

Shape-Persistent Molecular Architectures of Nanoscale Dimension

JEFFREY S. MOORE*

Departments of Chemistry and Materials Science & Engineering and The Beckman Institute for Advanced Science and Technology, University of Illinois, Urbana, Illinois 61801

Received April 23, 1997

Introduction

While there can be no questioning the importance of synthetic polymeric materials, it is worth remembering that these substances are chemical mixtures and that mixtures are fundamentally different from pure substances. In many ways, the distinction between mixtures and pure substances lies at the root of the historical separation of organic and polymer chemistry. It is interesting to briefly examine how this separation came to be. In 1907, at a time when many chemists believed that high molecular weight organic molecules simply did not exist, Emil Fischer succeeded in preparing a polypeptide chain of 18 amino acid residues.¹ Fischer wrote, "In studying substances of high molecular weight, molecular physics should restrict itself to synthetic products of known structure. I shall therefore continue experiments on the build-up of giant molecules."² Fischer apparently held the belief that, just as physical chemistry is concerned with the details of atomic and molecular structure, synthetic organic chemistry should strive to clarify the limits of molecular size.

It was 1920 when Staudinger proposed the existence of "*hochmolekulare Verbindungen*,"³ and within the short span of seven years, he unambiguously established this hypothesis.⁴ Soon after, the practical and industrial significance of these materials became apparent and synthetic efforts to make discrete, high molecular weight products of known structure lost appeal. Industrial polymer chemist Wallace Carothers set the agenda for the next 60 years. In a *Chemical Reviews* article titled "Polymerization" published in 1931, Carothers wrote, "The step-by-step synthesis of long molecular chains containing a repeating unit is illustrated by Fischer's synthesis of polypeptides. Reactions of polymerization, however, lead to the formation of polymeric chains in a single operation.... It is true that synthetic linear high polymers are invariably mixtures whose molecules are chains of slightly

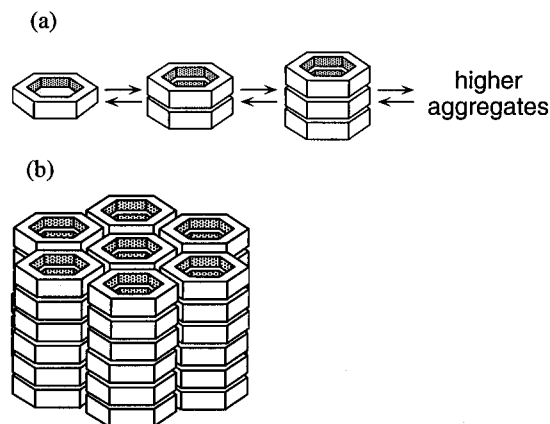


FIGURE 1. Schematic representation of (a) the solution aggregation of hexakis(phenylacetylene) macrocycles and (b) columnar hexagonal order exhibited by hexakis(phenylacetylene) macrocyclic mesogens.

Table 1. Comparison of Monodendron Yields Prepared by Scheme 1 and Scheme 7

generation	monodendron	yield (%)	
		Scheme 1	Scheme 7
1	3-mer	93	88
2	7-mer	80	82
3	15-mer	51	84
4	31-mer	27	81
5	63-mer	0	85

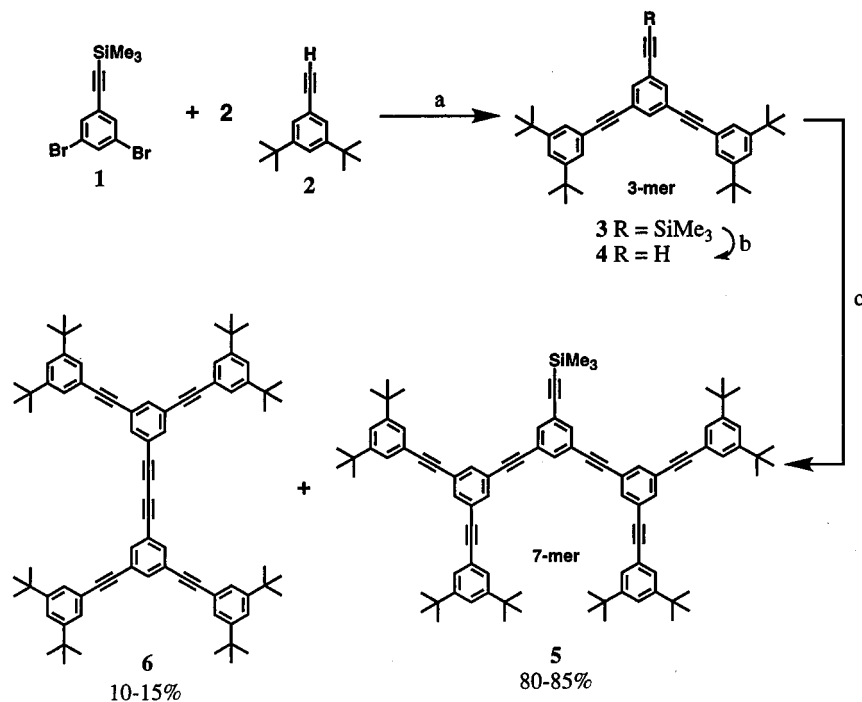
differing lengths.... Nevertheless, it must be admitted that a molecule does not lose any of its definiteness as an entity [because] it cannot be completely separated from other similar but slightly different molecules."⁵ So began the polymer industry, leaving mostly only those chemists interested in biopolymers to study discrete, high molecular weight substances. Fortunately, the situation changed dramatically in 1985, when Don Tomalia and George Newkome disclosed their invention of dendritic macromolecules,^{6,7} paving the way for us and others to revisit Fischer's vision of high molecular weight "products of known structure."

