Geometrically-Controlled and Site-Specifically-Functionalized Phenylacetylene Macrocycles†

Jinshan Zhang,§,⊥ Douglas J. Pesak,‡ James L. Ludwick,§ and Jeffrey S. Moore*,§,‡

Contribution from The Willard H. Dow Laboratories, Department of Chemistry, The University of Michigan, Ann Arbor, Michigan 48109-1055, and Roger Adams Laboratory, Departments of Chemistry and Materials Science & Engineering, University of Illinois, Urbana, Illinois 61801

Received December 31, 1993®

Abstract: A convergent, stepwise synthesis of linear phenylacetylene sequences (PASs) is described. The methodology allows for complete control over chain length, sequence order of monomers, and functional group placement. Chain growth follows geometric progression thus allowing sequences of length 2^n, where n is the number of repetitive cycles, to be assembled in a total of just $3 \cdot n$ steps (two deprotections and one coupling for each cycle). Sequences of length other than 2^n as well as sequences having a particular arrangement of co-monomer units, can also be realized by merging parallel repetitive cycles. Upon deprotection of the termini, these PASs can be cyclized to phenylacetylene macrocycles (PAMs) in high yield. Control over the ring structure of PAMs is determined by the chemistry of precursor PASs; the size of the macrocycle is related to the sequence length, while the geometry of the macrocycle and the position of the pendant functional groups on the macrocycle is governed by co-monomer sequence order. PAMs with four, five, six, seven, and twelve phenylacetylene monomer units, as well as a variety of site-specifically-functionalized PAMs, have been synthesized with this method. Finally, functional group transformations have been performed on some of the PAMs which lead to PAMs with new functionality. The versatile and efficient approach to this family of geometrically well-defined macrocycles offers potential for producing a set of modular building blocks to rationally assemble molecular crystals and liquid crystals. For this reason, the solid-state characteristics of the hydrocarbon skeletons are of interest. In spite of their solubility in common solvents, hydrocarbon PAMs are shown to yield crystals with remarkable thermal stability and high melting points. Three PAM hydrocarbons are shown not to exhibit melting transitions up to ca 400 °C, at which point an abrupt thermal irreversible reaction occurs, apparently involving a solid-state polymerization of the acetylene units.

Introduction

Supramolecular chemistry has experienced rapid development within the last two decades.[1,2] As this subject matures, it is becoming increasingly clear that the synthesis of well-defined molecular architectures will play a very crucial role because the incorporation of spatially-defined and orientationally-controlled steric and/or electronic features into molecules is essential for dictating noncovalent interactions. The incorporation of these features can be viewed as the encoding of information into molecular components—information that makes up the complete set of instructions for all of the subsequent noncovalent chemistry.[3]

In order to develop supramolecular chemistry into a more systematic science, methods will need to be available for encoding molecular building blocks in a way that is simple, yet offers total specificity. In order to mimic the best-known natural supramolecular systems such as the nucleic acids and proteins, synthetic methods that allow efficient, but versatile construction of complex molecular objects from simple building blocks are desirable.[4] Examples toward this endeavor are becoming more common.[5] Here, we report the development of a new famaily of geometrically well-defined or "shape persistent" macrocyclic skeletons.

In our preliminary communications, we reported a convergent and efficient approach to phenylacetylene sequences (PASs) of tightly controlled structure.[6] These PASs were converted to phenylacetylene macrocycles (PAMs) in high yield upon cyclization.[7] The phenylacetylene unit was chosen because of its rigidity and simple geometry. Combinations of *ortho*-, *meta*-, and *para*-phenylacetylene monomers (60°, 120°, and 180° angles, respectively) can give essentially any framework consistent with fragments of the trigonal lattice. In addition to control over geometry, the functional groups introduced in the synthesis of PASs can be carried over to PAMs. The synthetic advantage is that functional group placement on the outside and inside of PAMs can easily be controlled. The geometrically-controlled and site-specifically-functionalized PAMs synthesized by this

* Author to whom correspondence should be addressed. Current address: Departments of Chemistry and Materials Science & Engineering, University of Illinois at Urbana-Champaign, Urbana, IL 61801.

† Nanoarchitectures. 5. For Part 4 see: Wu, Z.; Lee, S.; Moore, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 8730.

§ The University of Michigan.

‡ The University of Illinois.

⊥ Current Address: Motorola Inc., 8000 W. Sunrise Blvd., Fort Lauderdale, FL 33322.

® Abstract published in *Advance ACS Abstracts*, April 1, 1994.

(1) (a) *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J.; Durr, H., Eds.; VCH: New York, 1991. (b) *Advances in Supramolecular Chemistry*; Gokel, G. W., Ed.; JAI Press: Greenwich, CT, 1992; Vol. 2. (c) *Supramolecular Chemistry*; Balzani, V., De Cola, L., Eds.; Kluwer Academic: Norwell, 1991. (d) *Design and Synthesis of Organic Molecules Based on Molecular Recognition*; Binst, G. van, Ed.; Springer-Verlag: Berlin, 1986.

(2) (a) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 89; **1990**, *29*, 1304. (b) Cram, D. J. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1009. (c) Hong, J.-I.; Feng, Q.; Rotello, V.; Rebek, J., Jr. *Science* **1992**, *255*, 848. (d) Whitesides, G. M.; Mathias, J. P.; Seto, C. T. *Science* **1991**, *254*, 1312. (e) Muehldorf, A. V.; Van Engen, D.; Warner, J. C.; Hamilton, A. D. *J. Chem. Soc.* **1988**, *110*, 6561. (f) Zimmerman, S. C.; Wu, W. *J. Am. Chem. Soc.* **1989**, *111*, 8054.

(3) Lehn, J.-M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1304.

(4) Lindsey, J. S. *Nouv. J. Chem.* **1991**, *15*, 153.

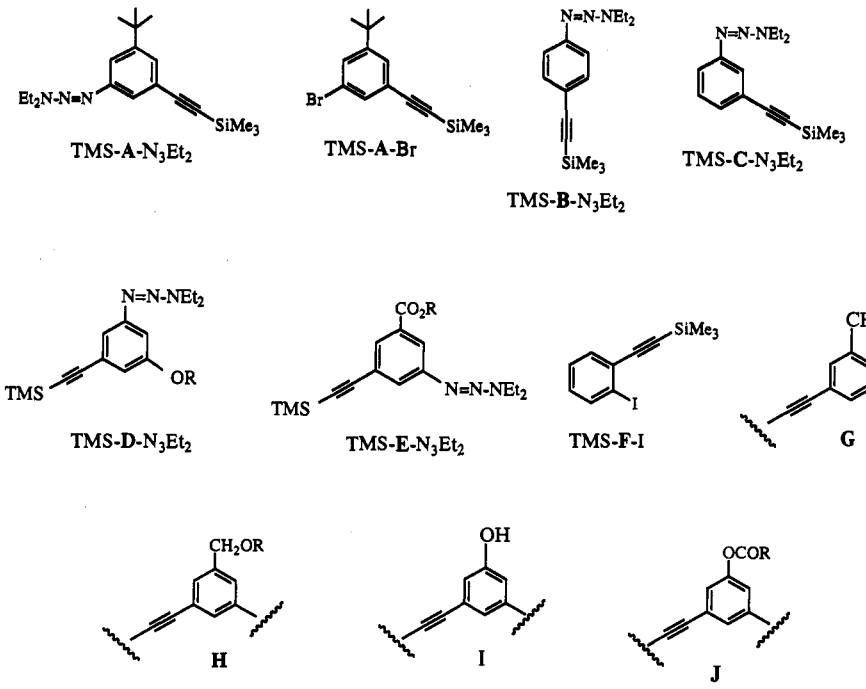
(5) (a) Kaszynki, P.; Friedli, A. C.; Michl, J. *J. Am. Chem. Soc.* **1992**, *114*, 601. (b) Ashton, P. R.; Brown, G. R.; Isaacs, N. S.; Giuffrida, D.; Kohnke, F. H.; Mathias, J. P.; Slawin, A. M. Z.; Smith, D. R.; Stoddart, J. F.; Williams, D. J. *J. Am. Chem. Soc.* **1992**, *114*, 6330.

(6) Zhang, J.; Moore, J. S.; Xu, Z.; Aguirre, R. *J. Am. Chem. Soc.* **1992**, *114*, 2273.

(7) Moore, J. S.; Zhang, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 922.

0002-7863/94/1516-4227$04.50/0

Chart 1



approach should be useful for constructing novel mesogens or building blocks for self-assembled monolayers[8] and rationally-designed organic crystals.[9]

Results and Discussions

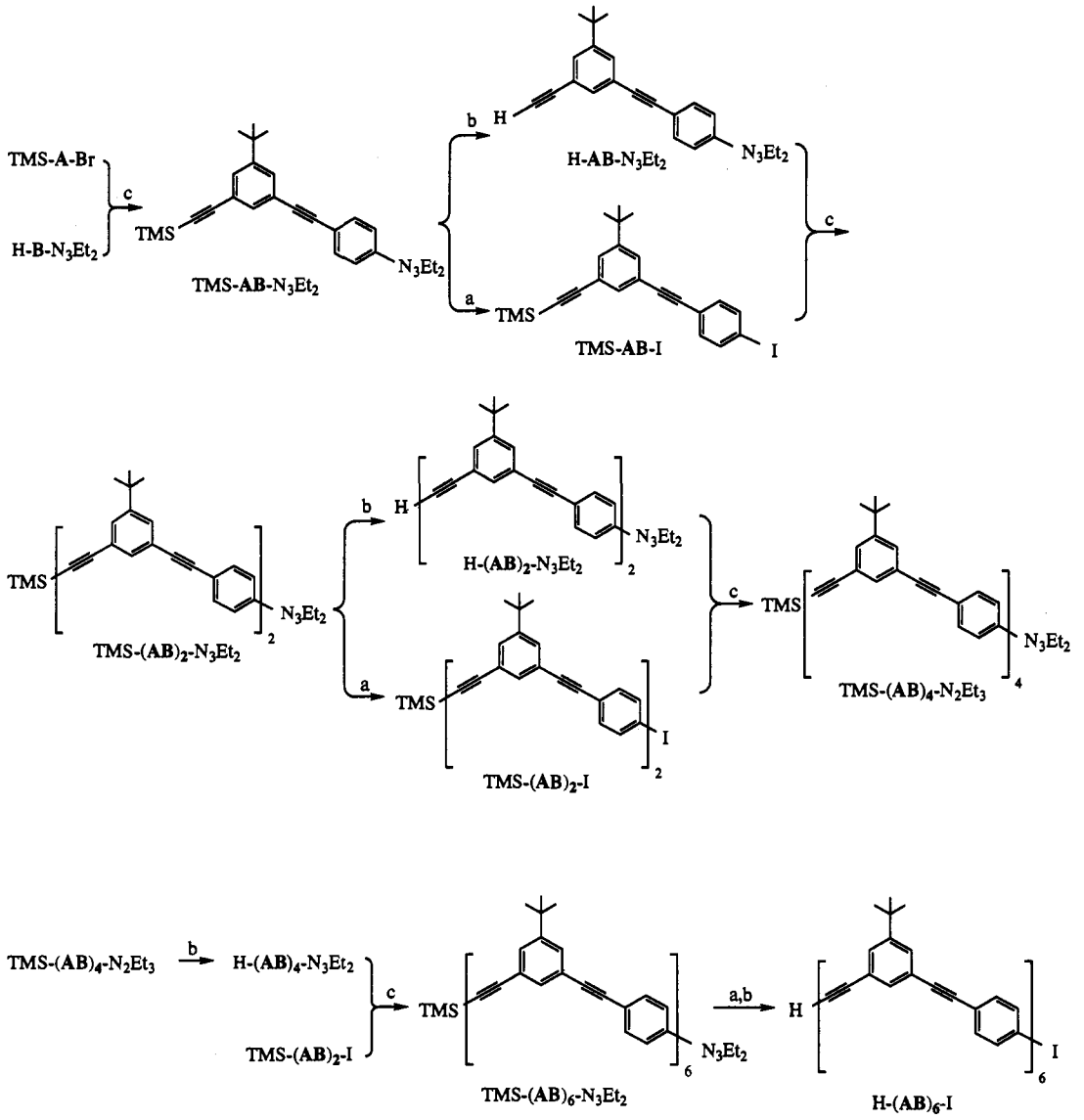
Monomer Synthesis. The monomers used to prepare the PASs were based on terminal acetylenes protected as the corresponding trimethylsilyl derivatives (TMS) and aryl iodides protected as dialkyltriazenes (–N=N—NEt_2). To simplify the format and to aid in visualizing subtle differences in the macrocyclic chemical structures, we have chosen to represent each monomer with an alphabetic character. Chart 1 shows the monomers (TMS-**A**-**Br**, TMS-**A**-N_3Et_2, TMS-**B**-N_3Et_2, TMS-**C**-N_3Et_2, TMS-**D**-N_3Et_2, TMS-**E**-N_3Et_2, and TMS-**F**-I) and repeat units that were used in this study. All of the monomers were readily synthesized from commercially available materials (Scheme 1, see supplementary material).

Sequence Synthesis. There has been considerable interest in well-defined oligomeric sequences because they represent ideal models for polymers.[10,11] A great deal of effort has been devoted to the synthesis of this class of compounds.[12] One of the most notable examples is Merrifield's solid-phase synthesis of peptides.[13] In the classic Merrifield approach, chain growth takes place at one end of the oligomer while the other end is attached to a solid support. This method is especially useful for complex polypeptides in which each successive unit is different from the previous. However, this method is not necessarily the most efficient method for other systems. For oligomers which have periodic or extended periodic segments, if chain growth can occur at both ends, then one can synthesize these oligomers much more efficiently by taking advantage of the geometric progressive growth. This idea has been utilized in the synthesis of oligomeric alkanes[14] and polyurethane segments.[15] We have used the same strategy in the synthesis of PASs.

