Photoresponsive peptoid oligomers bearing azobenzene side chains†

Neel H. Shah and Kent Kirshenbaum*

Received 20th March 2008, Accepted 23rd April 2008
First published as an Advance Article on the web 21st May 2008
DOI: 10.1039/b804802a

N-Substituted glycine peptoid oligomers were synthesized to incorporate a photoresponsive azobenzene side chain. The ability of this side chain to undergo reversible photoisomerization was established, and the *cis*- to *trans*-azobenzene thermal isomerization of this side chain was investigated. Circular dichroism studies indicated that *trans*- to *cis*-azobenzene isomerization does not significantly alter the backbone conformation in a series of peptoids thought to have well-defined structures.

Introduction

Many biomolecular systems are capable of recognizing and responding to external stimuli. Typically, an exogenous influence such as ligand binding, a change in pH or temperature, or absorbance of a photon can modulate biomolecular structure to subsequently activate a biochemical signal cascade. In recent years, extensive efforts have been made to mimic the responsiveness of biomolecules to their environment for biosensor and other biomedical applications.[1–5] Within these novel synthetic systems, light has emerged as a useful and convenient external stimulus due to the fact that it can be spatially and temporally controlled. In particular, research has focused on the irreversible photorelease of chemically caged compounds[6–9] and the reversible structural changes of photochromic compounds such as azobenzene.[10–16]

Our research is focused on developing structural control in a class of peptidomimetics known as *N*-substituted glycine oligomers, or peptoids. These molecules can be readily synthesized in a sequence-specific manner to yield a wide array of chemically diverse products.[17–19] Additionally, peptoids have the propensity to form stable, ordered conformations,[20–22] and a number of these oligomers have shown biological activity.[23–27] Despite their similarities to biopolymers, however, only a small number of peptoid oligomers have been shown to be responsive to their environment.[21,28,29] Thus far, such systems have relied on solvent or pH changes to induce conformational changes.

Although photosensitive functional groups have not yet been incorporated into peptoids, many azobenzene-functionalized peptides have been shown to undergo photo-induced conformational switching, suggesting that this strategy could be extrapolated to peptidomimetic systems.[1,10,16] Here, we report the incorporation of an azobenzene moiety into a peptoid scaffold and the ability to reversibly photoisomerize this side chain. The introduction of photoresponsive functionalities within this important class of biomimetic oligomers may allow for unique structural control and may expand the scope of their potential applications.

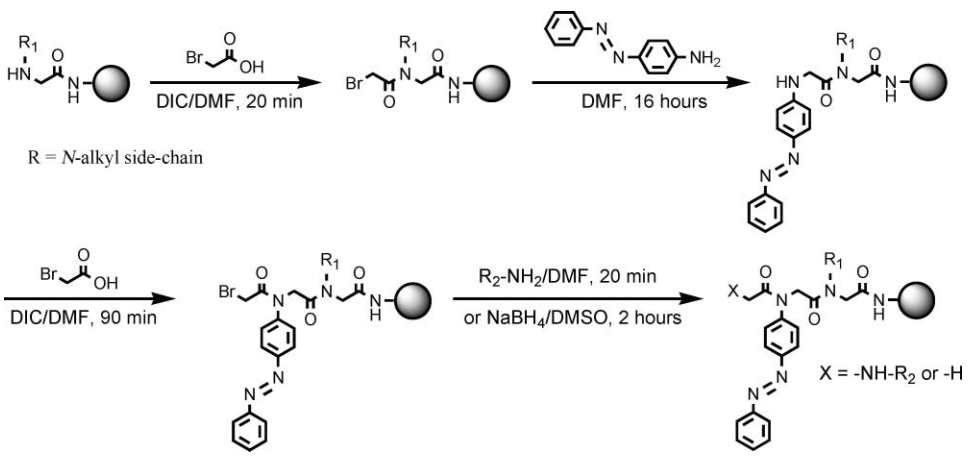
Results and discussion

Synthesis of photoresponsive peptoid oligomers

Azobenzene-containing peptoids were synthesized using a modified version of the solid-phase submonomer protocol developed by Zuckermann *et al.* (Scheme 1).[17] Typically, *N*-substituted glycine oligomers are generated through iterative bromoacetylation

Department of Chemistry, New York University, 100 Washington Square East, New York, NY, 10003-6688, USA. E-mail: kent@nyu.edu; Fax: +1 212 260 7905; Tel: +1 212 998 8487

† Electronic supplementary information (ESI) available: Structures and characterization of peptoid oligomers, RP-HPLC analysis of photoisomerization, and calculation of thermal isomerization rates. See DOI: 10.1039/b804802a



Scheme 1 Synthesis of azobenzene-containing peptoid oligomers.