For large, conformationally flexible molecules used as bulk materials such as most all commercial polymers, Carothers' convictions on the suitability of mixtures can hardly be questioned. However, for large molecules that have *shape-persistent architectures*, there may be many good reasons to prepare them as pure substances. They may, for example, offer special opportunities in the area of supramolecular chemistry or in the quest for devices that function on the basis of single molecular events. The potential of mesoscopic and macromolecular structures in supramolecular chemistry is instantly evident upon inspection of almost any process in molecular biology. Biomolecular systems rely heavily on van der Waals and

Jeffrey S. Moore was born outside of Joliet, IL, in 1962. After receiving his B.S. in chemistry from the University of Illinois (1984), he completed his Ph.D. in Materials Science and Engineering, also at the University of Illinois, with Samuel Stupp (1989). He then went to Caltech as an NSF postdoctoral fellow to study with Robert Grubbs. In 1990 he joined the chemistry faculty at the University of Michigan in Ann Arbor. He returned to the University of Illinois in 1993, where he is currently a Professor of Chemistry and Materials Science and Engineering. In 1995 he became a part-time Beckman Institute faculty member, where he now serves as a co-chairman of the Molecular and Electronic Nanostructures Main Research Theme.

* Phone: (217) 244-4024. FAX: (217) 244-8068. E-mail: moore@aries.scs.uiuc.edu.

- (1) Fischer, E. *Ber. Dtsch. Chem. Ges.* **1907**, *40*, 1754.
- (2) Morawetz, H. *Polymers: The Origins and Growth of a Science*; Wiley-Interscience: New York, 1985.
- (3) Staudinger, H. *Ber. Dtsch. Chem. Ges.* **1920**, *53*, 1073.
- (4) Staudinger, H.; Johner, H.; Signer, H.; Mie, G.; Hengstenberg, J. Z. *Phys. Chem. Stöchiom. Verwandtschaftsl.* **1927**, *126*, 425.
- (5) Carothers, W. H. *Chem. Rev.* **1931**, *8*, 353.
- (6) Tomalia, D. A.; Baker, H.; Dewald, J. R.; Hall, M.; Kallos, G.; Martin, S.; J., R.; Ryder, J.; Smith, P. *Polymer J. (Tokyo)* **1985**, *17*, 117.
- (7) Newkome, G. R.; Yao, Z.-Q.; Baker, G. R.; Gupta, V. K. *J. Org. Chem.* **1985**, *50*, 2003.

Scheme 1^a

^a Conditions: (a) $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PPh}_3/\text{Et}_3\text{N}/75^\circ\text{C}$ (93%). (b) $\text{K}_2\text{CO}_3/20^\circ\text{C}$ MeOH/ CH_2Cl_2 . (c) 2.1 equiv of **4**/ $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PPh}_3/\text{Et}_3\text{N}/75^\circ\text{C}$.

hydrophobic interactions for self-organization, but such interactions have been difficult to use by design in synthetic systems. Perhaps, by engineering large, information-rich molecular surfaces in shape-persistent molecules, it will become possible to use collections of these weak, nondirectional forces in a more controlled way. Thus, if we are to assemble chemical species that possess the structural and functional complexity of biological macromolecules, or if we are interested in exploiting single molecules in device applications, it is desirable to have large molecules that possess homogeneity at the levels of composition and constitution, as well as conformation.

The “poly” “mer” construction approach, i.e., the buildup of molecular structure from a common repeating unit, offers synthetic economy while allowing for enormous structural variation through pendant group modification. Nowhere is this more evident than by considering that all of the diversity in structure and function exhibited by biological macromolecules is realized from just three backbone constitutions. With this model as a guide, a pertinent question is then, “What is a suitable non-natural platform on which to base a new building block set?” This article describes synthetic methods that allow for the versatile and efficient construction of oligo- and macromolecular architectures from phenylacetylene monomers. Recognizing the advantages of stepwise, repetitive syntheses that follow geometric progressive growth, we developed chemistry leading to both straight chain and branched, monodisperse, sequence-specific oligomers and polymers. Acetylene-based macromolecules share features common to the best-known natural macromolecular systems, such as nucleic acids and proteins, in that they have a high level of shape persistence and many architectural variations can be realized by the ordered catenation of a small set of monomers.