A typical sequence synthesis is illustrated in Scheme 2. Palladium-catalyzed[16] cross-coupling of monomers TMS-**A**-**Br** and H-**B**-N_3Et_2 gives dimer TMS-**AB**-N_3Et_2 which has trimethylsilylacetylene and 1-aryl-3,3-diethyltriazene end group functionalities. Reaction of TMS-**AB**-N_3Et_2 with methanol in the presence of a catalytic amount of potassium carbonate gives terminal acetylene H-**AB**-N_3Et_2.[17] In contrast, reaction of TMS-**AB**-N_3Et_2 with methyl iodide gives aryl iodide TMS-**AB**-I.[18] Intermediates H-**AB**-N_3Et_2 and TMS-**AB**-I are then cross-coupled to give tetramer TMS-$(\mathbf{AB})_2$-N_3Et_2 which has exactly the same end group functionalities as dimer TMS-**AB**-N_3Et_2. This process can be repeated n times to give a sequence of length 2^n. A key finding which has made this particular chemistry feasible is that trimethylsilylacetylene and 1-aryl-3,3-diethyltriazene function very effectively as complementary protecting groups for terminal acetylene and aryl iodide, respectively. Each of the two protecting groups can be selectively removed in the presence of the other, and both protecting groups are stable to the cross-coupling conditions. The deprotection of triazene with methyl iodide proceeds cleanly at 110 °C. Filtration of the reaction mixture through a short plug of silica gel affords an analytically pure compound, usually without further purification and in isolated yields of over 95%. The deprotection of trimethylsilylacetylene with methanol is performed at room temperature, and also gives

(8) Whitesides, G. M.; Laibinis, P. E. *Langmuir* **1990**, *6*, 87–96.
(9) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989.
(10) (a) Huijts, R. A.; Hesselink, G. L. J. *Chem. Phys. Lett.* **1989**, *156*, 209; (b) Barzoukas, M.; Blanchard-Desce, M.; Josse, D.; Lehn, J.-M.; Zyss, J. *Chem. Phys.* **1989**, *133*, 323.
(11) (a) ten Hoeve, W.; Wynberg, H.; Havinga, E. E.; Meijer, E. W. *J. Am. Chem. Soc.* **1991**, *113*, 5887. (b) Khanna, R. K.; Jiang, Y. M.; Creed, D. *J. Am. Chem. Soc.* **1991**, *113*, 5451. (c) Knoll, K.; Schrock, R. R. *J. Am. Chem. Soc.* **1989**, *111*, 7989.
(12) (a) Rothe, M. In *Chemistry and Physics of Macromolecules*; Fischer, E. W., Schulz, R. C., Sillescu, H., Eds.; VCH: New York, 1987; pp 39–58. (b) *Synthesis and Characterization of Oligomers*; Uglea, C. V., Negulescu, I. I., Eds.; CRC Press: Boca Raton, 1991.
(13) Merrifield, R. B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 799.
(14) (a) Paynter, O. I.; Simmonds, D. J.; Whiting, M. C. *J. Chem. Soc., Chem. Commun.* **1982**, 1165–1166. (b) Bidd, I.; Whiting, M. C. *J. Chem. Soc., Chem. Commun.* **1985**, 543–544. (c) Igner, E.; Paynter, O. I.; Simmonds, D. J.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 1* **1987**, 2447–2454.
(15) Eisenbach, C. D.; Hayen, H.; Nefzger, H. *Makromol. Chem., Rapid Commun.* **1989**, *10*, 463.
(16) (a) Sonogashira, K.; Tohda, Y.; Hagihara, N. *Tetrahedron Lett.* **1975**, 4467. (b) Cassar, L. *J. Organomet. Chem.* **1975**, *93*, 253. (c) Dieck, H. A.; Heck, R. F. *J. Organomet. Chem.* **1975**, *93*, 259.
(17) (a) Eastmond, R.; Walton, D. R. M. *Tetrahedron* **1972**, *28*, 4591. (b) Eaborn, C.; Walton, D. R. M. *J. Organomet. Chem.* **1965**, *4*, 217.
(18) Moore, J. S.; Weinstein, E. J.; Wu, Z. *Tetrahedron Lett.* **1991**, *32*, 2465.

Scheme 2



Reagents: (a) CH_3I, 110°C, 12h. (b) MeOH ,CH_2Cl_2, K_2CO_3, r.t., 1h. (c) $Pd(dba)_2$, CuI, PPh_3, NEt_3, 80°C, 12 h.

an analytically pure compound without further purification. The yield of this deprotection is 95–98%.

Sequences of length other than 2^n, as well as sequences having a particular arrangement of co-monomer units, can be realized by merging parallel repetitive cycles. For example, hexamer sequence TMS-**(AB)**$_3$-N_3Et_2 is realized by combining dimer sequence TMS-**AB**-N_3Et_2 and tetramer sequence TMS-**(AB)**$_2$-N_3Et_2. With this repetitive method, the phenylacetylene sequence with up to 16 repeating units (i.e. TMS-**(AB)**$_8$-N_3Et_2) has been synthesized. Attempts to obtain the 32-mer (i.e. TMS-**(AB)**$_{16}$-N_3Et_2) have thus far been hampered by poor solubility. The synthetic chemistry does not appear to have reached its limitation but rather purification and characterization of this poorly soluble species have proven to be difficult.

The sequences have been characterized as their α-iodo-ω-(trimethylsilyl)acetylene or α-iodo-ω-ethynyl derivatives using ^1H and ^{13}C NMR, mass spectrometry (MS), elemental analysis, and size exclusion chromatography (SEC). As the number of monomer units increases, elemental analysis and SEC have proven to be the most effective characterization techniques. No molecular ion signal in MS for sequences TMS-**(AB)**$_6$-I and TMS-**(AB)**$_8$-I could be detected using FAB or EI methods. While ^1H NMR was useful for end group analysis, dispersion in chemical shift was typically insufficient to allow complete assignment, especially in the larger sequences. However, elemental analyses as well as SEC traces show distinct differences (Figure 1). The SEC trace also indicated that sequence TMS**(AB)**$_8$-**I** is slightly contaminated by high molecular weight impurity (ca. 5%). This contamination is presumably due to the fact that no purification, except precipitation, was done to this particular sequence because of its extremely low solubility in organic solvents.

The repetitive chemistry used to synthesize the PASs should be compatible with a wide variety of functional groups. Table 1 shows examples of other PASs that we have used as macrocyclic precursors (*vide infra*). Homo-sequences with ether and ester functional groups, such as TMS-**D**$_6$-N_3Et_2 and TMS-**E**$_n$-N_3Et_2 (n = 4, 5, 6, 7), have been synthesized from TMS-**D**-N_3Et_2 and TMS-**E**-N_3Et_2 monomers, respectively (Table 1, entries 1–5). While the synthesis of TMS-**D**$_6$-N_3Et_2 was straightforward, the synthesis of the TMS-**E**$_n$-N_3Et_2 sequences was initially complicated by their low solubility. For instance, sequence TMS-**E**$_6$-N_3Et_2 with six methyl ester groups was found insoluble in the reaction solvent. The butyl ester, on the other hand, was found to have adequate solubility. Transesterification replacement of

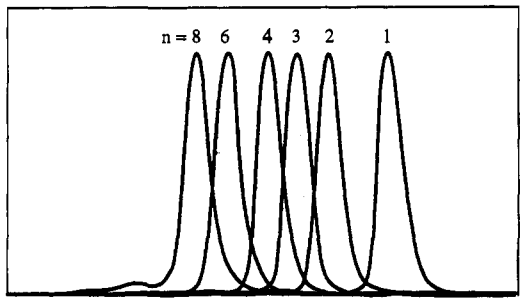


Figure 1. Normalized size exclusion chromatographs for TMS-$(AB)_n$-I sequences. From right to left: n = 1, 2, 3, 4, 6, 8.

Table 1. Precursor Sequences for Phenylacetylene Macrocycles

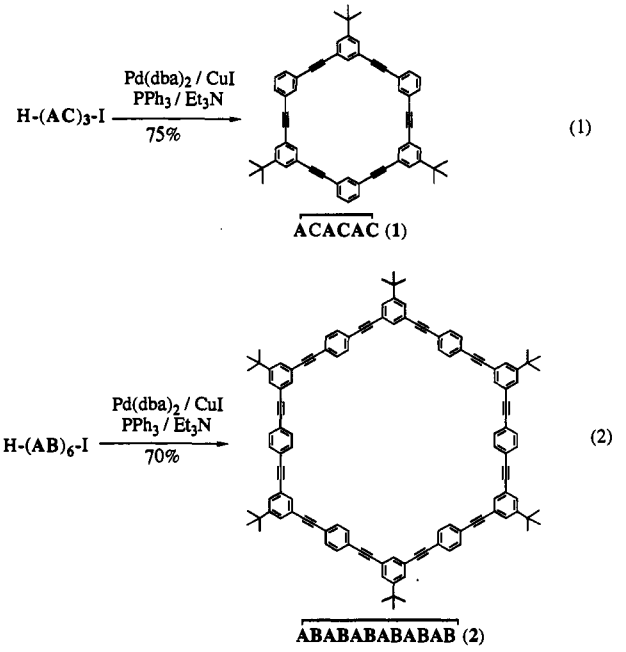
			elemental analysis			
			calcd		found	
entry	sequence	sequence length	C	H	C	H
1	H-E_4-I	4	67.24	5.32	66.98	5.38
2	H-E_5-I	5	69.14	5.36	69.29	5.32
3	H-E_6-I	6	70.48	5.54	70.32	5.44
4	H-E_7-I	7	71.46	5.60	71.20	5.34
5	H-D_6-I	6	74.47	6.32	74.67	6.40
6	H-$(FA)_2$-I	4	75.00	5.19	75.25	5.28
7	H-$(AC)_3$-I	6	80.35	5.51	79.96	5.45
8	TMS-$(ED)_3$-I	6	72.34	5.91	72.13	5.70
9	TMS-E_3D_3-I	6	72.34	5.91	72.28	5.64
10	TMS-EC$(AC)_2$-I	6	77.50	4.82	77.63	5.06

the methyl ester was realized simultaneously with the deprotection of the trimethylsilyl group when butyl alcohol, instead of methanol, was used along with a catalytic amount of 18-crown-6 ether and potassium carbonate.

Combination of two or more than two monomers can lead to co-sequences with different functionalities such as TMS-$(ED)_3$-N_3Et_2, TMS-E_3D_3-N_3Et_2, TMS-EC$(AC)_2$-N_3Et_2, and TMS-CE$(AC)_2$-N_3Et_2 (see Table 1, entries 6–10). By controlling the order of the coupling steps, placement of the functional groups at any position along the sequences can be achieved. An example is the controlled oligomerization of the isomers TMS-$(ED)_3$-N_3Et_2 and TMS-E_3D_3-N_3Et_2 from monomers TMS-E-N_3Et_2 and TMS-D-N_3Et_2. The sequence TMS-$(ED)_3$-N_3Et_2 is made through co-dimer TMS-ED-N_3Et_2, while TMS-E_3D_3-N_3Et_2 is obtained by merging a pair of homo-trimeric sequences (i.e. TMS-E_3-N_3Et_2 and TMS-D_3-N_3Et_2). Controlled manipulation of the sequences is demonstrated by the synthesis of the sequence TMS-EC$(AC)_2$-N_3Et_2 which contains a single heteroatom functional group (Table 1, entry 10). As will be shown below, this deliberate control over the functional group placement in PASs allows the synthesis of site-5-specifically-functionalized PAMs.

Cyclization. Macrocylic compounds have been particularly interesting because of their increasing importance in supramolecular chemistry. Numerous methods have been reported to synthesize macrocyclic compounds.[19] Theoretical treatments,[20] as well as synthetic strategies such as high dilution,[21] *gem*-dimethyl participation,[22] template effects,[23] rigid group effects,[24] and oxygen effects,[25] have been investigated in order to facilitate the ring-closure reactions. With very few exceptions,[26] most of these methods involve the oligomerization and ring closure reaction in one pot. However, this one-pot approach often suffers from low yield, mixture of different products, and lack of control over the ring structure.

The well-defined PASs synthesized above can be used to prepare PAMs. Deprotection of both masking groups from the sequence's termini gave difunctional intermediates such as H-$(AC)_3$-I, H-$(AB)_6$-I, H-D_6-I, H-E_n-I (n = 5, 6, 7), H-$(ED)_3$-I, H-E_3D_3-I, H-EC$(AC)_2$-I, H-CE$(AC)_2$-I, and H-$(FA)_2$-I. Upon intramolecular cyclication, they afforded the macrocycles ACACAC (**1**), ABABABABABAB (**2**), DDDDDD (**3**), EEEEE (**4**), EEEEEE (**5**), EEEEEEE (**6**), DEDEDE (**7**), DDDEEE (**8**), ECACAC (**9**), CEACAC (**10**), and AFAF (**11**), respectively. The efficiency of the cyclization can be illustrated with hydrocarbon macrocycles **1** and **2** (eqs 1 and 2). Rigid macrocycles with large internal diameters are obtained in high yield under optimized cyclization conditions.



