

## PHOTOCONTROLLING THE HELIX-COIL TRANSITION: AZOBENZENE-CONTAINING FOLDAMERS

Anzar Khan, Christian Kaiser, and Stefan Hecht\*

Institut für Chemie / Organische Chemie, Freie Universität Berlin  
Takustr. 3, 14195 Berlin, Germany  
Max-Planck-Institut für Kohlenforschung  
Kaiser-Wilhelm-Platz 1, Mülheim an der Ruhr, Germany  
hecht@mpi-muelheim.mpg.de

### Introduction

Recent years have witnessed enormous progress in the design of artificial backbones capable to adopt well-defined secondary structures, in particular of the helix type, in solution.<sup>1</sup> The helical folding process is governed by non-covalent interactions such as hydrogen bonding, metal coordination, electrostatic and  $\pi,\pi$ -stacking interactions among others. Therefore, the helix-coil transition is most frequently induced by increasing the temperature, changing solvent composition or adding denaturants. Such denaturation experiments provide insight into the stability of the helical conformation and the cooperativity involved in the folding process. However, methods to control this important conformational transition using light as perhaps the most convenient external stimulus have been limited. Photochromic molecules,<sup>2</sup> displaying two independently addressable switching states, have been used to affect structure and function at the molecular level.<sup>3</sup> The considerable structural reorganization accompanying the classical *trans-cis*-photoisomerization of azobenzene derivatives has for instance been explored to control the conformation in various peptides.<sup>4</sup>

Here, we report on our attempts to incorporate azobenzene moieties into amphiphilic phenylene ethynylene foldamers.<sup>5</sup> Several designs have been followed in order to obtain helices that can be turned on and off, respectively. These results represent the first example of photocontrolling the helix-coil transition in artificial, helically folding backbones (Figure 1).

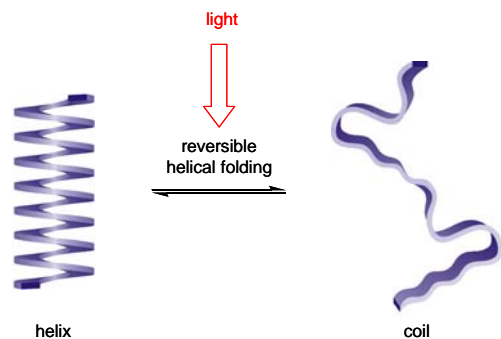


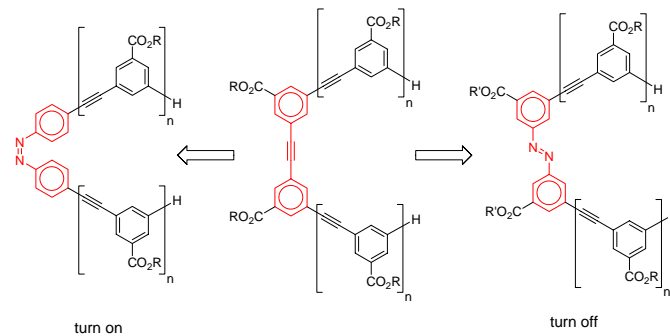
Figure 1. Photocontrol of the helix-coil transition in helical foldamers.

### Results and Discussion

In polar solvents amphiphilic oligo(*meta*-phenyleneethynylene)s<sup>5</sup> adopt a stable helical conformation, in which most likely six repeat units constitute one turn of the helix<sup>6</sup> that is stabilized primarily by solvophobic forces as well as  $\pi,\pi$ -stacking interactions between electron deficient aromatic repeat units. Our working hypothesis was to replace a single internal diphenylacetylene unit by differently substituted *trans*-azobenzene chromophores (Figure 2).<sup>7</sup> Thereby, either (thermally) stable helices or coils should be accessible and hence the helical conformation could be turned off or on using irradiation. The length of the oligomeric sequences attached to the photochromic unit has to be adjusted in such way that they cannot adopt a stable helical conformation by themselves but isomerization either breaks or creates a kinked connection to lead to helix denaturation or formation.