Hydrocarbon Dendrimers by the Convergent Method

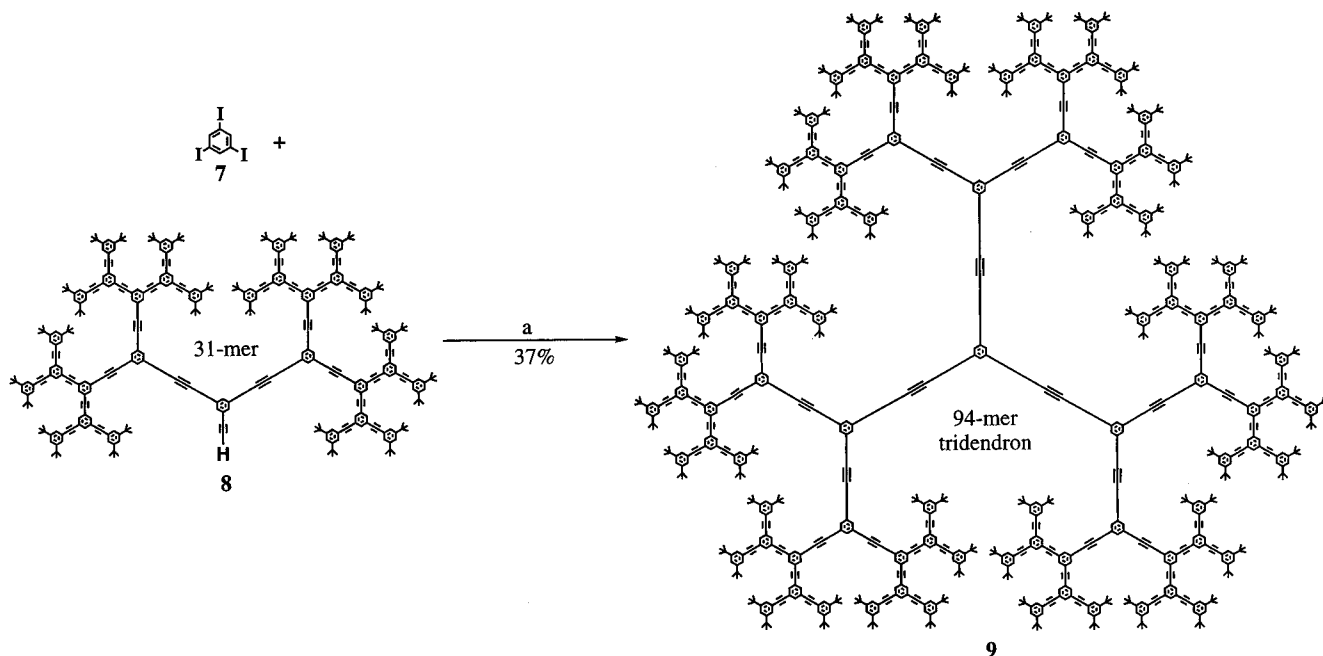
In October of 1990, my group at the University of Michigan initiated a program of research on the preparation and study of stiff, carbon-rich dendrimers with the hope that these molecules might possess a highly defined three-dimensional shape within a few generations of growth. The convergent method for synthesizing dendrimers had recently been reported by Hawker and Fréchet,⁸ and this appeared to be the best method for making well-defined structures. Dibromophenylacetylene **1** was readily synthesized and appeared to meet the criteria of a suitable “AB₂” monomer for convergent construction. The iterative chemistry involved palladium-catalyzed cross-coupling followed by deprotection of the focal point trimethylsilyl group.⁹ Early efforts were hampered by poor solubility of the growing monodendrons and by the low intrinsic reactivity of dibromo monomer **1**. Many of our early attempts to obtain even the third-generation dendrimer (a 15-mer) from **1** failed for these reasons. At that time, we speculated on the possibility that steric inhibition around the focal point must be more severe in rigid dendrimers,⁹ but as described below, this turns out not to be as significant as we first thought.

The solubility problem was solved by my graduate student Zhifu Xu, who examined a variety of peripheral groups and found that monodendrons containing 3,5-di-*tert*-butylbenzene termini maintained good solubility throughout all of the early generations (Scheme 1).¹⁰ Interestingly, and to our delight, solubility increased with increasing generation beyond the 15-mer. Despite their large aromatic content, the higher-generation dendrimers were quite soluble in a variety of solvents including

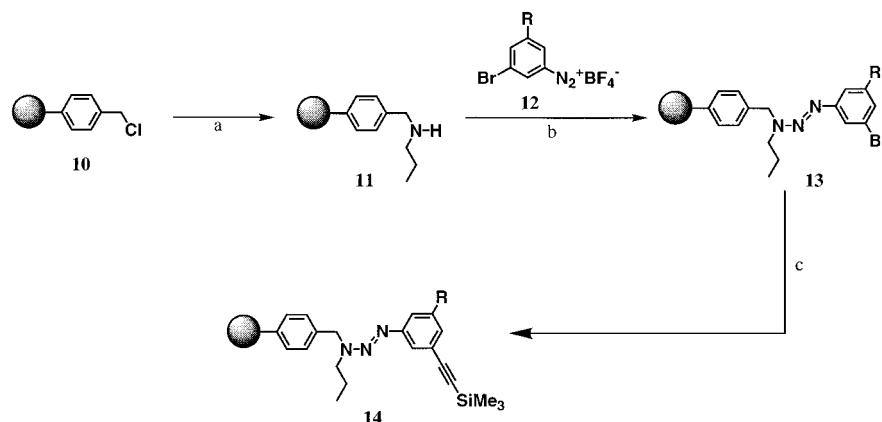
(8) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638.

(9) Moore, J. S.; Xu, Z. *Macromolecules* **1991**, *24*, 5893.

(10) Xu, Z.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 246.