The cyclization was carried out under pseudo-high-dilution conditions by slowly adding a solution of the desired sequence to an active solution of palladium catalyst using a syringe pump. Oxygen was determined to be the major cause of deactivating the catalyst over the time scale of the addition. Therefore in order to keep the catalyst active during the whole addition period which usually lasted for more than 12 h, it was essential to exclude oxygen from the reaction system. An active catalyst solution was characterized by its bright golden yellow color and a deactivated catalyst was dark brown or black. Typically, up to a gram of sequence could be cyclized in a total volume of 250 mL of solvent in a single run. The cyclization proceeded exceptionally well in terms of yield and purity of the products. In all cases only the desired product was isolated and no evidence for contamination by catenanes or oligomeric product has been found. Due to this fact, the separation of most PAMs was relatively straightforward. After flash chromatography on silica gel, the products were

(19) Rossa, L.; Vögtle, F. In *Top. Curr. Chem.* **1983**, *113*, 1–86.
(20) Mandolini, L. In *Advances in Physical Organic Chemistry*; Gold, V., Bethell, D., Eds.; Academic: Orlando, 1986; pp 1–111.
(21) (a) Ziegler, K.; Eberle, H.; Ohlinger, H. *Justus Liebigs Ann. Chem.* **1933**, *504*, 94.
(22) (a) Capon, B.; McManus, S. P. *Neighboring Group Participation*; Plenum: New York, 1976. (b) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.
(23) Laidler, D. A.; Stoddart, J. F. In *Synthesis of Crown Ethers and Analogues*; Patai, S., Ed.; The Chemistry of Functional Groups, Suppl. E, Part 1; John Wiley & Sons: New York, 1980, p 1–15.
(24) (a) Baker, W.; McOmie, J. F. W.; Ollis, W. D. *J. Chem. Soc.* **1951**, 200. (b) Drewes, S. E.; Riphagen, B. G. *J. Chem. Soc. Perkin Trans.* **1974**, *323*, 1908, 2578.
(25) Dale, J. *Tetrahedron* **1974**, *30*, 1683.
(26) For the synthesis of calixarenes with preassembled sequences, see: (a) Hayes, B. T.; Hunter, R. F. *Chem. Ind.* **1956**, 193. (b) Hayes, B. T.; Hunter, R. F. *J. Appl. Chem.* **1958**, *8*, 743. (c) Kämmerer, H.; Happel, G.; Caesar, F. *Makromol. Chem.* **1972**, *162*, 179. (d) Happel, G.; Mathiasch, B.; Kämmerer, H. *Makromol. Chem.* **1976**, *176*, 3317.

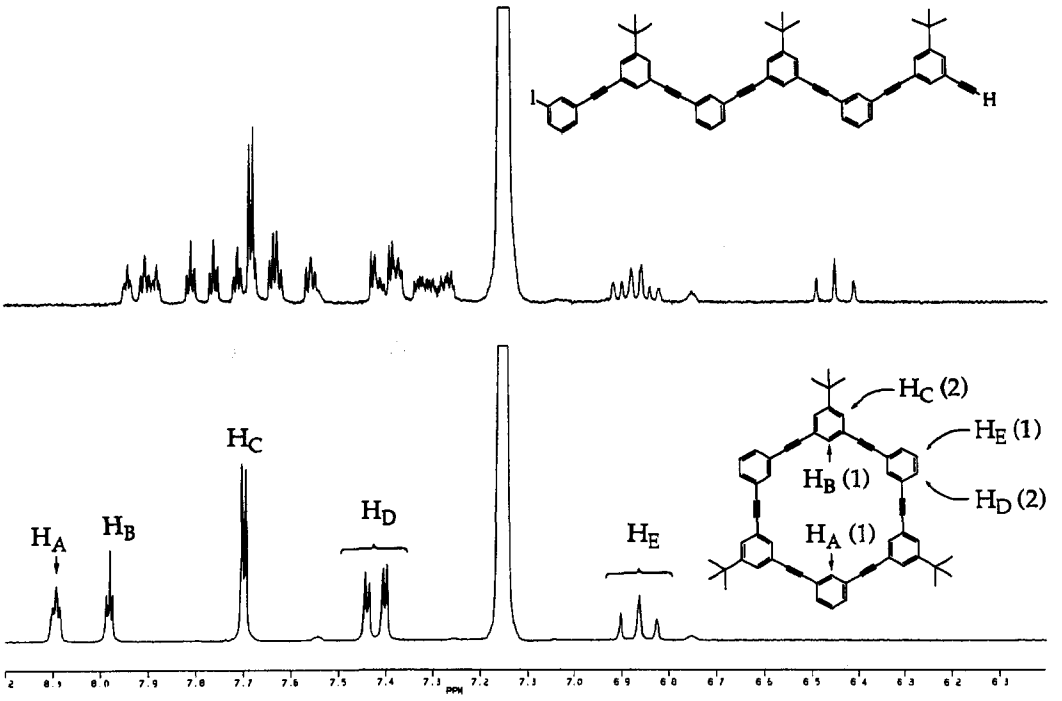
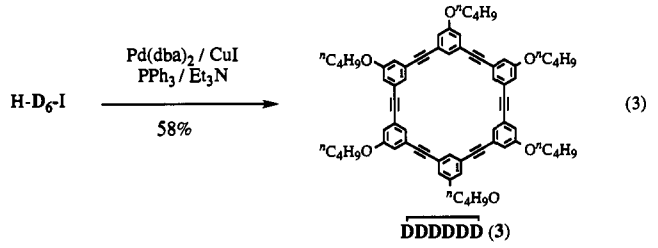


Figure 2. ^{1}H NMR (200 MHz) of PAM **ACACAC** and its precursor H-(AC)$_3$-I (in benzene-d_6).

sometimes slightly colored presumably due to the contamination by residual palladium catalyst. Precipitation of the product from a dichloromethane solution into methanol yielded colorless products in most cases. Alternatively, recrystallization was used to purify some of the PAMs. The isolated yield of the cyclization ranges from 70 to 80%. Except for **3**, macrocycles **1–11** werereadily soluble in aromatic hydrocarbon or chlorinated hydrocarbon solvents.

The cyclic structure of the products can be easily confirmed by ^{1}H, ^{13}C NMR, MS, and elemental analysis because the product and its precusor are very distinct spectroscopically. This is illustrated in Figure 2 which shows the ^{1}H NMR spectra of **ACACAC** and its precursor H-(AC)$_3$-I in benzene-d_6. The aromatic region of the ^{1}H NMR spectrum of the macrocycle shows the symmetry of its structure while the end group resonances which were observed in the precursor (terminal acetylene proton at 2.72 ppm and the aromatic proton ortho to iodide at 6.42 ppm) completely disappear.

Homo-monomer sequences cyclized smoothly to give the corresponding symmetrical macrocycles such as **DDDDDD** (eq 3).



(3)

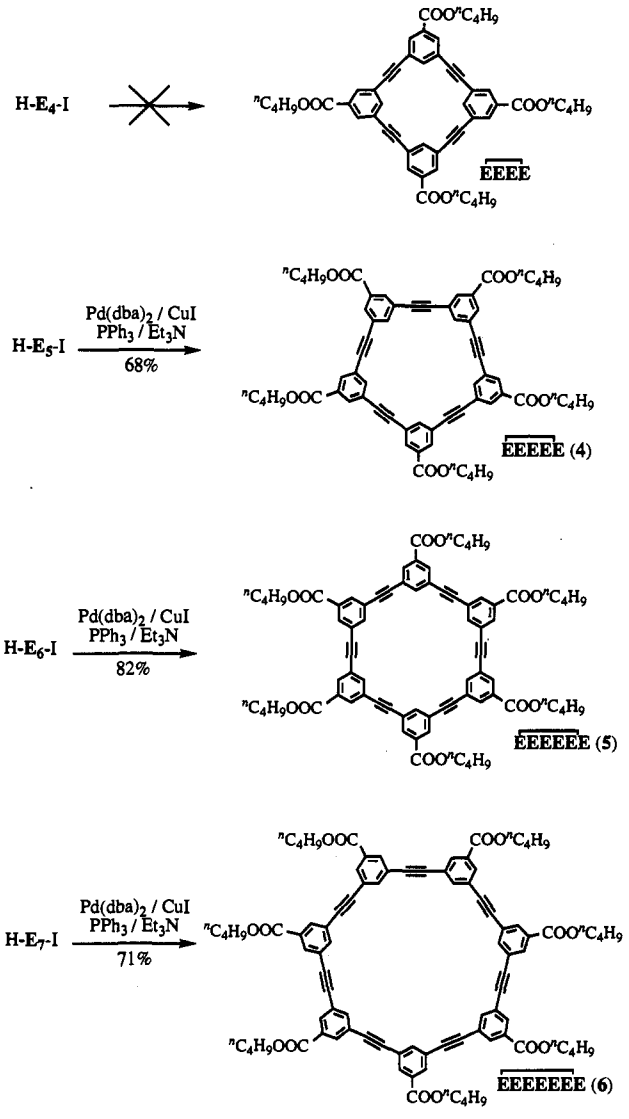
DDDDDD (3)

In this particular case, the solubility of the linear sequence and corresponding macrocyclic product differed greatly. Macrocycle **DDDDDD** exhibited poor solubility in chlorinated solvents which is the best solvent for its precursor, H-**D**$_6$-I. The poor solubility of this compound is at least partially responsible for the lower isolated yield in this case (due to mechanical losses). Cyclization of the series of homo-monomer sequences based on unit **E** shows that macrocycles with deviations from the natural valence angles can also be obtained (Scheme 3). PAMs with five (**EEEEE**), six (**EEEEEE**), and seven (**EEEEEEE**) phenylacetylene repeating units all underwent smooth cyclization in high yield. These examples demonstrate that the size of PAM can easily be controlled by using a precursor sequence of various lengths. Attempts to make the PAM with four phenylacetylene units (i.e. **EEEE**), however, from the tetrameric sequence (H-**E**$_4$-I) were unsuccessful. In this case, no desired product was isolated; instead, a mixture of polymers was obtained in 80% combined yield. Failure in this case is attributed to the high strain energy of this PAM. Molecular mechanics calculations on PAMs with four, five, six, and seven phenylacetylene monomer units indicate that the PAM with four monomer units has a strain energy of about 11 kcal/mol. For PAM with five monomer units, the strain energy is only ca. 2.2 kcal/mol, while it is essentially zero for PAMs with six and seven monomer units. Most of the strain is concentrated in valence angle deformations.[27]

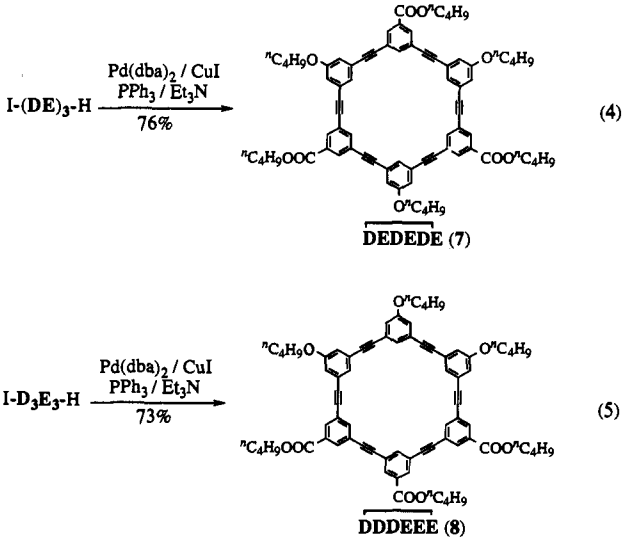
There are a number of advantages of using preassembled sequences to synthesize large macrocyclic structures. The present method should be compared to the more commonly used one-pot approach. Although the one-pot approach can potentially generate products in a single step, it suffers from a number of structure limitations. For example, only cyclic geometries that result from a single monomer type can easily be realized. Thus, **ABABABABABAB** could not be prepared from a one-pot reaction but instead would require prior synthesis of the *meta–para* dimer. For these same reasons, specific placement of functional groups on macrocyles is virtually impossible. In contrast, the approach described here offers a great deal of synthetic versatility. First, it can precisely control the size of the macrocyclic ring. Secondly, this approach lends itself to site-specific functionalization on PAMs. For example, macrocyclic isomers **DEDEDE**, with alternating ester and ether groups, and **DDDEEE**, with segregated ester and ether groups, were easily prepared from the cor-

(27) The phenylacetylene force field parameters were those reported by: Mannfors, B.; Pietilä, L.-O.; Palmö, *J. Mol. Struct.* **1986**, *114*, 287–299. Calculations were performed using the programs Insight II and Discover developed by Biosym Technologies.

Scheme 3



responding sequences (see eqs 4 and 5). Interestingly, these two



(4)

(5)

PAMs are easily differentiated by NMR, particularly by ^{13}C NMR because the former gives two acetylene carbon resonances, while the latter gives six well-resolved resonances (Figure 3). Thus, using preformed sequences as macrocyclic precursors, one

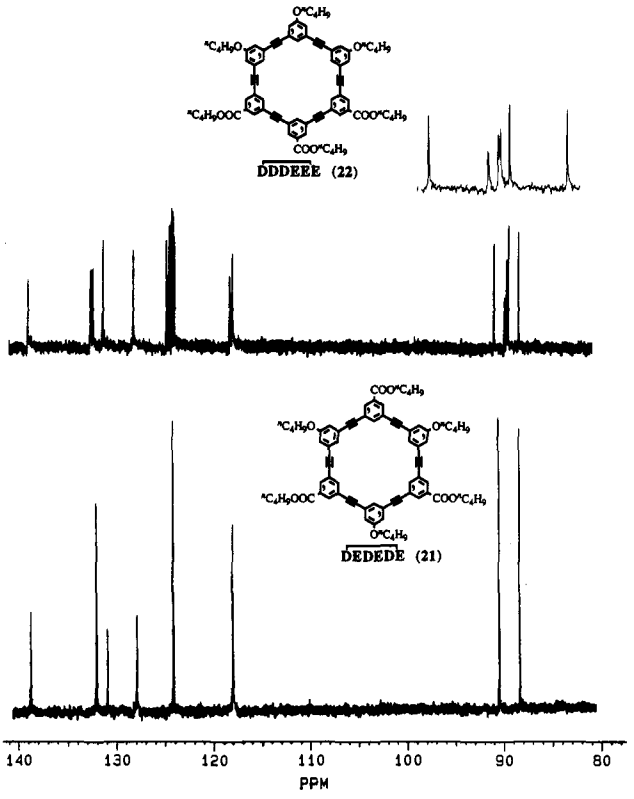
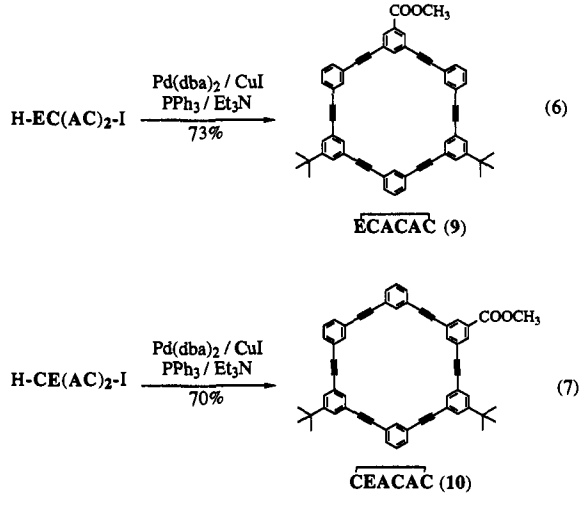


Figure 3. ^{13}C NMR (90 MHz in $CDCl_3$) of DDDEEE (top) and DEDEDE (bottom) isomers in the aromatic and acetylene regions. The spectra reveal six well-resolved acetylene carbon resonances for DDDEEE and two for DEDEDE consistent with the symmetry of these macrocycles.

can in principle place any particular group in any particular position of the PAMs. This is illustrated even further by the two monofunctional isomers ECACAC (9) and CEACAC (10) from H-EC(AC)$_2$-I and H-CE(AC)$_2$-I sequences (eqs 6 and 7). Macrocycles having only one functional group "handle" are ideally suited for attachment to polymeric backbones as pendant groups. Such materials could lead to new polyrotaxanes,[28] side-chain liquid crystalline polymers, or low-density amorphous films.



