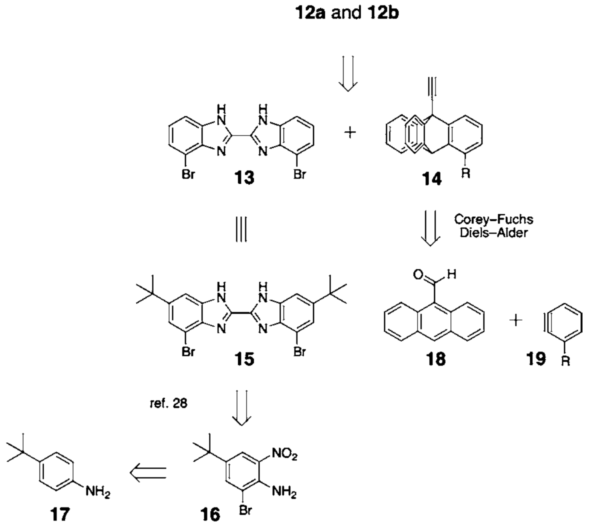
As expected from Figure 4, the distances between the axles of rotation[33] in the Tp groups increase from C_2 to C_{2v} to C_s in **12a** and **12b**. Distances of 6.84 Å (**12a**) and 6.85 (**12b**) for C_2 conformations and 7.98 (**12a**) and 7.99 (**12b**) for C_s conformations are ∼0.10−0.15 Å shorter than those shown in Figure 2, due to inward bending of the Tp groups. In the C_2 conformations, the proximal benzene rings display close face-to-face and edge-to-face arene distances the correlative of which places the Tp groups close together, with the axles bending inward. Analysis of the HOMOs shows in-phase orbital interactions between the two Tp groups.

The inward bending of the Tp groups in the C_s conformations and their lower energies compared to the C_{2v} conformations suggests that a slight attraction may exist between the Tp groups. As a consequence of the molecular symmetry, the C_s structures exhibit nearly degenerate HOMOs, each containing significant density on one of the Tp groups (one of which is shown for each in Figure 6).

The interaxle distances in the C_{2v} structures [7.71 Å (**12a**), 7.74 Å (**12b**)], though shorter than their C_s counterparts, are ∼0.5 Å longer than would be required from steric exclusion alone. This widening suggests a destabilizing repulsion between the blades of the Tp groups, which is further supported by the higher energy of the C_{2v} conformations. The HOMO orbital also shows antibonding interactions between the Tp groups.

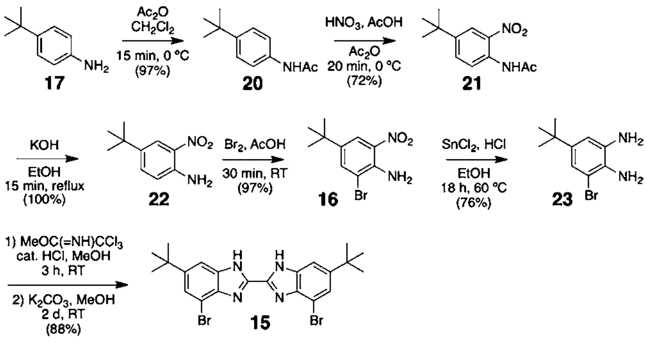
The computations clearly indicate that gear-meshed conformations C_2 and C_s are favored over the gear-clashed C_{2v} conformation and provide computed (**12b**) and estimated (**12a**) values for $\Delta G^{\ddagger}_{\text{geared rotation}}$ and $\Delta G^{\ddagger}_{\text{gear slippage}}$. From these data, gearing efficiency in terms of F_{gear} and T_{gear} can be assessed. The computations thus predict F_{gear} values of 1300 (**12a**) and 1100 (**12b**) and T_{gear} values of 138 K (**12a**) and 133 K (**12b**).[34] The results from the calculations support the molecular design and provided motivation for the chemical synthesis and investigation of BBI-based molecular spur gears.