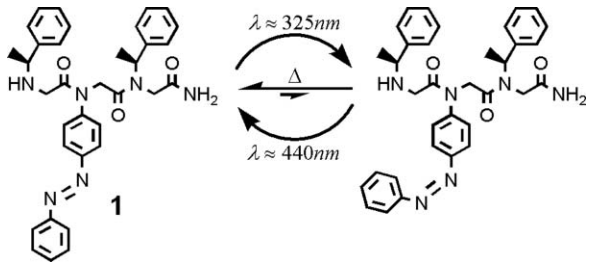
and primary amine displacement steps. *N*-(*p*-Phenylazo-phenyl)-glycine (*N*azb) was incorporated as a monomer unit in this manner by reacting the *N*-terminal bromoacetyl group of an elongating peptoid chain with commercially available 4-aminoazobenzene. Given the reduced nucleophilicity of this aryl amine with respect to the more common alkyl amines used in peptoid synthesis, the submonomer was allowed to react for 16 hours rather than 20 minutes. Additionally, the subsequent bromoacetylation was carried out for 90 minutes rather than 20 minutes. For those peptoid sequences bearing *N*-terminal *N*azb monomers, a 90 minute bromoacetylation reaction was followed by treatment with sodium borohydride to provide the corresponding acetylated oligomers. Overall, syntheses of azobenzene-containing peptoid oligomers yielded crude products with >85% purity which were subsequently purified by reverse-phase high performance liquid chromatography (RP-HPLC).[30]

Photoisomerization of azobenzene-containing peptoids

The capacity for azobenzene-functionalized peptoids to photoisomerize was evaluated using UV–vis spectroscopy before and after photoirradiation of the oligomers within select wavelength ranges. An initial absorbance spectrum of peptoid trimer **1** with azobenzene at the second residue showed an intense π–π* transition around 325 nm and a weak n–π* transition around 440 nm, characteristic of *trans*-azobenzene. Analytical RP-HPLC of the compound showed the presence of only one isomer.[31] Upon irradiation between 275 nm and 375 nm to the photostationary state, the intensity of the π–π* transition decreased while that of the n–π* transition increased (Fig. 1a). RP-HPLC showed two peaks representing the *cis*- and *trans*-azobenzene isomers of peptoid **1** with distinct polarities. Integration of these peaks indicated approximately 75% conversion from a *trans*- to a *cis*-azobenzene side chain.[31] Subsequent irradiation of the trimer in the visible region (>400 nm) completely recovered the *trans*-azobenzene-containing oligomer (Fig. 1b).

Kinetic stability of *cis*-azobenzene peptoid side chains

cis-Azobenzene is known to be thermally less stable than *trans*-azobenzene, and the isomer is often short-lived, reducing the utility of azobenzene as a photoswitch for practical applications.[32,33] Thus, upon establishing the efficacy of azobenzene photoisomerization on a peptoid scaffold, the kinetic stability of the unstable *cis*-azobenzene isomer was investigated. Absorbance spectra of molecule **1** after *trans*- to *cis*-photoisomerization showed that the *cis*-azobenzene isomer underwent rapid thermal back-isomerization in the dark at room temperature, reconverting to *trans*-azobenzene with a half-life of approximately 5 hours (Scheme 2). Interestingly, upon acetylation of the *N*-terminus, the thermal back-isomerization of resulting oligomer **2** slowed drastically, reconverting with a half-life of over 6 days. To better understand the nature of this disparity, a small library of oligomers (**3–9**, **11**, **12**) with varying lengths, side chains, and *N*-terminal functionalities were synthesized incorporating azobenzene at different positions along the peptoid scaffold (Table 1 and 2).[34]



Scheme 2 Photoisomerization and thermal back-isomerization of **1**.

