JOC The Journal of Organic Chemistry

ARTICLE

pubs.acs.org/joc

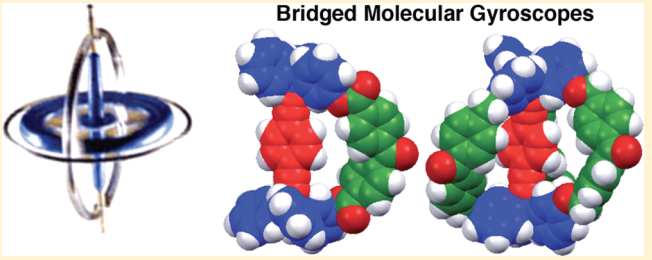
Synthesis of Bridged Molecular Gyroscopes with Closed Topologies: Triple One-Pot Macrocyclization

Patrick Commins, Jose E. Nuñez,† and Miguel A. Garcia-Garibay*

Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569, United States

Supporting Information

ABSTRACT: We describe the synthesis and characterization of six bridged molecular gyroscopes with *m*-alkoxy-substituted trityl stators and dialkynylphenylene rotators. All of the bridged molecular gyroscopes were synthesized convergently to form the phenolic stator−rotator framework, while the alkyl and benzophenone bridges were installed in one step by relatively efficient one-pot reactions to form macrocyclic diether or diester linkages. The isolated yield per bond-forming reaction varied from ca. 42% to 80%, with one exception where macrocyclization failed to produce the desired product. The molecular structure and crystal packing of each of the bridged molecular gyroscopes were determined via single crystal X-ray diffraction. Like most molecular gyroscopes with open topologies previously studied, the singly bridged structures pack by interdigitating one trityl stator in one molecule next to the rotator of an adjacent molecule in the lattice. In contrast, the triply bridged molecular gyroscopes were found to pack in lamellar sheets that prevent the rotator−stator interdigitation of adjacent molecules. However, solvent molecules and conformationally flexible bridges tend to fill in the packing volume by collapsing next to the rotator or by extending one of their bridges into the cavity of a neighboring molecule.



INTRODUCTION

The field of artificial molecular machines has been the subject of intense interest for the past 30 years.[1] Recent interest in the development of functional materials has led to the exploration of amphidynamic crystals built with a combination of rigid components and moving parts.[2−4] It has been suggested that amphidynamic crystals will have physical properties that are a function of their internal dynamics and will provide opportunities for the development of new types of functional materials.[2,5] One of the simplest and most promising strategies involves the preparation of molecular rotors[6] with structures that emulate the architecture and dynamics of macroscopic gyroscopes, which we[2,7] and others[8,9] have addressed from synthetic and functional perspectives. Gyroscopes possess a rotating mass linked by an axle to a shielding structure that provides a frame of reference and acts as the stator to help describe the internal motion (Figure 1). At the molecular level, we have pursued these features with axially linked rotators such as a *p*-phenylene[2,7] and more symmetric groups,[10] two triple bonds acting as the rotary axle, and two bulky triarylmethyl groups serving as the stator (Figure 1b).

It is well-known that rotation of groups linked to triple bonds is essentially barrierless in the gas phase,[11] and we have shown that rotation in the solid state is determined by the hindrance imposed by close neighbors and solvent molecules packing in the vicinity of the rotator.[12] We have shown that molecular gyroscopes with open topologies create low-density regions in the center of their structures, and that they are able to support rotational dynamics that range from a few hertz up to the gigahertz (10^{12} s^{-1})[2a,13] regime. Not surprisingly, we have found that these structures have a tendency for adjacent molecules to interdigitate and solvent molecules to pack close to the rotator (Figure 2A), making a strong case for the development of methods for the synthesis of triply bridged structures with closed topologies (Figure 2B).

As illustrated in Figure 2B, molecular gyroscopes with closed topologies require structures with longitudinal bridges that span from the top to the bottom of the structure to shield the rotator from contacts with the environment. Our first efforts on the synthesis of triply bridged molecular gyroscopes by direct macrocyclization with simple alkyl chains met with problems due to the formation of one "meridional" and two "zonal" bridges (Scheme 1, compound **4**).[14] We discovered that all-axial bridged structures with 8- and 10-carbon alkanediyl chains were not formed by reaction of 3 equiv of the corresponding α,ω-dibromoalkanes with hexaphenol **1**, or by ring-closing metathesis of the hexaalkenyl ethers **2**, a procedure that had been successfully used by Gladyzs and co-workers with metal-coordinated triarylphosphines.[7] The synthesis of compound **3** required a stepwise, directed macrocyclization with a nonsymmetric precursor (**5**) bearing the alkyl chains and the phenols on trityl groups at opposite ends.[13]

A qualitative analysis of molecular models indicates that zonal bridges are probably formed because the chain conformations

Received: August 1, 2011
Published: September 13, 2011

required for side-to-side cyclization are more easily attained than those required for the meridional bridges. In fact, while the distance between zonal phenols ranges from ca. 6.5 to 8.5 Å, the distances between meridional phenols span from 10.5 to 12.5 Å, suggesting that meridional alkyl bridges require entropically more demanding extended conformations. On the basis of this analysis, it should be possible to avoid zonal bridging by using rigid bridges with end-to-end distances that are longer than ca. 8.5 Å. In order to test this hypothesis, we decided to explore the use of 4,4′-dibromomethyl benzophenone and 4,4′-benzophenone dicarboxylic acid dichloride as bridging groups. While the relatively long distance between the reactive 4,4′-carbon atoms (ca. 10 Å) in the substituted benzophenones is not expected to lead to zonal bridges, we envisioned the stereoelectronic demands of the corresponding tetragonal and trigonal cyclization reactions to be different and worth exploring. To evaluate the efficiency of the macrocyclization reaction with ether and ester bridges, we decided to analyze the formation of the singly bridged structures **6** and **9** with 10-carbon chains starting from the diphenol **17**. With good results in both of those reactions, we next confirmed the formation of the benzophenone monobridged structures **7** and **8**, both of which were found to proceed in reasonable yields. A series of four singly bridged molecular gyroscopes and three triply bridged ones were synthesized (Figure 3), and their packing motifs were analyzed by single crystal X-ray diffraction. Compound **12** is not a bridged gyroscope but was obtained during the synthesis of **8** in significant yields. The formation of dimer **12** indicates that the synthesis of **11** would be unlikely, as each bridge could dimerize and prevent a fully intramolecularly cyclized product. The synthesis of a triply bridged ester linked alkyl rotor analogous to **11** was not performed using this method, as there would be competing regioselectivity between the meridional and zonal bridges, as shown in the one-step synthesis of **3**.[14]

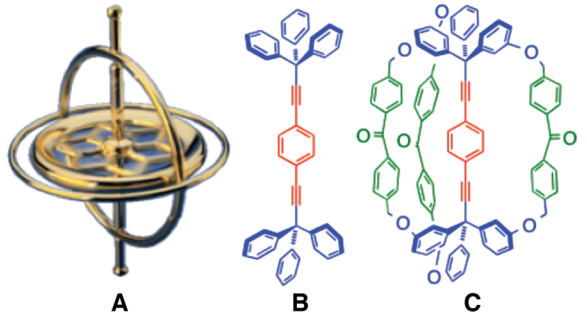


Figure 1. (a) A macroscopic toy gyroscope is assembled with a rotating mass (rotator) that is linked to a stator made by two circles that enclose the rotator. (b) A molecular gyroscope with an open topology consists of a phenylene rotator (red) and two trityl stators in blue, and (c) a molecular gyroscope with a closed topology consists of a phenylene rotator, two trityl stators, and three benzophenone bridges.

