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A Helicene-Containing Foldamer Displaying Highly Solvent-Dependent CD Spectra

Matthew T. Stone,[‡] Joseph M. Fox,[†] and Jeffrey S. Moore*[,‡]

Department of Chemistry and Materials Science & Engineering,
600 South Mathews Avenue, The University of Illinois at Urbana-Champaign,
Urbana, Illinois 61801, and Department of Chemistry and Biochemistry,
University of Delaware, Newark, Delaware 19716

moore@scs.uiuc.edu

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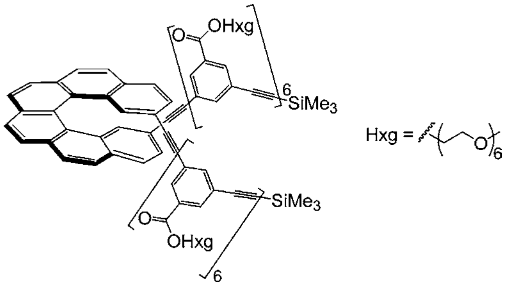
ABSTRACT



A *m*-phenylene ethynylene oligomer containing a helicene unit was synthesized to bias the twist sense of the folded helical conformation. The CD spectra of the helicene oligomer exhibited large Cotton effects that varied greatly with the solvent composition, including three separate conformational transitions.

Helical molecules can be divided into two categories.[1] The first group is epitomized by helicenes, which have a well-defined helical shape locked in place by strong steric interactions.[2] This helical structure is evident in the CD spectra of enantiomerically pure helicenes, which have characteristically large Cotton effects. These structures have been used as building blocks to construct chiral macromolecules such as cyclophanes and polymers.[3] In contrast to these rigid structures, the second category of helical molecules assumes its shape through folding, and in the absence of any chiral influence these are a racemic mixture of interconverting left- and right-handed helices in solution at room temperature. This category is typified by *m*-phenylene ethynylene (*m*PE) oligomers, which have been demonstrated to fold into a helical conformation in polar solvents.[4,5] Chiral bias of the folded *m*PE oligomers has been accomplished by inclusion of a binaphthol unit in the oligomer backbone or attachment of chiral side chains.[6−8] However, it might be predicted that, as a result of its complementary helical shape, a particularly efficient structure to nucleate the helical handedness of a *m*PE oligomer would be a member of the first category, such as helicene. The result of combining these two types of helices should give a molecule that has a strong chiral bias, but whose structure would be dependent on its

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[‡] University of Illinois at Urbana-Champaign.
[†] University of Delaware.
(1) Nakano, T.; Okamoto, Y. *Chem. Rev.* **2001**, *101*, 4013−4038.
(2) Laarhoven, W. H.; Prinsen, W. J. C. *Top. Curr. Chem.* **1984**, *125*, 63−130.
(3) Fox, J. M.; Lin, D.; Itagaki, Y.; Fujita, T. *J. Org. Chem.* **1998**, *63*, 2031−2038.
(4) Nelson, J. C.; Saven, J. G.; Moore, J. S.; Wolynes, P. G. *Science* **1997**, *277*, 1793−1796.
(5) Prince, R. B.; Saven, J. G.; Wolynes, P. G.; Moore, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 3114−3121.
(6) Gin, M. S.; Yokozawa, T.; Prince, R. B.; Moore, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 2643−2644.
(7) Prince, R. B.; Brunsveld, L.; Meijer, E. W.; Moore, J. S. *Angew. Chem., Int. Ed.* **2000**, *39*, 228−230.
(8) Brunsveld, L.; Prince, R. B.; Meijer, E. W.; Moore, J. S. *Org. Lett.* **2000**, *2*, 1525−1528.