Scheme 1. Retrosynthesis of Derivatives of Molecular Spur Gears 12a and 12b



Synthesis of Molecular Spur Gears. Retrosynthetic analysis of **12a** and **12b** leads to stator component 4,4′-dibromo-BBI (**13**) and rotator/axle component 9-ethynyltriptycene (**14**) (Scheme 1). To increase the solubility of the synthetic targets, 4,4′-dibromo-6,6′-di-*tert*-butyl-BBI (**15**) was substituted for **13**. Bibenzimidazole **15** can be disconnected to bromonitroaniline (**16**), which could be prepared from commercially available 4-*tert*-butylaniline (**17**). 9-Ethynyltriptycene, and 4-substituted derivatives thereof, can be disconnected from anthracene-9-carboxaldehyde (**18**) and 3-substituted benzynes (**19**).

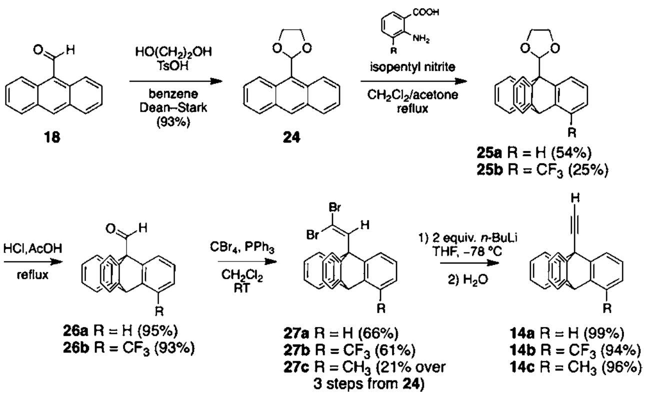
Scheme 2. Synthesis of Stator Intermediate 15



Bibenzimidazole **15** was synthesized in six steps from **17** (Scheme 2). Protection of the amino group in **17** with an acetyl group afforded acetanilide **20**, which underwent nitration to generate **21**. Deprotection yielded nitroaniline **22** and subsequent bromination yielded **16**.[35] Reduction of the nitro group with $SnCl_2$ afforded bromodiamine **23**. Treatment of **23** with 0.5 molar equiv of methyl 1,1,1-trichloroacetimidate and a catalytic amount of HCl, followed by basification with K_2CO_3, provided bibenzimidazole **15**.[36]

Rotator/axle components 9-ethynyltriptycene **14a** and 4-labeled derivatives **14b,c** were prepared by slightly modifying a published synthesis[37] (Scheme 3). Aldehyde **18** was converted to cyclic acetal **24**, which was treated with derivatives of benzyne, generated in situ from derivatives of anthranilic acid to yield triptycene **25**. Deprotection gave aldehyde **26**, which could be converted to ethynyltriptycenes **14a**−**c** by a Corey−Fuchs[38] homologation via dibromoalkenes **27a**−**c**. An alternate synthesis employing a Sonogashira cross-coupling is known[39] and also provided access to **14a**, but the Corey−Fuchs method was preferable in our hands. Reaction of **24** with 3-methylbenzyne gave the 1-methyl and 4-methyl derivatives of **25**. These isomers were not separated but carried on in the synthesis as a mixture until the Wittig step of the Corey−Fuchs methodology, which selectively reacted with the anti isomer

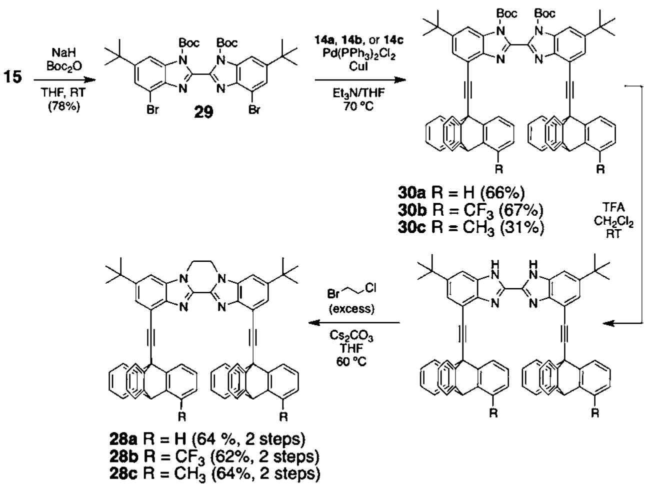
Scheme 3. Synthesis of Rotator/Axle Components 14a−c



and allowed for straightforward purification of **27c** by column chromatography.

