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Molecules with Shape Memory Based on Restricted Rotation

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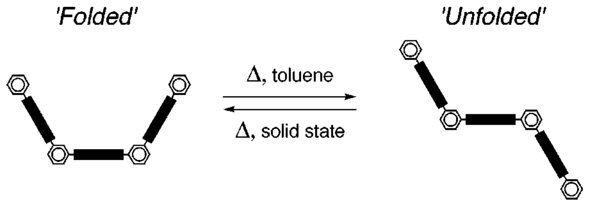
ABSTRACT



Diimide 1 and octaimide 2 both adopt two stable conformations at room temperature as a result of restricted rotation about two C_{aryl}−N_{imide} single bonds, a compact "folded" and an open "unfolded" structure. Predictable ratios of folded and unfolded rotamers can be achieved by heating in solvents of appropriate polarity as measured by the Reichardt's parameter (E_{T30}). On cooling to room temperature, the resulting conformational changes are "locked in" as restricted rotation is reestablished.

One of the most attractive aspects of polymers is their ability to be cast and recast into different forms and shapes at the bulk level. Our goal has been to achieve this level of control on the molecular level. Conformational control can be an effective strategy to introduce new or tune existing properties in molecular and macromolecular systems. One route is to identify systems that adopt different conformations in different solvents.[1] However, in most cases, these solvent-induced conformations are fragile and disappear upon removal from their promoting environments. We set out to design a class of polymers based on restricted rotation that could be shaped at elevated temperatures but would become rigid and shape-persistent on cooling, thereby preserving the solvent-induced conformations.[2] In this manner, they could be cast and recast into different shapes simply by heating and cooling in different environments and would retain these new shapes even upon transfer to a different environment.

To demonstrate the feasibility of this strategy diimide **1** and octaimide **2** were synthesized and studied. Both diimide **1** and octaimide **2** adopt two stable conformations: convergent "folded" and divergent "unfolded" states that are well-differentiated in terms of shape, size, and polarity (Scheme 1). These conformations arise from restricted rotation about connecting C_{aryl}−N_{imide} bonds within the rigid 1,4,5,8-naphthalene diimide framework.[2a,3] Restricted rotation about the C_{aryl}−N_{imide} bonds was imposed by the steric presence of *ortho*-ether substituents.[4] The long octadecyl *ortho*-ethers serve to endow the rigid polyimide framework with excellent organic solubility and also accentuate the differences in size and shape between the two conformers. Finally, the systems contain pendent nitrile groups that serve as strong polarizing groups,[5] by conferring very different dipole moments on the

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[1] For recent examples of solvent-induced conformational changes, see: (a) Leis, J.; Klika, K. D.; Karelson, M. *Tetrahedron* **1998**, *54*, 7497−7504. (b) Palyulin, V. A.; Emets, S. V.; Chertkov, V. A.; Kasper, C.; Schneider, H. J. *Eur. J. Org. Chem.* **1999**, 3479−3482. (c) Gardner, R. R.; McKay, S. L.; Gellman, S. H. *Org. Lett.* **2000**, *2*, 2335−2338. (d) Paliwal, S.; Geib, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1994**, *116*, 4497−4498. (e) Clegg, W.; Gimenez-Saiz, C.; Leigh, D. A.; Murphy, A.; Slawin, A. M. Z.; Teat, S. J. *J. Am. Chem. Soc.* **1999**, *121*, 4124−4129. (f) Leigh, D. A.; Moody, K.; Smart, J. P.; Watson, K. J.; Slawin, A. M. Z. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 306−310. (g) Janout, V.; Lanier, M.; Regen, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 1573−1574. (h) Hoger, S.; Meckenstock, A. D.; Muller, S. *Chem. Eur. J.* **1998**, *4*, 2423−2434. (i) Moore, J. S. *Acc. Chem. Res.* **1997**, *30*, 402−413.