Scheme 2^a

^a Conditions: (a) $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PPh}_3/\text{Et}_3\text{N}/40\text{ }^\circ\text{C}/2\text{ d}$.

Scheme 3^a

^a Conditions: (a) *n*-propylamine (neat)/70 °C/5 d. (b) $\text{K}_2\text{CO}_3/\text{DMF}/0\text{ }^\circ\text{C}$, 2 h. (c) $[\text{Pd}_2(\text{dba})_3]/\text{PPh}_3/\text{CuI}$, Et_3N , $\text{H}=\text{SiMe}_3$.

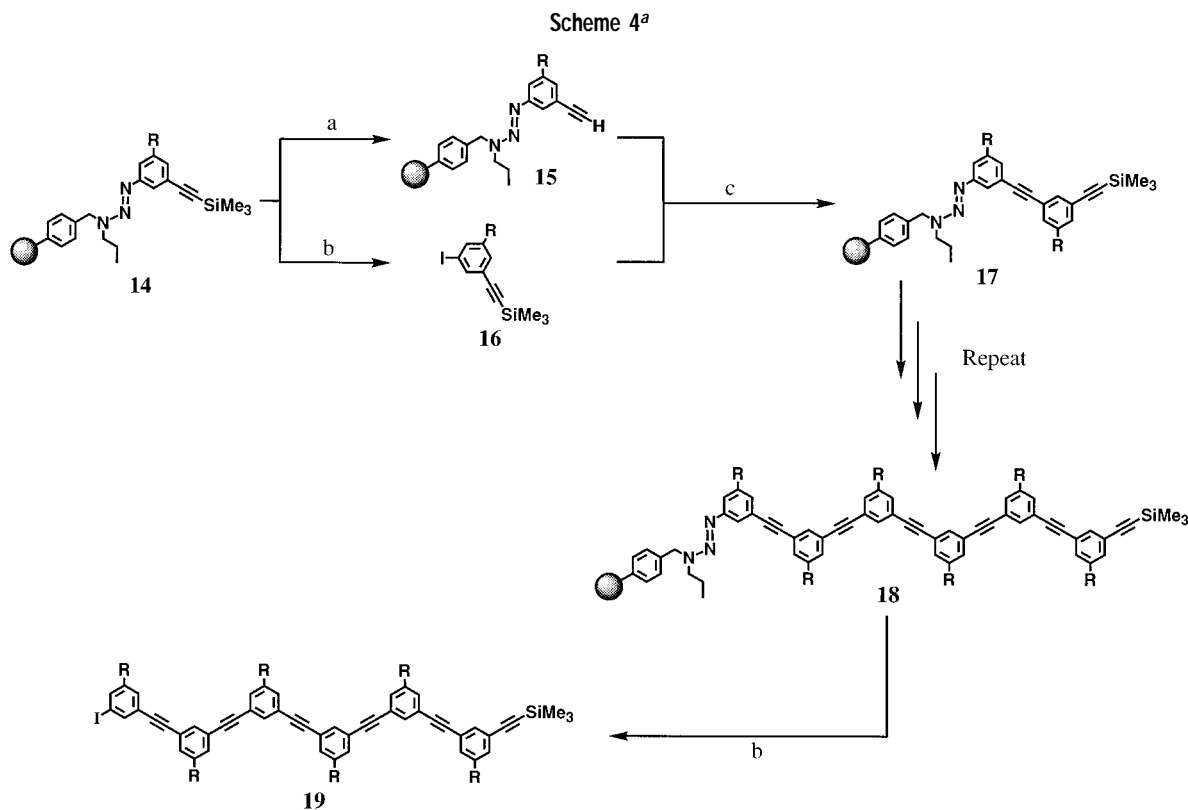
pentane. The solubility of the reaction products made it possible to elucidate the chemical structure of the major side reactions. We discovered that the only significant side reaction involved the oxidative dimerization of the monodendrons to give symmetrical diacetylenes (e.g., **6**). Surprisingly, the amount of these diacetylene byproducts increased with each generation and resulted in a dramatic reduction in monodendron yield (Table 1). We managed to prepare small quantities of the fourth-generation (31-mer) monodendron (**8**) using Scheme 1, but all attempts to continue this process to make higher generations failed. Changes in reactivity as a function of size are relatively rare among polymers,¹¹ and it is surprising that such behavior was observed so early in dendritic growth. Our original notion was to alleviate the crowding around the focal point by using expanded monomers.⁹ While this approach was successful, we later learned that the problem could be solved by using more reactive, iodo-bearing focal point monomers instead of dibromide **1**. The

importance of aryl iodides was realized when we found that the 94-mer tridendron **9** could be prepared in 37% by coupling monodendron **8** with triiodobenzene (Scheme 2),¹⁰ while the smaller 63-mer monodendron could not be synthesized from **8** and dibromide **1**. Molecular models indicate that tridendron **9** possesses a globular shape with a diameter of roughly 55 Å.

Rigorous characterization of the 94-mer tridendron, a 14.8 kDa $\text{C}_{1134}\text{H}_{1146}$ hydrocarbon, proved to be an arduous task. After extensive experimentation, conditions were found which gave good proton chemical shift dispersion, making it possible to observe each concentric layer. A small singlet was observed which integrated to three protons consistent with that expected for the central core.¹⁰ To prove this assignment, a 94-mer tridendron labeled with a deuterated core was synthesized from **7-*d***.¹² The small singlet in the ^1H NMR was absent from this deuterated analogue, while the remainder of the spectrum was identical to the original material. Shortly

(11) Flory, P. J. *Principles of Polymer Chemistry*; University Press: Ithaca, NY, 1953.