(6)

(7)

Cyclization at different feed rates should allow for optimization of the cyclization conditions for PAM synthesis. Figure 4 shows the feed rate dependence of the yield of EEEEEE determined by SEC on the crude reaction mixture. As the addition rate increases,

(28) Gibson, H. W.; Marand, H. *Adv. Mater.* **1993**, *26*, 2408.

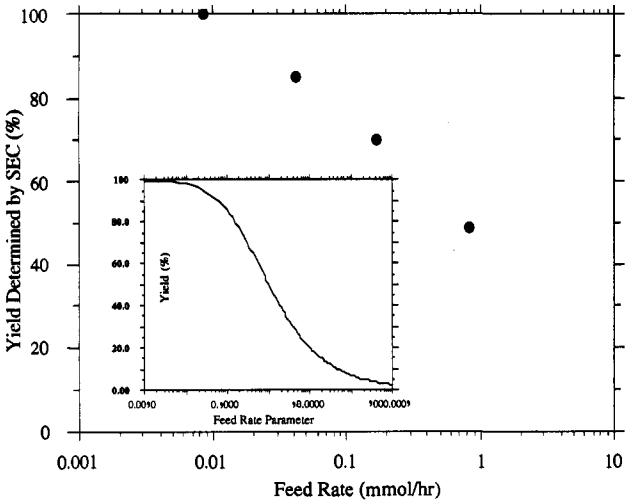
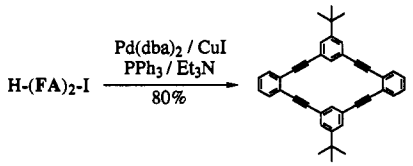


Figure 4. The feed rate dependence of the cyclization yield for **EEEEEE** as determined by SEC. These experiments involved adding 25 mL of a 4.0 mM solution of sequence H-(**E**)$_6$-I to 15 mL of a solution of palladium catalyst initially at a concentration of 4.0 mM. The inset shows the theoretical calculation.

the yield of hexa-phenylacetylene macrocycle smoothly decreases. For example, at an addition rate of 0.0083 mmol/h, a single cyclic product resulted as the only observable species. A 5-fold increase in addition rate (0.0417 mmol/h) gave a mixture that was predominately (85%) **EEEEEE**. The experimental data observed in Figure 4 display the same trend as theoretically predicted for cyclization yield vs influx rate[29] (see inset, Figure 4).

The above results suggest that the use of pre-assembled sequences to synthesize large cyclic compounds not only provides a means for precisely controlling molecular structure but also should allow higher yields to be obtained than the one-pot approach. This is because uncontrolled polymerization and the formation of larger cyclic products can be suppressed by adjusting the rate of precursor addition. In the one-pot approach, oligomerization favors high concentration (being a bimolecular reaction) while the high dilution condition favors unimolecular cyclization. To illustrate a specific example, the one-pot synthesis of the parent hexaphenylacetylene macrocycle has been reported to proceed in only 4.6% yield.[30] Comparison to the overall yields (including the entire sequence synthesis) for PAMs **1**–**11**, shows that by the precursor route, yields are nearly an order of magnitude higher (Table 2).

Entry to the many geometrical variations in the PAM family can be accomplished by using ordered sequences of *ortho*, *meta*, and *para* monomers corresponding to the desired macrocycle. As a simple example, the tetra-phenylacetylene macrocycle **AFAF** was prepared (see eq 8). This example brings up an additional

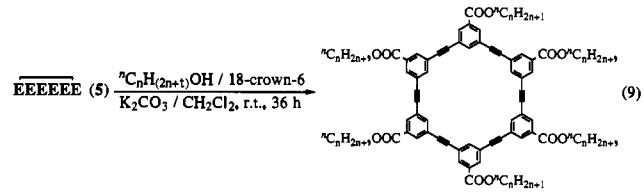


AFAF (**11**) (8)

point to consider in planning the most suitable precursor sequence for a given cyclic. Sequences such as H-(**AF**)$_2$–I and H-(**FA**)$_2$-**I** would, in principle, lead to macrocycle **AFAF**. Nonetheless, we find it advantageous to design the sequences in a way that results in the simplest cyclization reaction. Cyclization of sequence H-(**AF**)$_2$-I would require closure that involves coupling an iodide *ortho* to an acetylene. In contrast, cyclization of sequence H-(**FA**)$_2$-**I** requires closure that involves coupling an iodide *meta* to an acetylene. Because the rate of coupling is faster in the latter case, this sequence was chosen over H-(**AF**)$_2$-**I**.

Functional Group Transformations of PAMs. Transformation of the functional groups of PAMs provides an efficient way to chemically modify these macrocyclic compounds. The difficulties are that these transformations may involve simultaneous manipulation of multiple functional groups in a single molecule. Problems of solubility as well as incomplete conversion must be recognized. It is therefore essential to find conditions such that each of the functional groups undergo complete transformation.

Transesterification with alkanols in the presence of 18-crown-6 ether and potassium carbonate provides access to a family of esters which have the potential for developing liquid crystals (eq 9). The completion of this reaction can be monitored by 300-



(9)

EEEEEE
12: n = 7
13: n = 8
14: n = 16

MHz ^{1}H NMR because the methyl protons in the starting material are distinguishable from the methyl and methylene protons in the product. Reduction of **EEEEEE** (**5**) by diisobutylaluminum hydride (DIBAL-H)[31] gives **GGGGGG** with the pendant benzyl alcohol group (Scheme 4). This reaction proceeds smoothly at room temperature and the product is soluble in polar organic solvents such as DMSO and DMF. The isolated yield for this reduction reaction is ca. 60%. The low yield is at least partly due to mechanical losses in purification of this highly polar compound. When the same reaction is performed on **ECACAC**, the yield is nearly quantitative. Alkylation of **GGGGGG** with alkyl bromide gives a family of benzyl ethers, such as **HHHHHH** (**16**), as well as interesting liquid crystal mesogen (Scheme 4).

The phenyl ether linkage in **DDDDDD** can be cleaved with boron tribromide at room temperature to give **IIIIII**, a hexaphenol derivative (Scheme 5).[32] Due to the low solubility of **DDDDDD**, boron tribromide solution is added to its suspension in dichloromethane. Upon addition of boron tribromide, the suspension gradually dissolves to give a homogenous solution. The yield of this reaction is ca. 60%, and again this low yield has been attributed to the mechanical losses during purification. Surprisingly, **IIIIII** is very soluble in most polar organic solvents such as ethanol, DMF, DMSO, and dioxane as well as aqueous base solution. By condensation with carboxylic acids in the presence of 1,3-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridinium-4-toluenesulfonate (DPTS),[33] **IIIIII** can be converted to the family of alkanoate derivatives (**JJJJJJ**) (Scheme 5). PAMs **JJJJJJ** and **EEEEEE** are isomers, and the only difference between them is that they have a reversed ester linkage. However, such

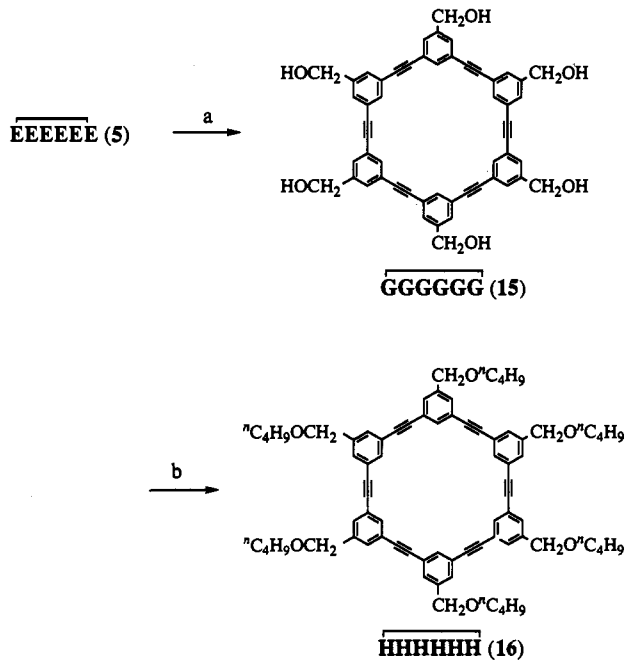
(29) Galli, C.; Mandolini, L. *Gazz. Chim. Ital.* **1975**, *105*, 367.
(30) Staab, H. A.; Neunhoeffer, K. *Synthesis* **1974**, 424.
(31) (a) Winterfeld, E. *Synthesis* **1975**, 617. (b) Yoon, N. M.; Gyoung, Y. S. *J. Org. Chem.* **1985**, *50*, 2443.
(32) Press, J. B. *Synth. Commun.* **1979**, *9*, 407.
(33) Moore, J. S.; Stupp, S. I. *Macromolecules* **1990**, *23*, 65.

Table 2. Cyclization Yield and Overall Yield[a] for PAMs 1–11

	1	2	3	4	5	6	7	8	9	10	11
cyclization yield (%)	75	70	59[b]	68	82	71	76	73	73	70	80
overall yield (%)	38	30	32	36	43	34	40	39	37	36	32

[a] Overall yield from monomer including all steps involved in the linear precursor synthesis and cyclization. [b] Low yield of cyclization in this case is due to the poor solubility of the product.

Scheme 4



Reagents: (a) DIBAL-H, PhH, THF, r.t., 2 hrs, 61%.
(b) $^{n}C_4H_9Br$, 18-crown-ether, KOH, DMF, 80°C, 36 h, 50%.

a seemingly slight modification to the chemical structure of PAMs can alter their solution and solid-state properties dramatically.[34] Alkylation of **IIIIII** with alkyl bromides converts the hexaphenol back to PAMs with phenyl ether linkages of various chain length (**22–25**). Unlike **3**, these compounds display reasonable solubility. In summary, the transformations shown in Scheme 5 provide a very efficient way to adjust the length of the side chains of PAMs. This is particularly important for the investigation of discotic liquid crystal properties of this class of molecules.[35]

Solid-State Behavior of PAMs. PAM molecules are potentially interesting as building blocks for tubular liquid crystals and porous molecular crystals. It is therefore useful to examine the solid-state structure and behavior of the simplest members of this family such as hydrocarbons **AFAF**, **ACACAC**, and **ABABABABABAB**. These unfunctionalized PAMs may establish a baseline regarding melting transitions and thermal stability. Although single crystals of **ACACAC** have been grown, the X-ray structure has not yielded to refinement, presumably due to considerable disorder. High resolution electron microscopy (HREM) and selected area electron diffraction (SAED) studies are currently being pursued and will be reported separately.[35]

Interestingly, in spite of their good solubility characteristics, none of the PAM hydrocarbons exhibit a melting transition. Instead, each of these undergoes an irreversible exothermic reaction prior to melting as determined by differential scanning calorimetry (DSC). These solid-state reactions occur between 400 and 450 °C (Figure 5). Thermogravimetric analysis (TGA) shows that no mass loss occurs up to this temperature. The color of the thermal product is black in the case of **AFAF** and light brown in the case of the other two macrocycles. None of the thermal products are soluble in common solvents. The enthalpy associated with this reaction is −135, −66, and −49 kcal/mol for **ABABABABABAB**, **ACACAC**, and **AFAF**, respectively. This corresponds to a nearly constant values of ca. 11–12 kcal/mol per phenylacetylene unit for the three different macrocycles (see Table 3). On the basis of the onset temperature, **AFAF** appears to be the most reactive. This macrocycle also gives the sharpest exotherm as measured by $\Delta_{1/2}$ (the width of the peak at half-height). More studies are needed to determine the structures of these thermal products as well as the nature of these chemical transformations. The possibility that these reactions are topochemical[36,37] solid-state polymerizations involving acetylenic groups is an intriguing consideration which is under current investigation. The thermal behavior of other PAMs has proven to be interesting in the melting transitions and even liquid crystal phases have been observed. The details of these findings will be reported in the near future.