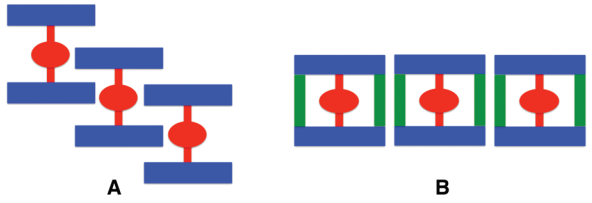
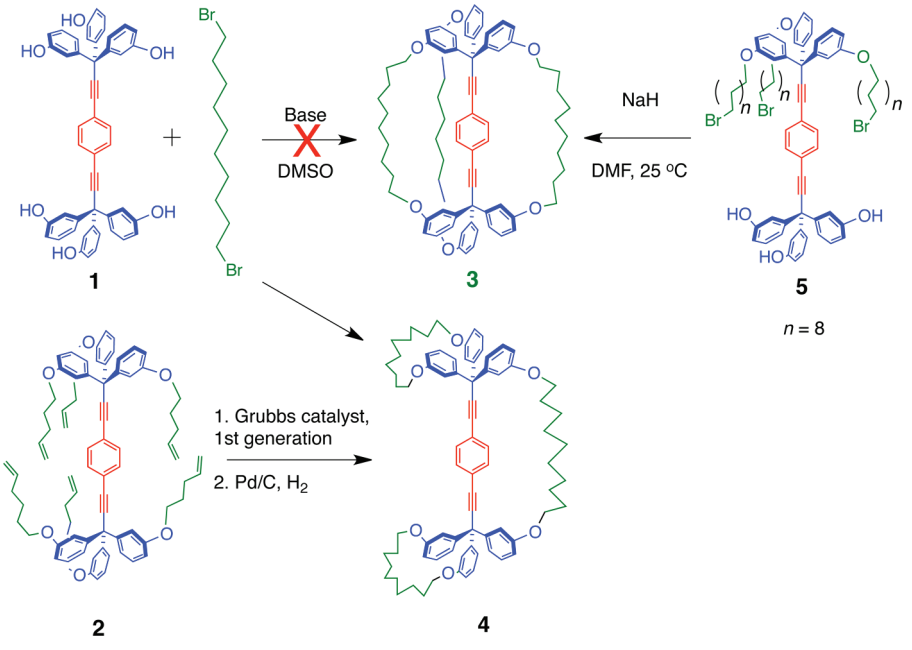


Figure 2. (A) Nonbridged molecular gyroscopes have a tendency to interdigitate one molecule's trityl stator into another molecule's phenylene rotator. (B) Bridged molecular gyroscopes are unable to interdigitate a trityl stator into the adjacent molecules' rotator. Rotators are shown in red, stators in blue, and bridges in green.

RESULTS AND DISCUSSION

Synthesis and Characterization. The synthesis of diphenol **17**, which is the common intermediate for compounds **6**, **7**, **8**, **9**, and **12**, was completed by a straightforward four-step synthesis (Scheme 2). The mono-*m*-methoxy trityl alcohol **14** was synthesized by lithiation of 3-bromoanisole using *n*-butyllithium, which

Scheme 1



dx.doi.org/10.1021/jo201513y |J. Org. Chem. 2011, 76, 8355–8363

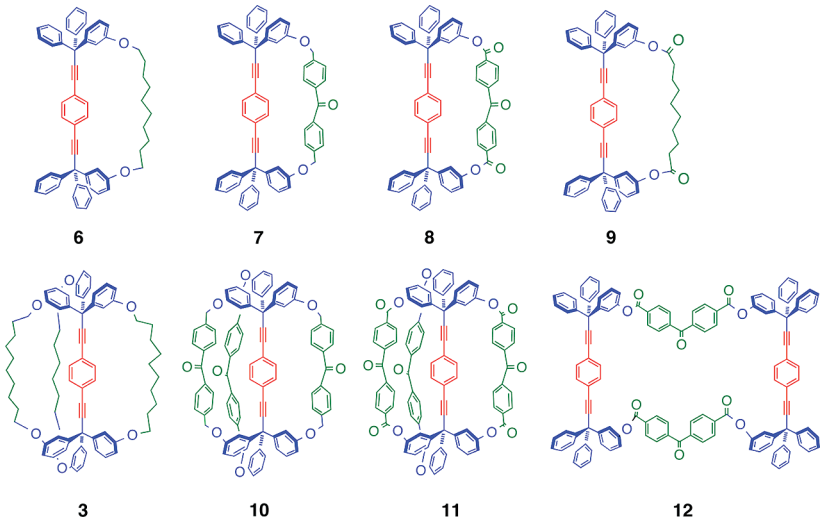
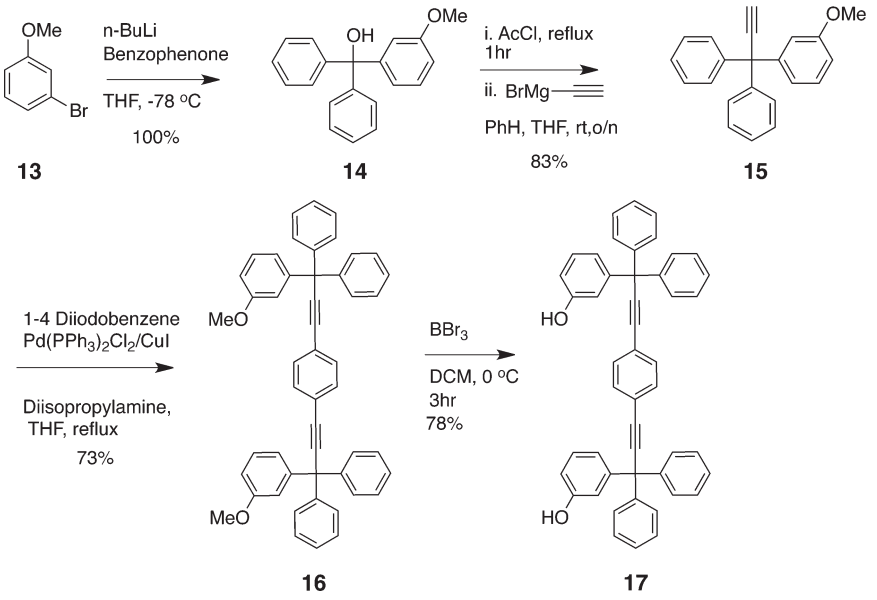


Figure 3. The eight bridged molecular gyroscopes synthesized via a one-pot reaction.

Scheme 2



was followed by reaction with benzophenone. The resulting alcohol was converted to the mono-*m*-methoxy trityl chloride by refluxing in acetyl chloride, which was subsequently refluxed in ethynylmagnesium bromide to generate the mono-*m*-methoxy trityl alkyne **15**. This compound was converted to the di-*m*-methoxy derivative **16** using diiodobenzene and standard Sonogashira conditions. Compound **16** was demethylated using BBr_3 to afford diphenol **17** in an overall yield of 47%.

The synthesis of **1** has been previously described[15] following a reaction sequence similar to that used for the preparation of **17** with the exception that diethyl carbonate instead of benzophenone is used to react with the lithium reagent obtained from 3-bromoanisole in the first reaction. The synthesis affords the hexa-*m*-phenol gyroscope **1** in four steps with an overall yield of 54%. The general one-step synthesis of the bridged compounds **6**−**10** and **12** is illustrated in Scheme 3. Freshly prepared solutions of **1** or **17** and the α,ω-dihalo-substituted bridge precursor are slowly added over 8 h into a solution of DMF containing K_2CO_3 as a mild base. The slow and concomitant addition of the phenol and bridge precursor into the reaction helps maintain a high dilution, which promotes the intramolecular cyclization and prevents oligomerization. The resulting molecular gyroscopes were purified using column chromatography and characterized by ^{13}C NMR, ^{1}H NMR, attenuated total reflectance (ATR) FTIR, high resolution MALDI-TOF mass spectrometry, and single crystal X-ray analysis. Compounds **3**, **6**−**10**, and **12** were isolated in moderate yields as detailed in Table 1.