(12) Xu, Z.; Kahr, M.; Walker, K. L.; Wilkins, C. L.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4537.

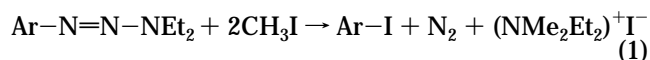


^a Conditions: (a) TBAF/THF/1 min. (b) CH₃I/110 °C. (c) [Pd₂(dba)₃]/PPh₃/CuI/Et₃N.

after we communicated the synthesis of **9** in the spring of 1993,¹⁰ I was contacted by Professor Charles Wilkins of the University of California at Riverside, who suggested that we collaborate on the characterization of these hydrocarbon dendrimers by mass spectrometry. The timing of his suggestion could not have been better since we were fast exceeding the limits of NMR to elucidate chemical structure. Professor Wilkins used several mass spectral techniques including matrix-assisted ultraviolet laser desorption (MALDI-TOF) and direct and silver chemical ionization infrared laser desorption Fourier transform mass spectrometry (LD-FTMS and LDCI-FTMS) to provide convincing evidence that we had been successful in preparing compositionally homogeneous substances, rather than mixtures.¹³

Oligomers and Macrocycles by Repetitive Methods

At the time we started our dendrimer program, we began a parallel effort using repetitive methods to synthesize linear oligomers from related phenylacetylene monomers. To construct these oligomers by the most efficient process, a set of complementary protecting groups for both partners of the cross-coupling reaction was required. Fortunately, we identified early on that *N,N*-dialkylaryl-triazenes could be transformed to aryl iodides in high yield by treatment with iodomethane at ca. 100 °C (eq 1).^{14,15}



(13) Walker, K. L.; Kahr, M. S.; Wilkins, C. L.; Xu, Z.; Moore, J. S. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 731.

(14) Moore, J. S.; Weinstein, E. J.; Wu, Z. *Tetrahedron Lett.* **1991**, *32*, 2465.

The triazene group served the role of a diazonium equivalent and was stable to conditions used in cross-coupling as well as those used to unmask the terminal alkyne. Since the trimethylsilyl group proved to be stable to the conditions used in the triazene to iodide transformation, a reasonable set of complementary protecting groups was in hand.

The growth of sequence-specific phenylacetylene oligomers by these methods is an efficient process. While our original procedures were carried out in solution,¹⁶ Jim Nelson and Jim Young in my laboratory at the University of Illinois developed solid-phase methods to simplify purification and increase the rate at which these oligomers could be produced.^{17,18} Scheme 3 shows the chemical reactions we used to initiate oligomer growth on the solid support. Propylbenzylamine **11** is readily obtained from Merrifield's resin¹⁹ as indicated, and this serves as an efficient reagent to sequester "start-monomer" **12**, which when applied to the resin in the form of a diazonium salt links directly to the support through triazene group (**13**). Reaction of this aryl halide with trimethylsilylacetylene produces a support-bound bifunctional monomer. Elaboration of the repetitive steps shown in Scheme 4 produces discrete oligomers containing up to 32 monomers in high purity. Thus, cleavage of the triazene tether produces iodoarene **16**, while briefly washing the support with tetrabutylammonium fluoride produces **15**. Coupling these two monomers generates dimer **17** functionalized