An initial comparison of trimers **1**, **3** and **5** to their acetylated derivatives **2**, **4**, and **6** suggested that the drastic change in the rate of thermal back-isomerization was simply a result of the loss of a free *N*-terminal amine. This free amine could establish an electrostatic influence or associate with a counterion that can destabilize the nearby *cis*-azobenzene moiety. However, molecule **14**, which does not contain a free amine but displays

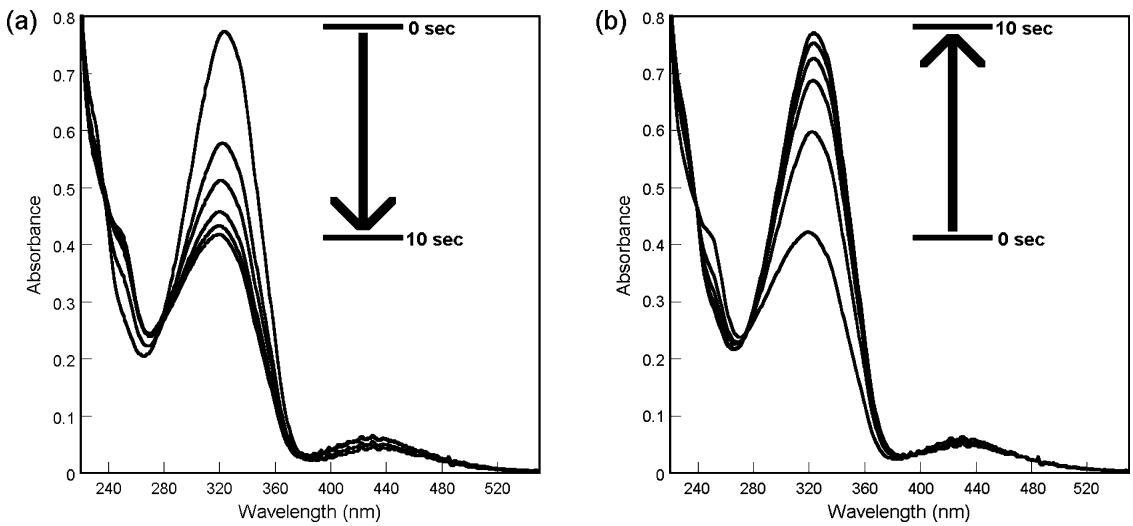


Fig. 1 Photoisomerization of a peptoid trimer monitored by UV–vis spectroscopy (a) *trans*- to *cis*- photoisomerization of **1**: 0, 2, 4, 6, 8 and 10 sec irradiation accompanied by decreasing absorbance intensity at 325 nm (b) *cis*- to *trans*- photoisomerization of **1**: 0, 2, 4, 6, 8 and 10 sec irradiation accompanied by increasing absorbance intensity at 325 nm.

Table 1 *N*-Substituted glycine monomer units

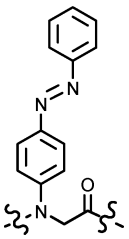
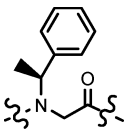
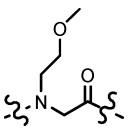
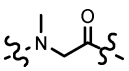
Monomer	Designator
	*N*azb = *N*-(*p*-phenylazo-phenyl)glycine
	*N*spe = (*S*)-*N*-(1-phenylethyl)glycine
	*N*me = *N*-(2-methoxyethyl)glycine
	Sar = *N*-(methyl)glycine or sarcosine

