Oligonucleotide-Directed Assembly of Materials: Defined Oligomers

Shane M. Waybright, Chainey P. Singleton, Kimberly Wachter, Catherine J. Murphy, and Uwe H. F. Bunz*

Contribution from the Department of Chemistry and Biochemistry, The University of South Carolina, Columbia, South Carolina 29208

Received March 16, 2000

Abstract: A nano-architectural system that has high variability while maintaining component specificity is described. Tetraphenylcyclobutadiene(cyclopentadienyl)cobalt complexes and phenyleneethynylene trimers were synthesized and subsequently modified with oligonucleotides utilizing standard phosphoramidite chemistry. The resulting oligonucleotide modified organics (OMOs) were characterized by UV−vis spectroscopy, fluorescence spectroscopy, and phosphate analysis. Hybridization of these OMOs resulted in a series of self-assembled oligomeric hybrids of varying length and topology. These hybrids were characterized by melting temperature, polyacrylamide gel electrophoresis, and fluorescence spectroscopy. This model system demonstrates the power of DNA to self-assemble modules of interest—independent of the module itself.

Introduction

The rational construction of nanoscale devices having desired mechanical, optical, electronic, or other physical properties has been a major thrust for many researchers.[1] Applications of nanoscale devices are expected in molecular electronics, photonics, and the field of organic semiconductors. Exploitation of supramolecular chemistry has generated many exciting macromolecular architectures. The inherent power of supramolecular forces (hydrogen bonding, π-stacking interactions, electrostatic interactions, and van der Waals interactions) lies in their ability to preassemble components and "self-correct" defects through reversible thermodynamic processes.

For the advancement of nano-science, it is fundamental to arrange matter on the nanoscale.[2] In an effort to create novel molecular architectures, oligonucleotides are a powerful tool in assembling structural units in a desired arrangement due to base specificity, sequence programmability, and stiffness.[3] Seeman and co-workers have done extensive work in creating DNA junctions,[4] polygons,[5] and polyhedra,[6,7] which DiMauro and Hollenberg[8] contend may be useful for electronic circuit construction through chemical vapor deposition methods. The groups of Mirkin,[9] Schultz,[10] and Bergstrom[11] have demonstratedthe ability of oligonucleotides to arrange the molecules to which they are attached into supramolecular assemblies.[12,13]

We aim to further expand and generalize this field by creating a variety of organic and organometallic hubs, vertices, and termini that can be linked together forming complex architectures. Initial investigations include attaching oligonucleotides to (a) cyclobutadiene(cyclopentadienyl)cobalt complexes, which show significant optical properties in an extended system,[14a] and to (b) highly fluorescent poly(phenylene ethynylene)s, which have applications in organic semiconductor devices.[14b] Subsequent hybridization of these oligonucleotide-modified organic (OMO) moieties results in a system reminiscent of Meijer's hydrogen-bonded polymers.[15] This self-assembly directed system, however, allows for oligomers of *defined* size by simple hybridization of its constituents.

In this report, we communicate an initial thrust into creating novel structures. We demonstrate (1) the incorporation of organic molecules into oligonucleotides through exploitation of current oligonucleotide synthesis technology,[16] (2) the characterization of these oligonucleotides including methods of concentration determination, and (3) the hybridization of oligonucleotide-modifed organic (OMO) modules into defined, oligomeric structures. It is critical to understand that the organic molecules we use are by no means inclusive, but rather the idea of oligonucleotides arranging molecules can be extrapolated to molecules of any researcher's interest.

Results and Discussion

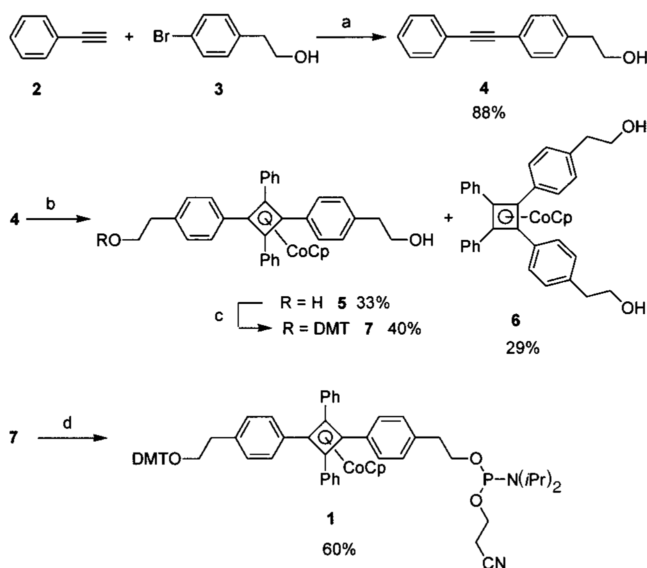
Synthesis of Organic Cores. To facilitate attachment of a molecule to an oligonucleotide, the molecule should be ap-

* To whom correspondence should be addressed. E-mail: bunz@mail.chem.sc.edu.