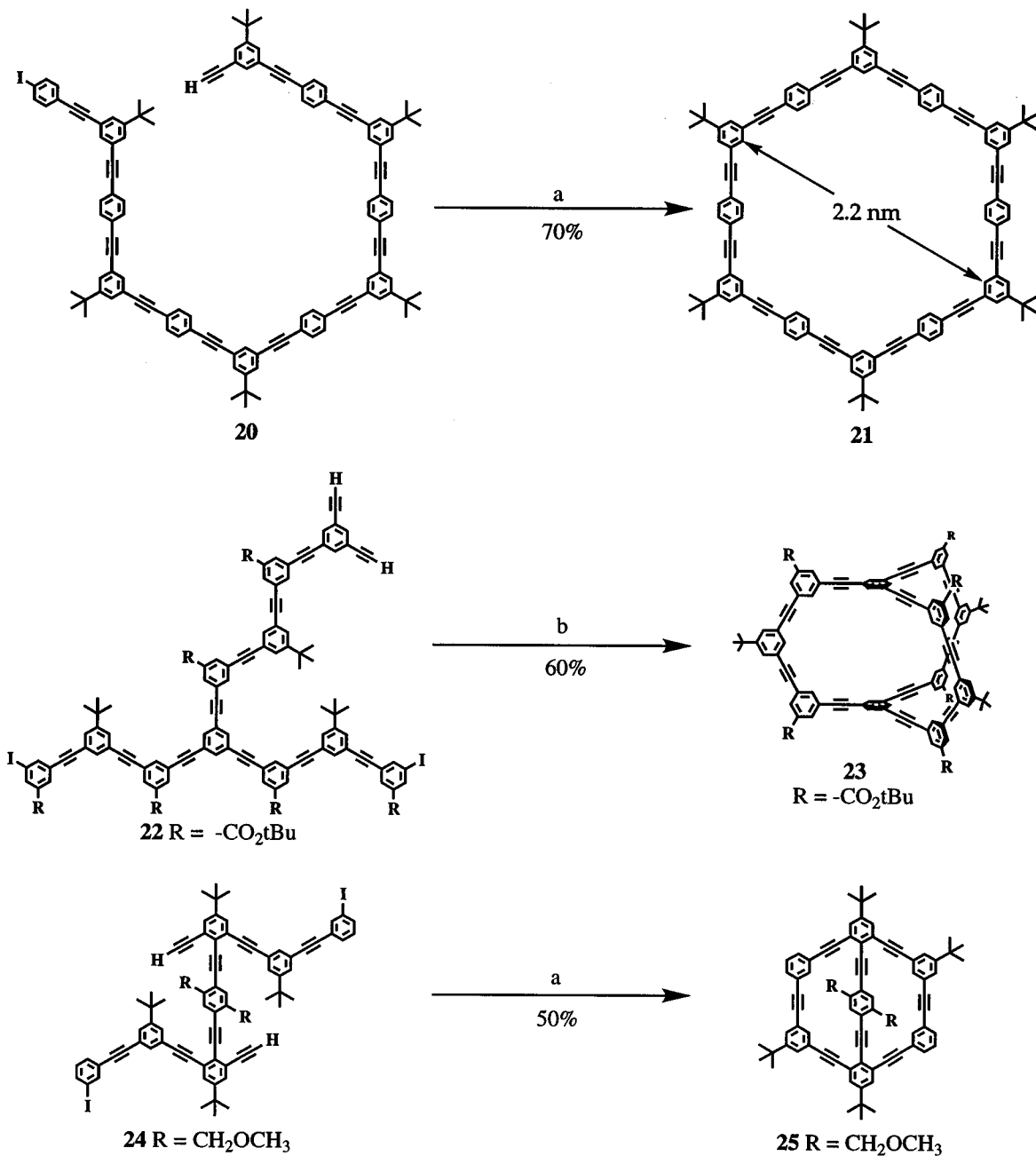
(15) Wu, Z.; Moore, J. S. *Tetrahedron Lett.* **1994**, *35*, 5539.

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

(17) Young, J. K.; Nelson, J. C.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 10841.

(18) Nelson, J. C.; Young, J. K.; Moore, J. S. *J. Org. Chem.* **1996**, *61*, 8160.

(19) Merrifield, R. B. *J. Am. Chem. Soc.* **1963**, *85*, 2149–2154.

Scheme 5^a

^a Conditions: (a) [Pd₂(dba)₃]/PPh₃/CuI/Et₃N/70 °C. (b) [Pd₂(dba)₃]/PPh₃/CuI/Et₃N/C₆H₆/70 °C.

in the same way as **14**. This same sequence of reactions can be repeated to obtain a support-bound tetramer. Hexamer **18** can then be prepared by reacting the supported tetramer with the iodo-terminated dimer derived from **17**. Each step of the sequence can be followed by infrared analysis directly on the solid support to help ensure the integrity of the growing oligomer.

These sequence-specific oligomers have proven to be extremely valuable in the preparation of large, site-specifically functionalized and geometrically controlled macrocycles such as **21** (Scheme 5). As first demonstrated by Jin Zhang, dropwise addition of α - ω -functionalized oligomers to an active solution of a palladium catalysts gives macrocycles in good yield.^{20,21} Macrocycles such

as **23** and **25** are readily prepared by double cyclization of branched sequences **22** and **24**.^{22,23} Even more complex macrocyclic topologies such as tricycle **29**, synthesized by Ziyang Wu, are possible by these methods (Scheme 6).²⁴ By inspection of molecular models, one realizes that **29** possesses an unusual conformational behavior in that it can be folded down flat by a hinged-like motion that involves concerted rotation about the eight parallel bonds. In the key step, 9-mer **26** was combined with 9-mer **27** under conditions that permitted bimolecular coupling of the two halves, followed by intramolecular cyclization in the same flask. Deprotection of **28** followed by cyclization yielded **29** as the only possible topological isomer. The

