[21] Since metal complexation and dehydrogenation both take place at elevated temperature in ethylene glycol, it is feasible to execute both steps as a "one-pot" transformation. Typical overall yields for the two-step transformation (that is, metal coordination followed by dehydrogenation) are approximately 50%.
[22] The removal of aromatic rings from the eilatin core, as in complexes **6** and **8**, results in higher susceptibility of the complexes toward oxidation. Products **6** and **8** have been isolated as a mixture of the Ru^{II} and Ru^{III} forms (see Supporting Information).
[23] J.-P. Sauvage, J.-P. Collin, J.-C. Chambron, S. Guillerez, C. Coudret, V. Balzani, F. Barigelletti, L. De Cola, L. Flamigni, *Chem. Rev.* **1994**, *94*, 993–1019; V. Balzani, A. Juris, M. Venturi, S. Campagna, S. Serroni, *Chem. Rev.* **1996**, *96*, 759–833; F. R. Keene, *Coord. Chem. Rev.* **1997**, *166*, 121–159; M. D. Ward, F. Barigelletti, *Coord. Chem. Rev.* **2001**, *216–217*, 127–154.
[24] The overall yield for the two steps is 30%.
[25] It is likely that a thermodynamic impetus to redirect the "misdirected" metal–ligand bonds in the unfused precursors contributes to the driving force of these transformations. See ref. [9] for a discussion regarding the bonding in the fluxional unfused complex **1**.

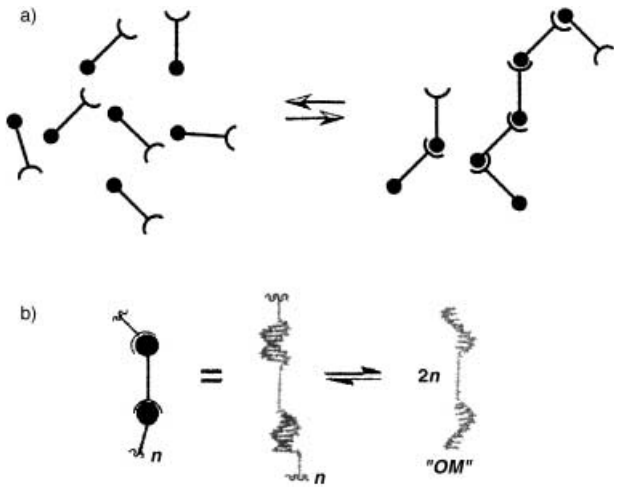

Figure 1. a) Schematic representation of reversible polymers; b) an OM-based reversible polymer. The spacer is extended for illustrative clarity only.

Modular, Well-Behaved Reversible Polymers from DNA-Based Monomers**

Elizabeth A. Fogleman, Wayne C. Yount, Jun Xu, and Stephen L. Craig*

Reversibly formed linear polymers (Figure 1a) have received increasing attention in recent years.[1–8] Reversible association of monomers leads to extended assemblies whose structure and properties depend on the strength and specificity of the association, the conformational flexibility of the molecule, the concentration of the monomer, and the chemical and physical environment of the system. These dissipative polymers undergo conformational changes and diffusion on much shorter timescales than their covalent counterparts, assemble with minimal imperfections, and repair themselves on useful timescales.[1,9] They encompass a range of structural motifs, phase behaviors,[1,3,10] solution and solid-state mechanical properties,[2,11,12] and environmental responsiveness,[12] and offer promise as environmentally benign materials as a result of the ease of processing and recycling and the absence of a polymerization catalyst. Meijer and co-workers[2,13,14] were the first to show that reversible polymers may possess properties that are similar to traditional covalent polymers despite the transient interaction (approximately seconds) defining the main chain.

[*] Prof. S. L. Craig, E. A. Fogleman, W. C. Yount, J. Xu
Department of Chemistry
P.M. Gross Chemical Laboratory, Duke University
Durham, NC 27708-0346 (USA)
Fax: (+1) 919-660-1605
E-mail: stephen.craig@duke.edu

[**] This work was supported by the Petroleum Research Fund of the American Chemical Society and Duke University. Partial support was provided by the North Carolina Biotechnology Center and Research Corp. S.L.C. gratefully acknowledges a DuPont Young Professor Award and a Camille and Henry Dreyfus New Faculty Award.