(1) Ball, P. *Nature* **1995**, *375*, 101.
(2) See July 1999 issue: *Chem. Rev.* **1999**, *99*.
(3) Seeman, N. C.; Zhang, Y. *J. Am. Chem. Soc.* **1992**, *114*, 2656.
(4) (a) Ma, R.-I.; Kallenbach, N. R.; Sheardy, R. D.; Petrillo, M. L.; Seeman, N. C. *Nucleic Acids Res.* **1986**, *14*, 9745. (b) Petrillo, M. L.; Newton, C. J.; Cunningham, R. P.; Ma, R.-I.; Kallenbach, N. R.; Seeman, N. C. *Biopolymers* **1988**, *27*, 1337. (c) Wang, Y.; Mueller, J. E.; Kemper, B.; Seeman, N. C. *Biochemistry* **1991**, *30*, 5667.
(5) Chen, J.-H.; Kallenbach, N. R.; Seeman, N. C. *J. Am. Chem. Soc.* **1989**, *111*, 6402.
(6) Chen, J.-H.; Seeman, N. C. *Nature* **1991**, *350*, 631.
(7) Zhang, Y.; Seeman, N. C. *J. Am. Chem. Soc.* **1994**, *116*, 1661.
(8) Di Mauro, E.; Hollenberg, C. P. *Adv. Mater.* **1993**, *5*, 384.
(9) Mirkin, C. A.; Letsinger, R. L.; Mucic, R. C.; Storhoff, J. J. *Nature* **1996**, *382*, 607. Elghanian, R.; Storhoff, J. J.; Mucic, R. C.; Letsinger, R. L.; Mirkin, C. A. *Science* **1997**, *277*, 1078.
(10) Alivisatos, P. A.; Johnsson, K. P.; Peng, X.; Wilson, T. E.; Loweth, C. J.; Bruchez, M. P., Jr.; Schultz, P. G. *Nature* **1996**, *382*, 609.
(11) Bergstrom, D. E.; Shi, J. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 111
(12) For reviews see: (a) Storhoff, J. J.; Mirkin, C. A. *Chem. Rev.* **1999**, *99*, 1848. (b) Niemeyer, C. M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 585.
(13) An, Y.-Z.; Chen, C.-H. B.; Anderson, J. L.; Sigman, D. S.; Foote, C. S.; Rubin, Y. *Tetrahedron* **1996**, *52*, 5179.
(14) (a) Altmann, M.; Bunz, U. H. F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 569. (b) Bunz, U. H. F. *Chem. Rev.* **2000**, *100*, 1605.
(15) Sijbesma, R. P.; Beijer, F. H.; Brunsveld, L.; Folmer, B. J. B.; Hirschberg, J. H. K. K.; Lange, R. F. M.; Lowe, J. K. L.; Meijer, E. W. *Science* **1997**, *278*, 1601.
(16) (a) Caruthers, M. H. *Acc. Chem. Res.* **1991**, *24*, 278. (b) Caruthers, M. H. *Science* **1985**, *230*, 281.

10.1021/ja000950k CCC: $20.00 © 2001 American Chemical Society
Published on Web 02/07/2001

Scheme 1[a]



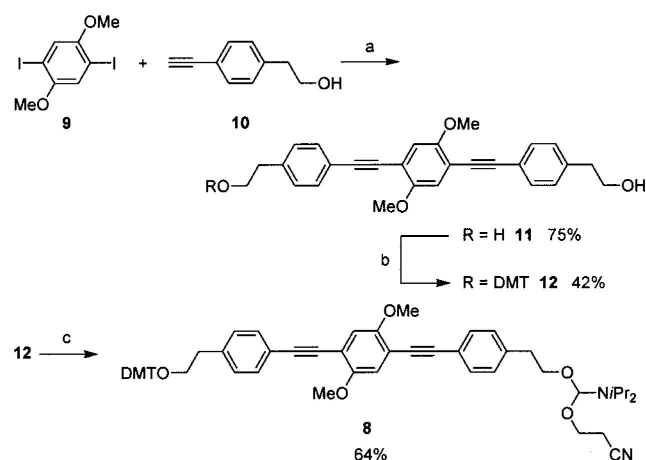
[a] Conditions: (a) $PdCl_2(PPh_3)_2$/CuI/PPh_3/NEt_3; (b) $CpCo(CO)_2$/p-xylene; (c) DMTCl/pyridine; (d) 2-cyanoethyl diisopropylchlorophosphoramidite/diisopropylethylamine/THF.