Comparing the yields per bond formed for a singly bridged gyroscope (e.g., compounds **6** and **7** with two bonds each) to its corresponding triply bridged analogue (compounds **3** and **10** with six bonds each) demonstrates that they are similar. Although

dx.doi.org/10.1021/jo201513y |*J. Org. Chem.* 2011, 76, 8355–8363

this analysis is based only on two examples, this indicates that the addition of the final bridging group was as probable as the addition of the first. One can see from the table that the yields of bridging using ether linkages tend to be higher (67−80%) than those obtained using esters (42−45%). In fact, the low yield for compound **8** correlates with the formation of product **12**, which is a 58-membered macrocycle.[16] That dimerization is favored over intramolecular cyclization, which is shown by the increased yields per bond formed, 42% for **8** vs 68% for **12**. The "dimer" **12** was observed when DMAP was used as a base to synthesize **8**, as potassium carbonate only afforded minor amounts of product. The use of models shows that the phenol has a poor angle of attack on the activated acylpyridinium monolinked intermediate, such that the inefficient intramolecular cyclization causes the intermediate to accumulate and dimerize and form the larger macrocycle. We speculate that the ether-forming compounds do not have a poor angle of attack on the monolinked intermediate and are able to cyclize efficiently. Comparing the results from the reactions leading to **7** and **8** indicates that trigonal cyclizations are unfavorable when bridging the gyroscope as compared to the tetragonal cyclization reactions. The synthesis of compound **11** was attempted, but none of the desired product was detected. However, considering the low yield per bond of **8** and dimerization product for compound **12**, it seems unlikely that compound **11** could be made using this method. No dimerizations or oligomeric products could be isolated from the attempted syntheses of **11**.

Compounds **3**, **6**−**10**, and **12** dissolve well in chloroform, methylene chloride, and toluene and are insoluble in polar solvents such as acetonitrile and methanol. The ^{1}H NMR spectra for all of the bridged molecular gyroscopes show the typical motif of the *m*-alkoxy-substituted aryl ring and the signals of the central phenylene along with those of the unsubsituted phenyl groups in the case of **7**, **8**, **9**, and **12**. With reference to the numbering shown in Scheme 3, the *m*-alkoxy-substituted aryl rings are characterized by an apparent triplet assigned to H10, a doublet of doublets assigned to H7 and two doublet of doublets of doublets assigned to H9 and H11 in the range of 6.29−7.58 ppm. The ^{1}H NMR also showed a singlet corresponding to the four protons (H2) in the central phenylenes between 6.86 and 7.44 ppm, indicating a high degree of average symmetry in all the molecules. The H7 proton for compounds **3**, **6**−**10**, and **12** is significantly deshielded with a chemical shift at 7.23−7.84 ppm, which is 0.45−1.06 ppm higher than that in the *m*-phenol precursors. The increased shielding is due to its forced proximity above the alkynyl axles as indicated in the crystal structures. The ^{13}C NMR spectra of compounds **3**, **6**−**10**, and **12** shows a single quaternary trityl carbon (C5, Scheme 3) at 56.0−56.3 ppm and only two alkyne signals at 84.7−85.2 (C3) and 95.9−97.4 (C4) ppm, further indicating a high degree of symmetry in the structure.

The ^{1}H NMR spectrum of compound **6**, with a single alkyl bridge, has a multiplet from 7.20 to 7.35 ppm attributed to the 20 phenyl protons in its trityl stators. There is a multiplet at 1.20−1.80 ppm assigned to the 16 internal hydrogens of the 10-carbon chain as well as a triplet at 3.90 ppm assigned to the methylene group adjacent to the ether oxygen. There are 12 aromatic carbons in the ^{13}C NMR as well as the quaternary and alkynyl carbons as previously mentioned. There are 4 alkyl carbons between 25 and 31 ppm that are assigned to the bridge, and one signal at 67 ppm corresponding to the carbon adjacent to the oxygen. The ^{1}H NMR spectrum of the triply bridged molecular gyroscope **3** is similar to that of **6**, with the exception that the molecule is now D_{3h} symmetric with a simpler appearance in the aromatic region. In analogy to **6**, compound **7** has 20 aryl protons from 7.20 to 7.30 ppm, two doublet of doublets of doublets with J = 8.2, 2.5, 0.9, and J = 7.8, 1.8, 0.9 Hz at 6.96 and 6.34 ppm, respectively, that integrate for 2H, and a singlet at 5.23 ppm for 4H. The latter are assigned to the benzophenone bridge and the methylene protons, respectively. A ^{13}C NMR signal at 195 ppm corresponds to the carbonyl group of the benzophenone bridge, which can be fully accounted for with four aromatic signals from 131 to 120 ppm and a methylene ether signal at 68 ppm. The ^{1}H and ^{13}C NMR spectra of tribridged compound **10** are similar to those of **7**, and similar assignments could be made for compounds **8** and **12**. However, the correct structure for the latter was suggested from its ESI mass spectrum with a strong signal at m/z = 1753.583 (2M + H) and by a 2D diffusion ordered correlation spectroscopy (2D DOSY) comparison of

Scheme 3

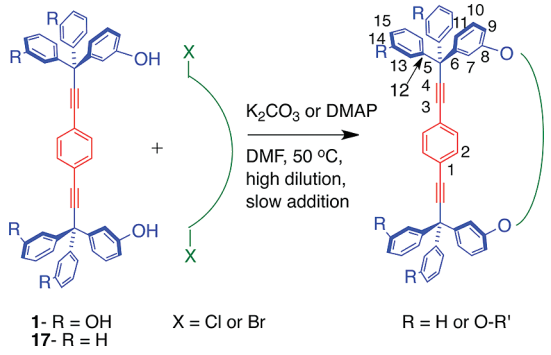


Table 1. Yields from Synthesis of Singly and Triply Bridged Molecular Gyroscopes

compound	bridge precursor	isolated yield (%)	isolated yield per bonds formed (%)
3	*a*	27	65
6	1,10-dibromodecane	46	67
7	bis[4-(bromomethyl)phenyl]methanone	57	75
8	4,4′-carbonyldibenzoyl chloride	18	42
9	1,10-decanedioyl dichloride	20	45
10	bis[4-(bromomethyl)phenyl]methanone	11	69
11	4,4′-carbonyldibenzoyl chloride	0	0
12	4,4′-carbonyldibenzoyl chloride	22	68

[a] Synthesized using asymmetric precursor **5**, as shown in Scheme 1.

dx.doi.org/10.1021/jo201513y |*J. Org. Chem.* 2011, 76, 8355–8363

Table 2. Crystallographic Characteristics of Bridged Molecular Gyroscopes

compound	space group	asymmetric unit	Z	propeller chirality	packing coefficient
3	$P\bar{1}$	$C_{78}H_{88}O_6$ 1.5 ($C_6H_5CH_3$) 0.15 (C_6H_6)	2	$(M, M)/(P, P)$	0.732
6	$C2/c$	$C_{58}H_{52}O_2$	4	$(M, M)/(P, P)$	0.715
7	$P\bar{1}$	$C_{63}H_{44}O_3$ 0.7 (CH_2Cl_2)	2	$(M, M)/(P, P)$	0.679[a]
8	$P\bar{1}$	$C_{63}H_{40}O_5$ 0.3 ($C_4H_{10}O$) 0.7 (CH_2Cl_2)	2	$(M, M)/(P, P)$	0.719
9	$C2/c$	$C_{58}H_{48}O_4$	4	$(M, M)/(P, P)$	0.798
10	$P\bar{1}$	$C_{93}H_{63}O_9$ 1.5 ($C_4H_{10}O$) 4.5 (CH_2Cl_2)	2	(M, P)	0.703

[a] SQUEEZE theorem was applied to remove undeterminable disordered solvent in the crystal.