Here we report that the reversible polymeric properties of a system based on oligonucleotide base pairing are well-behaved. The system is intrinsically modular and is therefore amenable to "physical organic chemistry of materials", that is, systematically varying the structure of the components and observing the concomitant changes in the properties of the assemblies. The monomers (hereafter, oligonucleotide-based monomers (OMs)) comprise oligonucleotide sequences that are covalently linked directly or through a synthetic spacer (Figure 1b). Duplex formation creates a linear, polymeric assembly that resembles larger duplex DNA,[15] but in which the main chain is defined by the reversible base pairing. The specificity between complementary DNA strands is such that monomers can be synthesized that associate head-to-tail or in alternating patterns. DNA base pairing is a popular motif for self-assembly,[16,17] and similar systems have been used to characterize DNA curvature and ring-closure probabilities,[18,19] to sequentially align synthetic moieties,[20,21] and to fabricate linear DNA–protein nanostructures.[22] Surprisingly, their properties in the context of reversible polymerization have not been previously reported. We find that OMs are well-suited to systematic studies of reversible polymerization.

Representative OMs are reported in Table 1. OMs **1a–d** are self-complementary and form single-component homopolymers, while **2A**:**2B** and **3A**:**3B** are two-component heteropolymer systems. Melting curves give effective free energies of dimerization[23] (ΔG_{dim}) that are in line with empirically derived expectations;[24,25] polymerization does not have a significant impact on duplex formation. Polymer formation is revealed in all cases by an increased viscosity in the OM solutions relative to solutions of nonpolymerizing analogues. For example, the viscosity of **2A**:**2B** (3 mg mL^{-1} or 0.29 mM in each monomer, 1M NaCl/10 mM sodium phosphate buffer, pH 7.0, 25.0 °C, Cannon–Ubbellohde viscometer) is 1.25 times that of the same concentration of **2B** alone, and that of **3A**:**3B** (5.8 mg mL^{-1} or 0.22 mM) is 2.5 times that of **3A** alone. The molecular weight of the polymer can be easily controlled by varying the ratios of **2A**:**2B** and **3A**:**3B**; an excess of any monomer serves as an effective "chain

  0044-8249/02/4121-4026 $ 20.00+.50/0

Table 1. Composition, complementarity, and free energies of dimerization of oligonucleotide-based monomers. Red and blue colors denote complementarity within each OM system.

OM	Sequence	$\Delta G_{dim}(298)$ [kcal mol^{-1}][21]
1	(5′→3′)GGTATACC-X-GCTTAAGC	
1a	no spacer	−10.0
1b	X = −T−	−8.5
1c	X = $-CH_2CH_2CH_2-$	−8.5
1d	X = $-(CH_2CH_2O)_6-$	−9.2
2A	(5′→3′)GGCTCCCTTCTACCAC	−12.4
2B	(5′→3′)AGGGAGCCGTGGTAGA	
3A	(5′→3′)GCCCGGGCTCTCAAAAACTCTCGGGCCCTAGAGGGGCCCTAGA	−13.2
3B	(5′→3′)CCCGGGCTCTAGGGCCCCTCTAGGGCCCGAGAGTTTTTGAGAG	

terminator" for the polymerization. Expected molecular weights are calculated from the free energies of the duplexes and monomer ratio, and the viscosity observed scales as $MW^{(1.2\pm0.1)}$ for **2** and **3** (Figure 2). The exponents indicate semirigid rod polymers, which is consistent with the known structure of duplex DNA.