propriately functionalized. Thus, cyclobutadiene complex **1** (a functionalized diol) was chosen as an initial target for synthesis. This molecule contains a DMT protecting group and a phosphoramidite activating group, which make it conducive for automated oligonucleotide synthesis. These functionalized hydroxyl groups will have similar reactivity as the nucleotides used to synthesize oligonucleotides, making the target molecule (**1**) compatible with the chemistry of the automated synthesizer. It is readily recognized that any diol,[17−20] after appropriate functionalization, will meet the requirements for automated synthesis.

Preparation of the cyclobutadiene complex (**1**, Scheme 1) began with the Pd/Cu-catalyzed coupling[21] of phenylacetylene (**2**) with 4-bromophenethyl alcohol (**3**). Cyclization of the resulting tolane (**4**) with cyclopentadienylcobaltdicarbonyl ($CpCo(CO)_2$) gave a mixture of isomers designated *ortho* and *para* with regard to substitution around the cyclobutadiene ring. These isomers were separated by chromotography.[22] While the *ortho* isomer (**6**) has the potential to form cycles when modified with oligonucleotides, the *para* isomer (**5**) was protected to create linear DNA structures. Monoprotected **7** was treated with 2-cyanoethyldiisopropylchlorophosphoramidite to give **1** after isolation.[23]

(17) Waybright, S. M.; Singleton, C. P.; Tour, J. M.; Murphy, C. J.; Bunz, U. H. F. *Organometallics* **2000**, *19*, 368.
(18) Kool, E. T.; Breslow, R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1617.
(19) (a) Thuong, N. T.; Chassignol, M. *Tetrahedron Lett.* **1988**, *26*, 5905. (b) Durand, M.; Chevrie, K.; Chassignol, M.; Thuong, N. T.; Maurizot, J. C. *Nucleic Acids Res.* **1990**, *18*, 6353. (c) Giovannangeli, C.; Montenay-Garestier, T.; Rougee, M.; Chassignol, M.; Thuong, N. T.; Helene, C. *J. Am. Chem. Soc.* **1991**, *113*, 7775.
(20) (a) Manikrao, S.; Wu, T.; Letsinger, R. L. *J. Am. Chem. Soc.* **1992**, *114*, 8768. (b) Letsinger, R. L.; Wu, T. *J. Am. Chem. Soc.* **1994**, *116*, 811. (c) Letsinger, R. L.; Wu, T. *J. Am. Chem. Soc.* **1995**, *117*, 7323. (d) Lewis, F. D.; Helvoigt, S. A.; Letsinger, R. L. *J. Chem. Soc., Chem. Commun.* **1999**, 327.
(21) Zhang, Y.; Schuster, G. B. *J. Org. Chem.* **1997**, *59*, 11855.
(22) Given that the *ortho* isomer should have a greater dipole moment than the *para* isomer, the faster running spot on TLC was assigned the *para* isomer. This was confirmed with ^{13}C NMR with the line width set at zero. The spectra of the DMT-protected, phosphoramidite-activated forms of each isomer were compared. There were four cyclobutadiene peaks distinguishable for the *ortho* isomer and only three for the *para* isomer (C_s symmetry).

Scheme 2[a]



[a] Conditions: (a) $PdCl_2(PPh_3)_2$/CuI/piperidine; (b) DMTCl/pyridine; (c) 2-cyanoethyl diisopropylchlorophosphoramidite/diisopropylethylamine/THF.

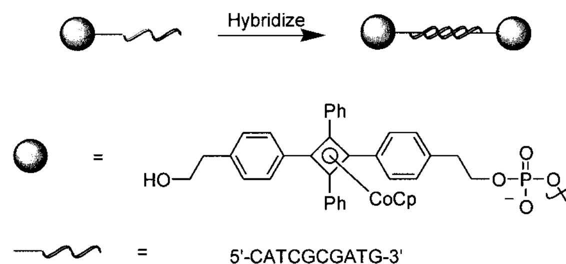


Figure 1. Schematic illustration of a duplex oligonucleotide modified organic (OMO).

