

## Helical Bias in Solvophobiclly Folded Oligo(Phenylene Ethynylene)s

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The design and synthesis of nonbiological chain molecules that adopt ordered conformations in solution has been an active area of research in recent years.<sup>1</sup> The aim of this research is to understand the forces that drive self-organization and, ultimately, to mimic the behavior of natural biopolymers. Toward this end, several strategies have been used to impart a bias on the screw sense of helical structures.<sup>2</sup> Previous work in this group on solution conformations of phenylene ethynylene oligomers has demonstrated a solvent-induced transition from a random, disordered conformation in “good” solvents such as chloroform to an ordered, putative helical conformation in “poor” solvents such as acetonitrile.<sup>3,4</sup> Herein we report the use of an optically active binaphthol derivative inserted into the oligomer chain to impart a bias in the twist sense of the helical structure, as evidenced by solvent-dependent changes in the circular dichroism spectra (Figure 1).

Binaphthol derivative **1** was prepared from (*R*)-binaphthol in 86% overall yield following sequential treatment with bromine<sup>6</sup> (−78–23 °C, 3 h) and TgOMs (K<sub>2</sub>CO<sub>3</sub>, 18-crown-6, 75 °C, 2 days). Palladium-catalyzed coupling of oligomers **2–5** with **1** was achieved under standard conditions<sup>7</sup> (Pd(dba)<sub>2</sub>, CuI, Ph<sub>3</sub>P, Et<sub>3</sub>N, 75 °C, 18 h) to afford bis-coupled products **6–9** in 60–90% yields

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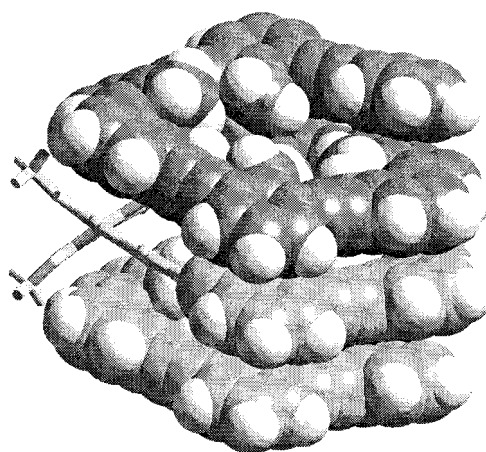
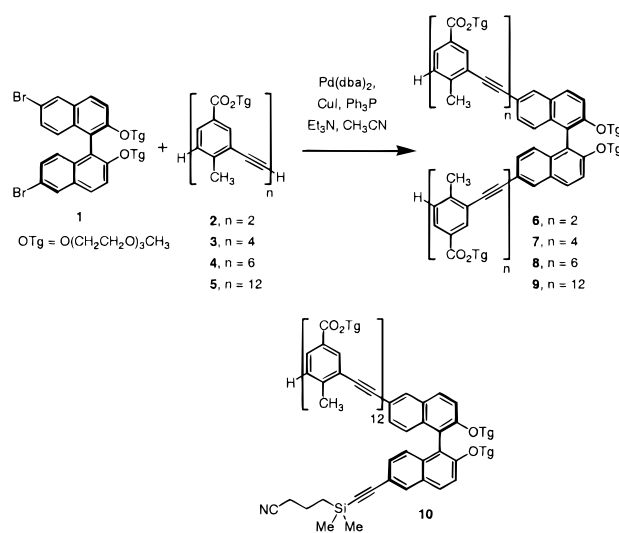


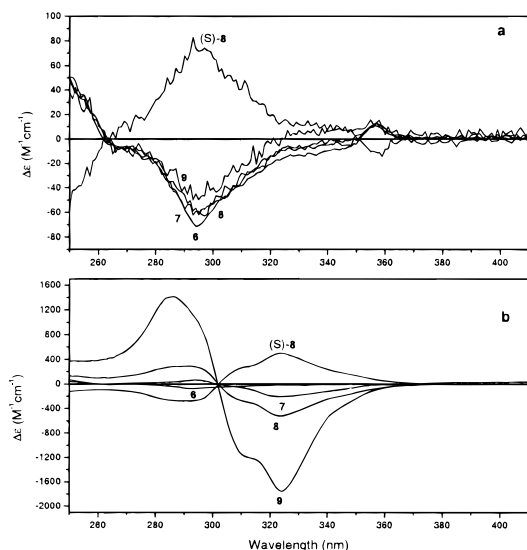
Figure 1. Minimized structure of a phenylene ethynylene octamer bis-coupled to binaphthol.<sup>5</sup>