"monomer" **8** and "dimer" **12**. Compound **8** was found to have a diffusion coefficient of $\log(-9.26)$ m^2/s whereas the larger compound **12** has a value of $\log(-9.40)$ m^2/s. Compound **9** was also identified and characterized from its ^1H and ^{13}C NMR which were consistent with the expected structure.

Single Crystal X-ray Diffraction Analyses. X-ray quality single crystals of compound **9** were grown by slow evaporation from a 50:50 mixture of benzene and toluene. Single crystals of **6** and **10** and single crystal solvates of **7** and **8** were obtained by slow evaporation of 50:50 mixtures of dichloromethane and diethyl ether. The crystal structure for the trialkyl-bridged compound **3** was described previously,[14] and diffraction quality single crystals of **12** could not be obtained. Data acquisition for crystals of compounds **6**−**10** was carried out at 100 K. A summary of the space groups, asymmetric unit contents, molecules per unit cell, trityl chirality, and packing coefficients are included in Table 2.

As shown in Table 2, all of the bridged molecular gyroscopes crystallize in centrosymmetric space groups in low symmetry triclinic ($P\bar{1}$) or monoclinic ($C2/c$) crystal systems. Like the crystal structure of trialkyl bridged compound **3**, crystals of molecular gyroscopes **7**, **8**, and **10** were found to contain disordered solvent molecules with partial occupancies in the unit cell. In fact, some of the solvent could not be accounted for in the case of **7**, and the structure had to be solved using the squeeze theorem to remove the most highly disordered solvent molecules in the structure. Only the alkyl monobridged compounds **6** and **9** crystallize without solvent in the structure. It is also notable that all but compound **10** adopt conformations with both trityl propellers in every molecule adopting homochiral helical configurations, either (M, M) or (P, P). However, as required by the space group, each crystal is racemic with both enantiomers related by the symmetry operations in the unit cell.

Packing coefficients calculated by the group increment method described by Gavezzotti[17] showed no apparent correlation with the number of bridges, even though the triply bridged molecular gyroscopes were initially expected to have more empty space. The packing coefficient (C_k) is a measure of crystal density obtained by computing the relation between the van der Waals volume of all the molecules in the unit cell ($Z \cdot V_{mol}$) divided by the unit cell volume ($C_k = (Z \cdot V_{mol})/V_{u\text{-}cell}$). As shown in Table 2, all the structures solved without the SQUEEZE[18] algorithm have a similar packing coefficient in the range of 0.703−0.798, which is a common value for molecular crystals. The packing structures of the bridged molecular gyroscopes take advantage of aromatic edge-to-face interactions between adjacent trityl stators in the form of distorted 6-fold and 4-fold phenyl embraces.[19] The 6-fold (6PE) and 4-fold phenyl embraces (4PE) are illustrated in Figure 4 with molecular gyroscopes **10** and **8**, respectively.

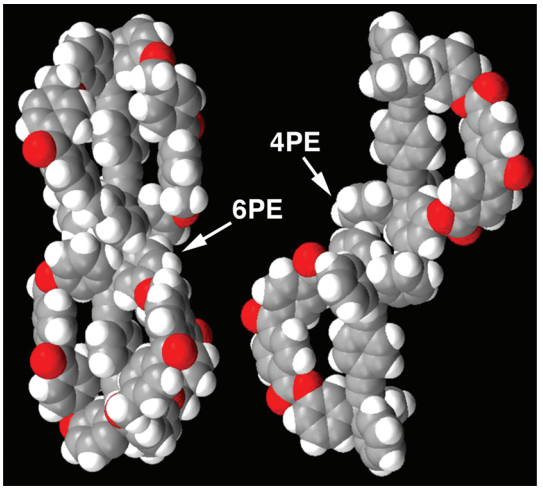


Figure 4. Space-filling models of pairs of molecular gyroscopes **10** (left) and **8** (right) illustrating the complementary face-to-edge interactions of their 6-fold (6PE) and 4-fold (4PE) phenyl embraces, respectively. With phenyl embraces on both sides of their structure, molecular gyroscopes align in infinite chains.

An ideal 6PE positions the triphenylmethyl groups in a configuration where every ring directs its own edge to the π-face of a ring in the interacting trityl group partner, while its own π-face interacts with the edge of another ring of the same trityl neighbor. It is well-known that the complementary edge-to-face interactions of the form $XPh_3 \cdots Ph_3X$ are quite robust and result in linear arrays that in the ideal case possess a local S_6 point group.[19] The 6PE of molecular gyroscopes **3**, **7**, **9**, and **10** are locally distorted, some with the presence of solvent molecules. The interaction observed in the case of monobridged benzophenone diether, **7**, resembles a 6PE, but the chain-like alignment between adjacent molecules is

dx.doi.org/10.1021/jo201513y |J. Org. Chem. 2011, 76, 8355–8363

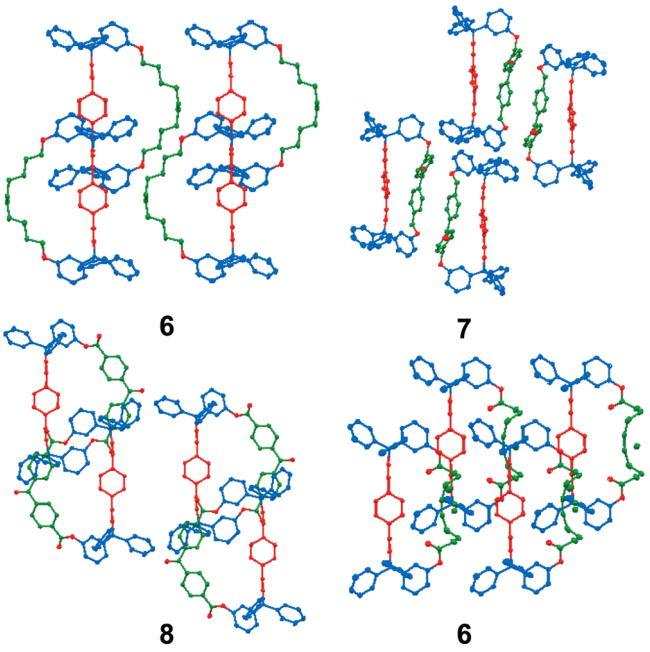


Figure 5. View of the crystal structures of the four singly bridged molecular gyroscopes **6**, **7**, **8**, and **9**. All four monobridged molecular gyroscopes adopted an interdigitated packing motif where the trityl group of one molecule approaches the phenylene rotator of an adjacent molecule in the lattice. Hydrogen atoms and solvent molecules have been omitted for clarity.

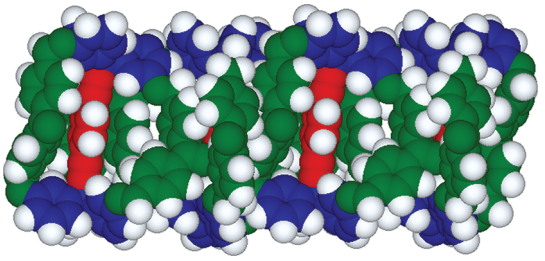


Figure 6. Space-filling model of triply benzophenone-bridged molecular gyroscopes **10** with the phenylene rotators in red, the trityl stators in blue, and the benzophenone bridges in green, illustrating the formation of layers.

mediated by solvent molecules rather than by edge-to-face interactions. As shown in Figure 4, the 4-fold phenyl embrace of molecular gyroscope **8** has one phenyl ring from each adjacent molecule directed away, so that only four rings are involved in self-complementary edge-to-face interactions. A common characteristic of all four monobridged structures, **6**−**9**, is that their "infinite" chains of molecules aligned by their 6PE and 4PE are displaced along the chain axis in a manner that the trityl group of one molecule tends to occupy the space that is available near the rotator of an adjacent molecule in the lattice (Figure 5).