A methoxy phenyleneethynylene trimer (**8**) was also synthesized (Scheme 2). Pd/Cu-catalyzed coupling of 1,4-diiodo-2,5-dimethoxybenzene (**9**) and 4-ethynylphenethyl alcohol (**10**) results in phenyleneethynylene trimer **11**, which was treated with dimethoxytrityl chloride to give a mixture of diprotected, monoprotected, and unprotected trimers. The desired monoprotected trimer **12** was isolated by flash chromatography and was treated with 2-cyanoethyl diisopropylchlorophosphoramidite to obtain **8**.

Construction and Hybridization of a Cyclobutadiene OMO for a Dimer Hybrid. We have recently described the formation of an oligonucleotide-modified organometallic (OMO) conjugate by attaching cyclobutadiene complex **1** to the 5′ end of an oligonucleotide with a palindromic sequence of 5′ GTAGCGCTAC 3′. Thus, a dimer was formed upon annealing (Figure 1).[17] We now have applied the concepts of this simple system to the more complex situation of having multiple components.

Construction and Characterization of OMOs for Oligomeric and Polymeric Hybrids. To obtain polymeric and oligomeric motifs, the cyclobutadiene complex **1** and the methoxy-substituted phenyleneethynylene trimer **8** were modified with oligonuclotides on both sides rather than on only one as previously described.[17] The oligonucleotides are dodecamers containing palindromic restriction sites to allow subsequent enzymatic lysis of the duplex DNA. Fourteen random sequences were designed, each containing a restriction site such that no two sequences (or their complements) are similar.[24] Thus when mixed together, a single strand will pair only with its complement and not with some other undesired strand.

(23) Coleman, R. S.; Kesicki, E. A. *J. Am. Chem. Soc.* **1994**, *116*, 11636.
(24) Seeman, N. C. *J. Theor. Biol.* **1982**, *99*, 237.

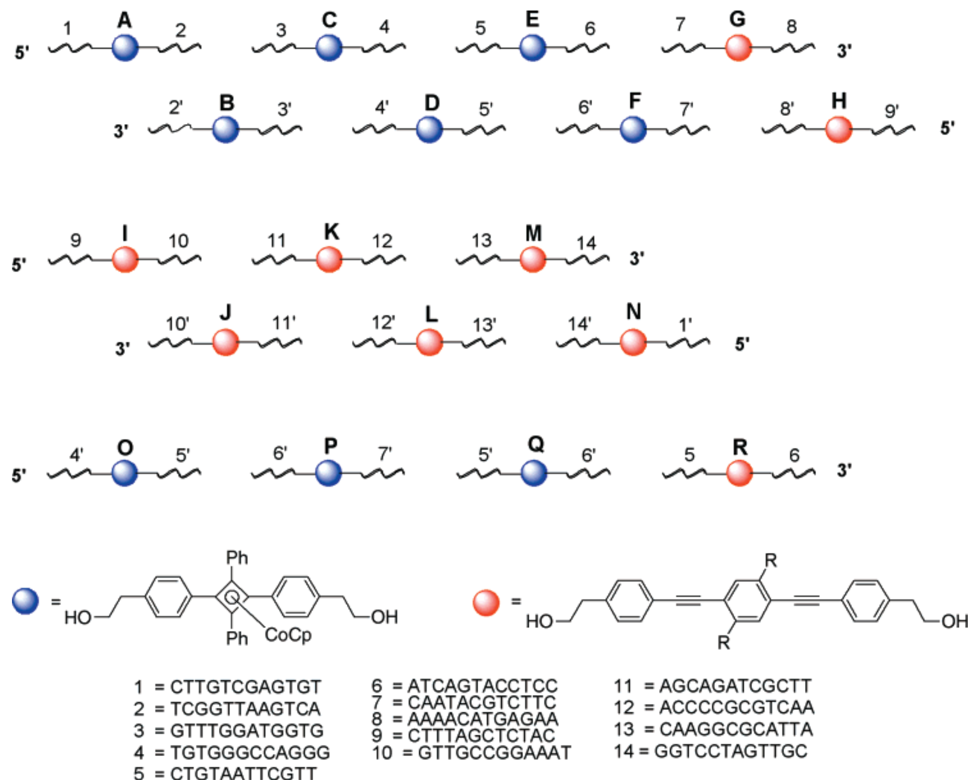


Figure 2. Schematic illustration of OMO constructs.

A series of oligonucleotides of the DNA-organic-DNA motif were constructed (Figure 2). The OMOs were assembled as follows: (1) The 12-base sequence was synthesized on an automated synthesizer. (2) Cyclobutadiene complex **1** (blue balls in Figure 2) or phenyleneethynylene trimer **8** (red balls) in THF was added to the growing oligonucleotide. (3) A second 12-base sequence was synthesized onto the strand.