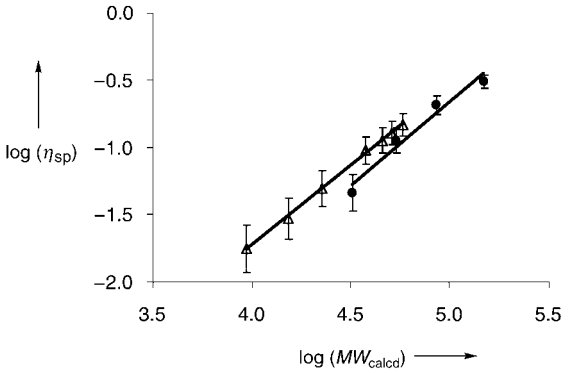

Figure 2. Specific viscosity η_{sp} as a function of calculated molecular weight determined from chain-termination studies for **2AB** (△, 3.0 mg mL^{-1}, 20 °C) and **3AB** (●, 2.9 mg mL^{-1}, 20 °C).

The concentration dependence of the solution viscosity also reveals the reversible nature of the system. The specific viscosity of **1a** scales with $[\mathbf{1a}]^{3.3\pm0.2}$, which is in good agreement with theoretical expectations[26] and previous observations for reversible systems.[2,12] Static multiangle and dynamic light scattering studies on 1 mM solutions of **1a** confirm the expected average molecular weights of approximately 200 kDa and the presence of semirigid rod structures with persistence lengths of about 50 nm. The OM polymers behave like true reversible counterparts of high MW duplex DNA.

Enzymatic manipulations provide further insight. Quick T4 DNA ligase (New England Biolabs) covalently captures polymers of **1a** on the timescale of OM dissociation (approximately minutes), and the ligated polymers can be characterized by gel electrophoresis (Figure 3). All equilibrium polymerizations are candidates for some degree of cyclization, and these can be characterized for **1a**. Digestion by Lambda exonuclease removes any linear polymers,[27] and the remaining small band of cyclic structures (approximately 10 % of total) is clearly seen in the gel.

Polymeric properties are determined not only by primary and secondary structure but also by inter- and intrachain

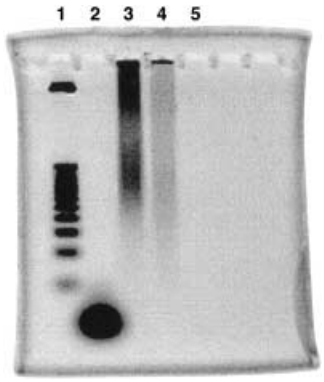

Figure 3. Denaturing polyacrylamide gel electrophoresis (PAGE) of OM **1a** samples. Lane 1: 25-bp step ladder; lane 2: OM **1a**; lane 3: ligated polymer of **1a**; lane 4: ligated and exonucleased **1a**; Lane 5: exonucleased **1a**.

interactions. In OMs, the interactions—reflected by the Huggins constant (k')—are largely electrostatic, and they are mediated by the ionic strength of the buffer. Similar to the results of Shruggs and Ross,[28] k' varies from 0.49 to 0.84, and passes through a maximum value at about 1 M NaCl. The nonlinear dependence on ionic strength can be ascribed to screening effects,[29] and its consequence is that polymer–polymer interactions can be varied from good solvent to strongly interacting conditions. The variation is pseudo-independent of duplex thermodynamics, thus providing another handle for fundamental studies.

In conclusion, DNA-based modules appear to be generally suitable systems for fundamental studies of reversible polymerizations. As such, they possess several attractive characteristics. The thermodynamics and kinetics of association are determined by the variable OM base sequence. The linear density of the reversible interactions and the conformational flexibility along the polymer backbone are each dependent on a spacer in which much variation is possible. Inter- and intrachain interactions may be tuned by the salt concentration in the buffer. Finally, robust enzymology offers covalent capture of transient structures and structural analyses of cyclizations. Many properties of assembled materials directly reflect the nature of the reversible interaction defining the polymerization. An understanding of the relationship between the structural, mechanical, and dynamic properties of the polymer and the structural, thermodynamic, and dynamic properties of the molecular constituents might therefore create an avenue for the rational synthesis of materials with

  0044-8249/02/4121-4027 $ 20.00+.50/0

specific properties. Studies with OMs should therefore provide insight into the molecular basis of novel properties of reversible polymeric systems, for example, at surfaces and interfaces.[8]