With compounds **14a−c** and **15** in hand, ethylene-bridged molecular spur gears **28a−c** were synthesized (Scheme 4).

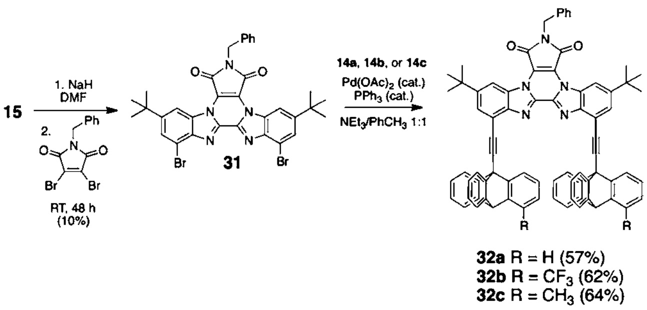
Scheme 4. Synthesis of Ethylene-Bridged Molecular Spur Gears 28a−c



The 1- and 1′-positions of **15** were protected with Boc groups, affording **29**, which was treated with alkynes **14a**, **14b**, or **14c** under standard Sonogashira cross-coupling conditions to yield **30a−c**. Subsequent deprotection, followed by treatment with an excess of 1-bromo-2-chloroethane, afforded **28a−c** in yields ranging from 62% to 64%.

Synthesis of analogs of unsaturated gear **12b** presented a different challenge. Several initial attempts to introduce a vinylene bridge to compound **15** failed, but deprotonation with NaH, followed by treatment with *N*-benzyl-2,3-dibromomaleimide,[40] successfully introduced an unsaturated C−C bond at the desired position, affording dibromoimide **31** (Scheme 5). The yield of this reaction was routinely ∼10%, lower than the reported yield of 36% for the same reaction with unsubstituted BBI.[41] Copper-free cross-coupling reactions[42] with alkynes **14a−c** afforded spur gears **32a−c**. Standard Sonogashira conditions using CuI failed, presumably due to complexation of the Cu(I) by **31**.

Scheme 5. Synthesis of Dioxopyrrole-Fused Spur Gears 32a−c



X-ray Structure of Molecular Spur Gear 28a. Single crystals of **28a** were obtained from chlorobenzene, and the crystal structure was determined by X-ray crystallography. The asymmetric unit contains one molecule of **28a** and approximately two molecules of chlorobenzene, which are distributed across three partially occupied sites with high disorder. The unit cell contains two molecules of **28a** and the space group is $P\overline{1}$, with the center of inversion located at a point elevated above the plane of the heterocyclic stator component.

The molecular structure, though unsymmetrical, closely resembles the calculated C_s conformation of **12a** (Figure 7).

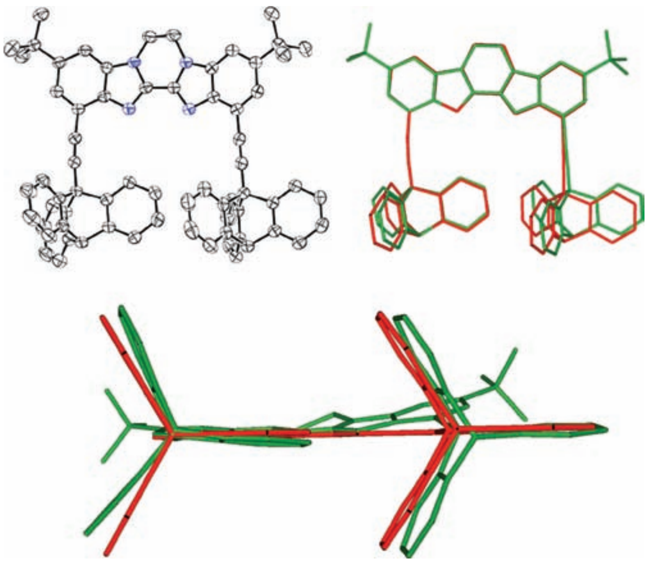


Figure 7. (Top left) The X-ray molecular structure of **28a** [50% thermal ellipsoids; hydrogen atoms removed for clarity. (Top right and bottom) An overlay of experimental structure of **28a** (green) and the calculated C_s structure of **12a** (red).