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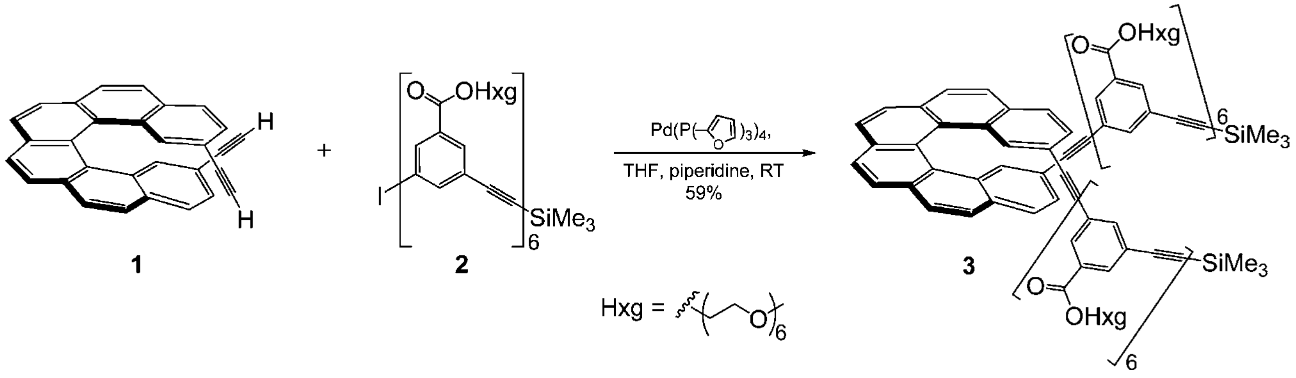
Scheme 1



environment.[9] This Letter describes the synthesis and characterization of helicene-containing *m*PE oligomer **3**, which was found to exhibit highly solvent-dependent circular dichroism spectra.

Helicene-containing oligomer **3** was designed with water-soluble hexaethylene glycol side chains, so that it could be studied in aqueous solutions where there is a strong hydrophobic driving force.[10] The helicene moiety was incorporated in the center of the chain to ensure that the *m*PE arms would be incapable of folding independently of its influence. Helicene oligomer **3** was synthesized by reacting (−)-(*M*)-2,15-diethynylhelicene **1**[3] with 2 equiv of iodide-terminated *m*PE hexamer **2**[10] under palladium-coupling conditions to give **3** with an isolated yield of 59% (Scheme 1). The structure and purity of **3** was determined by mass spectrometry (MALDI), ^{1}H NMR spectroscopy, and high performance liquid chromatography. The solvent-dependent nature of helicene oligomer **3** was then investigated using UV and CD spectroscopy at a concentration of 3.1 μM (Figure 1). Spectra were collected in mixed solvents whose composition was varied in 10% increments from pure chloroform where *m*PE oligomers exist in a random, denatured state to pure acetronitrile where they adopt a helical conformation.[11] The solvent composition was also tracked in 10% increments from acetonitrile to water where a strong hydrophobic driving force exists.

The UV absorbance spectra of **3** in different solvent compositions displayed features similar to those of previously reported *m*PE oligomers.[4] As the solvent composition changed from chloroform to acetonitrile, there was a decrease in the absorption band centered around 305 nm, indicative of *m*PE oligomers adopting a helical conformation.[11] The absorbance band at 305 nm did not recede completely in 100% acetonitrile, which suggests that the helicene unit in the backbone has a destabilizing effect on the folded conformation. From 10% to 90% water in acetonitrile there was pronounced hypochromic effect, which has been noted in previous studies of *m*PE oligomers at higher water compositions.[10,12] This hypochromic effect is also observed in the UV spectra of DNA during thermal denaturation and is attributed to the close packing of aromatic chromophores.[13] The tight packing of the *m*PE backbone chromophores in water could be caused by the tightening of the helical shape and/or aggregation of folded oligomer **3**. The spectrum in pure water deviates from the trend in that a higher maximum absorbance is observed compared to the spectrum recorded in 90% water. Similar behavior was also seen in the solvent titration of a water-soluble *m*PE oligomer and is likely an effect of preferential solvation of the backbone by acetonitrile.[10]

The CD spectra of helicene oligomer **3** displayed strong Cotton effects in all solvent compositions. Three distinct spectral transitions were identified as the solvent composition was incrementally changed, and two of these were accompanied by isodichroic points. The variations between spectra were most pronounced from 250 to 340 nm, which is a region where chirally biased *m*PE oligomers typically exhibit Cotton effects.[6−8] The rigid structure of helicene is unlikely to account for these changes in the CD spectra; therefore, the differences over this region were attributed to the helical conformations of the *m*PE arms.[2] Although a specific, well-defined conformation cannot be inferred on the basis of these CD spectra alone, the direction of the Cotton effect does indicate the spatial disposition or twist sense of the backbone chromophores.[14] To gain further insight, computer modeling was used to examine the feasibility of various structures.