### Scheme 1

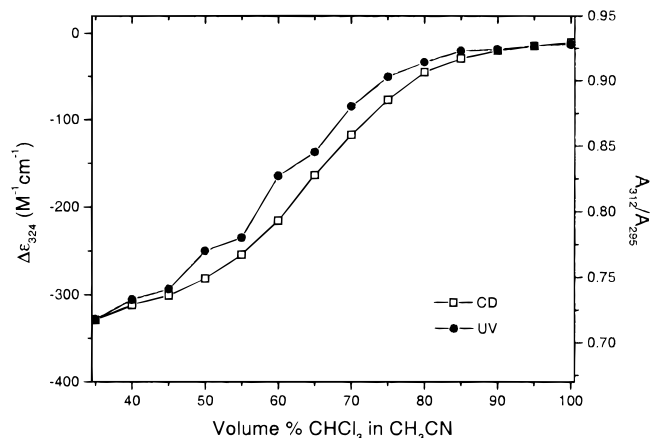


(Scheme 1). The enantiomer (*S*)-**8** was prepared from (*S*)-binaphthol, and monocoupled oligomer **10** was prepared from the corresponding binaphthol derivative under similar coupling conditions. All products were characterized by <sup>1</sup>H NMR, HPLC, and mass spectrometry. As in our previous studies on the oligomers, the UV absorption and fluorescence emission spectra were solvent-dependent for all products except **6**, which, as expected from our earlier work,<sup>3a</sup> is too short to form a stable helical conformation.

For CD studies, all solutions were prepared with an OD at λ<sub>max</sub> of ca. 1.0 (2–11 μM; molarity based on moles of oligomer). As shown in Figure 2a, the CD spectra of **6–9** in chloroform (i.e., a good solvent) are independent of chain length. The only observed signal is due to the chiral binaphthol unit in the chain. In contrast, large signals are evident in acetonitrile (Figure 2b). The shape and magnitude of the CD signal from the shortest oligomer **6** (Δε<sub>294</sub> = −75 M<sup>−1</sup> cm<sup>−1</sup>) is the same in both solvents. For (*R*)-**7–9**, however, the values at 294 nm become positive, and a new band appears at 323 nm, corresponding to the electronic transition in the backbone chromophores.<sup>3</sup> Whereas in chloroform the magnitude of the Δε values are the same for the four oligomers, there is a dramatic increase in the Δε values in acetonitrile as the size of the chain increases, indicating that the observed signal arises from the chiral environment of the helical backbone and that this environment persists as the chain lengths.



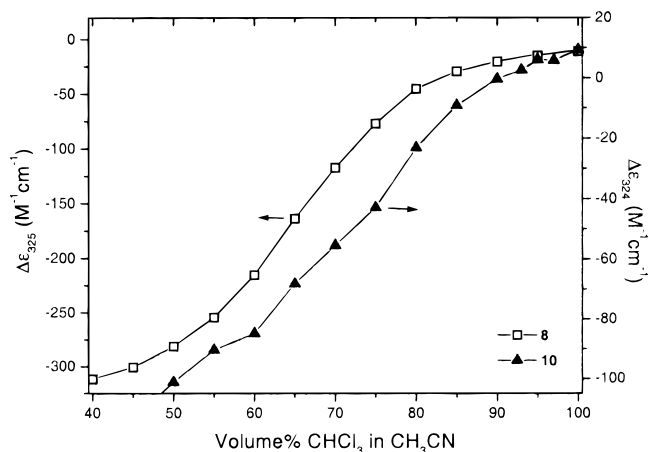
**Figure 2.** CD spectra of 6–9 in (a) chloroform, and (b) acetonitrile. Note the different ordinate scales. All samples were prepared with OD ca. 1.0 (2–11  $\mu\text{M}$  in oligomer), and spectra were recorded at ambient temperature (23  $^{\circ}\text{C}$ ).