Table 2 Peptoid sequences and half-lives of thermal back-isomerization

Compound	Sequence	Half-life[a]/hours
1	*N*spe*N*azb*N*spe	5.7
2	Ac*N*spe*N*azb*N*spe	153.5
3	*N*me*N*azb*N*me	5.5
4	Ac*N*me*N*azb*N*me	137.2
5	Sar*N*azbSar	7.8
6	AcSar*N*azbSar	149.8
7	(*N*spe)$_2$*N*azb(*N*spe)$_2$	108.9
8	Ac(*N*spe)$_2$*N*azb(*N*spe)$_2$	84.8
9	Ac*N*azb(*N*spe)$_4$	106.6
10	Ac(*N*spe)$_5$	—
11	Ac(*N*spe)$_3$*N*azb(*N*spe)$_3$	122.5
12	Ac*N*azb(*N*spe)$_6$	109.0
13	Ac(*N*spe)$_7$	—
14	*N*-methyl-*p*-phenylazo-acetanilide	5.0

[a] Half-life is based on a first-order decay.

the same core chromophore as **1–6**, also showed a rapid rate of back-isomerization. The fact that peptoid pentamer **7**, bearing a free *N*-terminus, had a slow rate of thermal back-isomerization also indicated that this disparity in thermal stability cannot be attributed exclusively to *N*-terminal acetylation. Additionally, oligomers **1–6** showed that this phenomenon was not side chain dependent. Ultimately, it was found that acetylated trimers and longer oligomers underwent thermal back-isomerization nearly one order of magnitude slower than non-acetylated trimers and the small-molecule analogue **14** (Table 2).[35] This trend may be attributable to non-local stereoelectronic interactions between the azobenzene and monomer units more than one residue away that stabilize the *cis*-azobenzene state or increase the energetic barrier to back-isomerization by destabilizing the transition state of this process.

Circular dichroism of photoresponsive peptoids

Peptoids rich in (S)-*N*-(1-phenylethyl)glycine (*N*spe) monomer units have been shown to populate compact helical conformations and display distinct circular dichroism (CD) spectra in their backbone amide absorbance region (between 195 nm and 225 nm).[20] Additionally, CD has been used to detect backbone conformational changes in peptoids by monitoring changes in the local electronic environment around the main-chain amide chromophores.[21,29] We sought to examine the ability of peptoids incorporating *N*azb to populate stable backbone conformations. The effect of *trans*- to *cis*-azobenzene photoisomerization on the peptoid backbone was monitored using CD (Fig. 2). Since distinct conformational states typically display unique CD spectra, a change in CD spectrum upon photoisomerization would indicate a photoswitching of the peptoid backbone structure.

Prior to photoisomerization, pentamers **8** and **9** and heptamers **11** and **12** showed qualitatively similar CD spectra to their corresponding *N*spe homo-oligomers **10** and **13**. Upon photoisomerization, the general spectral shape of each oligomer was retained, however compounds **9** and **12**, bearing *N*-terminal azobenzene side chains, showed a small decrease in signal intensity, suggesting a subtle change in backbone conformation. Since the azobenzene side chain in these oligomers was at the *N*-terminus, this change is most likely only a realignment of the terminal residue. Surprisingly, peptoids **8** and **11**, bearing azobenzene side chains in the middle of the sequence, showed virtually no change in their CD spectra upon photoisomerization, indicating retention of general backbone conformation features.

The CD spectra of oligomers **8**, **9**, **11** and **12** were not dramatically altered after *trans*- to *cis*-azobenzene photoisomerization. These results indicate that structural perturbations in the azobenzene side chain may not strongly influence the peptoid backbone. Previous studies of peptoids comprising *N*-alkyl glycine monomers have described conformational rearrangements in response to pH and solvent changes,[21,28,29] reinforcing the notion that these oligomers can exhibit substantial structural plasticity.[36] On the other hand, the local conformational preferences of *N*-aryl glycine units, such as *N*azb, have not been as carefully defined. *N*-Aryl glycine monomers may exhibit distinct structural characteristics. In particular, the presence of *N*-aryl glycines may rigidify the peptoid backbone, thereby precluding dramatic conformational rearrangements, even upon photoisomerization of a bulky azobenzene side chain. Research in our lab is currently focused on investigating the properties of *N*-aryl glycine peptoid oligomers to better understand their structural preferences.