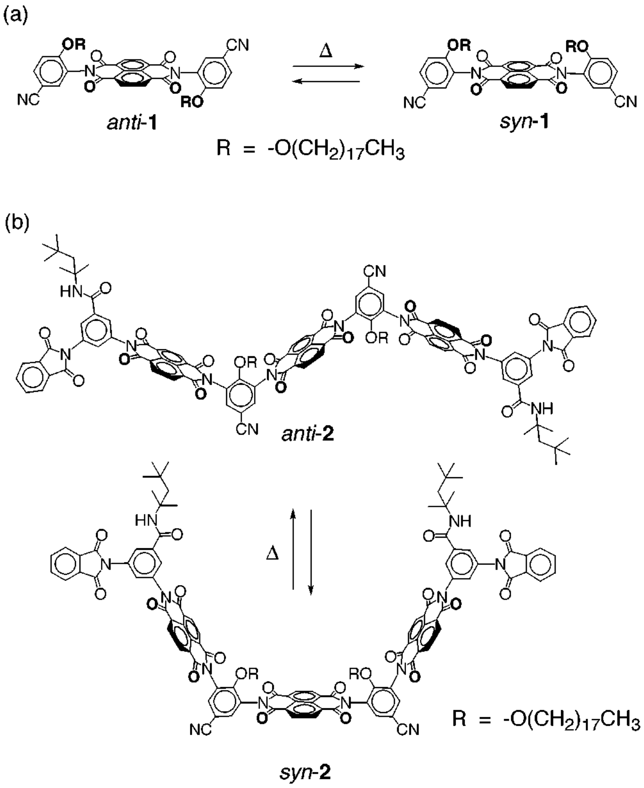
[2] (a) Chong, Y. S.; Smith, M. D.; Shimizu, K. D. *J. Am. Chem. Soc.* **2001**, *123*, 7463−7464. (b) Degenhardt, C., III; Shortell, D. B.; Adams, R. D.; Shimizu, K. D. *J. Chem. Soc., Chem. Commun.* **2000**, 929−930.

[3] (a) Curran, D. P.; Geib, S.; DeMello, N. *Tetrahedron* **1999**, *55*, 5681−5704. (b) Verma, S. M.; Singh, N. D. *Aust. J. Chem.* **1976**, *29*, 295−300.

[4] Shimizu, K. D.; Dewey, T. M.; Rebek, J. *J. Am. Chem. Soc.* **1994**, *116*, 5145−5149.

10.1021/ol0167098 CCC: $20.00

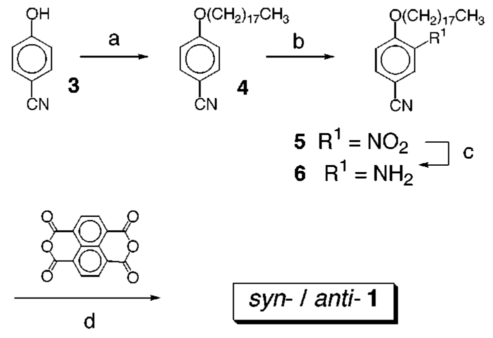
Scheme 1



syn and *anti* conformers. This enables control over the *syn*/*anti* equilibrium, and therefore shape, by choice of the dielectric constant of the surrounding medium.

An attractive feature of this rigid shape-persistent framework is the ease with which it can be assembled. For example, diimide **1** was synthesized in 86% yield by simply condensing the appropriate aniline and anhydride components, **6** and 1,4,5,8-naphthalenetetracarboxylic dianhydride (NTDA), in DMF (Scheme 2). The requisite *ortho*-aniline **6** was synthesized in three steps from 4-cyanophenol **3** via alkylation, nitration, and reduction.

Scheme 2[a]



[a] (a) K_2CO_3, $Br(CH_2)_{17}CH_3$, acetone, Δ (98%). (b) fuming HNO_3, 23 °C (93%). (c) cyclohexene, 10% Pd/C, EtOH, reflux (99%). (d) DMF, 130 °C, 12 h (86%).