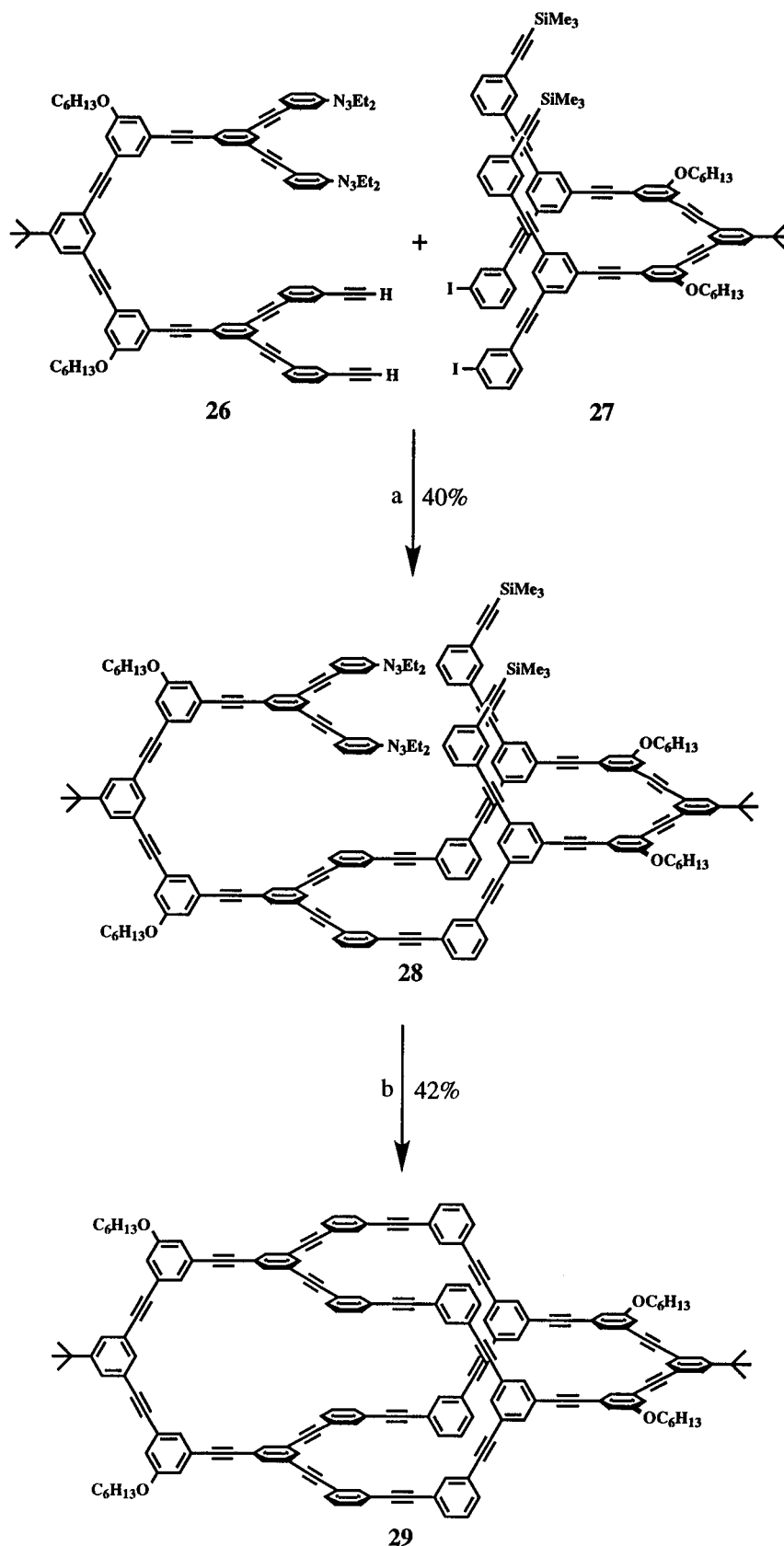
(20) Moore, J. S.; Zhang, J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 922.

(21) Zhang, J.; Pesak, D. J.; Ludwick, J. J.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 4227.

(22) Wu, Z.; Lee, S.; Moore, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 8730.

(23) Bedard, T. C.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 10662.

(24) Wu, Z.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 297.

Scheme 6^a

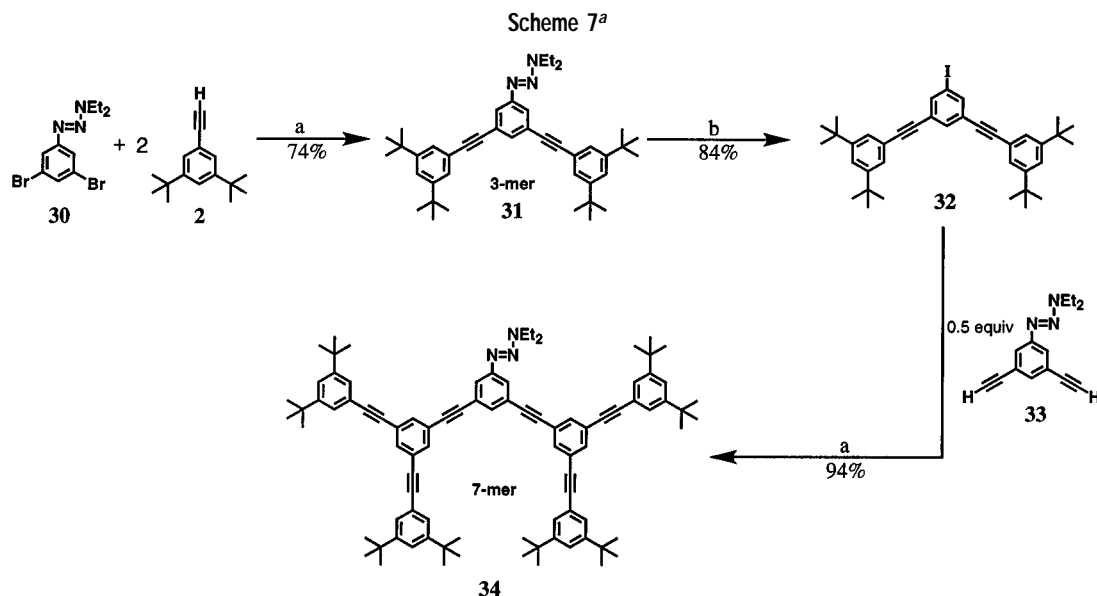
^a Conditions: (a) [Pd₂(dba)₃]/PPh₃/CuI/Et₃N/45 °C. (b) (i) MeI/100 °C. (ii) K₂CO₃ (cat.) MeOH/CH₂Cl₂. (iii) [Pd₂(dba)₃]/PPh₃/CuI/Et₃N/PhCH₃/70 °C.

symmetry of the structure was confirmed by ¹H NMR, and the composition was determined by mass spectrometry.