Conclusions

In conclusion, we have shown that a photoresponsive azobenzene side chain can be readily incorporated within a peptoid scaffold and reversibly interconverted between two states. Additionally, the kinetic stability of the thermally less stable *cis*-azobenzene side chain can be significantly enhanced by elongating the oligomer beyond trimer length, thereby allowing access to this state for practical applications or structural studies. Ultimately, the ability to photocontrol both the backbone and side chain conformations of these well-ordered peptidomimetics could provide a convenient

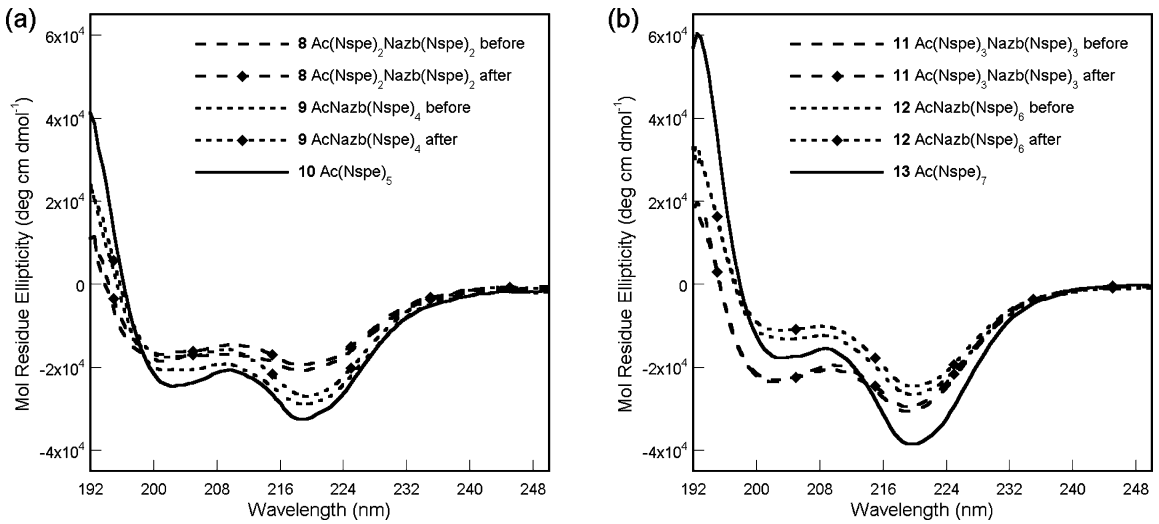


Fig. 2 CD spectra of (a) pentamers and (b) heptamers before and after *trans*- to *cis*- photoisomerization.

way to control their functions. Azobenzene-containing peptoids may provide a useful scaffold for photoactive materials in optical or sensor devices. Furthermore, the incorporation of this photoresponsive side chain into bioactive peptoids may provide a precise method to modulate and probe their interactions with biological molecules.

Experimental

Materials

Bromoacetic acid, 4-aminoazobenzene, piperidine, and methylamine in tetrahydrofuran (2.0 M) were purchased from Sigma-Aldrich (St. Louis, MO). *S*-(−)-1-Phenylethylamine was purchased from TCI (Portland, OR). 2-Methoxyethylamine, acetic anhydride, sodium borohydride, iodomethane and sodium hydride (60% w/w dispersion in mineral oil) were purchased from Alfa Aesar (Ward Hill, MA). *N*,*N*′-Diisopropylcarbodiimide and *N*,*N*-diisopropylethylamine were purchased from Chem-Impex International (Wood Dale, IL). Trifluoroacetic acid was purchased from Acros (Belgium). Fmoc-protected Rink amide resin (0.69 mmol g^{-1} loading level) was purchased from Nova Biochem (San Diego, CA).

Peptoid synthesis

Solid-phase synthesis of peptoid oligomers was carried out in fritted syringes on Rink amide resin using a variation of the peptoid submonomer synthesis reported by Zuckermann *et al.*[17] *N*-Substituted glycine monomers were generated from their corresponding amine submonomers. *N*-(2-Methoxyethyl)-glycine was generated by incorporation of 2-methoxyethylamine. *N*-(Methyl)glycine was generated by incorporation of methylamine. *N*-(4-Phenylazo-phenyl)glycine was generated by incorporation of 4-aminoazobenzene. (*S*)-*N*-(1-Phenylethyl)glycine was generated by incorporation of *S*-(−)-1-phenylethylamine. All equivalencies are given with respect to resin loading level.