The plane of the inward-facing, wedged benzene ring and the planes of the flanking, proximal benzene rings of the neighboring Tp group intersect at angles of 56.6(2)° and 67.2(2)°. The plane of this wedged benzene ring and the plane of the distal benzene ring on the other Tp group are close to parallel, intersecting at an angle of 10.4(2)°. The distances between the (9−9′) and (10−10′) bridgehead atoms of the Tp groups are 8.420(4) and 8.257(4) Å, respectively, longer than those found in the calculated C_s structures **12a** and **12b**.

The molecular structure in the crystal, considered in the context of the calculations, provides further evidence for the preference of the C_s conformation over the C_{2v} conformation. The similarity of the experimental structure to a C_s conformation illustrates that the transition state to geared rotation is a favorable conformation of relatively low energy and provides additional validation to the calculated structures.

Deviation from the C_2 conformation, the most stable conformation according to calculations, is attributable to crystal packing forces.

VT-NMR Experiments. Although the energy barriers for gear slippage were calculated to be in the range 7−8 kcal/mol (at the detection limit for VT-NMR studies) compounds **28b**, **28c**, **32b**, and **32c** were probed in an attempt to uncover phase isomerism at low temperature.[43] Determination of coalescence temperatures for the interconversion of meso and enantiomeric phase isomers could experimentally confirm the molecular preference for geared rotation over gear slippage and quantitatively establish the barrier to gear slippage. ^{1}H NMR Samples were measured in the low-freezing solvent $CDCl_2F$[44] at temperatures as low as 150 K.[45]

The VT-^{1}H NMR signals of all of the studied molecules significantly broaden upon cooling but show no clear signs of decoalescence (see Supporting Information). ^{19}F-NMR spectra of **28b** and **32b** in CD_2Cl_2 were measured at temperatures as low as 180 K and also showed broadening, but no splitting, of the signals.

The absence of decoalescence in VT-NMR experiments precludes the determination of the barrier to gear slippage and experimental demonstration that the rotators prefer to undergo geared rotation over gear slippage. Several explanations could account for the absence of observable decoalescence:

(1) The chemical shift differences between signals from the enantiomeric and meso phase isomers may be so small as to render them unobservable. Considering the common peak broadening that results from shimming, tumbling and other experimental issues at low temperature, it is possible that independent signals could be hidden within the broad peaks.

(2) The calculated values for the barriers to gear slippage may be higher than those for the experimental systems under the conditions of observation. If the barriers to gear slippage for the experimental systems lie below 7 kcal/mol, rather than ~8 kcal/mol, decoalescence would not be observable even at temperatures as low as 150 K.

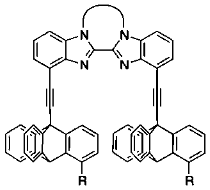
OUTLOOK

As technical issues did not allow for conclusive experimental observation of the presence (or absence) of phase isomers, the logical next step is to synthesize systems that would lead to greater chemical dispersion of the NMR signals, increasing the likelihood of observing phase isomers, should they exist. The labeling groups remain distant from each other in the meso phase isomer and come close in three of the six energy-minimum conformations in the enantiomeric phase isomers. This difference could be exploited in systems incorporating strongly anisotropic units, including π-systems, which are known to induce significant changes in the chemical shifts of local nuclei.[46]

According to the Gutowsky−Holm approximation[47] and the Eyring equation, increasing $\Delta\nu$ between decoalesced signals not only makes observation of decoalesced signals easier to observe but also increases the temperature of coalescence. By increasing chemical shift dispersion, coalescence occurs at faster exchange rates; therefore, T_c will be higher and hence more accessible.

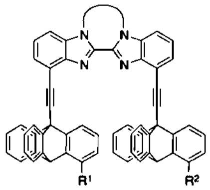
Design of next-generation targets incorporates chemical shift anisotropy (CSA) inducers. For example, a construct containing triple bonds such as alkynes or nitriles (**33**) can be envisioned and ^{13}C-labeled derivatives thereof would allow one to exploit the high resolution of ^{13}C NMR spectroscopy.