Received: June 4, 2002 [Z19455]

[1] J.-M. Lehn, *Makromol. Chem. Macromol. Symp.* **1993**, *69*, 1.
[2] R. P. Sijbesma, F. H. Beijer, L. Brunsveld, B. J. B. Folmer, J. H. K. K. Hirschberg, R. F. M. Lange, J. K. L. Lowe, E. W. Meijer, *Science* **1997**, *278*, 1601 – 1604.
[3] R. K. Castellano, D. M. Rudkevich, J. Rebek, Jr.,*Proc. Natl. Acad. Sci. USA* **1997**, *94*, 7132 – 7137.
[4] N. Zimmerman, J. S. Moore, S. C. Zimmerman, *Chem. Ind.* **1998**, 604 – 610.
[5] P. S. Corbin, S. C. Zimmerman in *Supramolecular Polymers, Vol. 1* (Eds: A. Ciferri), Marcel Dekker, New York, NY, **2000**, pp. 147 – 176.
[6] C. Alexander, C. P. Jariwala, C. M. Lee, A. C. Griffin, *Polym. Prepr. (Am. Chem. Soc. Div. Polym. Chem.)* **1993**, *34*, 168 – 169.
[7] U. Michelsen, C. A. Hunter, *Angew. Chem.* **2000**, *112*, 780 – 783; *Angew. Chem. Int. Ed.* **2000**, *39*, 764 – 767.
[8] J. van der Gucht, N. A. M. Bessling, M. A. C. Stuart, *J. Am. Chem. Soc.* **2002**, *124*, 6202 – 6205.
[9] G. M. Whitesides, J. P. Mathias, C. T. Seto, *Science* **1991**, *254*, 1312 – 1319.
[10] R. K. Castellano, C. Nuckolls, S. H. Eichhorn, M. R. Wood, A. J. Lovinger, J. Rebek, Jr., *Angew. Chem.* **1999**, *111*, 2764 – 2768; *Angew. Chem. Int. Ed.* **1999**, *38*, 2603 – 2606.
[11] A. J. Canty, J. Patel, B. W. Skelton, A. H. While, *J. Organomet. Chem.* **2000**, *599*, 195 – 199.
[12] R. K. Castellano, R. Clark, S. L. Craig, C. Nuckolls, J. Rebek, Jr.,*Proc. Natl. Acad. Sci. USA* **2000**, *97*, 12418 – 12421.
[13] B. J. B. Folmer, R. P. Sijbesma, E. W. Meijer, *Polym. Mater. Sci. Eng.* **1999**, *80*, 20 – 21.
[14] L. Brunsveld, B. J. B. Folmer, E. W. Meijer, *MRS Bull.* **2000**, *25*, 49 – 53.
[15] The spacers are only a small fraction of the reversible polymers and their influence on the properties is largely limited to conformational flexibility.
[16] N. C. Seeman, *Nano Lett.* **2001**, *1*, 22 – 26.
[17] J. J. Storhoff, C. A. Mirkin, *Chem. Rev.* **1999**, *99*, 1849 – 1862.
[18] D. Shore, J. Langowski, R. Baldwin, *Proc. Natl. Acad. Sci. USA* **1981**, *78*, 4833 – 4837.
[19] M. Dlakic, R. Harrington, *J. Bio. Chem.* **1995**, *270*, 29945 – 29952.
[20] S. M. Waybright, C. P. Singleton, K. Wachter, C. J. Murphy, U. H. F. Bunz, *J. Am. Chem. Soc.* **2001**, *123*, 1828 – 1833.
[21] Y. Ohya, K. Yabuki, M. Komatsu, T. Ouchi, *Polym. Adv. Technol.* **2000**, *11*, 845 – 855.
[22] C. M. Niemeyer, M. Adler, B. Pignataro, S. Lenhert, S. Gao, L. Chi, H. Fuchs, D. Blohm, *Nucleic Acids Res.* **1999**, *27*, 4553 – 4561.
[23] In each of **1a**–**d** and **2AB**, there are two duplexes of comparable calculated free energies (within 1–2 kcal mol^{-1}). The individual transitions are not resolved in UV melting experiments, and the experimental free energy reported is very close to an average of the two. The free energy of **3AB** is assigned to the weaker duplex; the larger duplex is effectively permanently fixed in our experimental conditions and serves as an effective "duplex spacer": J. Xu, S. L. Craig, unpublished results.
[24] K. J. Breslauer, R. Frank, H. Blocker, L. A. Marky, *Proc. Natl. Acad. Sci. USA* **1986**, *83*, 3746.
[25] K. M. Guckian, B. A. Schweitzer, R. X.-F. Ren, C. J. Sheils, D. C. Tahmassebi, E. T. Kool, *J. Am. Chem. Soc.* **2000**, *122*, 2213 – 2222.
[26] M. E. Cates, *Macromolecules* **1987**, *20*, 2289.
[27] R. I. Ma, N. R. Kallenbach, R. D. Sheardy, M. L. Petrillo, N. C. Seeman, *Nucleic Acids Res.* **1986**, *14*, 9745 – 9753.
[28] R. L. Shruggs, P. D. Ross, *Biopolymers* **1964**, *2*, 593 – 609.
[29] M. Shibayama, M. Uesaka, S. Inamoto, H. Mihaua, M. Nomura, *Macromolecules* **1996**, *29*, 885 – 891.