Trityl cleavage data confirmed the addition of the organic molecule (**1** or **8**) and the subsequent addition of the next nucleotide. It was also noted that the solutions of oligonucleotides modified with cyclobutadiene (**1**) were yellowish in color—obviously due to the intrinsic color of the cyclobutadiene complex. Concurrently, oligonucleotides modified with the trimer (**8**) fluoresced when excited with long-wave UV light from a hand-held lamp. In fact, this attribute became an efficient way to verify the trityl data in the context of the desired OMO.

High-performance LC of the resulting OMOs revealed two major peaks. The peak eluting at approximately 19 min corresponded to DNA without an organic molecule attached. The UV−vis spectrum of this component was characteristic of DNA with a broad band at 260 nm. The peak eluting at approximately 25 min was a result of the OMO whether the organic was the cyclobutadiene complex (**1**) or the phenylene-ethynylene trimer (**8**). The UV−vis spectrum of this peak showed the characteristic DNA absorption at 260 nm and a shoulder at 310 nm for the cyclobutadiene OMO case, and absorptions at 318 and 375 nm for the trimer OMO case.

Figure 3 depicts the spectrum of the cyclobutadiene OMO (OMO **A**, Figure 2)[25] compared to the spectra of the oligonucleotide control and the free cyclobutadiene complex (**5**). Comparing the control spectrum with the cyclobutadiene OMO spectrum, it is clear that the additional shoulder at 310 nm must be due to the organometallic complex as this feature is present in the spectrum of **5**. As a consequence of the differing solvent conditions, the units of the *y*-axis are arbitrary. Regardless of the solvent, the new features of the cyclobutadiene OMO must be assigned to the covalent attachment of the cyclobutadiene complex.

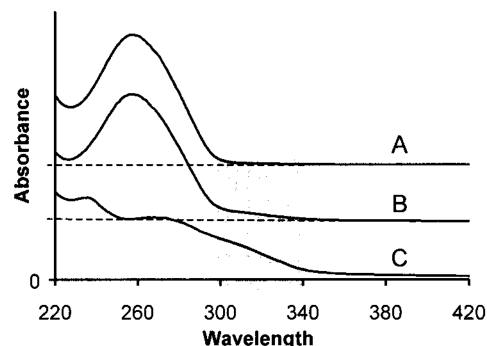


Figure 3. UV−vis spectra of DNA (A), cyclobutadiene OMO **C** (B), and cyclobutadiene complex **5** (C). The dotted baselines are added for clarity. Wavelength [nm]

Figure 4 shows the spectrum of the trimer OMO (OMO **G**, Figure 2) overlaid with spectra of free DNA and free trimer (**11**; note that the trimer spectrum was taken in chloroform while both DNA spectra were taken in water; thus, the units of the *y*-axis are arbitrary). The UV−vis spectra of the trimer OMOs show transitions at 318 and 375 nm that DNA alone does not display, but are reflected in the spectra of the free trimer (**11**).

Enzymatic digestion of the OMOs to the corresponding nucleosides also supported the incorporation of **1** or **8** into the sugar-phosphate backbone. Utilizing a solvent gradient from 2% acetonitrile to 70% acetonitrile in aqueous buffer resulted in elution of **1** after 25 min and **8** after 31 min. Integrated areas of the nucleoside peaks were consistent with the composition of the corresponding OMOs (Table 1). Therefore, the cyclobuta-

(25) To aid the reader's understanding, all organic molecules are numbered with Arabic numerals (Schemes 1 and 2), all OMOs are indicated with letters (Figure 2), and all self-assembled structures are labeled with Roman numerals (Figure 7).

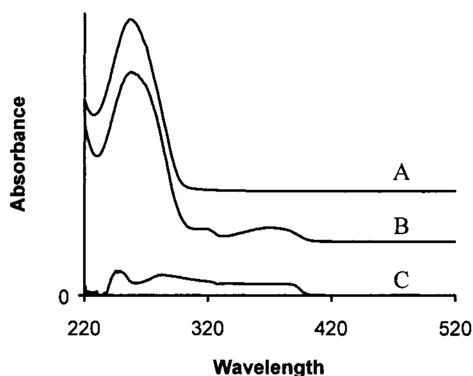


Figure 4. UV−vis spectra of DNA (A), trimer OMO **G** (B), and trimer **11** (C). Wavelength [nm]

Table 1. Typical Enzyme Digestion Data for OMOs[a]

	I (trimer)			**P** (cyclobutadiene)		
OMO base	ret. time	actual comp.	calcd comp.	ret. time	actual comp.	calcd comp.
C	3.55	5.9	6	3.57	1.2	2
G	6.46	5.2	5	6.47	8.9	9
T	8.27	8.4	8	8.16	6.5	6
A	14.38	4.5	5	14.36	7.4	7
Organic	30.77			25.83		

[a] The retention times for nucleoside in minutes and organic peaks are presented along with the integrated area of nucleoside peaks compared to calculated composition of the OMO.