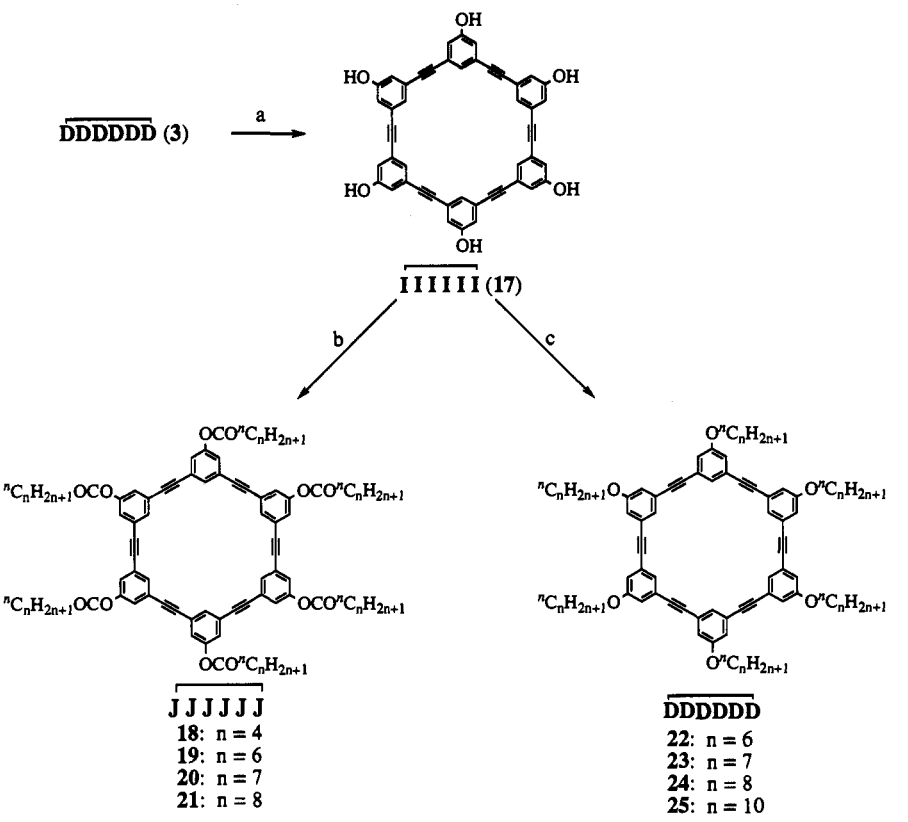
Conclusions

We have described in efficient method for synthesizing oligomeric sequences of phenylacetylene monomers. By this method, chain growth occurs at both ends and therefore the size of the oligomer grows nonlinearly against the number of synthetic steps. This method also allows the placement of various functional groups at any specific positions along the sequence chain. The phenylacetylene sequences can be cyclized to give phenylacetylene macrocycles, PAMs, in high yield. The control introduced in the sequence synthesis is carried over to the macrocyclic compounds, making it suitable to prepare geometrically-controlled and site-specifically functionalized variants. Compared with the more commonly used one-pot approach to macrocyclic compounds, the method described here has many advantages in terms of efficiency, product purity, and control over the ring structure. Simple functional group transformations on the PAMs have been successfully performed. The chemistry which has been used for sequence synthesis and cyclization is the palladium-catalyzed cross-coupling of aryl iodide and terminal acetylene. However, the generality of this approach to the synthesis of sequences and macrocycles should go beyond this particular chemistry as long as suitable protecting group schemes can be found.

Apart from the synthetic challenge that they present, PAMs are of interest because they potentially represent a set of useful molecular building blocks for new materials. The large interior cavity (the hydrogen-to-hydrogen distance is ca. 21 Å for **ABABABABABAB** and ca. 8 Å for other hexa-phenylacetylene PAMs) and shape-persistent, non-collapsible skeleton make PAMs especially attractive for porous organic materials including tubular mesophases,[38] low density nanocellular solids,[39] and organic crystals that may be functionally reminiscent of zeolites.

(34) Zhang, J.; Moore, J. S. Manuscript in preparation.
(35) Buchko, C. J.; Wilson, P. M.; Martin, D. C. Unpublished results.
(36) (a) Perrin, R.; Lamartine, R. In *Structure and Properties of Molecular Crystals*; Pierrot, M., Ed.; Elsevier: The Netherlands, 1990; pp 107–159. (b) Desiraju, G. R. *Crystal Engineering: The Design of Organic Solids*; Elsevier: New York, 1989.
(37) (a) *Polydiacetylenes*; Bloor, D., Chance, R. R., Eds.; Martinus Nijhoff Dordrecht: Boston, 1985.
(38) Zhang, J.; Moore, J. S. Manuscript in preparation.
(39) Gibson, L. J.; Ashby, M. F. *Cellular Solids: Structure and Properties*; Pergamon: New York, 1988.

Scheme 5



Reagents: (a) BBr_3, $ClCH_2CH_2Cl$, r.t., 12 h, 60%. (b) $^nC_nH_{(2n+1)}COOH$, DCC, DPTS, r.t, 3 h. (c) $^nC_nH_{(2n+1)}Br$ (n = 4, 6, 7, 8), K_2CO_3, DMF, 90°C, 12 h.

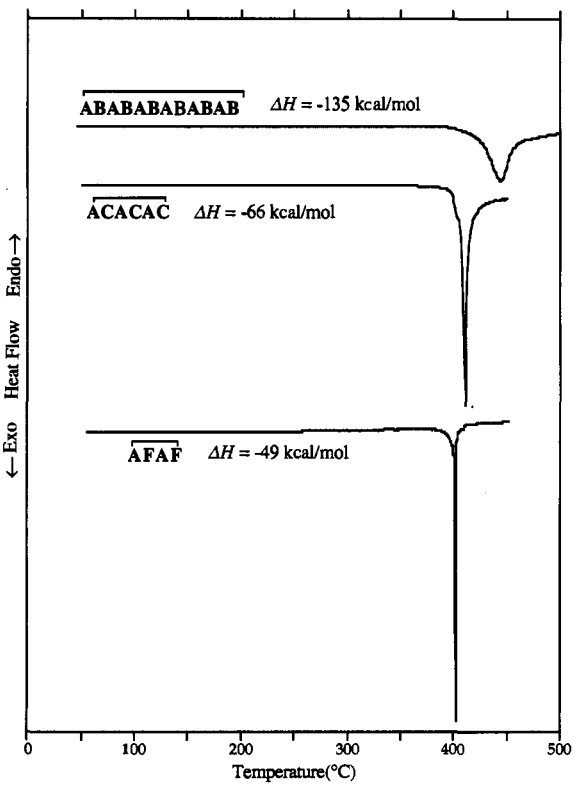


Figure 5. DSC traces of hydrocarbon PAMs.

Table 3. Solid-State Thermal Reaction Data on PAM Hydrocarbons

macrocycle	T_{onset} (°C)	$\Delta_{1/2}$ (°C)	ΔH (kcal/mol)	ΔH/monomer (kcal/mol repeat unit)
AFAF	399	0.8	−49	−12.3
ACACAC	423	4.9	−66	−11.0
ABABABABABAB	430	19.8	−135	−11.3

Experimental Section

General Method. Unless otherwise indicated, all starting materials were obtained from commercial suppliers and used without further purification. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and were uncorrected or they were reported as the onset temperature from differential scanning calorimetry traces run at a heating rate of 20 °C-min^{-1}. Dry triethylamine was obtained by vacuum transfer from calcium hydride. Dry THF and benzene were obtained by vacuum transfer from sodium and benzophenone. Methyl iodide was vacuum transferred from molecular sieves. The ^1H and ^{13}C NMR spectra were recorded on Bruker AM-360, AM-300, AM-200, Varian XL 200, or Unity 400 in chloroform-*d* (unless otherwise indicated) at the indicated fields; chemical shifts are expressed in parts per million (δ) with residual solvent peak as the internal standard. Splitting patterns are designed as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). In some cases the ^1H NMR chemical shifts highly depend on concentration and temperature, and these parameters are also indicated. Gas chromatography (GC) was performed on an HP-5890 Series II gas chromatograph equipped with a 25 m × 0.2 mm × 0.33 mm HP-1 silicone column. Analytical thin layer chromatography (TLC) was performed on KIESELGEL F-254 pre-coated TLC plates. Flash chromatography was carried out with Silica Gel 60 (230–400 mesh) from EM Science. Low resolution mass spectra (LRMS) were recorded on a Finigan 4021 mass spectrometer, Finnigan GC-MS equipped with a 30 m SE-54 capillary column (EI), Finnigan-MAT CH5 mass spectrometer (EI) or a VG ZAB-SE mass spectrometer (FAB). High resolution mass spectra were obtained on a VG 70-S mass spectrometer (EI or FAB), Finnigan-MAT 731 mass spectrometer (EI), or VG 70-SE-4F mass spectrometer (FAB). Size-exclusion chromatography (SEC) was performed using a Waters 6000 Å solvent delivery system and a

Model 440 absorbance detector at 254 nm. A series of three styragel columns of pore sizes 500, 10^3, and 10^4 Å were used and calibrated with narrow molecular weight polystyrene standards. SEC data were obtained in THF at 23 °C. Elemental analyses were performed either on a Perkin-Elmer P2000 or 2400 CHN Elemental Analyzer or in the Spang Microanalytical Laboratory, Eagle Harbor, MI 49951.

Sequence Synthesis. General Procedure for Deprotecting (Trimethylsilyl)acetylenes. (a) The starting material was dissolved in methanol with a catalytic amount of potassium carbonate. After the mixture was stirred at room temperature for an hour, the solvent was removed under vacuum. The residual solid or oil was dissolved in dichloromethane and filtered through a plug of silica gel to give the product. The yield ranged from 95% to 98%. (b) If the starting material was not soluble enough in methanol, dichloromethane was used as the co-solvent. Longer time was needed when the co-solvent was used. The reaction may be monitored by ^{1}H NMR and TLC. The rest of the procedure was the same as in (a). (c) In order to increase the solubility of some of the sequences with ester functional groups, methyl ester was replaced with ethyl or *n*-butyl ester by transesterification simultaneously with this deprotection step. The procedure for such cases was as follows: To a mixture of the sequence and a catalytic amount of potassium carbonate and 18-crown-6 ether in dichloromethane, absolute ethanol or 1-butanol was added. After the mixture was stirred under nitrogen at room temperature for 12 h, the solvent was removed under vacuum and fresh solvent was added to repeat the process again. The mixture was then stirred at room temperature for another 12 h. The rest of the procedure was the same as in (a).

General Procedure for Deprotecting Phenyltriazenes. A solution of the starting material dissolved methyl iodide was degassed three times and then stirred at 110 °C for 12 h. The reaction may be monitored by TLC and ^{1}H NMR. Unreacted methyl iodide was distilled out for recycling. The residual was redissolved in dichloromethane and filtered through a plug of silica gel. Upon removal of solvent, the product was obtained in 90% to 95% yield.

General Procedure for Coupling Terminal Acetylenes and Aryl Iodides. A heavy-walled flask was charged with terminal acetylene (1 equiv), aryl iodide (1.05–1.10 equiv), $Pd(dba)_2$ (0.02 equiv), PPh_3 (0.06 equiv), CuI (0.01 equiv), and dry triethylamine. For some sequences, benzene was used as a co-solvent due to poor solubility of the reactants. The concentrations of the reactions varied from 0.3 to 0.05 M depending on the solubility of the reactants. The flask was then evacuated and backfilled with nitrogen three times, sealed with a Teflon screw cap, and stirred at 80 °C for 12 h. The disappearance of starting materials may be monitored by TLC. After completion, the solvent was removed and the reaction mixture was purified by flash column chromatography.

Sequence TMS-**AB**-N_3Et_2 (18.4 g, 42.8 mmol, 86% yield) was prepared from Br-**A**-N_3Et_2 (16.9 g, 54.6 mmol) and H-**B**-N_3Et_2 (10.0 g, 49.7 mmol). The terminal acetylene H-**AB**-N_3Et_2 (5.30 g, 14.8 mmol, 98% yield, CH_2Cl_2 as co-solvent) was prepared from TMS-**AB**-N_3Et_2 (6.50 g, 15.1 mmol). The aryl iodide TMS-**AB**-I (7.79 g, 17.0 mmol, 94% yield) was prepared from TMS-**AB**-N_3Et_2 (7.80 g, 18.2 mmol). Characterization of TMS-**AB**-I: ^{1}H NMR (200 MHz) 7.68 (dt, J = 8.6 Hz, 2.0 Hz, 2H), 7.50–7.45 (m, 3H), 7.24 (dt, J = 8.6 Hz, 2.0 Hz, 2H), 1.32 (s, 9H), 0.26 (s, 9H); ^{13}C NMR (90 MHz) 151.6, 137.6, 133.1, 132.3, 129.2, 128.8, 123.6, 122.83, 122.78, 104.8, 94.3, 94.1, 90.6, 88.4, 34.7, 31.1, –0.1; HRMS (EI) calcd for $C_{23}H_{25}SiI$ 456.0772, found 456.0768. Anal. Calcd for $C_{23}H_{25}ISi$: C, 60.52; H, 5.52. Found: C, 60.07; H, 5.41.

Sequence TMS-$(AB)_2$-N_3Et_2 (8.15 g, 11.9 mmol, 87% yield) was prepared from TMS-**AB**-I (6.50 g, 14.2 mmol) and H-**AB**-N_3Et_2 (4.85 g, 13.6 mmol). The terminal acetylene H-$(AB)_2$-N_3Et_2 (3.47 g, 5.65 mmol, 97% yield, CH_2Cl_2 as co-solvent) was prepared from TMS-$(AB)_2$-N_3Et_2 (4.00 g, 5.83 mmol). The aryl iodide TMS-$(AB)_2$-I (4.32 g, 6.06 mmol, 92% yield) was prepared from TMS-$(AB)_2$-N_3Et_2 (4.52 g, 6.59 mmol). Characterization of TMS-$(AB)_2$-I: ^{1}H NMR (200 MHz), 7.70 (d, J = 8.7 Hz, 2H), 7.50 (m, 10H), 7.27 (d, J = 8.7 Hz, 2H), 1.36 (s, 9H), 1.33 (s, 9H), 0.27 (s, 9H); ^{13}C NMR (75 MHz) 151.9, 151.7, 137.7, 133.2, 132.4, 131.9, 131.7, 129.2, 129.0, 128.9, 123.3, 123.1, 122.8, 104.9, 94.4, 94.2, 91.2, 91.1, 90.6, 89.3, 89.1, 88.6, 34.8, 34.7, 31.1, 0; HRMS (EI) calcd for $C_{43}H_{41}ISi$ 712.2024, found 712.1996. Anal. Calcd for $C_{43}H_{41}SiI$: C, 72.46; H, 5.80. Found: C, 72.63; H, 5.74.