Molecular Clips that Undergo Heterochiral Aggregation and Self-Sorting**

Anxin Wu, Arindam Chakraborty, James C. Fettinger, Robert A. Flowers II,* and Lyle Isaacs*

Biological systems offer exquisite examples of the ways in which spatially and temporally controlled self-processes—self-organization, self-assembly, and self-recognition—can lead to the creation of higher order functional structures.[1] To approach the design of supramolecular systems that display complex biomimetic behavior, chemists have developed metal coordination, donor-acceptor interaction, and hydrogen-bond-driven self-assembly to a level of sophistication that has allowed these assemblies to be endowed with desirable chemical or physical properties.[2] Within the area of self-assembly driven by hydrogen bonds, these activities have resulted in intriguing discoveries including quadruple hydrogen bonding modules[3] that form the basis of supramolecular polymers,[4] molecular capsules,[5] systems that display enantiomeric self-recognition,[6] and complete asymmetric induction.[7] The use of hydrogen bonding as a tool in these applications depended on the design of robust, functionalizable, and tightly associated H-bonding modules. The further implementation of H-bonding modules as instructed components[1] in self-organizing systems additionally requires systems capable of self-sorting.[8] Such systems display high levels of discrimination between self and non-self species and consequently operate simultaneously and orthogonally within complex mixtures. One strategy to create robust H-bonding modules relies on increasing the number of hydrogen bonds and tailoring their geometrical arrangement. In this paper we employ a strategy using molecular clips,[9,10] based on molecular shape and chirality. We report that compounds **1a**, **1b**, (±)-**2a**, and (±)-**2b** form tightly self-associated dimers in $CDCl_3$ driven by the simultaneous formation of π–π interactions and two hydrogen bonds. The dimers possess a confluence of properties—tight binding, high levels of chiral discrimination, and self-sorting—that make them prime modules for use in advanced applications.

[*] Prof. L. Isaacs, Dr. A. Wu,[+] Dr. A. Chakraborty, Dr. J. C. Fettinger
Department of Chemistry and Biochemistry
University of Maryland
College Park, MD 20742 (USA)
Fax: (+1) 301-314-9121
E-mail: LI8@umail.umd.edu

Prof. R. A. Flowers II
Department of Chemistry and Biochemistry
Texas Tech University
Lubbock, TX 79409 (USA)
Fax: (+1) 806-742-1289
E-mail: rflowers@ttu.edu

[+] National Laboratory of Applied Organic Chemistry
Lanzhou University
Lanzhou 730000 (P. R. China)

[**] We thank the National Institutes of Health (GM61854) for generous financial support. L.I. is a Cottrell Scholar of Research Corporation.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

  0044-8249/02/4121-4028 $ 20.00+.50/0