In pure chloroform the CD spectrum displayed a Cotton effect with a negative chirality that resembled the previously reported spectra of (+)-(*P*)-2,15-diarylethynylhelicene **4** in both shape and magnitude (Figure 1a and b).[3] This would be expected because the *m*PE arms are denatured in chloroform, leaving the diarylethynylhelicene center as the only optically active chromophore (Figure 2a). The broad

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[9] Katz, T. J. *Angew. Chem., Int. Ed.* **2000**, *39*, 1921−1923.

[10] Stone, M. T.; Moore, J. S. *Org. Lett.* **2004**, *6*, 469−472.

[11] Hill, D. J.; Moore, J. S. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5053−5057.

[12] Prince, R. B.; Moore, J. S.; Brunsveld, L.; Meijer, E. W. *J. Am. Chem. Soc.* **2001**, *123*, 7978−7984.

[13] Barr, G. C.; Norman, D. *Techniques Applied to Nucleic Acids. Nucleic Acids in Chemistry and Biology*, 2nd ed.; Oxford University Press Inc.: New York, 1996; pp 446−447.

[14] Harada, N.; Nakanishi, K. *Circular Dichroic Spectroscopy-Exciton Coupling in Organic Stereochemistry*; University Science Books: Mill Valley, CA, 1983; pp 4−8.