**Figure 3.** Solvent denaturation of **8** measured by UV absorbance ratios (●) and CD intensity (□).

The presence of an isodichroic point at 302 nm suggests a similarity in the structures of 7–9, and the opposite sign of the signal arising from (S)-**8** confirms that the induction of chirality in the backbone is caused by the binaphthol segment. The shape of the CD signals from monocoupled oligomer **10** are similar; however, the intensity of the signal in acetonitrile is less than one-half that of comparably sized bis-coupled **8**. This may reflect a decrease in the effectiveness of the binaphthol segment toward biasing the twist sense of the helix when positioned at the end of the chain. An assay for determining the absolute bias of these helices has not yet been identified.

We have previously invoked a two-state model to analyze the transition between unfolded and helical conformations of oligomers such as **5**. This assumption allows us to use solvent composition titration data to approximate free energies of unfolding ( $\Delta G_u$ ).<sup>3a,8</sup> In this study solvent composition titrations were performed on bis-hexamer **8** and mono-dodecamer **10** in an effort to probe the degree of helical destabilization caused by the presence of the binaphthol moiety in the center of the chain. Figure 3 shows the titration curves for **8** obtained by monitoring  $\Delta\epsilon$  at 324 nm (□), and by monitoring the relative intensities of the UV absorption bands at 312 and 295 nm (●). The transition



**Figure 4.** Solvent denaturation of **8** (□) and **10** (▲) measured by CD.

**Table 1.**  $\Delta G_{\text{CH}_3\text{CN}}$  and  $[\text{CHCl}_3]_{1/2}$  Obtained from Solvent Denaturation of **8** and **10**.<sup>a,b</sup>

oligomer	$[\text{CHCl}_3]_{1/2}^c$		$\Delta G_{\text{CH}_3\text{CN}}^d$	
	CD	UV	CD	UV
<b>8</b>	67	64	6.7	5.9
<b>10</b>	81	80	10.5	9.6

<sup>a</sup> See ref 8 and Supporting Information for details of the calculations.

<sup>b</sup> For comparison, fluorescence titration of **5** gave  $[\text{CHCl}_3]_{1/2} = 75$  and  $\Delta G_{\text{CH}_3\text{CN}} = 7.3$ .<sup>9</sup> <sup>c</sup> Volume % in  $\text{CH}_3\text{CN}$ . <sup>d</sup> kcal/mol.

between folded and unfolded conformations, whether measured by UV or CD, occurs at similar chloroform concentrations (i.e., 60–70%  $\text{CHCl}_3$ ).

Titrations performed on **10** gave curves analogous to those of **8**. Comparison of the CD titration curves of **8** (□) and **10** (▲) illustrates that the unfolding transition for **10** occurs at higher chloroform composition (Figure 4). Analysis of the four titration curves to extricate  $\Delta G_u$ 's (kcal/mol) invoked the linear free energy relationship shown in eq 1.<sup>8</sup>

$$\Delta G_u = \Delta G_{\text{CH}_3\text{CN}} - m(\% \text{CHCl}_3) \quad (1)$$

The midpoint of the transition occurs when  $\Delta G_u = 0$ , or at  $[\text{CHCl}_3]_{1/2} = \Delta G_{\text{CH}_3\text{CN}}/m$  (Table 1). Extrapolating to 0%  $\text{CHCl}_3$ , the free energy of unfolding in acetonitrile,  $\Delta G_{\text{CH}_3\text{CN}}$ , was obtained. From these data, one can see that the folded structure of **10** in acetonitrile is 3–5 kcal/mol more stable than that of **8**, indicating that the binaphthol in the center of **8** produces a destabilizing kink in the helix.

We have demonstrated that the introduction of an optically active binaphthol derivative into the backbone of phenylene ethynylene oligomers imparts a bias on the helical structures formed in acetonitrile. Using solvent denaturation methods, the amount of destabilization incurred when the binaphthol is positioned in the middle of the chain is estimated to be 3–5 kcal/mol. The extent to which the binaphthol biases the twist sense of the helix, however, is significantly greater when positioned in the center of the oligomer chain. The chiral cavity of these helices may prove to be effective as asymmetric recognition elements.

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**Supporting Information Available:** Experimental procedures, UV, fluorescence, additional CD spectra, and the details of the  $\Delta G_u$  calculations (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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