More advanced targets (**34**) include gears with differentially labeled Tp groups, in which one Tp group contains a CSA inducer and the other Tp group contains an NMR-active reporter substituent. Potential CSA inducers include alkynes and nitriles, strongly anisotropic aryl or arylethynyl groups, or possibly stable radicals. NMR-active reporter substituents could include the methyl (^{1}H NMR) and trifluoromethyl (^{19}F-NMR) groups described in this study as well as a variety of ^{13}C-labeled substituents (^{13}C NMR).



33

R = CCH
R = CN



34

R^1 = CSA inducer
R^2 = NMR-active reporter

CONCLUSIONS

Encompassing molecular design, density functional theory calculations, chemical synthesis, structural examination, and dynamic stereochemical analysis, this work illustrates a rigorous investigation into molecular spur gears. Computational results regarding **12a** and **12b**, combined with structural data of **28a**, strongly suggest that the Tp rotators on these molecules preferentially undergo geared rotation over gear slippage, although VT-NMR studies did not experimentally confirm the presence of phase isomers in **28b**,**c** and **32b**,**c**. The syntheses and investigations reported here form the basis for future work in the field of molecular rotors and machinery. An emphasis is placed on the importance of engineering molecular features not attributable to the classical hard sphere/mechanical model. Along these lines, macro-engineering principles like those of magnetic gearing may provide the insight necessary to achieve high gearing fidelity at practical temperatures.

ASSOCIATED CONTENT

Ⓢ Supporting Information

Full experimental synthesis procedures and characterization data, including ^{1}H-NMR and ^{13}C-NMR spectra of all new compounds; computational methods; VT-NMR spectra of **28b**, **28c**, **32b**, and **32c**; and CIF file of **28a**. This material is available free of charge via the Internet at http://pubs.acs.org/.

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■ REFERENCES

(1) (a) Balzani, V.; Credi, A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348. (b) Browne, W. R.; Feringa, B. L. *Nat. Nanochem.* **2006**, *1*, 25. (c) Kay, E. R.; Leigh, D. A.; Zerbetto, F. *Angew. Chem., Int. Ed.* **2007**, *46*, 72. (d) Carella, A.; Coudret, C.; Guirado, G.; Rapenne, G.; Vives, G.; Launay, J.-P. *Dalton Trans.* **2007**, 177.

(2) (a) Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281. (b) Feringa, B. L. *Acc. Chem. Res.* **2001**, *34*, 504. (c) Broer, D. J.; Feringa, B. L. *Nature* **2006**, *440*, 163.

(3) (a) Khuong, T.-A. V.; Nunez, J. E.; Godinez, C. E.; Garcia-Garibay, M. A. *Acc. Chem. Res.* **2006**, *39*, 423. (b) Godinez, C. E.; Zepeda, G.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 4701.

(4) (a) Clarke, L. I.; Horinek, D.; Kottas, G. S.; Varaska, N.; Magnera, T. F.; Hinderer, T. P.; Horansky, R. D.; Michl, J.; Price, J. C. *Nanotechnology* **2002**, *13*, 533. (b) Hou, S.; Sagara, T.; Xu, D.; Kelly, T. R.; Ganz, E. *Nanotechnology* **2003**, *14*, 566. (c) van Delden, R. A.; ter Wiel, M. K. J.; Pollard, M. M.; Vicario, J.; Koumura, N.; Feringa, B. L. *Nature.* **2005**, *437*, 1337.

(5) Dynamic gearing is defined as the "special effect on the rate or mechanism of a process that may be attributed to the intermeshing of a chemical rotor with a neighboring group" in: Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65.

(6) (a) Iwamura, H.; Mislow, K. *Acc. Chem. Rev.* **1988**, *21*, 175. (b) Mislow, K. *Chemtracts: Org. Chem.* **1989**, *2*, 151.

(7) Ōki, M. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 87.

(8) Hounshell, W. D.; Johnson, C. A.; Guenzi, A.; Cozzi, F.; Mislow, K. *Proc. Natl. Acad. Sci.* **1980**, *77*, 6961. References 3a,b.