In a typical oligomer synthesis, 100 mg of resin with a loading level of 0.69 mmol g^{-1} was swollen in 2 mL of *N*,*N*′-dimethylformamide (DMF) for 30 minutes. Following swelling, the Fmoc protecting group was removed by treatment with 1.5 mL of 20% piperidine in DMF twice for 20 minutes. After deprotection and after each subsequent synthetic step, the resin was washed twice with 2 mL of DMF, twice with 2 mL of dichloromethane, and twice again with 2 mL of DMF, one minute per wash.

Peptoid synthesis was carried out with alternating bromoacylation and amine displacement steps. For each bromoacylation step, 20 eq. bromoacetic acid (1.2 M in DMF) and 24 eq. *N*,*N*′-diisopropylcarbodiimide (neat) were added to the resin, and the mixture was agitated for 20 minutes. After washing, 20 eq. of the required amine (1.0 M in DMF) were added to the resin and agitated for 20 minutes. Incorporation of methylamine was carried out in 50% tetrahydrofuran in DMF. Additionally, a modified reaction time of 16 hours was used for the amine displacement with 4-aminoazobenzene, and the subsequent bromoacylation of the *N*-terminal 4-aminoazobenzene was conducted for 90 minutes.

When required, peptoid *N*-termini were acetylated on solid-phase by one of two methods. For oligomers with an *N*-terminal 4-aminoazobenzene, acetylation was carried out in two steps. First, the *N*-terminus was bromoacetylated as described above. After washing, the bromide was displaced by adding 5 eq. of sodium borohydride (0.25 M in dimethylsulfoxide) to the resin and agitating the mixture for 2 hours. All other oligomers were acetylated by adding 10 eq. of acetic anhydride (0.5 M in DMF) to the resin and agitating the mixture for 1 hour.

Peptoid characterization and purification

Peptoid products were cleaved from the Rink amide resin by treatment with 95% aqueous trifluoroacetic acid for 10 minutes (40 mL g^{-1} resin). After filtration, the cleavage cocktail was concentrated by rotary evaporation under reduced pressure for large volumes or under a stream of nitrogen gas for volumes less than 1 mL. Cleaved samples were then re-suspended in 50% acetonitrile in water to the desired concentration.

Peptoid oligomers were characterized by analytical reversed-phase high performance liquid chromatography (RP-HPLC) using an analytical C_{18} column on a Beckman Coulter System Gold

HPLC system. Products were detected by UV absorbance at 214 nm during a linear gradient from 5 to 95% solvent B (0.1% trifluoroacetic acid in HPLC-grade acetonitrile) in solvent A (0.1% trifluoroacetic acid in HPLC-grade water) in 10 minutes with a flow rate of 0.7 ml min^{-1}. The expected molecular mass of each product was confirmed using liquid chromatography/mass spectrometry (LC/MS) on an Agilent 1100 Series LC/MSD Trap XCT with an electrospray ion source in positive ion mode.[30]

Peptoid products were purified to >95% purity using the same RP-HPLC apparatus described above with a preparatory C_{18} column. Products were detected by UV absorbance at 230 nm during a linear gradient from 5 to 95% solvent B in solvent A in 50 minutes with a flow rate of 2.5 ml min^{-1}. Compounds were then lyophilized to powders.

Synthesis and purification of *N*-methyl-4-phenylazo-acetanilide (14)

Acetic anhydride (44 μL, 46.9 mmol) and *N*,*N*-diisopropyl-ethylamine (122 μL, 70.4 mmol) were added to a solution of 4-aminoazobenzene (50 mg, 23.5 mmol) in dichloromethane (1 mL) and the mixture stirred at room temperature for 1 hour. The solvent was then evaporated under a stream of nitrogen gas, and the resulting residue was re-dissolved in diethyl ether (8 mL). The ether solution was washed twice with 5% aqueous citric acid (5 mL per wash). The organic layer was then dried, and the solvent was removed under reduced pressure.