Diimide **1** is the shortest model system in which restricted rotation can be easily observed. The presence of restricted rotation in diimide **1** was immediately apparent by the isolation of two spectroscopically similar compounds that interconverted on heating. A particularly useful method for identifying rotamers was the utilization of two-dimensional TLC. The isomers were first separated on a square TLC plate. The plate was heated to re-equilibrate the rotamers and then run in the perpendicular direction. The appearance of new spots off of the diagonal identified the compounds that are conformational rotamers. The individual *syn* and *anti* conformers of **1** were sufficiently stable at room temperature to be separated and isolated by flash chromatography (1.5% EtOAc in CH_2Cl_2, Merck silica gel 60). The rotational barriers about the $C_{aryl}-N_{imide}$ bonds were measured from the equilibration rates of the pure *syn* and *anti* isomers at 64 °C in $CHCl_3$. Both isomers concur on a rotational barrier of 27 kcal/mol, which corresponds to a half-life of 11 h at 64 °C or 93 days at 23 °C.[6]

Assignments of the *syn* and *anti* isomers of model compound **1** were initially complicated by the high symmetries of the isomers, which thwarted their structural assignment by NMR spectroscopy. However, the differences in symmetry of the isomers did enable differentiation and assignment by their different dipole moments, as measured by TLC and by their nonequivalent equilibrium ratios. The use of elution order in TLC has been successfully applied elsewhere in the atropisomers of tetraarylporphyrins and *N*,*N*′-diaryl-1,4,5,8-perylenediimides.[4,7] The more polar *syn* isomer was assigned as the lower R_f compound. Further support for the TLC-based assignments was provided by the observed differences in equilibrium ratios in different solvents. For example, the rotational barrier studies revealed that diimide **1** attains a 43:57 equilibrium ratio in chloroform with the higher R_f less polar *anti* rotamer being favored. We assigned the major isomer as the *anti* conformer, which is presumably preferred in nonpolar solvents as a result of its smaller dipole moment. These differences in dipole moment were expected to be expressed to different extents depending upon the medium, and accordingly in a more polar solvent such as DMSO, a 1:1 equilibrium ratio was observed.

Octaimide **2** was then synthesized to demonstrate the ease with which this platform can be extended to larger systems. In the case of oligomer **2**, restricted rotation is present only about the central naphthalene diimide surface, again yielding two conformational isomers, as only the four central of the eight $C_{aryl}-N_{imide}$ bonds show restricted rotation. The larger octaimide **2** was assembled in a stepwise fashion from the appropriate amine and anhydride components and could be accomplished without the necessity of protecting groups (Scheme 3). For example, diamine **9** was formed selectively by condensation of aniline **8** with 1,4,5,8-naphthalenetetracarboxylic at 150 °C. Condensation reactions carried out at higher temperatures (160 °C) led to oligomerization, whereas

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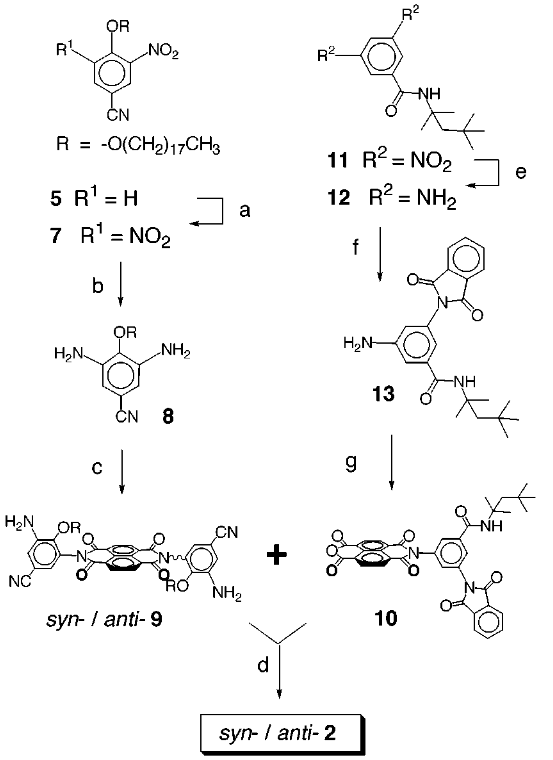
(5) Bezborodov, V. S.; Petrov, V. F. *Liq. Cryst.* **1997**, *23*, 771−788.

(6) Calculated from the Arrhenius equation assuming an ideal value of $A = 2.08 \times 10^{10}$ s^{-1} deg^{-1}. The ratio of isomers was monitored by HPLC.

(7) Sanders, G. M.; Van Dijk, M.; Machiels, B. M.; van Veldhuizen, A. *J. Org. Chem.* **1991**, *56*, 1301−1305.