In remarkable contrast, the structures of the triply bridged molecular gyroscopes **3** and **10** have their 6PE chains in register so that molecular gyroscopes occur in layers (Figure 6). The space in the tribridged structures is filled by positioning the bridges of a given molecule into the space left by the two bridges of an adjacent one (Figure 7), and in the case of the triply bridged benzophenone derivative **10**, by collapsing one of the bridges

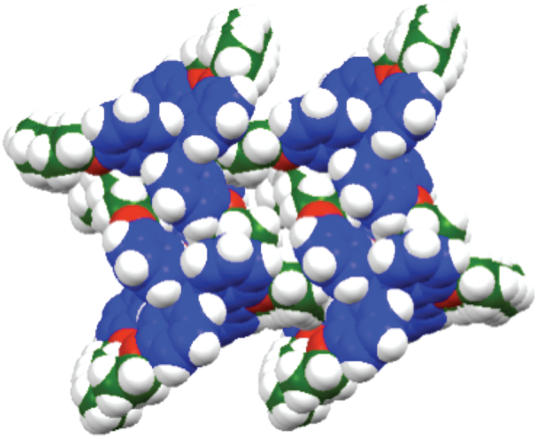


Figure 7. Crystal structures of **3** viewed down the principal axis illustrating the formation of layers orthogonal to the molecular rotor axis. The figure also illustrates how next neighbors interdigitate by directing one of the three bridges on one structure (in green) into the vicinity of the rotator of another molecule.

into the space of the rotator. This collapse is clearly visible in Figure 6 for the benzophenone on the left side of the first molecule from the left.

The molecular structures of all the molecular gyroscopes present deviations from their maximum possible symmetry. The three phenyl blades of each trityl propeller have different torsion angles, and the alkyne axles are not straight and collinear. The alkyne axles in the structure of **6** deviate from linearity with angle of 178°, which reaches the largest value of 173.4° for the structure of **7** and has an average value of 176.6° for all the structures determined in this study. Some interesting differences are observed between the various types of bridges. The thin diether alkyl bridges in molecular gyroscopes **3** and **6** extend radially outside the center of the molecule, leaving the proximity of the rotator interdigitated with neighboring bridges or stators and occupied with solvent molecules. The alkyl diester bridges of compound **9** tend to collapse at the center, occupying two disordered positions. Similarly, the bridging benzophenone diether in compound **7** and one of the three bridges in compound **10** tend to adopt conformations that collapse toward the rotator, seemingly to take advantage of aromatic−aromatic interactions. One may conclude that benzophenone bridges do not provide the molecular gyroscopes with sufficient shielding to prevent the inclusion of solvent molecules or the interdigitation of bridges from next neighboring molecules.

CONCLUSIONS

We have shown that the one-step triple-bridging procedure using a hexaphenol precursor works when the bridging groups are rigid and the two reaction sites extend beyond the distance needed for "zonal" macrocyclization within a given trityl stator. It is interesting that the yield per bond formed is not altered significantly, as the structure varies from one to three bridges, suggesting that there is no unfavorable strain introduced after the first or second bridges are formed. It was also shown that bridging reactions that form ether bonds are almost twice as efficient as bridging reactions that form esters. While it is notable that reasonably good quality crystals were obtained for all molecular gyroscopes, it was shown that the linked diaryl

benzophenone bridges are not sufficiently bulky to prevent interdigitation nor the inclusion of solvent molecules. It is also important to note that there are torsional degrees of freedom present in the structure of the bridge that allows it to collapse toward the central rotator. All the lessons learned in this study will be used to design the next generation of triply bridged molecular gyroscopes.

EXPERIMENTAL SECTION

IR spectra were obtained with a Perkin-Elmer spectrum 100 HATR-FTIR instrument. ^{1}H and ^{13}C NMR spectra were acquired on a Brüker NMR spectrometer at 400 and 100 MHz or 300 and 75 MHz, respectively, with $CDCl_3$ as the solvent. NMR coupling constants were calculated using gNMR. All the NMR assignments described below are based on the atom numbering shown in Scheme 3. Mass spectra were acquired on an Applied Biosystems Voyager-DE-STR MALDI-TOF. The 3-bromoanisole, benzophenone, 2.5 M *n*-butyllithium in hexanes, acetyl chloride, 0.5 M ethynylmagnesium bromide in THF, diisopropylamine, CuI, bis(triphenylphosphine)palldium(II) chloride, 1,4-diiodobenzene, 1,10-dibromodecane, decandioyl chloride, 1 M boron tribromide in DCM, and potassium carbonate were commercially available and were used without further purification. THF and benzene were distilled from sodium and kept under argon. Samples of bis[4-(bromomethyl)phenyl]methanone (for the synthesis of **7** and **10**) and 4,4′-carbonyldibenzoyl chloride (for the synthesis of **8** and **12**) were prepared as described in the literature.[20] The synthesis and characterization of **3** has been described previously.[14]

General Synthesis of Monobridged Molecular Gyroscopes. An oven-dried 100 mL round-bottom flask was charged with potassium carbonate (0.92 mmol) and dry DMF (20 mL) under an argon atmosphere. Compound **17** (0.127 mmol) and the respective bridge precursor (0.127 mmol) were added into two separate oven-dried 10 mL round-bottom flasks and dissolved in dry DMF (4 mL). Compound **17** and the coresponding bridge precursor were added via syringe slowly at 0.5 mL/h over 8 h to the flask containing potassium carbonate and dry DMF at 40 °C, and the mixture was left to react overnight. Afterward, the solution was quenched with a saturated ammonium chloride solution (20 mL) and partitioned with ethyl acetate. The organic phase was washed with saturated lithium chloride (3 × 10 mL) and then brine (20 mL). Combined organic fractions were dried over $MgSO_4$ and concentrated on a rotary evaporator. The residue was then purified by flash chromatography on silica gel.

General Synthesis of Tribridged Molecular Gyroscopes. An oven-dried 100 mL round-bottom flask was charged with potassium carbonate (1.52 mmol) and dry DMF (20 mL) under an argon atmosphere. Compound **1** (0.127 mmol) and the respective bridge (0.382 mmol) were added into two separate oven-dried 10 mL round-bottom flasks and dissolved in dry DMF (4 mL). Compound **1** and the coresponding bridge precursor were added via syringe slowly at 0.5 mL/h over 8 h to the flask containing potassium carbonate and dry DMF at 50 °C and stirred overnight. After 24 h, the solution was quenched with saturated ammonium chloride (20 mL) and partitioned with ethyl acetate. The organic phase was washed with saturated lithium chloride (3 x10 mL) and brine (20 mL). Combined organic fractions were dried over $MgSO_4$ and concentrated on a rotary evaporator. The residue was then purified by flash chromatography on silica gel.