The resulting crude acetylated product (4-phenylazo-acetanilide) was then re-dissolved in *N*,*N*-dimethylformamide (2 mL). Iodomethane (36.5 μL, 58.7 mmol) and sodium hydride in mineral oil (1.97 mg, 58.7 mmol) were added to the solution and the mixture was stirred at room temperature for 2 hours. Diethyl ether (8 ml) was added to the reaction mixture, and the mixture was washed twice with 5% aqueous citric acid (5 mL per wash). The organic layer was then dried, and the solvent was removed under reduced pressure. The crude compound was purified on a silica-gel column (5% ethyl acetate in dichloromethane to 20% ethyl acetate in dichloromethane) to yield the desired product (41 mg, 68.9%). Product was confirmed by ^{1}H-NMR in $CDCl_3$.[37]

UV–Vis spectroscopy of azobenzene derivatives

All UV–Vis spectroscopy experiments were carried out in sealed 1 cm path-length quartz cuvettes on 50 μM solutions of each compound in methanol. Photoisomerization of azobenzene derivatives was monitored using an Agilent 8453 UV–Visible spectrophotometer. Each sample was irradiated with the appropriate wavelengths of UV or visible light for successive one second intervals, obtaining an absorbance spectrum in between each interval. Thermal *cis*- to *trans*- isomerization of azobenzene derivatives was monitored using a Varian Cary 50 UV–Vis spectrophotometer. Absorbance was measured before photoirradiation. Then samples were irradiated from 275 nm to 375 nm for 2 minutes, and then placed in the dark spectrophotometer chamber. Typically, absorbance was measured each minute for the first 10 minutes, every 10 minutes for the following 20 minutes, and then every 30 minutes until the sample was scanned for a minimum of 6 hours.

Circular dichroism spectroscopy of azobenzene derivatives

All CD spectroscopy experiments were carried out in capped 1 mm path-length quartz cuvettes on 50 μM solutions of each compound in methanol or acetonitrile. CD spectra were obtained using an Aviv Stopped Flow CD Spectropolarimeter Model 202SF. CD spectra were obtained for each compound before and after irradiation between 275 nm and 375 nm for 2 minutes.

Acknowledgements

We thank Professor Vladimir Shafirovich for the use of his xenon light source and Dr Robert Cerpa for his helpful discussions. This work was supported by a National Science Foundation CAREER Award (CHE-0645361) and the NYU College of Arts and Science Dean's Undergraduate Research Fund. We also thank the NCRR/NIH for a Research Facilities Improvement Grant (C06RR-165720) at NYU.