Scheme 3[a]



[a] (a) 90% HNO_3, 23 °C (49%). (b) H_2, 10% Pd/C, EtOH (92%). (c) 0.5 equiv of 1,4,5,8-naphthalenetetracarboxylic dianhydride, CH_2Cl_2, 23 °C then neat, 150 °C in vacuo, 3 days (44%). (d) CH_2Cl_2 23 °C, then neat 170 °C in vacuo, 12 h (36%). (e) H_2, 10% Pd/C, EtOH (97%). (f) phthalic anhydride, DMF, reflux 12 h (59%). (g) 6 equiv of 1,4,5,8-naphthalenetetracarboxylic dianhydride, DMF, reflux.

at lower temperatures (140 °C) no reaction was observed. Reaction of the first amine of **8** apparently reduces the nucleophilicity of the second such that oligomerization is suppressed, eliminating the need for protecting groups. The final condensation reaction between diamine **9** and monoanhydride **10** was carried out under more forcing conditions (170 °C, neat, in vacuo) because of lower reactivity of the amines in **9**, and the product, octaimide **2**, was isolated in 36% yield.

Like model system **1**, oligoimide **2** was isolated as a mixture of stable *syn* and *anti* conformers. The *syn* and *anti* conformers were separated by preparative TLC and assigned on the basis of polarity arguments and also by differences in size and shape (vide infra). The rotational barrier of **2** (26.5 kcal/mol) was similar to that of model system **1** (27 kcal/mol) and was calculated from the rate of reequilibration of the pure *syn* and *anti* isomers in acetonitrile at 80 °C.

Molecular models predicted that the two conformational isomers would have drastically different shapes. The rigid framework coupled with the limited conformational freedom enabled an accurate measure of the dimensions of *syn*- and *anti*-**2**. The *syn* isomer has a curved compact shape; whereas, the *anti* isomer has a larger extended shape (Scheme 1). Similar differences in hydrodynamic volume have been observed for the *cis* and *trans* isomers of photoresponsive azobenzene containing polymers.[8] The differences in size were experimentally apparent from gel permeation chromatography (GPC) (Figure 1). Despite the identical molecular weight of the isomers, GPC was able to differentiate *syn*- and *anti*-**2**, yielding estimated molecular weights (M_n) of 2665 and 2457, respectively, on the basis of polystyrene standards. The unfolded *anti* isomer eluted first, demonstrating that it had a larger hydrodynamic volume and giving additional support for the initial dipole-based assignments. In addition, the GPC measured molecular weights of both *syn*-**2** and *anti*-**2** were inflated in comparison to their absolute molecular weights (2286), which is consistent with what has been observed for other shape-persistent systems.[9]

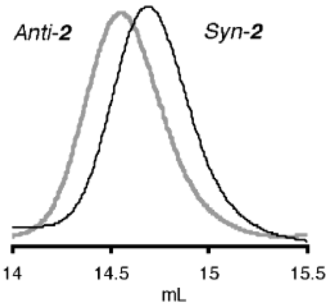


Figure 1. GPC traces of *anti*-**2** and *syn*-**2**. Conditions: Waters Styragel HMW 2 column at 1 mL/min, in chloroform.

The unique aspect of octaimide **2** is its dynamic shape-persistent and shape-adaptable qualities. Control of the *anti/syn* equilibria at elevated temperatures would enable the oligomers to be “molded” into one shape or the other and then to hold that shape. A possible strategy was suggested from studies of the model compound **1** of using differences in dipole moment of the conformers to control morphology.[10] These differences should be expressed to a different extent depending upon the dielectric constant of the medium. To test this strategy, oligomer **2** was equilibrated in a range of different solvents, by heating for greater than 10 half-lives. On cooling to room temperature, the *anti*/*syn* equilibria ratios were preserved as a result of the re-establishment of restricted rotation even when removed from the promoting environment. The *anti/syn* ratios were then measured by integration of the central naphthalene proton by ^{1}H NMR in $CDCl_3$. The heating experiments demonstrated that in more polar solvents such as acetonitrile the differences in dipole are minimized, and the *anti/syn* ratio approaches 1:1. In nonpolar solvents

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[8] (a) Junge, D. M.; McGrath, D. V. *J. Am. Chem. Soc.* **1999**, *121*, 4912−4913. (b) Izumi, A.; Teraguchi, M.; Nomura, R.; Masuda, T. *Macromolecules* **2000**, *33*, 5347−5352. (c) Beattie, M. S.; Jackson, C.; Jaycox, G. D. *Polymer* **1998**, *39*, 2597−2605.