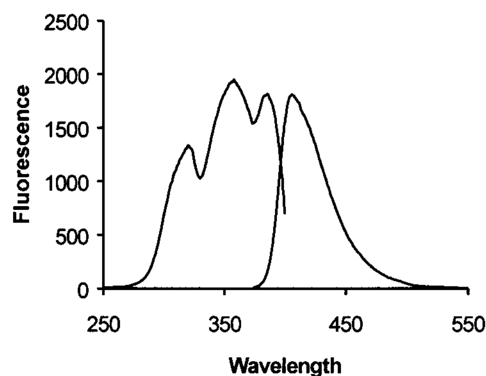


Figure 5. Fluorescence excitation and emission spectra for trimer OMO (**G**). Wavelength [nm]

diene complex (**1**) or the phenyleneethynylene trimer (**8**) *must* have been included into the oligonucleotide strand as desired. This is verified by UV−vis, enzyme digestion, qualitative visual inspection, and, most convincingly, trityl cleavage data. These data show cleavage of trityl groups from the nucleotides linked to the growing oligonucleotide *after* the addition of **1** or **8**—an observation that occurs only if **1** or **8** has been successfully added.

Fluorescence measurements were performed on the trimer OMOs (OMO **G**, see Figure 5). Excitations at 323, 370, and 388 nm resulted in a single emission at 410 nm. This observation was consistent for all pheneyleneethynylene trimer OMOs. Both the phenyleneethynylene trimer and the trimer OMOs have quantum yields of near unity (0.95 to 1.0 at 370 nm excitation).[26] Neither the cyclobutadiene modified nor the unmodified oligonucleotides showed any fluorescence.

To ensure correct molar ratios of single-stranded OMOs in the creation of the desired double-stranded structures, the exact concentrations of the OMO solutions must be known. Traditional concentration analysis of oligonucleotides involves the absorbance of the 260 nm signature band of DNA and subsequent calculation of the concentration from known extinction coefficients. However, this method was not applicable as the organic molecule (**1** or **8**) had a contribution to the 260 nm band of the DNA resulting in skewed concentration results. Thus, a more fundamental tool had to be employed. Phosphate analysis, in which the total amount of inorganic phosphate in a sample was measured allowed the correct OMO concentration to be determined.

Our primary goal in this methodology was to obtain the OMO concentration; our secondary goal was to establish a relationship between the *measured* concentration via the traditional method (absorption spectroscopy) and the *actual* concentration via the phosphate analysis. Not surprisingly, when actual concentration was plotted versus the measured concentration at 260 nm for each organic, the relationship was linear (Figure 6). This relationship allows us to avoid the time-consuming phosphate analysis and utilize the data from the simpler 260-nm-absorbance protocol. It should be noted that this entire exercise could have been avoided by knowing the extinction coefficient of **1** or **8** at 260 nm. This measurement is trivial in organic solvents; however, it is much less so in aqueous solvents in which the OMOs are soluble but, of course, not **1** or **8**.

Hybridization of OMOs into Oligomeric and Polymeric Hybrids. The OMOs in Figure 2 were annealed to form duplex DNA resulting in hybrids (Table 2). By hybridizing OMOs **E** and **Q**, or **Q** and **R** we can produce self-assembled polymers of high molecular weight. Hybridizing OMOs **E** and **Q** will result in polymer containing all cyclobutadiene OMOs while hybridizing OMOs **Q** and **R** will lead to a polymer of alternating cyclobutadiene and trimer OMOs. Oligomeric motifs can be achieved similarly. These include the following: All trimer OMO oligomers {**G**+**H**}, {**G**+**H**+**I**}, {**G**+**H**+**I**+**J**}, {**G**+**H**+**I**+**J**+**K**}, {**G**+**H**+**I**+**J**+**K**+**L**}, and {**G**+**H**+**I**+**J**+**K**+**L**+**M**}; all cyclobutadiene OMO oligomers {**C**+**D**}, {**C**+**D**+**E**}, and {**C**+**D**+**E**+**F**}; and mixed cyclobutadiene/trimer OMO oligomers {**F**+**G**}, {**C**+**D**+**R**}, and {**E**+**F**+**G**+**H**}. The pictorial representations are given in Table 2.