Sequence TMS-$(AB)_3$-N_3Et_2 (0.203 g, 0.215 mmol, 86% yield) was prepared from TMS-$(AB)_2$-I (0.188 g, 0.264 mmol) and H-**AB**-N_3Et_2 (0.0898 g, 0.251 mmol). The aryl iodide TMS-$(AB)_3$-I (0.196 g, 0.202 mmol, 94% yield) was prepared from TMS-$(AB)_3$-N_3Et_2 (0.203 g, 0.215 mmol). Characterization of TMS-$(AB)_3$-I: ^{1}H NMR (200 MHz) 7.70 (d, J = 8.5 Hz, 2H), 7.55–7.45 (m, 17H), 7.27 (d, J = 8.5 Hz, 2H), 1.36 (s, 9H), 1.35 (s, 9H), 1.33 (s, 9H), 0.26 (s, 9H); ^{13}C NMR (90 MHz) 151.7, 151.5, 137.5, 133.1, 132.3, 131.8, 131.6, 129.2, 128.9, 123.0–122.6 (m), 104.7, 94.3, 94.2, 91.0, 90.9, 90.5, 89.2, 89.12, 89.14, 89.0, 88.5, 34.7, 34.6, 31.1, 0.0; HRMS (EI) calcd for $C_{63}H_{57}SiI$ 968.3276, found 968.3259. Anal. Calcd for $C_{63}H_{57}ISi$: C, 78.08; H, 5.93. Found: C, 78.36; H, 6.21.

Sequence TMS-$(AB)_4$-N_3Et_2 (3.80 g, 3.17 mmol, 82% yield) was prepared from TMS-$(AB)_2$-I (2.92 g, 4.09 mmol) and H-$(AB)_2$-N_3Et_2 (2.39 g, 3.89 mmol). The terminal acetylene H-$(AB)_4$-N_3Et_2 (2.29 g, 2.04 mmol, 98% yield) was prepared from TMS-$(AB)_4$-N_3Et_2 (2.50 g, 2.09 mmol). The aryl iodide TMS-$(AB)_4$-I (0.768 g, 0.627 mmol, 94% yield) was prepared from TMS-$(AB)_4$-N_3Et_2 (0.800 g, 0.667 mmol). Characterization of TMS-$(AB)_4$-I: ^{1}H NMR (360 MHz) 7.75 (d, J = 8.3 Hz, 2H), 7.50 (m, 24H), 7.27 (d, J = 8.3 Hz, 2H), 1.35 (m, 36H), 0.27 (9H); ^{13}C NMR (90 MHz) 151.8, 151.6, 137.6, 133.1, 132.3, 131.9, 131.6, 129.2, 129.0, 123.1–122.7 (m), 104.8, 94.2, 91.1, 91.0, 90.5, 89.2, 89.1, 88.5, 34.8, 31.1, 0; HRMS (EI) calcd for $C_{83}H_{73}ISi$ 1224.4528, found 1224.4517. Anal. Calcd for $C_{83}H_{73}ISi$: C, 81.35; H, 6.00. Found: C, 81.50; H, 5.97.

Sequence TMS-$(AB)_6$-N_3Et_2 (2.22 g, 1.30 mmol, 86% yield) was prepared from TMS-$(AB)_2$-I (1.83 g, 1.65 mmol) and H-$(AB)_4$-N_3Et_2 (1.70 g, 1.51 mmol). The aryl iodide TMS-$(AB)_6$-I (1.43 g, 0.823 mmol, 86% yield) was prepared from TMS-$(AB)_6$-N_3Et_2 (1.63 g, 0.953 mmol). The difunctionalized sequence H-$(AB)_6$-I (1.20 g, 0.720 mmol, 96% yield, CH_2Cl_2 as co-solvent) was prepared from TMS-$(AB)_6$-I (1.30 g, 0.748 mmol). Characterization of TMS-$(AB)_6$-I: ^{1}H NMR (200 MHz), 7.70 (d, J = 8.2 Hz, 2H), 7.51 (m, 38H), 7.27 (d, J = 8.2 Hz, 2H), 1.35 (m, 54H), 0.27 (s, 9H); ^{13}C NMR (90 MHz) 151.8, 151.6, 137.6, 133.1, 132.3, 131.9, 131.6, 129.0, 129.0, 128.9, 123.1–122.7 (m), 104.8, 94.2, 91.1, 91.0, 90.5, 89.2, 89.1, 88.54, 34.8, 31.1, 0. Anal. Calcd for $C_{123}H_{105}ISi$: C, 84.99; H, 6.09. Found: C, 84.66; H, 6.16.

Sequence TMS-$(AB)_8$-N_3Et_2 (0.552 g, 0.248 mmol, 70% yield after recrystallization from toluene) was prepared from TMS-$(AB)_4$-I (0.443 g, 0.362 mmol) and H-$(AB)_4$-N_3Et_2 (0.400 g, 0.355 mmol). The aryl iodide TMS-$(AB)_8$-I (0.431 g, 0.191 mmol, 85% yield) was prepared from TMS-$(AB)_8$-N_3Et_2 (0.500 g, 0.225 mmol). Characterization of TMS-$(AB)_8$-I: ^{1}H NMR (200 MHz), 7.70 (d, J = 8.4 Hz, 2H), 7.51 (m, 60H), 7.27 (d, J = 8.4 Hz, 2H), 1.35 (m, 72H), 0.27 (s, 9H); ^{13}C NMR (90 MHz) 151.8, 151.6, 137.6, 133.1, 132.3, 131.8, 131.6, 131.4, 129.2, 128.9, 123.1–122.7 (m), 104.7, 94.2, 91.0, 90.5, 89.1, 89.0, 88.5, 34.7, 31.1, 0. Anal. Calcd for $C_{163}H_{137}ISi$: C, 86.98; H, 6.14. Found: C, 87.13; H, 6.15.

Sequence H-$(AC)_3$-I was prepared from TMS-**A**-Br and H-**C**-N_3Et_2 (overall 51% yield). ^{1}H NMR (360 MHz) 7.91 (dd, J = 1.7, 1.7 Hz, 1H), 7.69 (dd, J = 1.0, 1.7 Hz, 1H), 7.67 (dd, J = 1.0, 1.7 Hz, 2H), 7.50 (m, 1H), 7.48 (m, 2H), 7.09 (m, J = 7.9 Hz, 1H), 1.34 (s, 1H), 0.28 (s, 9H); ^{13}C NMR (90 MHz) 151.5, 140.2, 137.3, 132.3, 130.6, 129.8, 129.3, 128.7, 125.2, 123.1, 122.6, 104.5, 94.3, 93.7, 90.4, 87.5, 34.7, 31.0, 0.0. HRMS (EI) calcd for $C_{60}H_{49}I$ 896.2881, found 896.2861. Anal. Calcd for $C_{60}H_{49}I$: C, 80.35; H, 5.51. Found: C, 79.96; H, 5.45.

Sequence H-D_6-I was prepared from TMS-**D**-N_3Et_2 (overall 54% yield). ^{1}H NMR (360 MHz), 7.45 (t, J = 1.6 Hz, 1H), 7.29 (m, 12H), 7.01 (m, 5H), 4.00 (m, 12H), 3.07 (s, 1H), 1.80 (m, 12H), 1.47 (m, 12H), 0.99 (m, 18H); ^{13}C NMR (90 MHz) 159.25, 158.82, 158.74, 132.49, 127.59, 127.21, 125.42, 124.52, 124.21, 124.17, 124.11, 123.96, 123.29, 118.54, 118.21, 118.06, 117.96, 116.81, 93.73, 89.47, 88.86, 88.81, 88.70, 87.90, 82.77, 77.46, 31.17, 31.13, 31.09, 19.17, 19.13, 13.79; MS (EI) calcd for $C_{72}H_{73}O_6I$ 1161.29, found 1160 (0.6%), 1161 (0.4%), 1162 (0.2%). Anal. Calcd for $C_{72}H_{73}O_6I$: C, 74.47; H, 6.32. Found: C, 74.67; H, 6.40.

Sequence H-E_4-I was prepared from TMS-**E**-N_3Et_2 (overall 58% yield). ^{1}H NMR (360 MHz), 8.35 (t, J = 1.6 Hz, 1H), 8.16 (m, 6H), 8.13 (t, J = 1.6 Hz, 1H), 7.88 (m, 2H), 7.83 (t, J = 1.6 Hz, 1H), 4.36 (m, 8H), 3.17 (s, 1H), 1.80 (m, 8H), 1.48 (m, 8H), 1.02 (m, 12H); ^{13}C NMR (90 MHz) 164.92, 164.89, 164.27, 143.82, 138.63, 138.32, 138.13, 132.95, 132.66, 132.59, 132.51, 132.49, 132.23, 131.80, 131.29, 131.19, 124.69, 123.48, 123.43, 123.33, 123.29, 122.98, 93.28, 89.48, 89.02, 88.92, 88.89, 88.23, 81.64, 78.92, 65.46, 65.38, 65.34, 30.68, 30.64, 30.61, 19.18, 19.15, 13.71, 13.68; HRMS (EI) calcd for $C_{52}H_{49}O_8I$ 928.2474, found 928.2408. Anal. Calcd for $C_{52}H_{49}O_8I$: C, 67.24; H, 5.32. Found: C, 66.98; H, 5.38.

Sequence H-E_8-I was prepared from TMS-**E**-N_3Et_2 (overall 53% yield). ^{1}H NMR (360 MHz), 8.34 (t, J = 1.5 Hz, 1H), 8.17 (m, 8H), 8.12 (t, J = 1.5 Hz, 1H), 7.88 (m, 3H), 7.82 (t, J = 1.5 Hz, 1H), 4.36 (m, 10H), 3.17 (s, 1H), 1.80 (m, 10H), 1.49 (m, 10H), 1.00 (m, 15H); ^{13}C NMR (90 MHz) 165.11, 165.08, 165.05, 164.43, 143.96, 138.74, 138.45, 138.26, 133.07, 132.77, 132.73, 132.65, 132.38, 131.90, 131.44, 131.31, 124.81,

123.57, 123.55, 123.41, 123.08, 93.34, 89.52, 89.07, 89.03, 88.98, 88.94, 78.91, 65.56, 65.49, 65.43, 30.72, 19.24, 19.20, 13.75; MS (EI) calcd for $C_{65}H_{61}O_{10}I$ 1129.11, found 1128 (1.6%), 1129 (1.4), 1130 (0.6%). Anal. Calcd for $C_{65}H_{61}O_{10}I$: C, 69.14; H, 5.36. Found: C, 69.29; H, 5.32.

Sequence H-E_6-I was prepared from TMS-E-N_3Et_2 (overall 53% yield). ^1H NMR (300 MHz) 8.33 (t, J = 1.6 Hz, 1H), 8.18 (m, 10H), 8.12 (t, J = 1.6 Hz, 1H), 8.06 (t, J = 1.6 Hz, 1H), 7.89 (m, 4H), 7.83 (t, J = 1.6 Hz, 1H), 4.40 (m, 12H), 3.17 (s, 1H), 1.80 (m, 12H), 1.50 (m, 12H), 1.00 (m, 18H); ^{13}C NMR (90 MHz) 165.07, 165.01, 164.39, 143.93, 138.73, 138.43, 138.24, 133.05, 132.75, 132.71, 132.64, 132.35, 131.89, 131.41, 131.30, 124.79, 123.56, 123.43, 123.40, 123.06, 93.34, 89.54, 89.04, 89.00, 88.96, 88.29, 81.71, 78.94, 65.55, 65.48, 65.42, 44.45, 30.72, 30.70, 19.25, 19.23, 13.77, 13.74, 11.26; MS (EI) calcd for $C_{78}H_{73}O_{12}I$ 1329.35, found 1329 (0.1%), 1328 (0.1%). Anal. Calcd for $C_{78}H_{73}O_{12}I$: C, 70.48; H, 5.54. Found: C, 70.32; H, 5.44.

Sequence H-E_7-I was prepared from TMS-E-N_3Et_2 (overall 48% yield). ^1H NMR (360 MHz) 8.34 (t, J = 1.6 Hz, 1H), 8.18 (m, 12H), 8.13 (t, J = 1.6 Hz, 8.06 (t, J = 1.6 Hz, 1H), 7.88 (m, 5H), 7.82 (t, J = 1.6 Hz, 1H), 4.36 (m, 14H), 3.17 (s, 1H), 1.81 (m, 14H), 1.50 (m, 14H), 1.00 (m, 21H); ^{13}C NMR (90 MHz) 165.07, 165.01, 164.39, 143.93, 138.73, 138.43, 138.24, 133.05, 132.76, 132.71, 132.64, 132.35, 131.89, 131.42, 131.30, 124.80, 123.56, 123.43, 123.40, 123.06, 93.34, 89.54, 89.04, 88.99, 88.96, 88.29, 81.71, 78.94, 65.55, 65.48, 65.42, 30.72, 19.25, 13.75, 13.74. Anal. Calcd for $C_{91}H_{85}O_{14}I$: C, 71.46; H, 5.60. Found: C, 71.20; H, 5.34.

Sequence H-(**DE**)$_3$-I was prepared from TMS-**D**-N_3Et_2 and TMS-E-N_3Et_2 (overall 53% yield). ^1H NMR (360 MHz), 8.32 (t, J = 1.6 Hz, 1H), 8.14 (m, 5H), 8.04 (t, J = 1.6 Hz, 1H), 7.84 (m, 2H), 7.33 (t, J = 1.3 Hz, 1H), 7.31 (t, J = 1.3 Hz, 1H), 7.08 (m, 3H), 7.05 (m, 3H), 7.01 (t, J = 1.3 Hz, 1H), 4.30 (m, 6H), 4.00 (m, 6H), 3.08 (s, 1H), 1.78 (m, 12H), 1.50 (m, 12H), 1.00 (m, 18H); ^{13}C NMR (90 MHz) 165.26, 158.92, 158.80, 143.93, 138.23, 138.16, 132.34, 132.30, 131.85, 131.28, 127.65, 127.26, 125.19, 123.97, 123.93, 123.84, 123.81, 123.71, 123.40, 118.84, 118.40, 118.28, 118.25, 93.30, 90.62, 89.97, 89.91, 87.98, 87.85, 87.08, 82.68, 77.58, 68.08, 68.01, 65.52, 65.40, 31.16, 31.13, 30.72, 30.68, 19.24, 19.19, 13.82, 13.79, 13.77, 13.74; MS (EI) calcd for $C_{75}H_{73}O_9I$ 1244.32, found 1244 (0.3%), 1245 (0.2). Anal. Calcd for $C_{75}H_{73}O_9I$: C, 72.34; H, 5.91. Found: C, 72.13; H, 5.70.