Several derivatives including model compounds have been synthesized and their folding behavior has been investigated in the dark and photostationary states. Important results are associated with the importance of linkage geometry of the azobenzene unit as well as the effect of helical structure on the rate of the *cis-trans*-isomerization. Detailed spectroscopic studies involving UV/vis-absorption, fluorescence, and CD-spectroscopy

reveal insight into the behavior of the azobenzene chromophore in the



presence of the phenylene ethynylene backbone.

Figure 2. Studied azobenzene-containing phenylene ethynylene foldamers.

### Conclusions

Introduction of photochromic azobenzene units into helically folding, amphiphilic oligo(*meta*-phenyleneethynylene)s leads to photocontrol over the helix-coil transition in this important class of foldamers. The spontaneous denaturation or generation of a helical secondary structure upon irradiation offers insight into the dynamics of folding related processes and a variety of potential applications for instance in the creation of photoresponsive smart materials.

**Acknowledgements.** Generous support by the Sofja Kovalevskaja Award of the Alexander von Humboldt Foundation, endowed by the Federal Ministry of Education and Research (BMBF) within the Program for Investment in the Future (ZIP) of the German Government, is gratefully acknowledged. Further support has been provided by the Collaborative Research Center SFB 448 (TP A14) of the German Research Foundation (DFG).

### References

- (1) For a comprehensive review on foldamers, see: Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893.
- (2) (a) *Photochromism - Molecules and Systems*, (Eds.: H. Dürr, H. Bouas-Laurent), Elsevier: Amsterdam, 2003; (b) *Molecular Switches*, (Ed.: B. L. Feringa), Wiley: Weinheim, 2001; (c) Special Issue: „Photochromism: Memories and Switches“; *Chem. Rev.* **2000**, *100*, 1683, and references therein.
- (3) (a) Balzani, V.; Credi, A.; Venturi, M. *Molecular Devices and Machines: A Journey into the Nanoworld*; Wiley-VCH: Weinheim, 2003; (b) Balzani, V.; Credi, A.; Raymo, F. C.; Stoddart, J. F. *Angew. Chem. Int. Ed. Engl.* **2000**, *39*, 3348; (c) Special Issue: „Molecular Machines“; *Acc. Chem. Res.* **2001**, *34*(6), 409; (d) Willner, I.; Rubin, S. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 367; (e) For a recent highlight, consult: Hecht, S. *Small* in press.
- (4) For linear peptides with azobenzene containing side chains: (a) Pieroni, O.; Fissi, A.; Angelini, N.; Lenci, F. *Acc. Chem. Res.* **2001**, *34*, 9-17; For linear peptides with azobenzene containing linkers: (b) Flint, D. G.; Kumita, J. R.; Smart, O. S.; Woolley, G. A. *Chemistry & Biology* **2002**, *9*, 391-397; For cyclic peptides with azobenzene containing linker: (c) Vollmer, M. S.; Clark, T. D.; Steinem, C.; Ghadiri, M. R. *Angew. Chem. Int. Ed. Engl.* **1999**, *38*, 1598-1601.
- (5) Foldamers based on amphiphilic oligo(*meta*-phenyleneethynylene)s have been pioneered by Moore and coworkers: (a) Nelson, J. C.; Saven, J. G.; Moore, J. S.; Wolynes, P. G. *Science* **1997**, *277*, 1793; (b) Prince, R. B.; Saven, J. G.; Wolynes, P. G.; Moore, J. S. *J. Am. Chem. Soc.* **1999**, *121*, 3114.
- (6) Experimental evidence for this structure arises from ESR double spin labeling experiments: Matsuda, K.; Stone, M. T.; Moore, J. S. *J. Am. Chem. Soc.* **2002**, *124*, 11836.
- (7) Khan, A.; Kaiser, C.; Hecht, S. unpublished results.