(9) (a) Cozzi, F.; Guenzi, A.; Johnson, C. A.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 957. (b) Johnson, C. A.; Guenzi, A.; Mislow, K. *J. Am. Chem. Soc.* **1981**, *103*, 6240. (c) Guenzi, A.; Johnson, C. A.; Cozzi, F.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1438.

(10) (a) Kawada, Y.; Iwamura, H. *J. Am. Chem. Soc.* **1981**, *103*, 958. (b) Kawada, Y.; Iwamura, H. *Tetrahedron Lett.* **1981**, *22*, 1533.

(11) Bürgi, H.-B.; Hounshell, W. D.; Nachbar, R. B.; Mislow, K. *J. Am. Chem. Soc.* **1983**, *105*, 1427.

(12) Thioether: (a) Kawada, Y.; Ishikawa, J.; Yamazaki, H.; Koga, G.; Murata, S.; Iwamura, H. *Tetrahedron Lett.* **1987**, *28*, 445. Carbinol: ref 10c. Ketone: (b) Johnson, C. A.; Guenzi, A.; Nachbar, R. B. Jr.; Bount, J. F.; Wennerström, O.; Mislow, K. *J. Am. Chem. Soc.* **1982**, *104*, 5163. Silane ref 5o in ref 7. Amine: (c) Kawada, Y.; Yamazaki, H.; Koga, G.; Murata, S.; Iwamura, H. *J. Org. Chem.* **1986**, *51*, 1472.

(13) Kawada, Y.; Sakai, H.; Oguri, M.; Koga, G. *Tetrahedron Lett.* **1994**, *35*, 139.

(14) Setaka, W.; Nirengi, T.; Kabuto, C.; Kira, M. *J. Am. Chem. Soc.* **2008**, *130*, 15762.

(15) (a) Koga, N.; Kawada, Y.; Iwamura, H. *J. Am. Chem. Soc.* **1983**, *105*, 5498. (b) Koga, N.; Kawada, Y.; Iwamura, H. *Tetrahedron* **1986**, *42*, 1679.

(16) Chance, J. M.; Geiger, J. H.; Mislow, K. *J. Am. Chem. Soc.* **1989**, *111*, 2326.

(17) Vide infra; see Figure 5.

(18) Stevens, A. M.; Richards, C. J. *Tetrahedron Lett.* **1997**, *38*, 7805.

(19) Bryan, J. C.; Sachleben, R. A.; Gakh, A. A.; Bunick, G. J. *J. Chem. Cryst.* **1999**, 513.

(20) Frantz, D. K.; Baldridge, K. K.; Siegel, J. S. *Chimia* **2009**, *63*, 201.

(21) Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. *Isr. J. Chem.* **1980**, *20*, 65.

(22) Nakamura, M.; Ōki, M.; Nakanishi, H.; Yamamoto, O. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2415.

(23) Imashiro, F.; Takegoshi, K; Terao, T.; Saika, A. *J. Am. Chem. Soc.* **1982**, *104*, 2247.

(24) Cases in which the steric bulk of a group is not well represented by its hydrodynamic radius can often be found in systems that demonstrate interlocking of groups (e.g., the rotators in gear constructs **1**−**8**). Other examples include the solid state structure of a 1:1 mixture of tris(phenylethynyl)benzene and tris[(pentafluorophenyl)ethynyl]benzene, which exhibits interlocked packing of alternating molecules (see: Ponzini, F.; Zagha, R.; Hardcastle, K.; Siegel, J. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 2323). The structural differences between corannulene, which is well represented as a circular bowl, and 1,3,5,7,9-pentamethylcorannulene, which resembles a pentagon, also illustrate this point (see: Bauert, T.; Merz., L.; Bandera, D.; Parschau, M.; Siegel, J. S.; Ernst, K.-H. *J. Am. Chem. Soc.* **2009**, *131*, 3460).

(25) The point groups given in this discussion assume axles on one side of the rotators that are connected by a stator. By this treatment, a C_{2h} orientation of lone rotators becomes C_2-symmetric, D_{2v} becomes C_{2v}, and C_{2v} becomes C_s. The C_{2v}* orientation positions the blades of each rotator directly toward each other.