Notes and references

1 R. Cerpa, F. E. Cohen and I. D. Kuntz, *Folding Des.*, 1996, **1**, 91.
2 E.-H. Ryu and Y. Zhao, *J. Org. Chem.*, 2006, **71**, 9491.
3 K. Chockalingam, M. Blenner and S. Banta, *Protein Eng., Des. Sel.*, 2007, **20**, 115.
4 K.-S. Moon, H.-J. Kim, E. Lee and M. Lee, *Angew. Chem.*, 2007, **119**, 6931.
5 T. Haneda, M. Kawano, T. Kojima and M. Fujita, *Angew. Chem., Int. Ed.*, 2007, **46**, 1.
6 D. D. Young and A. Deiters, *Org. Biomol. Chem.*, 2007, **5**, 999.
7 G. C. R. Ellis-Davies, *Nat. Methods*, 2007, **4**, 619.
8 C. J. Bosques and B. Imperiali, *J. Am. Chem. Soc.*, 2003, **125**, 7530.
9 J. E. T. Corrie, Y. Katayama, G. P. Reid, M. Anson and D. R. Trentham, *Philos. Trans. R. Soc. London, Ser. A*, 1992, **340**, 233.
10 M. S. Vollmer, T. D. Clark, C. Steinem and M. R. Ghadiri, *Angew. Chem., Int. Ed.*, 1999, **38**, 1598.
11 J. A. Ihalainen, J. Bredenbeck, R. Pfister, J. Helbing, L. Chi, I. H. M. van Stokkum, G. A. Woolley and P. Hamm, *Proc. Natl. Acad. Sci. USA*, 2007, **104**, 5383.
12 A. Khan, C. Kaiser and S. Hecht, *Angew. Chem., Int. Ed.*, 2006, **45**, 1878.
13 M. Aoyama, J. Watanabe and S. Inoue, *J. Am. Chem. Soc.*, 1990, **112**, 5542.
14 C. J. Gabriel and J. R. Parquette, *J. Am. Chem. Soc.*, 2006, **128**, 13708.
15 S. Keiper and J. S. Vyle, *Angew. Chem., Int. Ed.*, 2006, **45**, 3306.
16 L. Ulysse, J. Cubillos and J. Chmielewski, *J. Am. Chem. Soc.*, 1995, **117**, 8466.
17 R. N. Zuckermann, J. M. Kerr, S. B. H. Kent and W. H. Moos, *J. Am. Chem. Soc.*, 1992, **114**, 10646.
18 T. Horn, B. Lee, K. A. Dill and R. N. Zuckermann, *Bioconjugate Chem.*, 2004, **15**, 428.
19 J. M. Holub, H. Jang and K. Kirshenbaum, *Org. Biomol. Chem.*, 2006, **4**, 1497.
20 K. Kirshenbaum, A. E. Barron, R. A. Goldsmith, P. Armand, E. K. Bradley, K. T. V. Truong, K. A. Dill, F. E. Cohen and R. N. Zuckermann, *Proc. Natl. Acad. Sci. USA*, 1998, **95**, 4303.
21 K. Huang, C. W. Wu, T. J. Sanborn, J. A. Patch, K. Kirshenbaum, R. N. Zuckermann, A. E. Barron and I. Radhakrishnan, *J. Am. Chem. Soc.*, 2006, **128**, 1733.
22 S.-B. Y. Shin, B. Yoo, L. Todaro and K. Kirshenbaum, *J. Am. Chem. Soc.*, 2007, **129**, 3218.
23 J. A. Patch, K. Kirshenbaum, S. L. Seurynck, R. N. Zuckermann and A. E. Barron, in *Pseudopeptides in Drug Development*, ed. P. E. Nielsen, Wiley-VCH, Weinheim, Germany, 2004, p. 1.
24 H.-Y. Lim, C. T. Archer and T. Kodadek, *J. Am. Chem. Soc.*, 2007, **129**, 7750.
25 Y. Utku, E. Dehan, O. Ouerfelli, F. Piano, R. N. Zuckermann, M. Pagano and K. Kirshenbaum, *Mol. BioSyst.*, 2006, **2**, 312.

26 J. A. Patch and A. E. Barron, *J. Am. Chem. Soc.*, 2003, **125**, 12092.
27 J. M. Holub, M. J. Garabedian and K. Kirshenbaum, *QSAR Comb. Sci.*, 2007, **26**, 1175.
28 B.-C. Lee, R. N. Zuckermann and K. Dill, *J. Am. Chem. Soc.*, 2005, **127**, 10999.
29 S.-B. Y. Shin and K. Kirshenbaum, *Org. Lett.*, 2007, **9**, 5003.
30 See ESI page S2 for a crude RP-HPLC chromatograph of **1**. All peptoid oligomers were characterized by electrospray mass spectrometry and purified by RP-HPLC (ESI pages S3–S7)†.
31 RP-HPLC was monitored at an isosbestic wavelength (273 nm). See ESI page S8 for chromatographs of **1** before and after irradiation†.
32 N. Pozhidaeva, M.-E. Cormier, A. Chaudhari and G. A. Woolley, *Bioconjugate Chem.*, 2004, **15**, 1297.
33 V. Borisenko and G. A. Woolley, *J. Photochem. Photobiol., A*, 2005, **173**, 21.
34 See ESI pages S2–S3 for structures of peptoid oligomers†.
35 See ESI pages S8–S9 for calculations used to determine the rates of thermal back-isomerization of azobenzene-derivatives†.
36 C. W. Wu, K. Kirshenbaum, T. J. Sanborn, J. A. Patch, K. Huang, K. A. Dill, R. N. Zuckermann and A. E. Barron, *J. Am. Chem. Soc.*, 2003, **125**, 13525.
37 ^{1}H-NMR spectrum of **14** in $CDCl_3$ can be found in the ESI on page S7†.