Synthesis of (3-Methoxyphenyl)diphenylmethanol 14. An oven-dried 500 mL round-bottom flask was charged with 3-bromoanisole **13** (23.1 g, 0.125 mol), dry THF (500 mL) under argon, and cooled to −78 °C in dry ice/acetone bath. Then 2.5 M *n*-BuLi (50 mL) in hexanes was added to the reaction and stirred for 30 min. Afterward, benzophenone (22.7 g, 0.125 mol) dissolved in 40 mL of dry THF was added to reaction at −78 °C, allowed to warm to room temperature, and stirred for an additional 12 h. The reaction was quenched with water and partitioned with diethyl ether. The organic phase was washed with water (3 × 50 mL) and brine (50 mL). The combined organic fractions were dried over $MgSO_4$ and concentrated on a rotary evaporator. The crude product was then purified by recrystallization in 70:30 hexanes:diethyl ether to afford clear crystals in 100% yield: mp = 91−92 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31−7.36 (m, 10H, phenyl-H), 7.23 (apparent t, J = 8.2, 7.8 Hz, 1H, H10), 6.88 (dd, J = 2.6, 1.8 Hz, 1H, H7), 6.83 (ddd, J = 7.8, 1.8, 0.9 Hz, 1H, H9), 6.81 (ddd, J = 8.2, 2.6, 0.9 Hz, 1H, H11), 3.75 (s, 3H, methoxy-H), 2.79 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 148.5, 146.7, 128.8, 127.9, 127.9, 127.3,120.5, 114.0, 112.4, 82.0, 55.2. FTIR (solid, HATR, cm^{-1}): 3462, 3071, 3008, 2972, 1595, 1489, 1463, 1448, 1414, 1361, 1318, 1244, 1166, 1148, 1032, 1013, 930, 869, 820, 794, 753, 699. HRMS (ESI) $C_{20}H_{18}O_2$. Calcd: 290.13. Found: 273.129 (loss of OH).

Synthesis of 3-(3-Methoxyphenyl)-3,3-diphenylpropyne 15. A 500 mL round-bottom flask equipped with a magnetic stir bar was charged with mono-*m*-methoxy trityl alcohol **14** (4.6 g, 16.6 mmol) and acetyl chloride (10 mL) and heated to reflux for 1 h. Excess acetyl chloride was removed via rotary evaporator, washed with dry benzene (3 × 20 mL), and concentrated on a rotary evaporator. The residue was dissolved in dry benzene (50 mL), and (100 mL) 0.5 M ethynylmagnesium bromide in THF was added under argon and stirred overnight at room temperature. Afterward, the reaction was quenched with aqueous saturated ammonium chloride solution and partitioned with diethyl ether. The organic phase was washed with water (2 × 50 mL) and brine (1 × 50 mL). The combined organic fractions were dried over Mg_2SO_4, filtered, and concentrated on a rotary evaporator. The residue was then purified by flash chromatography on silica gel (2:1 hexanes:DCM) to afford 83% yield of a yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.2−7.35 (m, 10H, phenyl-H), 7.22 (apparent t, J = 8.2, 7.8 Hz, 1H, H10), 6.88 (dd, J = 2.5, 1.8 Hz, 1H, H7), 6.83 (ddd, J = 7.8, 1.8, 0.9 Hz, 1H, H9), 6.81 (ddd, J = 8.2, 2.5, 0.9 Hz, 1H, H11), 3.74 (s, 3H, methoxy-H), 2.78 (s, 1H, H3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.3, 146.3, 144.6, 129.0, 128.8, 128.0, 126.9, 121.7, 115.4, 111.9, 89.6, 73.4, 55.5, 55.1. FTIR (solid, HATR, cm^{-1}): 3289, 3057, 2932, 2833, 1594, 1486, 1462, 1444, 1423, 1317, 1249, 1171, 1143, 1037, 967, 913, 866, 813, 786, 748, 697. HRMS (ESI) $C_{22}H_{18}O$. Calcd: 298.135. Found: 273.125 (loss of terminal alkyne).

Synthesis of 1,4-Bis[3-(3-methoxyphenyl)-3,3-diphenylpropynyl]benzene 16. A 250-mL oven-dried round-bottom flask equipped with a magnetic stir bar was charged with mono-*m*-methoxy trityl alkyne **15** (1.1 g, 3.69 mmol), diiodobenzene (607 mg, 1.89 mmol), diisopropylamine (5 mL), and dry THF (10 mL), and the solution was degassed with argon for 30 min. CuI (35 mg, 0.18 mmol) and Pd-$(PPh_3)_2Cl_2$ (130 mg, 0.18 mmol) were added, and the reaction was heated to reflux for 24 h. The reaction was quenched with aqueous saturated ammonium chloride and partitioned with diethyl ether. The organic phase was washed with water (2 × 40 mL) and brine (40 mL). The combined organic fractions were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The residue was then purified by flash chromatography on silica gel (2:1 hexanes:DCM) to afford 73% yield of a yellow solid: mp = 204−205 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36 (s, 4H, H2), 7.21−7.31 (m, 20H, phenyl-H), 7.15 (apparent t, J = 8.2, 7.8 Hz, 2H, H10), 6.84 (dd J = 2.6, 1.5 Hz, 2H, H7), 6.81 (ddd, J = 7.8, 1.8, 0.9 Hz, 2H, H9), 6.76 (dd, J = 8.2, 2.5, 0.9 Hz, 2H, H11), 3.66 (s, 6H, methoxy-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.3, 146.8, 145.0, 131.4, 129.1, 128.9, 128.0, 126.9, 123.2, 121.8, 115.5, 112.0, 97.2, 84.8, 56.2, 55.1. FTIR (solid, HATR, cm^{-1}): 3051, 2952, 2924, 2829, 1601, 1579, 1489, 1445, 1430, 1315, 1290, 1241, 1137, 1032, 881, 842, 780, 767, 756, 717. HRMS (MALDI-ICR) $C_{50}H_{38}O_2$. Calcd: 670.287. Found: 670.284.

Synthesis of 1,4-Bis(3-(3-hydroxyphenyl)-3,3-diphenylpropynyl)benzene 17. A 250 mL round-bottom flask equipped with magnetic stir bar was charged with dimethoxy-rotor **16** (600 mg, 0.89 mmol) and dry

dx.doi.org/10.1021/jo201513y |*J. Org. Chem.* 2011, 76, 8355–8363

DCM (10 mL) under argon atmosphere. The flask was cooled to 0 °C in an ice bath, and 1 M BBr in DCM (3.58 mL) was added. The reaction was stirred for 3 h at 0 °C, quenched by addition of ice, and partitioned with diethyl ether and water. The organic phase was washed with saturated sodium bicarbonate (2 × 20 mL) and brine (20 mL). Combined organic fractions were dried over $MgSO_4$, filtered, and concentrated on a rotary evaporator. The residue was purified by flash chromatography on silica gel (3:1 hexanes: acetone) to afford a yellow powder in 78% yield: mp = 250−252 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (s, 4H, H2), 7.21−7.40 (m, 20H, phenyl-H), 7.16 (apparent t, J = 8.2, 7.8 Hz, 2H, H10), 6.87 (ddd, J = 7.8, 1.8, 0.9 Hz, 2H, H9), 6.78 (dd, J = 2.5, 1.8 Hz, 2H, H7), 6.76 (ddd, J = 8.2, 2.5, 0.9 Hz, 2H, H11); ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.4, 147.0, 145.0, 144.2, 131.4, 129.1, 128.0, 126.9, 123.1, 121.7, 116.4, 114.0, 97.1, 84.8, 56.0. FTIR (solid, HATR, cm^{-1}): 3531, 3343 (broad), 3058, 2923, 1596, 1489, 1446, 1263, 1031, 873, 783, 754, 697. HRMS (MALDI-ICR) $C_{48}H_{34}O_2$. Calcd: 642.256. Found: 643.264 (M + H)