Each hybrid shown in Table 2 was annealed from its corresponding OMO monomers. Melting temperature studies were performed on each hybrid. These data are presented in Table 2. It was evident that oligonucleotide portions of each OMO acted independently, that is, each 12-base segment hybridizes independently of the other segments. Additionally, it was observed that the longer oligomers (series **I**−**VI**) exhibited sharper melting points (Figure 7). This is likely due to the decreasing contribution of the dangling single-stranded ends with longer oligomers.

Fluorescence spectra were taken of the hybrids (**I**−**VI, X**−**XII**) both before and after annealing. Quantum yields were calculated by using quinine sulfate as a standard.[26] The quantum yields for **I**−**VI** were essentially unity (Table 2). However, for hybrids **X**−**XII**, there was a noticeable decrease in quantum yield. It is known that organometallic π-complexes efficiently quench fluorescence;[27] thus, this decrease is likely due to the introduction of the cyclobutadiene complex.

A 12% native polyacrylamide analytical gel was run at 6 °C. The gel clearly showed the annealed DNA strands when stained with the intercalating dye ethidium bromide (Figure 8). To determine the size of the OMO hybrids, a standard size marker

(26) Quinine sulfate was used as the standard and quantum yields were determined as described in the following: Demas, J. N.; Crosby, G. A. *J. Phys. Chem.* **1971**, *75*, 991.

(27) Steffen, W.; Bunz, U. H. F. *Macromolecules* **2000**, *33*, 9518.

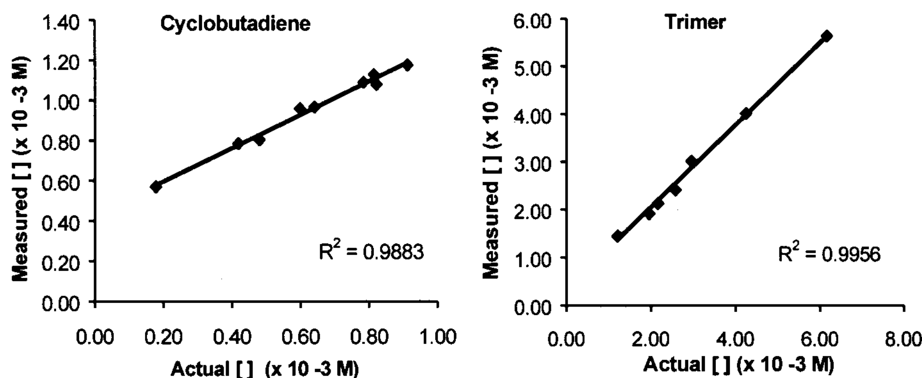


Figure 6. Relationship of actual and measured concentration of cyclobutadiene OMOs (**A**−**F**, **O**−**Q**) and phenyleneethynylene trimers (**G**−**N**, **R**). The actual concentration was determined by phosphate analysis; the measured concentration was determined by absorbance at 260 nm.

Table 2. Melting Temperature and Fluorescence Quantum Yields Compared to Quinine Sulfate for Annealed and Unannealed Oligomer and Polymer Hybrids of Phenylenethynylene Trimer (red balls) and Cyclobutadiene Complex (blue balls) OMOs[a]

	Structure	Tm °C	Unannealed φ	Annealed φ
I	G H	40	0.91	0.90
II	G H I	40	0.96	0.94
III	G H I J	50	0.97	0.96
IV	G H I J K	45	0.84	0.86
V	G H I J K L	40	1.0	1.0
VI	G H I J K L M	55	0.98	0.93
VII	C D		--	--
VIII	C D E	40	--	--
IX	C D E F	35	--	--
X	F G	40	0.60	0.60
XI	E F G		0.41	0.35
XII	E F G H	35	0.25	0.22
XIII	E Q E Q E Q E	47		
XIV	R Q R Q R Q R	47		
XV		--	--	--

[a] Polymers are represented by XIII and XIV; XV is a DNA control

of a 25 base pair ladder in lane 6 was used. The PCR standards show the 25, 50, 75, and 100 base pair fragments.

In typical gel electrophoresis the DNA fragment migrates as a function of the number of base pairs that it contains. The OMO hybrids (**I**−**VI**) contain a portion of the DNA that anneals to its complement and a portion at each end that does not have a complement and thus remains single-stranded. The OMO hybrids (**I**−**VI**) migrate through a native polyacrylamide gel as a function of the total number of bases including double- *and* single-stranded regions. This is evident when comparing the control DNA in lane 1 to the size standards in lanes 5 and 6. Control **XV** (lane 1) contains 24 double-stranded bases and 24 single bases for a total of 48 bases and migrates as a fragment of approximately 50 base pairs in size. This trend is consistent throughout all of the OMO hybrids.