Sequence H-D_3E_3-I was prepared from TMS-**D**-N_3Et_2 and TMS-E-N_3Et_2 (overall 54% yield). ^1H NMR (300 MHz) 8.18 (m, 5H), 8.13 (t, J = 1.5 Hz, 1H), 7.88 (m, 2H), 7.83 (t, J = 1.5 Hz, 2H), 7.45 (t, J = 1.4 Hz, 2H), 7.31 (t, J = 1.4 Hz, 1H), 7.28 (t, J = 1.4 Hz, 1H), 7.23 7.31 (t, J = 1.4 Hz, 1H), 7.00 (m, 5H), 4.36 (m, 6H), 3.97 (m, 6H), 3.17 (s, 1H), 1.78 (m, 12H), 1.50 (m, 12H), 1.00 (m, 18H); ^{13}C NMR (75 MHz) 165.07, 164.98, 164.93, 159.19, 158.80, 158.77, 138.66, 138.16, 132.97, 132.69, 132.51, 132.44, 132.24, 131.30, 131.22, 127.16, 125.35, 124.45, 124.22, 124.11, 123.92, 123.71, 123.54, 123.45, 123.37, 122.99, 118.18, 117.94, 117.86, 116.75, 93.92, 90.20, 89.42, 89.13, 88.96, 88.91, 88.88, 88.77, 87.88, 87.71, 81.68, 78.91, 67.98, 67.93, 65.41, 65.37, 31.13, 31.06, 30.68, 30.64, 19.21, 19.19, 19.15, 19.10, 13.79, 13.73, 13.70; MS (EI) calcd for $C_{75}H_{73}O_9I$ 1245.32, found 1244 (0.5%), 1245 (0.5%). Anal. Calcd for $C_{75}H_{73}O_9I$: C, 72.34; H, 5.91. Found: C, 72.28; H, 5.64.

Sequence H-EC(AC)$_2$-I was prepared from TMS-A-N_3Et_2, TMS-C-N_3Et_2, and TMS-E-N_3Et_2 (overall 51% yield). ^1H NMR (300 MHz) 8.18 (t, J = 1.5 Hz, 1H), 8.12 (t, J = 1.6 Hz, 1H), 7.92 (t, J = 1.5 Hz, 1H), 7.81 (t, J = 1.5 Hz, 1H), 7.75 (m, 2H), 7.67 (d, J = 8.0 Hz, 1H), 7.53 (m, 11H), 7.36 (m, 2H), 7.08 (t, J = 7.8 Hz), 1H), 3.95 (s, 3H), 3.15 (s, 1H), 1.37 (s, 9H), 1.36 (s, 9H); ^{13}C NMR (75 MHz), 165.50, 151.70, 140.17, 138.74, 137.31, 134.71, 132.78, 131.79, 131.40, 130.69, 129.84, 128.97, 128.54, 125.15, 123.89, 123.47, 122.98, 122.73, 93.70, 90.35, 90.10, 89.85, 89.63, 88.55, 88.37, 87.95, 78.84, 52.47, 34.73, 31.09. Anal. Calcd for $C_{58}H_{43}O_2I$: C, 77.50; H, 4.82. Found: C, 77.63; H, 5.06.

Sequence H-CE(AC)$_2$-I was prepared from TMS-A-Br, TMS-C-N_3-Et_2, and TMS-E-Et_2N_3 (overall 52% yield). ^1H NMR (300 MHz) 8.17 (t, J = 1.6 Hz, 1H), 8.15 (t, J = 1.6 Hz, 1H), 7.91 (t, J = 1.6 Hz, 1H), 7.86 (t, J = 1.5 Hz, 1H), 7.75 (t, J = 1.6 Hz, 1H), 7.68 (m, 2H), 7.53 (m, 11H), 7.33 (m, 2), 7.09 (t, J = 7.9 Hz, 1H), 3.96 (s, 3H), 3.10 (s, 3H), 1.38 (s, 9H), 1.37 (s, 9H); ^{13}C NMR (75 MHz) 166.12, 152.18, 140.57, 139.14, 137.10, 135.11, 135.07, 133.13, 132.14, 131.74, 131.18, 131.04, 130.17, 129.41, 129.33, 129.29, 129.24, 128.91, 128.84, 125.46, 123.89, 123.79, 123.31, 123.27, 93.78, 90.43, 90.18, 89.93, 89.75, 89.70, 88.64, 88.609, 88.42, 87.68, 76.53, 52.33, 34.48, 30.81; MS (EI) calcd for $C_{58}H_{43}O_2I$ 898.90, found 899 (5.5%), 898 (3.5%), 900 (1.5%), 901 (0.5%).

Sequence H-(**FA**)$_2$-I was prepared from TMS-**A**-N_3Et_2 and TMS-**F**-I (overall 40% yield). R_F 0.25 (1:7 dichloromethane–low petroleum ether); ^1H NMR (200 MHz, benzene-d_6), δ 7.94 (t, J = 1.7 Hz, 1H), 7.89 (t, J = 1.7 Hz, 1H), 7.71 (d, J = 1.6 Hz, 2H), 7.68–7.64 (m, 2H), 7.48–7.34 (m, 4H), 6.86–6.74 (m, 4H), 2.92 (s, 1H), 1.07 (s, 9H), 0.94 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 153.5, 151.6, 137.2, 135.0, 132.5, 131.82, 131.75, 131.7, 129.2, 129.0, 128.5, 128.2, 128.1, 128.0, 126.1, 125.8, 125.5, 124.7, 123.2, 123.0, 94.0, 93.4, 93.3, 92.4, 88.8, 88.0, 82.1, 81.2, 34.7, 31.1, 31.0; MS (FAB) m/e calcd for $C_{40}H_{34}I^+$ $(M+H)^+$ 641.1705, found 641.1705, 949.4 (28), 829.2 (23), 795.2 (64), 675.1 (63), 659.1 (41), 641 (49, $(M+H)^+$), 619.1 (33), 585.1 (32), 514.2 (40), 401.1 (27), 309.0 (17), 279.2 (20), 195.1 (14).

Cyclization. General Procedure. A Schlenk flask charged with triphenylphosphine (0.090 g), bis(dibenzylideneacetone)palladium(0) (0.030 g) and copper(I) iodide (0.015 g) was evacuated and back-filled with nitrogen three times. Then dry triethylamine was added to the flask. While the mixture was stirred under nitrogen at 75 °C, a solution of sequence precursor (ca. 0.400 g) in dry triethylamine (25 mL) and dry benzene (25 mL) was added to the flask by a syringe pump at a rate of ca. 2.5 mL/h. After addition, the solvent was removed with a rotary evaporator. The reaction mixture was then subject to flash chromatography, and the product was obtained with a yield of ca. 70–80%.

PAM $\overline{\text{ACACAC}}$ (**1**) (0.327 g, 0.425 mmol, 75% yield) was prepared from H-(**AC**)$_3$-I (0.509 g, 0.567 mmol). The product was purified by flash column chromatography (eluted with a 1:1 mixture of CH_2Cl_2–hexane) followed by recrystallization from benzene. ^1H NMR (200 MHz, benzene-d_6) 8.09 (t, J = 1.6 Hz, 1H), 7.98, (t, J = 1.4 Hz, 1H), 7.70 (d, J = 1.4 Hz, 1H), 7.42 (dd, J = 1.6 Hz, 7.9 Hz), 6.86 (t, J = 7.9 Hz, 1H), 1.10 (s, 9H); ^{13}C NMR (75 MHz) 151.7, 135.3, 132.4, 131.0, 128.6, 128.4, 123.6, 123.1, 89.8, 88.6, 34.8, 31.1; HRMS (EI) calcd for $C_{60}H_{48}$ 768.3756, found 768.3774. Anal. Calcd for $C_{60}H_{48}$: C, 93.71; H, 6.29. Found: C, 93.94; H, 6.33.

PAM $\overline{\text{ABABABABABAB}}$ (**2**) (0.324 g, 0.211 mmol, 70% yield) was prepared from H-(**AB**)$_6$-I (0.500 g, 0.300 mmol). The product was purified by flash column chromatography (eluted with a 1:1 mixture of CH_2Cl_2–hexane) followed by recrystallization from toluene. ^1H NMR (200 MHz, benzene-d_6) 7.84 (t, J = 1.3 Hz, 3H), 7.67 (d, J = 1.3 Hz, 6H), 7.42 (s, 12H), 1.10 (s, 27H); ^{13}C NMR (90 MHz) 151.8, 132.4, 131.6, 128.7, 123.1, 91.0, 89.2, 34.7, 31.2; MS (EI) calcd for $C_{120}H_{96}$ 1538.10, found 1537 (2.1%), 1538 (2.2%), 1539 (1.9%), 1540 (1.0%). Anal. Calcd for $C_{120}H_{96}$: C, 93.71; H, 6.29. Found: C, 93.66; H, 6.40.

PAM $\overline{\text{DDDDDD}}$ (**3**) (0.236 g, 0.228 mmol, 59%) was prepared from H-D_6-I (0.450 g, 0.388 mmol). Due to the low solubility of the product, flash column chromatography could not be performed. Instead, after cyclization, the reaction mixture was continuously washed with boiling ethanol for 24 h and then taken up to hot chloroform and decolorized with activated carbon. After removal of solvent, analytically pure product was obtained as a fairly white solid. ^1H NMR (360 MHz) 7.33 (t, J = 1.5 Hz, 6H), 7.04 (t, J = 1.5 Hz, 12 H), 4.00 (t, J = 6.5 Hz, 12H), 1.79 (m, 12H), 1.52 (m, 12H), 1.00 (t, J = 7.2 Hz, 18H); HRMS (EI) calcd for $C_{72}H_{72}O_6$ 1032.5329, found 1032.5255. Anal. Calcd for $C_{72}H_{72}O_6$: C, 83.69; H, 7.02. Found: C, 83.53; H, 6.94.

PAM $\overline{\text{EEEEE}}$ (**4**) (0.170 g, 0.170 mmol, 68% yield) was prepared from H-E_5-I (0.280 g, 0.249 mmol). The same purification method was used as for $\overline{\text{EEEEEE}}$. ^1H NMR (360 MHz, 3 mg/mL in $CDCl_3$) 8.10 (d, J = 1.6 Hz, 10H), 8.04 (t, J = 1.6 Hz, 15H), 4.38 (t, J = 6.6 Hz, 10H), 1.81 (m, 10H), 1.53 (m, 10H), 1.03 (t, J = 7.4 Hz, 5H); ^{13}C NMR (90 MHz) 164.7, 140.7, 131.3, 130.8, 123.4, 89.6, 65.4, 30.8, 19.3, 13.8; HRMS (EI) calcd for $C_{65}H_{60}O_{10}$ 1000.4186, found 1000.4262. Anal. Calcd for $C_{65}H_{60}O_{10}$: C, 77.98; H, 6.04. Found: C, 77.85; H, 6.03.

PAM $\overline{\text{EEEEEE}}$ (**5**) (0.298 g, 0.248 mmol, 82% yield) was prepared from H-E_6-I (0.400 g, 0.301 mmol). The product was purified by flash column chromatography (first eluted with pure CH_2Cl_2, then a 10:1 mixture of CH_2Cl_2–THF) followed by precipitation from the CH_2Cl_2 solution with methanol. ^1H NMR (300 MHz, 4.0 mg/mL) 7.96 (d, J = 1.5 Hz, 12H), 7.62 (t, J = 1.5 Hz, 6H), 4.35 (t, J = 6.6 Hz, 12H), 1.84 (m, 12H), 1.55 (m, 12H), 1.07 (t, J = 7.3 Hz, 18H); ^{13}C NMR (90 MHz) 164.8, 138.0, 132.2, 131.3, 123.5, 89.2, 65.4, 30.8, 19.3, 13.7; HRMS (EI) calcd for $C_{78}H_{72}O_{12}$ 1200.5023, found 1200.4927. Anal. Calcd for $C_{78}H_{72}O_{12}$: C, 77.98; H, 6.04. Found: C, 77.94; H, 6.09.

PAM $\overline{\text{EEEEEEE}}$ (**6**) (0.189 g, 0.134 mmol, 71% yield) was prepared from H-E_7-I (0.290 g, 0.190 mmol). The same purification method was

used as for EEEEEE. ^{1}H NMR (360 MHz, 2 mg/mL in $CDCl_3$) 8.17 (d, J = 1.5 Hz, 14H), 7.81 (t, J = 1.5 Hz, 7H), 4.39 (t, J = 6.6 Hz, 14H), 1.82 (m, 14H), 1.54 (m, 14H), 1.03 (t, J = 7.4 Hz, 21H); ^{13}C NMR (90 MHz) 164.7, 136.5, 132.8, 131.0, 123.4, 89.2, 65.4, 30.8, 19.2, 13.8; MS (EI) calcd for $C_{91}H_{84}O_{14}$ 1401.68, found 1400 (2.0%), 1401 (1.9%), 1402 (1.4%), 1403 (0.5%). Anal. Calcd for $C_{91}H_{84}O_{14}$: C, 77.98; H, 6.04. Found: C, 77.74; H, 6.32.