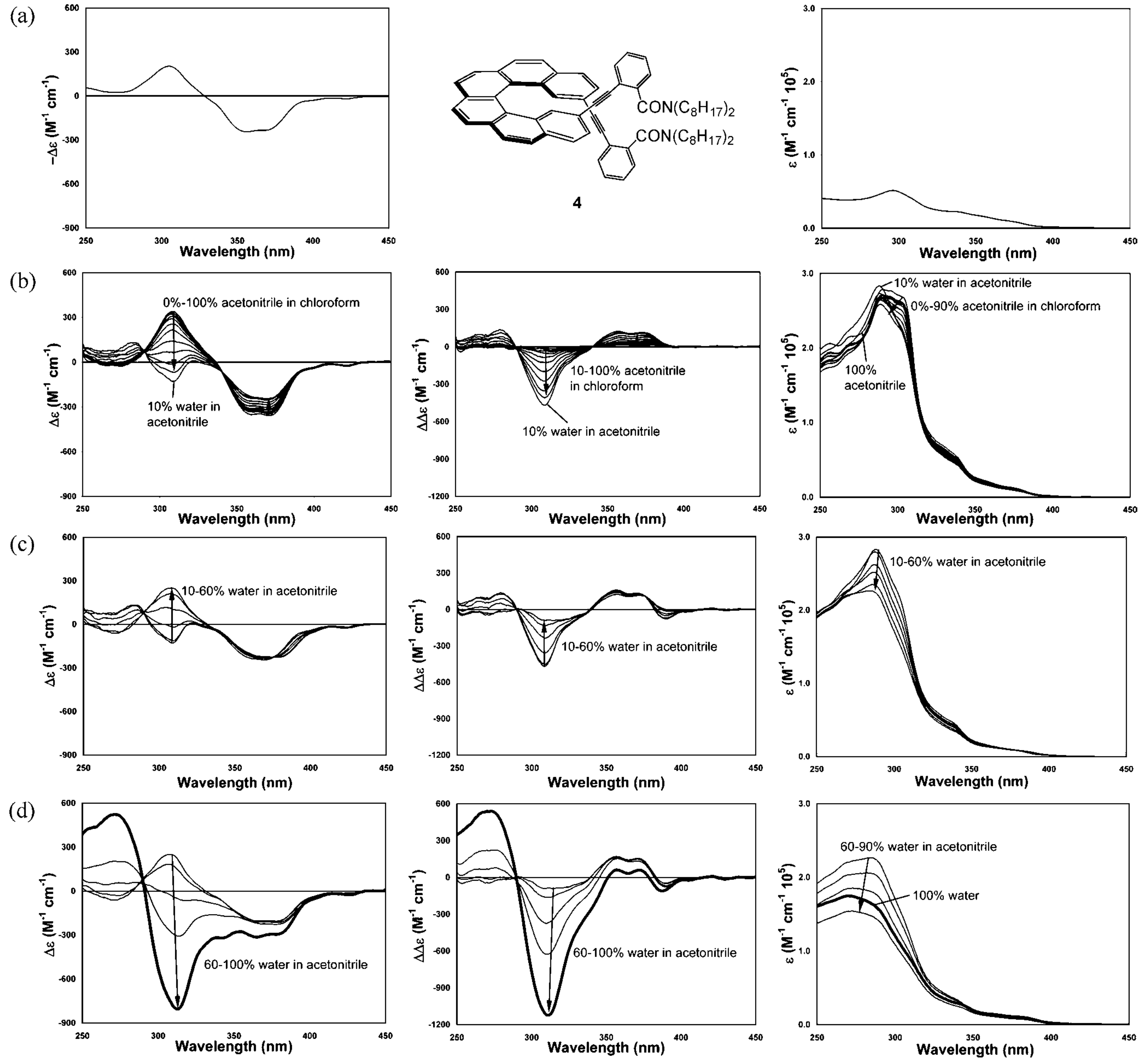

Figure 1. Figure 1. Room-temperature CD spectra (left), difference between CD spectra in 100% chloroform (center), and UV spectra (right) of (a) (+)-(*P*)-2,15-diarylethynylhelicene **4** in methylene chloride (note that CD spectrum is displayed as $-\Delta\epsilon$ for comparison), (b) **3** from 100% chloroform to 100% acetonitrile and 10% water in acetonitrile, (c) **3** from 10% to 60% water in acetonitrile, (d) **3** from 60% to 100% water in acetonitrile.

negative band centered at 375 nm was assigned to the rigid diarylethynylhelicene core as it lies outside the range where chirally biased *m*PE oligomers display significant Cotton effects. Consistent with this assignment, spectral features in this region varied little with solvent composition.

As the solvent was changed from pure chloroform to 10% water in acetonitrile, a transition was identified containing two isodichroic points at 290 and 341 nm, indicative of a single-step transition to a folded state. A second localized Cotton effect with a negative chirality developed from 250 to 340 nm, which suggests the *m*PE arms are folding into a *M*-helix. This localized Cotton effect appears weaker because it overlaps with the positive second Cotton effect of the diarylethynylhelicene core. The development of the negative Cotton effect during this transition is apparent when the CD signal in 100% chloroform is subtracted from the spectra. The structure proposed to account for this feature has the helicene moiety jutting out of a *M*-helix formed by the *m*PE arms (Figure 2b). This conformation allows all *m*PE repeat units to stack with each other except for the last two, which are able to stack with the helicene unit. The reasonableness of this structure was evaluated using a Monte Carlo conformational search in Macromodel. The search began from a structure in which the oligomer arms were arranged roughly