Hybrid **I** (lane 5) has 36 bases and runs as a fragment of approximately 35 base pairs when compared to the standards in lane 6. Hybrid **II** (lane 4) has 48 bases and when compared to standards in lane 6 runs slightly faster than the 50-base-pair standard. Lane 3 contained hybrid **III** and clearly had a mobility of a DNA fragment of 60 base pairs when compared to the standards in lane 7. These hybrids can be compared with the control hybrid **XV** (lane 1) that is 48 bases in size. Hybrid **II**

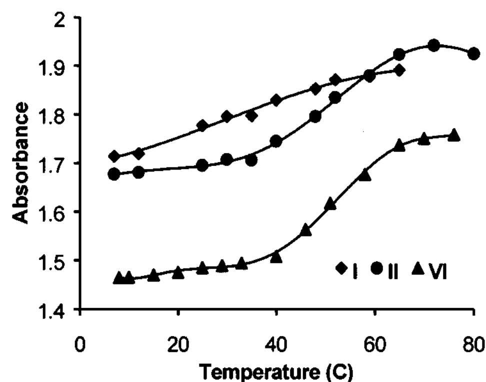


Figure 7. Melting temperature curves for dimer (**I**), trimer (**II**), and heptamer (**VI**).

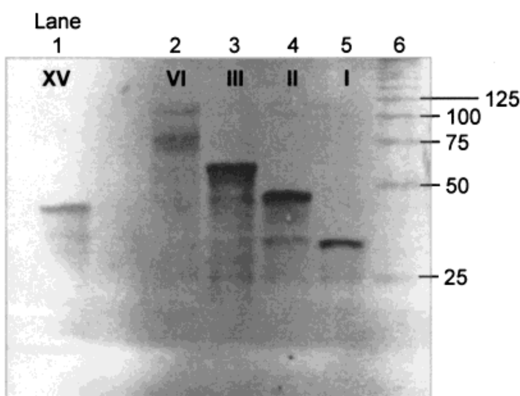


Figure 8. Polyacrylamide gel of four oligomeric hybrids. Lanes as follows: 1, DNA control **XV**; 2, heptamer **VI**; 3, tetramer **III**; 4, trimer **II**; 5, dimer **I**; and 6, 25 base pair PCR ladder.

(lane 4) and the control hybrid **XV** (lane 1) have comparable mobilities and therefore must be of similar size.

A step pattern formed by the increase in size of the oligomer hybrids is present when comparing lanes 3 (hybrid **III** of 60 bases), 4 (hybrid **II** of 48 bases), and 5 (hybrid **I** of 36 bases) to lane 1 (control **XV** of 48 bases) and to the size standards in lanes 6 and 7. The bands present in lanes 3, 4, and 5 correspond to the size of the fragments expected when estimated by the sequence taking into account the addition of the organic moiety. The organic molecule does not interfere with the ability of the DNA to anneal. Hybrid **VI** in lane 2 does not show one discrete band but several. The slowest moving migrates as a fragment of approximately 110 base pair in size and a larger band at 75 bases when compared with the size standards in lane 6. Hybrid **VI** is made by the annealing of 7 separate segments to produce a heptamer that migrates as a 96 base fragment. Due to partial annealing we see bands that correspond to 72 (pentamer) and 84 (hexamer) as well as the 96 (heptamer) base band. Also, lane 3 containing hybrid **III** shows bands corresponding to 48 and 36 bases. Lane 4 has an additional band at 36 bases as does lane 1 containing control **XV**. These additional bands are expected if any slight deviation from precise stoichiometric ratio occurs.

Conclusion

In conclusion, we have demonstrated that defined oligomeric materials can be formed by hybridization of DNA-containing organic modules. The concept is not restricted to the modules utilized here, but should be extendable to *any* organic building block containing hydroxy groups functionalized for automated synthesis. Thus, when designing a self-assembled system, one is not restricted to working with molecules that self-assemble on their own, but rather, one can use any molecule having a desirable property or function. This concept allows a general approach to nano-construction where *the structure is not dependent on the modules used*, *rather it is dependent only on the DNA used to link the modules together*!

Acknowledgment. The authors thank NSF-EPSCoR and USC start-up for funding. K.W. is an REU participant from UC Santa Cruz. U.H.F.B. is a recipient of the NSF CAREER award (2000−2003) and a Dreyfus Teacher Scholar 2000−2005.

Supporting Information Available: Experimental and spectroscopic details for **1**−**12**, synthesis and purification of OMOs **A**−**R**, phosphate analysis, melting curves, and PAGE details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

JA000950K