Monoalkyl Ether-Linked Bridged Molecular Gyroscope 6. A 46% yield of a white solid: mp = 230−232 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 (dd, J = 2.5, 1.8 Hz, 2H, H7), 7.44 (s, 4H, H2), 7.20−7.35 (m, 20H, phenyl-H), 7.11 (apparent t, J = 8.2, 7.8 Hz, 2H, H10), 6.80 (ddd, J = 8.2, 2.5, 0.9 Hz, 2H, H11), 6.29 (ddd, J = 7.8, 1.8, 0.9 Hz, 2H, H9), 3.97 (t, J = 4.8 Hz, 4H, alkyl-H), 1.76 (quintet, J = 5.4, 4.8 Hz, 4H, alkyl-H), 1.42−1.44 (m, 4H, alkyl-H), 1.26−1.30 (m, 8H, alkyl-H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1, 146.5, 145.1, 131.4, 129.1, 125.5, 128.0, 126.9, 123.2, 121.1, 115.4, 113.7, 97.4, 84.8, 67.8, 56.3, 29.2, 29.2, 29.0, 25.9. FTIR (powder, HATR, cm^{-1}): 3063, 3019, 2925, 2853, 1724, 1597, 1489, 1446, 1251, 1033. HRMS (MALDI-ICR) $C_{58}H_{52}O_2$. Calcd: 780.396. Found: 780.395

Monobenzophenone Ether-Linked Bridged Molecular Gyroscope 7. A 57% yield of white solid: mp = 246−247 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, J = 8.3 Hz, 4H, benzophenone H), 7.39 (d, J = 8.3 Hz, 4H, benzophenone-H), 7.28 (dd, J = 2.5, 1.8 Hz, 2H, H7), 7.22−7.27 (m, 20H, phenyl-H), 7.22 (s, 4H, H2), 7.16 (apparent t, J = 8.2, 7.8, 2H, H10), 6.96 (ddd, J = 8.2, 2.5, 0.9 Hz, 2H, H11), 6.34 (ddd, J = 7.8, 1.8, 0.9 Hz, 2H, H9), 4.79 (s, 4H, methylene-H); ^{13}C NMR (75 MHz, CDCl3): δ 195.8, 158.2, 146.4, 145.0, 142.2, 136.6, 131.3, 130.4, 129.1, 128.8, 128.0, 126.9, 126.4, 123.1, 121.9, 115.2, 115.0, 96.9, 84.7, 68.9, 56.2. FTIR (powder, HATR, cm^{-1}): 3051, 2956, 2916, 2849, 1670, 1260, 1008, 790, 697 cm^{-1}. HRMS (MALDI-ICR) $C_{63}H_{44}O_3$. Calcd: 848.329. Found: 871.320 (M + Na).

Monobenzophenone Ester-Linked Bridged Molecular Gyroscope 8. An 18% yield of white solid: mp = decomposes >411 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.4 Hz, 4H, benzophenone-H), 7.84 (dd, J = 2.5, 1.8 H, 2H, H7), 7.72 (d, J = 8.4 Hz 4H, benzophenone-H), 7.58 (ddd, J = 8.2, 2.5, 0.9 Hz 2H, H11), 7.49 (s, 4H, H2), 7.26−7.35 (m, 22H, phenyl-H and H10), 6.76 (ddd, J = 7.8, 1.8, 0.9 Hz 2H, H9); ^{13}C NMR (75 MHz, $CDCl_3$): δ 196.5, 163.2, 151.0, 146.5, 144.7, 142.0, 133.1, 131.6, 130.1, 129.8, 129.0, 128.7, 128.2, 127.1, 126.4, 123.3, 121.3, 119.8, 96.7, 85.2, 56.1. FTIR (powder, HATR, cm^{-1}): 3063, 2922, 2852, 1744, 1672, 1490, 1446, 1260, 1213, 1071, 905, 749, 695. HRMS (MALDI-ICR) $C_{63}H_{40}O_5$. Calcd: 876.287. Found: 876.285 and 899.275 (M + Na)

Monoalkyl Ester-Linked Bridged Molecular Gyroscope 9. A 20% yield of white solid: mp = 318−319 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, J = 2.5, 1.8 Hz, 2H, H7), 7.44 (s, 4H, H2), 7.22−7.31 (m, 22H, phenyl-H and H10), 7.03 (ddd, J = 8.2, 2.5, 0.9 Hz, 2H, H11), 6.63 (ddd, J = 7.8, 1.8, 0.9 Hz, 2H, H9), 2.54 (t, J = 7.2 Hz, 4H), 1.75 (quintet, J = 7.7, 7.6 Hz, 4H), 1.43 (m, 4H), 1.36 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 172.0, 150.9, 146.5, 144.8, 131.5, 129.1, 128.4, 128.1, 127.0, 126.1, 123.1, 122.8, 120.2, 96.8, 84.9, 56.0, 34.5, 28.8, 28.7, 24.8. FTIR (powder, HATR, cm^{-1}): 3055, 2939, 2853, 1752, 1587, 1489, 1445, 1211, 1155, 1138, 1115, 1033, 906, 837, 785, 758, 698. HRMS (MALDI-ICR) $C_{58}H_{48}O_4$. Calcd: 808.355. Found: 831.344 (M + Na).

Tribenzophenone Ether-Linked Bridged Molecular Gyroscope 10. An 11% yield of white solid: mp = decomposes >379 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, J = 8.0 Hz, 12H, benzophenone-H), 7.24 (d, J = 8.0 Hz, 12H, benzophenone-H), 7.23 (dd, J = 2.5, 1.8 Hz, 6H, H7), 7.16 (apparent t, J = 8.2, 7.8 Hz, 6H, H10), 6.96 (ddd, J = 8.2, 2.5, 0.9 Hz, 6H, H11), 6.86 (s, 4H, H2), 6.42 (ddd, J = 7.8, 1.8, 0.9 Hz, 6H, H9), 5.19 (s, 12H, methylene-H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 195.0, 158.0, 146.2, 142.1, 136.8, 131.2, 130.4, 128.8, 126.5, 122.9, 121.7, 115.8, 113.9, 95.9, 85.0, 68.7, 56.2. FTIR (powder, HATR, cm^{-1}): 3059, 2982, 2857, 2250, 1726, 1655, 1593, 1230, 731. HRMS (MALDI-ICR) $C_{93}H_{64}O_9$. Calcd: 1324.455. Found: 1347.447 (M+Na).

Monobenzophenone Ester-Linked Bridged Molecular Gyroscope Dimer 12. A 22% yield of white solid: mp = 225−227 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, J = 8.4 Hz, 8H, benzophenone-H), 8.27 (d, J = 8.4 Hz, 8H, benzophenone-H), 7.46 (s, 8H, H2), 7.42 (dd, J = 3.1, 2.3 Hz, 4H, H7), 7.25−7.40 (m, 44H, phenyl-H and H10), 7.19 (ddd, J = 10.7, 3.1, 1.2 Hz, 4H, H11), 7.02 (ddd, J = 10.5, 2.3, 1.2 Hz, 4H, H9); ^{13}C NMR (75 MHz, $CDCl_3$): δ 195.1, 164.1, 150.6, 147.2, 144.6, 141.0, 133.1, 131.5, 130.2, 129.9, 129.1, 128.9, 128.2, 127.1, 126.7, 123.1, 122.5, 120.2, 96.8, 85.1, 56.1. FTIR (powder, HATR, cm^{-1}): 3059, 1738, 1664, 1490, 1446, 1259, 1212, 1071, 905, 719. HRMS (ESI) $C_{126}H_{80}O_{10}$. Calcd: 1752.575. Found: 1753.583(M + H).

■ ASSOCIATED CONTENT

Supporting Information. Spectroscopic data for all compounds, and crystallographic information files (cif) for compounds **6**−**9**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author
*E-mail: mgg@chem.ucla.edu.

Present Addresses
†Chemistry Department, University of Texas, 500 West University Ave., El Paso, TX.

■ ACKNOWLEDGMENT

The National Science Foundation supported this work through grant DMR-0605688 and creativity extension DMR-0937243. P.C. acknowledges the National Science Foundation IGERT: Materials Creation Training Program (DGE-0654431) and the California Nanosystems Institute.