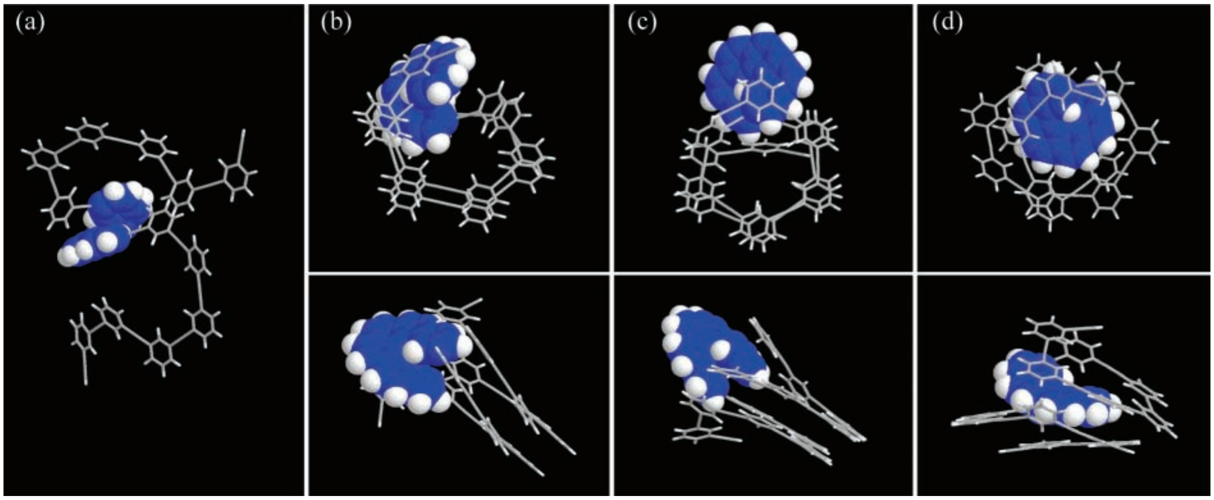

Figure 2. Figure 2. Molecular models of helicene oligomer **3** in different conformations: (a) unfolded, (b) *m*PE arms folded into a *M*-helix, (c) *m*PE arms folded into a *P*-helix, (d) *m*PE arms wrapped around helicene in a *M*-helix. Helicene moiety is displayed in blue as a space-filling model, and side chains were omitted to simplify calculation.

into a *M*-helix, and the oligomer was then allowed to reach a local minimum energy. The search produced a low energy structure that placed the *m*PE arms into a *M*-helix as proposed.

As the percentage of water in acetonitrile increased from 10% to 60%, a second transition was identified containing an isodichroic point at 376 nm, indicating that there is a single-step transformation to a second folded conformation (Figure 1c). During this transition the Cotton effect with negative chirality from 250 to 340 nm recedes, leaving a spectrum at 60% water in acetonitrile that resembles the spectrum of **3** in pure chloroform. It appears that above 10% water the folded *M*-helix is in equilibrium with a second folded *P*-helix. At a composition of 60% water, both the folded M- and *P*-helices are present at significant concentrations, which results in a small overall signal from the folded mPE arms. It was proposed that oligomer **3** could form a *P*-helix if the helicene unit protruded out from the folded *m*PE arms (Figure 2c). Computer modeling, as described above, was found to converge to such a conformation. Inspection of the model showed that the folded *P*-helix has a diameter smaller than that of the folded *M*-helix, and this would allow the oligomer to reduce its solvent-exposed surface area at these higher compositions of water.

As the percentage of water increased above 60% a dramatic inversion of the band centered at 310 nm was observed, which progressed into a strong Cotton effect with the positive chirality (Figure 1d). The lack of isodichroic points over this transition is probably due to aggregation of the folded helices, which is consistent with the hypochromic effect observed in the UV spectra. The Cotton effect in pure water was more than twice the magnitude found at any other solvent composition. Again the negative first Cotton effect of the folded *m*PE arms is even stronger than it appears, because it overlaps with the positive second Cotton effect of the diarylethynylhelicene core. The strong Cotton effect led us to propose a conformation where the *m*PE arms were wrapped around the *M*-helicene, forcing them into a complementary *M*-helix. This structure would in effect place the helicene within the hydrophobic cavity, minimizing unfavorable interactions with water molecules. Computer modeling of this structure included a force field to simulate water as solvent and revealed that there is a propensity for the *m*PE arms to wrap around the helicene moiety (Figure 2d). However, the actual conformation in solution might be more compact than is suggested by this calculated structure.

In conclusion, helicene-containing *m*PE oligomer **3** was synthesized, and it was found that inclusion of this rigid helicene structure was particularly effective at biasing the twist sense of the folded helical conformation. The solvent-dependent behavior of UV absorbance spectra was consistent with the folding ability of previously studied *m*PE oligomers. The CD spectra of **3** varied greatly with solvent composition, displaying three distinct transitions. Conformations of **3** were proposed to account for the observed CD spectra, and their feasibility was evaluated with computer modeling.

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Supporting Information Available: Detailed descriptions of all experimental procedures. This material is available free of charge via the Internet at http://pubs.acs.org.

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