PAM DEDEDE (7) (0.191 g, 0.171 mmol, 76% yield) was prepared from H-(DE)$_3$-I (0.281 g, 0.226 mmol). The product was purified by flash column chromatography (first eluted with a 1:3 mixture, then a 1:2 mixture of CH_2Cl_2–hexane) followed by precipitation from the CH_2Cl_2 solution with methanol. ^{1}H NMR (360 MHz, 3.2 mg/mL) 8.08 (d, J = 1.5 Hz, 6H), 7.81 (t, J = 1.5 Hz, 3H), 7.28 (t, J = 1.5 Hz, 3H), 7.03 (d, J = 1.5 Hz, 6H), 4.37 (t, J = 6.5 Hz, 6H), 4.00 (t, J = 6.5 Hz, 6H), 1.81 (m, 12H), 1.50 (m, 12H), 1.02 (m, 18H); ^{13}C NMR (90 MHz) 165.1, 158.4, 138.3, 131.6, 130.5, 127.4, 123.71, 123.66, 117.6, 90.1, 88.0, 67.7, 65.1, 31.3, 30.8, 19.29, 19.23, 13.94, 13.85; MS (EI) calcd for $C_{75}H_{72}O_9$ 1117.40, found 1116 (3.1%), 1117 (2.2%), 1118 (1.2%). Anal. Calcd for $C_{75}H_{72}O_9$: C, 80.62; H, 6.49. Found: C, 80.54; H, 6.39.

PAM DDDEEE (8) (0.138 g, 0.124 mmol, 73% yield) was prepared from H-D$_3$E$_3$-I (0.210 g, 0.169 mmol). The product was purified by flash column chromatography (first eluted with a 1:3, then a 1:2 mixture of CH_2Cl_2–hexane) followed by precipitation from the CH_2Cl_2 solution with methanol. ^{1}H NMR (360 MHz, 5.0 mg/mL) 8.11 (d, J = 1.5 Hz, 2H), 8.08 (m, 4H), 7.79 (m, 6H), 7.25 (m, 6H), 6.98 (m, 4H), 6.94 (d, J = 1.5 Hz, 2H), 4.38 (m, 6H), 3.96 (m, 6H), 1.81 (m, 12H), 1.53 (m, 12H), 1.02 (m, 18H); ^{13}C NMR (90 MHz) 165.05, 165.01, 158.39, 158.35, 138.3, 131.9 (m), 130.7, 127.5, 124.0 (m), 123.5 (m), 117.6, 117.3, 90.30, 89.21, 89.02, 88.99, 88.82, 87.77, 67.74, 67.68, 65.30, 65.24, 31.3, 31.7, 19.29, 19.22, 13.93, 13.85; MS (EI) calcd for $C_{75}H_{72}O_9$ 1117.40, found 1116 (3.3%), 1117 (2.7%), 1118 (1.5%). Anal. Calcd for $C_{75}H_{72}O_9$: C, 80.62; H, 6.49. Found: C, 80.59; H, 6.36.

PAM ECACAC (9) (0.216 g, 0.283 mmol, 73% yield) was prepared from H-EC(AC)$_2$-I (0.345 g, 0.384 mmol). The product was purified by flash column chromatography (eluted with a 1:1 mixture of CH_2Cl_2–hexane) followed by precipitation from the CH_2Cl_2 solution with methanol. ^{1}H NMR (300 MHz) 8.15 (d, J = 1.6 Hz, 2H), 7.89 (t, J = 1.5 Hz, 1H), 7.75 (m, 3H), 7.53 (m, 10H), 7.36 (m, 4H), 3.94 (s, 3H), 1.38 (s, 18H); ^{13}C NMR (90 MHz) 165.72, 151.82, 138.75, 135.34, 134.37, 134.22, 132.52, 132.06, 131.46, 131.25, 131.07, 129.70, 128.68, 128.61, 128.51, 124.11, 123.80, 123.71, 123.20, 123.13, 90.21, 90.03, 89.89, 88.72, 88.58, 88.32, 52.37, 34.79, 31.17; HRMS (EI) calcd for $C_{58}H_{42}O_2$ 770.3185, found 770.3136. Anal. Calcd for $C_{58}H_{42}O_2$: C, 90.36; H, 5.49. Found: C, 89.98; H, 5.67.

PAM CEACAC (10) (0.181 g, 0.235 mmol, 70% yield) was prepared from H-CE(AC)$_2$-I (0.302 g, 0.336 mmol). The product was purified by flash column chromatography (eluted with a 1:1 mixture of CH_2Cl_2–hexane) followed by precipitation from the CH_2Cl_2 solution with methanol. ^{1}H NMR (300 MHz) 8.11 (m, 2H), 7.85 (m, 1H), 7.73 (m, 3H), 7.46 (m, 10H), 7.32 (m, 4H), 3.96 (s, 3H), 1.39 (s, 9H), 1.39 (s, 9H); ^{13}C NMR (90 MHz) 165.71, 151.83, 151.71, 138.75, 135.35, 135.25, 132.57, 132.51, 132.00, 131.94, 131.49, 131.33, 131.20, 131.14, 131.07, 128.88, 128.78, 128.64, 128.49, 124.22, 124.06, 123.73, 123.53, 123.26, 123.20, 122.84, 90.83, 90.20, 89.96, 89.87, 89.48, 89.24, 88.84, 88.72, 88.42, 88.79, 52.34, 34.79, 31.19; HRMS (EI) calcd for $C_{58}H_{42}O_2$ 770.3185, found 770.3200.

PAM AFAF (11) (0.061 g, 0.119 mmol, 80% yield) was prepared from H-(FA)$_2$-I (0.092 g, 0.144 mmol). The product was purified by flash column chromatography (eluted with a 1:7 mixture of CH_2Cl_2–low petroleum ether) followed by precipitation from the CH_2Cl_2 solution with methanol. R_F 0.22 (1:7, dichloromethane–low petroleum ether); ^{1}H NMR (400 MHz, benzene-d_6) δ 8.32 (br t, 2H), 7.68 (d, J = 1.2 Hz, 4H), 4.54 (dd, 4H), 6.83 (dd, 4H), 1.07 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 132.9, 131.8, 128.7, 128.1, 125.7, 123.2, 93.2, 88.4, 34.8, 31.1; MS (EI 70 eV) m/e calcd for $C_{40}H_{32}^+$ 512.2504, found 512.2512; 512 (100), 440 (9), 424 (9), 411 (5), 400 (15), 256 (6), 241 (16), 227 (7), 213 (10), 205 (4), 57 (84), 41 (14).

Functional Group Transformations. PAM EEEEEE (13). To a solution of EEEEEE (5) (0.120 g, 0.10 mmol) in dichloromethane (10 mL) and 1-octanol (10 mL) was added potassium carbonate (20 mg) and 18-crown-6-ether (5 mg). After the mixture was stirred at 40 °C for 12 h, the solvents were removed under vacuum, and fresh solvents (dichloromethane and octanol) were added. The mixture was stirred for another 12 h, and the solvents were removed again under vacuum. The residual was dissolved in dichloromethane and filtered through a plug of silica gel. Concentration followed by precipitation with methanol gave as a white solid (0.131 g, 0.085 mmol, 85% yield). ^{1}H NMR (300 MHz) 8.04 (d, J = 1.5 Hz, 12H), 7.72 (t, J = 1.5 Hz, 6H), 4.35 (t, J = 6.8 Hz, 12H), 1.83 (m, 12H), 1.40 (m, 60H), 0.89 (t, J = 7.0 Hz, 18H); ^{13}C NMR (90 MHz) 164.6, 137.9, 132.0, 131.0, 123.3, 89.2, 65.7, 31.9, 29.7, 29.3, 28.7, 26.0, 22.7, 14.1; MS (EI) calcd for $C_{102}H_{120}O_{12}$ 1538.09, found 1537 (2.1%), 1538 (2.2%), 1539 (1.9%), 1540 (1.0%), 1541 (0.6%). Anal. Calcd for $C_{102}H_{120}O_{12}$: C, 79.65; H, 7.86. Found: C, 79.57; H, 8.09.

PAM GGGGGG (15). To a solution of EEEEEE (5) (0.240 g, 0.20 mmol) in dry benzene (3 mL) and THF (3 mL) was added a diisopropyl aluminum hydride solution in hexane (1.0 M, 4.8 mL) in the drybox at room temperature. After the solution was stirred for 2 h, a mixture of methanol (10 mL) and water (10 mL) was added slowly. Then the solvent was removed under vacuum and the residual solid was taken up to DMF and filtered through a plug of silica gel. After removal of DMF under vacuum, a fairly white solid was obtained (0.095 g, 0.122 mmol, 61% yield). ^{1}H NMR (300 MHz, DMSO-d_6) 7.65 (s, 6H), 7.54 (s, 12H), 5.42 (t, J = 5.6 Hz, 6H), 4.54 (d, J = 5.6 Hz, 12H); ^{13}C NMR (90 MHz, DMSO-d_6) 144.2, 132.7, 129.3, 122.4, 89.0, 61.9.

PAM HHHHHH (16). A solution of GGGGGG (0.156 g, 0.20 mmol) in DMF (10 mL) with 1-bromobutane (10 mL), potassium hydroxide (5 g), and 18-crown ether (10 mg) was stirred at 90 °C for 12 h. After workup with water and extraction with dichloromethane followed by concentration and precipitation with methanol three times, flash column chromatography afforded HHHHHH as a white solid (0.112 g, 0.10 mmol, 50% yield). ^{1}H NMR (360 MHz) 7.66 (t, J = 1.5 Hz, 6H), 7.48 (d, J = 1.5 Hz, 12H), 4.51 (s, 12H), 3.51 (t, J = 6.6 Hz, 12H), 1.65 (m, 12H), 1.43 (m, 12H), 0.95 (t, J = 7.4 Hz, 18H); ^{13}C NMR (90 MHz) 139.6, 134.3, 130.2, 123.5, 89.2, 72.0, 70.5, 31.8, 19.4, 14.0; MS (EI) calcd for $C_{78}H_{84}O_6$ 1117.54, found 1116 (1.6%), 1117 (1.5%), 1118 (0.8%). Anal. Calcd for $C_{78}H_{84}O_6$: C, 83.83; H, 7.58. Found: C, 83.73; H, 7.59.

PAM IIIII (17). To a suspension of DDDDDD (0.207 g, 0.20 mmol) in 1,2-dichloroethane (10 mL) was added boron tribromide (1 M in dichloromethane, 4 mL) dropwise in the drybox. Upon the addition, the suspension gradually turned homogeneous, and the reaction mixture was stirred at room temperature for an additional 12 h. After the removal of dichloromethane and the excess tribromide, triethylamine was introduced to the reaction mixture and then removed under vacuum. The final residual was dissolved in potassium hydroxide (w/w 10%) and was precipitated with HCl (6 N). After centrifuging, the precipitate was redissolved in ethanol and filtered through a plug of silica gel. Removal of ethanol afforded IIIII as a white solid (0.084 g, 60% yield). ^{1}H NMR (360 MHz, DMSO-d_6) 10.10 (br, 6H), 7.20 (s, 12H), 6.98 (s, 6H); ^{13}C NMR (90 MHz, DMSO-d_6) 157.5, 125.5, 123.4, 118.4, 88.5.

PAM JJJJJJ (18). To a solution of IIIII (0.070 g, 0.10 mmol) in DMSO (2 mL) was added valeric acid (0.5 mL), 1,3-dicyclohexylcarbodiimide (DCC, 0.031 mg, 0.45 mmol), a catalytic amount of 4-(dimethylamino)pyridinium-4-toluenesulfonate (DPTS), and dichloromethane (2 mL). The mixture was then stirred at room temperature for 3 h. After removal of insoluble byproduct, the solution was worked-up with water and extracted into dichloromethane. The organic layer was then dried over sodium sulfate and concentrated. The residual was subjected to flash chromatography, and JJJJJJ was obtained as a white solid (0.107 g, 89%). ^{1}H NMR (360 MHz): 7.53 (t, J = 1.6 Hz, 6H), 7.19 (d, J = 1.6 Hz, 12H), 2.58 (t, J = 7.4 Hz, 12H), 1.84 (m, 12H), 1.55 (m, 12H), 1.07 (t, J = 7.3 Hz, 18H); ^{13}C NMR (90 MHz) 171.4, 150.7, 132.5, 124.7, 124.3, 89.1, 34.1, 27.0, 22.2, 13.6; MS (EI) calcd for $C_{78}H_{72}O_{12}$ 1201.44, found 1201 (0.1%), 1202 (0.1%). Anal. Calcd for $C_{78}H_{72}O_{12}$: C, 77.98; H, 6.04. Found: C, 77.78; H, 6.28.

PAM DDDDDD (23). A solution of IIIII (0.070 g, 0.10 mmol) in DMF (5 mL) with 1-bromoheptane (0.5 mL) and potassium carbonate (0.5 g) was refluxed at 90 °C for 20 h. After workup with water and extraction with dichloromethane, flash column chromatography afforded KKKKKK as a white solid (0.090 g, 0.070 mmol, 70% yield). ^{1}H NMR

(360 MHz) 7.32 (t, J = 1.6 Hz, 6H), 7.03 (d, J = 1.6 Hz, 12H), 4.00 (t, J = 7.7 Hz, 12H), 1.81 (m, 12H), 1.42 (m, 48H), 0.91 (t, J = 8.1 Hz, 18H); ^{13}C NMR (90 MHz) 159.1, 128.1, 124.5, 118.0, 89.1, 68.6, 31.8, 29.3, 29.0, 26.0, 22.6, 14.0; HRMS (EI) calcd for $C_{90}H_{108}O_6$ 1284.8145, found 1284.8060. Anal. Calcd for $C_{90}H_{108}O_6$: C, 84.07; H, 8.45. Found: C, 83.73; H, 8.30.

Acknowledgment is made to the National Science Foundation for support through Grant CHE-9202095 and the NSF Young Investigator Program, Grant CHE-9257050 (1992–97). J.S.M. also thanks the 3M Company for support through their nontenured faculty awards program.

Supplementary Material Available: Scheme 1, experimental details for monomer syntheses, a table of SEC data and elemental analysis data for sequences of TMS-(**AB**)$_n$-I (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.