[9] (a) Rader, H. J.; Spickermann, J.; Mullen, K. *Macromol. Chem. Phys.* **1995**, *196*, 3967−3978. (b) Rader, H. J.; Spickermann, J.; Kreyenschmidt, M.; Mullen, K. *Macromol. Chem. Phys.* **1996**, *197*, 3285−3296.

[10] Dipole moments of *anti*- and *syn*-**2** were calculated as 0.66 and 6.05 D using MacSpartan (semiemperical, AM1).

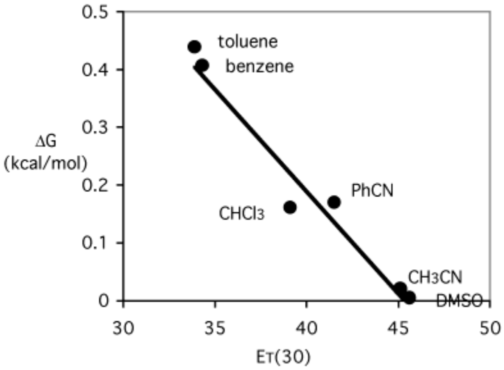

Figure 2. The observed energy differences between the *anti*-**2** and *syn*-**2** in different solvents plotted against the solvent polarity scale $E_{T(30)}$.

such as toluene and benzene, the less polar *anti* isomer is favored (64:36). A regular relationship between conformational ratio and solvent polarity was observed by a roughly linear relationship between $\Delta G°$ versus the solvent polarity scale $E_{T(30)}$ (Figure 2). This predictable relationship enabled precise control over the *anti/syn* ratio by choice of a solvent of appropriate polarity.

Alternatively, a 35:65 *anti/syn* ratio was observed on heating in the solid state (neat in vacuo at 80 °C for 24 h). This preference for the *syn* isomer is possibly due to the dominance of packing effects over dipole effects. The influence of effects other than differences in dipole moments on the *syn/anti* equilibrium is seen even in solution. If the equilibrium ratio were controlled solely by solvent polarity, then a linear relationship between $\Delta G°$ and the Kirkwood parameter $((\epsilon - 1)/(2\epsilon + 1))$ is predicted.[11] However, this plot shows considerably more scatter than the $\Delta G°$ versus $E_{T(30)}$ plot. Thus, the relatively linear relationship between $\Delta G°$ and $E_{T(30)}$ suggests that the conformational equilibrium is controlled not by dipole moment alone but also by other effects such as steric or attractive interactions.[12] Molecular models confirm that in the *syn* isomer there is the possibility for significant interactions between the octadecyl chains.

Although either conformer can be favored, complete control over the morphology of oligomer **2** was not observed, as the differences in dipole moment were not sufficient to shift the equilibria entirely to one conformation or the other. As a consequence, this system is more akin to a two-component polymer blend in which the ratios of each component can be adjusted simply by heating in different solvents. These ratios are then preserved on cooling. The properties of this "blend" can be tuned back and forth without reformulating the blend by addition of one or the other component.

Octaimide **2** represents an example of a molecule that can be shaped on the molecular level. This was accomplished by designing a shape-persistent/shape-adaptable system, which arises from restricted rotation about connecting $C_{aryl}-N_{imide}$ single bonds. At elevated temperatures the molecules can be predictably shaped into either a folded *syn* or an unfolded *anti* conformation having unique shapes, hydrodynamic volumes, and dipole moments by choice of a particular solvent environment. On cooling to room temperatures, these conformational preferences are saved and preserved as restricted rotation is reinstated. In this way, the properties of the oligomer can be modulated or tuned by controlling the percentage of the *syn* and *anti* conformations.

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Supporting Information Available: Synthetic procedures and characterization for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

OL0167098

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[11] Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*; VCH: Weinheim, 1990.

[12] Leis, J.; Klika, K. D.; Karelson, M. *Tetrahedron* **1998**, *54*, 7497−7504.