(26) Oberg, E.; Johnes, F. D.; Horton, H. L.; Ryffel, H. H. *Machinery's Handbook; A Reference Book for the Mechanical Engineer, Designer, Manufacturing Engineer, Draftsman, Toolmaker, and Machinist*, 26th ed.; Industrial Press: New York, 2000.

(27) In Figure 3, the Tp groups are rendered according to the following specifications: the thickness of a benzene ring is 3.4 Å, twice the van der Waals radius of a carbon atom. The hydrogen atoms at the tips of the benzene rings have a van der Waals radius of 1.2 Å. The minimum distances between axles are calculated from van der Waals contacts of inflexible Tp moieties.

(28) (a) Frantz, D. K.; Sullivan, A. A.; Yasui, Y.; Linden, A.; Baldridge, K. K.; Siegel, J. S. *Org. Biomol. Chem.* **2009**, *7*, 2347. (b) Yasui, Y.; Frantz, D. K.; Siegel, J. S. *Org. Lett.* **2006**, *8*, 4989.

(29) The distances between the 4- and 4′-positions in the X-ray crystal structure of 4,4′-diaryl-1,1′-ethylene-bridged derivatives of BBI range from 8.08−8.20 Å (see ref 28a).

(30) Reference 6a and references cited therein.

(31) There are two diastereomeric C_2 conformations, whose difference in energy is 0.58 kcal/mol, for molecule **12a**. The discussion considers only the lowest energy structure.

(32) 2,3-Dihydropyrazineprefers a twisted conformation. See: Wiberg, K. B.; Nakaji, D.; Breneman, C. M. *J. Am. Chem. Soc.* **1989**, *111*, 4178.

(33) Interaxle distances are measured as the distances between the centroids calculated from the bridgehead carbons at the 9- and 10-positions of the Tp groups.

(34) The values given are based on rates that were calculated from $\Delta G^{\ddagger}_{\text{geared rotation}}$ and $\Delta G^{\ddagger}_{\text{gear slippage}}$ using the Eyring equation.

(35) Preparation of **21** from **17** is reported in: Carpenter, M. S.; Easter, W. M.; Wood, T. F. *J. Org. Chem.* **1951**, *73*, 586.

(36) Holan, G.; Samuel, E. L.; Ennis, B. C.; Hinde, R. W. *J. Chem. Soc. C.* **1967**, 20.

(37) Our synthesis of **14a** closely followed a procedure given in: Kelly, T. R.; Sestelo, J. P.; Tellitu, I. *J. Org. Chem.* **1998**, *63*, 3655.

(38) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(39) Godinez, C. E.; Zepeda, G.; Garcia-Garibay, M. *J. Am. Chem. Soc.* **2002**, *124*, 470.

(40) Joyce, R. P.; Gainor, J. A.; Weinreb, S. M. *J. Org. Chem.* **1987**, *52*, 1177.

(41) Zhang, L.; Carroll, P.; Meggers, E. *Org. Lett.* **2004**, *6*, 521.

(42) Austin, W. B.; Bilow, N.; Kelleghan, W. J.; Lau, K. S. *J. Org. Chem.* **1981**, *46*, 2280.

(43) It should be noted that the nature of rotation of the benzyl group about the pyrrolodione moiety in **32b**,**c** would cause no complication in investigations of phase isomers in VT-NMR experiments. If gear slippage is fast compared to rotation of the benzyl group, the stereochemical outcome of two enantiomeric and one meso phase isomers does not change, as was pointed out and demonstrated by Mislow's investigations of bis(2,3-dimethyltriptycen-9-yl)methanol (ref 10c). The stereochemical consequences also do not change if rotation of the benzyl group is faster than gear slippage; a side-to-side flip of the benzyl group may change the nature through which the conformations in a phase isomer interconvert, but interconversion between phase isomers would not occur.

(44) Siegel, J. S.; Anet, F. A. L. *J. Org. Chem.* **1988**, *53*, 2629.

(45) NMR spectra were recorded at 20 K intervals from 250 to 150 K, then in 10 K intervals from 150 to 250 K. No hysteresis was observed. All spectra taken from 150 to 250 K are given in the Supporting Information.

(46) Klod, S.; Kleinpeter, E. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1893.

(47) Gutowsky, H. S.; Holm, C. H. *J. Chem. Phys.* **1956**, *25*, 1228.