■ REFERENCES

(1) (a) Karim, A. R.; Linden, A.; Baldridge, K. K.; Siegel, J. S. *Chem. Sci.* **2010**, *1*, 102. (b) Kay, E. R.; Leigh, D. A.; Zerbetto, F *Angew. Chem., Int. Ed.* **2007**, *46*, 72. (c) Koumura, N.; Zijlstra, R.; Delden, R.; Harada, N.; Feringa, B. *Nature* **1999**, *401*, 152. (d) Balzani, V.; Credi, A.; Raymo, F.; Stoddart, F. *Angew. Chem., Int. Ed.* **2000**, *39*, 3348. (e) Sauvage, J. P. *Acc. Chem. Res.* **1998**, *31*, 611. (f) Pérez, E. M.; Dryden, D. T. F.; Leigh, D. A.; Teobaldi, G.; Zerbetto, F. *J. Am. Chem. Soc.* **2004**, *126*, 12210. (g) Shirai, Y.; Osgood, A. J.; Zhao, Y.; Yao, Y.; Saudan, L.; Yang, H.; Yu-Hung, C.; Alemany, L.; Sasaki, T.; Morin, J.; Guerrero, J.; Kelly, K. F.; Tour, J. *J. Am. Chem. Soc.* **2006**, *128*, 4854. (h) Juluri, B. K.; Kumar, A. S.; Liu, Y.; Ye, T.; Yang, Y.; Flood, A. H.; Fang, L.; Stoddart, F.; Weiss, P.; Huang, T. J. *ACS Nano* **2009**, *3*, 291. (i) Kelly, T. R.; De Silva, H.; Silva, R. A. *Nature* **1999**, *401*, 150.

(2) (a) Khuong, T.-A. V.; Nuñez, J. E.; Godinez, C. E.; Garcia-Garibay, M. A. *Acc. Chem. Res.* **2006**, *39*, 413–422. (b) Karlen, S. D.; Garcia-Garibay,

M. A. *Top. Curr. Chem.* **2006**, *262*, 179. (c) Garcia-Garibay, M. A. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 10793.

(3) (a) Akimov, A. V.; Kolomeisky, A. B. *J. Phys. Chem. C* **2011**, *115*, 13584. (b) Comotti, A.; Bracco, S.; Valsesia, P.; Beretta, M.; Sozzani, P. *Angew. Chem., Int. Ed.* **2010**, *49*, 1760. (c) Horinek, D.; Michl, J. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 14175. (d) Tabe, Y.; Yokoyama, H. *Nat. Mater.* **2004**, *2*, 806. (e) Akutagawa, T.; Shitagami, K.; Nishihara, S.; Takeda, S.; Hasegawa, T.; Nakamura, T.; Hosokoshi, Y.; Inoue, K.; Ikeuchi, S.; Miyazaki, Y.; Saito., K. *J. Am. Chem. Soc.* **2005**, *127*, 4397.

(4) Sokolov, A. N.; Swenson, D. C.; MacGillivray, L. R. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, *105*, 1794.

(5) Garcia-Garibay, M. A. *Angew Chem., Int. Ed.* **2007**, *46*, 8945.

(6) For a recent review of molecular rotors, please see: Kottas, G. S.; Clarke, L. I.; Horinek, D.; Michl, J. *Chem. Rev.* **2005**, *105*, 1281.

(7) (a) Dominguez, Z.; Dang, H.; Strouse, M. J.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 2398. (b) Godinez, C. E.; Zepeda, G.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 4701. (c) Dominguez, Z.; Dang, H.; Strouse, J. M.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 7719. (d) Dominguez, Z.; Khuong, T. A. V.; Sanrame, C. N.; Dang, H.; Nuñez, J. E.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2003**, *125*, 8827.

(8) (a) Wang, L.; Hampel, F.; Gladysz, J. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 4372. (b) Narwara, A. J.; Shima, T.; Hampel, F.; Gladysz, J. A. *J. Am. Chem. Soc.* **2006**, *128*, 4962. (c) Shima, T.; Hampel, F.; Gladysz, J. A. *Angew. Chem., Int. Ed.* **2004**, *43*, 5537.

(9) (a) Khan, N. S.; Perez-Aguilar, J. M.; Kaufmann, T.; Hill, P. A.; Taratula, O.; Lee, O.-S.; Carroll, P. J.; Saven, J. G.; Dmochowski, I. J. *J. Org. Chem.* **2011**, *76*, 1418. (b) Setaka, W.; Ohmizu, S.; Kira, M. *Chem. Lett.* **2010**, *39*, 468. (c) Kitagawa, H.; Kobori, Y.; Yamanaka, M.; Yoza, K.; Kobayashi, K. *Proc. Natl. Acad. Sci. U.S.A.* **2009**, *106*, 10444. (d) Setaka, W.; Ohmizu, S.; Kabuto, C.; Kira, M. *Chem. Lett.* **2007**, *36*, 1076. (e) Gray, G. M.; Duffey, C. H. *Organometallics* **1994**, *13*, 1542.

(10) (a) Karlen, S. D.; Reyes, H.; Taylor, R. E.; Khan, S. I.; Hawthorne, M. F.; Garcia-Garibay, M. A. *Proc. Natl. Acad. Sci. U.S.A.* **2010**, *107*, 14973. (b) Karlen, S. D.; Ortiz, R.; Chapman, O. L.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2005**, *127*, 6554.

(11) (a) Saebo, S.; Almolof, J.; Boggs, J. E.; Stark, J. G. *J. Mol. Struct. (THEOCHEM)* **1989**, *200*, 361. (b) Sipachev, V. A.; Khaikin, L. S.; Grikina, O. E.; Nikitin, V. S.; Traettberg, M. *J. Mol. Struct.* **2000**, *523*, 1.

(12) (a) Khuong, T.-A. V.; Nuñez, J. E.; Godinez, C. E.; Garcia-Garibay, M. A. *Acc. Chem. Res.* **2006**, *39*, 413. (b) Garcia-Garibay, M. A. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 10793.

(13) Godinez, C. E.; Garcia-Garibay, M. A. *Cryst. Growth Des.* **2009**, *9*, 3124.

(14) Nunez, J. E.; Natarajan, A.; Khan, S. I.; Garcia-Garibay, M. A. *Org. Lett.* **2007**, *9*, 3559.

(15) Nunez, J.; Khuong, T.; Campos, L.; Farfán, N.; Dang, H.; Karlen, S.; Garcia-Garibay, M. *Cryst. Growth Des.* **2006**, *6*, 867.

(16) For previous examples of 58-membered macrocycles, please see: (a) Grave, C.; Lentz, D.; Schäfer, A.; Samorı, P.; Rabe, J. P.; Franke, P.; Schluter, A. D. J. *Am. Chem. Soc.* **2003**, *125*, 6907. (b) Grave, C.; Schlüter, A. D. *Eur. J. Org. Chem.* **2002**, 3075. (c) Belfrekh, N.; Dietrich-Buchecker, C.; Sauvage, J.-P. *Inorg. Chem.* **2000**, *39*, 5169.

(17) Gavezzotti, A. *J. Am. Chem. Soc.* **1990**, *105*, 5220–5225.

(18) Spek, A. L. *SQUEEZE*; University of Utrecht, Utrecht, The Netherlands, 1992.

(19) (a) Scudder, M.; Dance, I . *J. Chem. Soc., Dalton Trans.* **1998**, 329. (b) Scudder, M.; Dance, I. *Dalton* **2000**, 2909. (c) Dance, I.; Scudder, M. *New J. Chem.* **1998**, *22*, 481. (d) Lacour, J.; Bernardinelli, G.; Russell, V.; Dance, I. *CrystalEngComm* **2002**, *4*, 165.

(20) Grützmacher, H.; Husman, W. *Tetrahedron* **1987**, *43*, 3205.