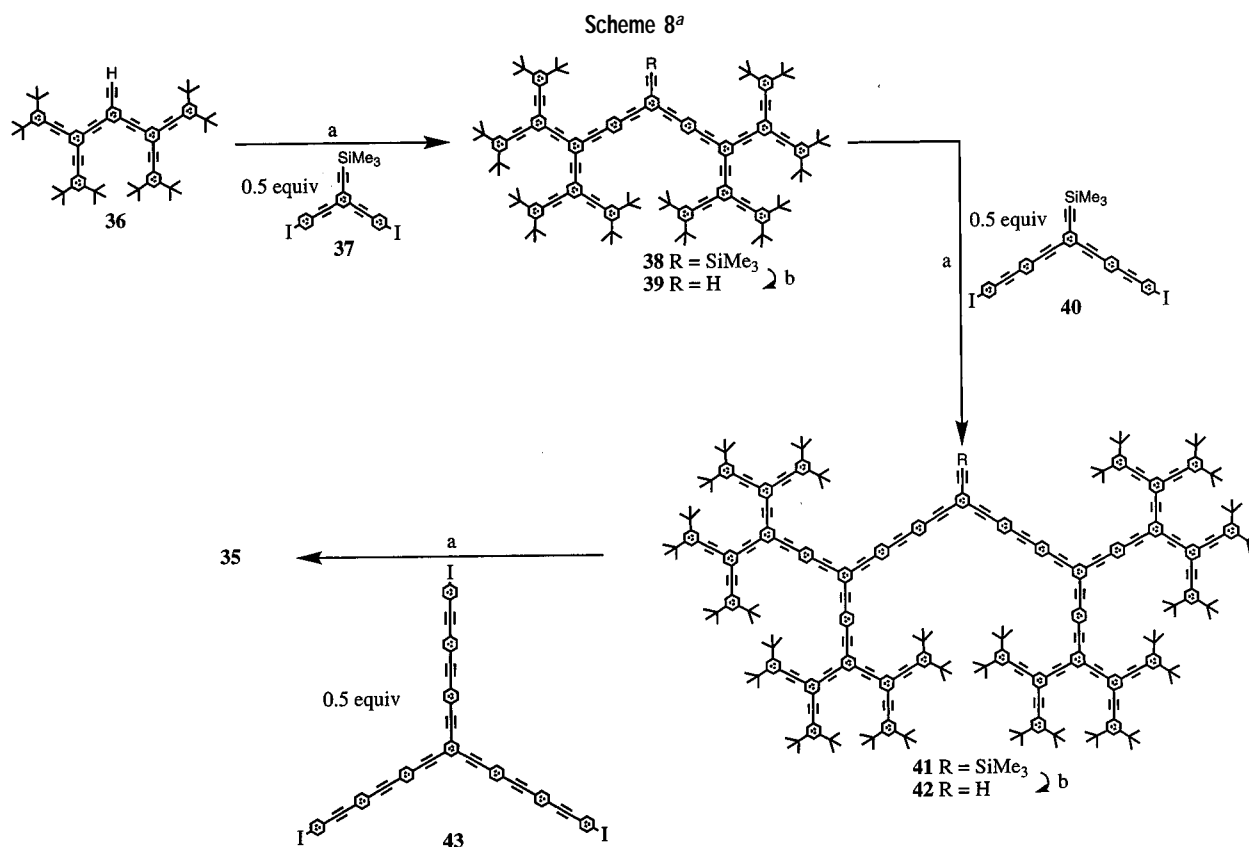
Many of the macrocycles prepared by these methods have shown interesting and sometimes unique behavior. One surprising observation was the discovery that hexakis-

(phenylacetylene) macrocycles aggregate in solution to a degree that is readily observable by ¹H NMR.²⁵ While the geometry of these aggregates is not known for certain,

(25) Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1992**, *114*, 9701.



^a Conditions: (a) $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PPh}_3/\text{Et}_3\text{N}/75^\circ\text{C}$. (b) $\text{MeI}/110^\circ\text{C}$.



^a Conditions: (a) $[\text{Pd}_2(\text{dba})_3]/\text{CuI}/\text{PPh}_3/\text{Et}_3\text{N}/75^\circ\text{C}$. (b) $\text{K}_2\text{CO}_3/20^\circ\text{C}/\text{MeOH}/\text{CH}_2\text{Cl}_2$.

studies carried out by Jin Zhang and Ashok Shetty strongly suggest the formation of stacked ring structures as depicted schematically in Figure 1a.²⁶ These findings led us to columnar liquid crystal phases based on these toroidal-shaped mesogens.²⁷ Such shape-persistent macrocycles should produce noncollapsible “tubular” mesophases as ideally represented in Figure 1b. These macrocycles were used as building blocks of other porous materials. In collaboration with Professor Stephen Lee at the University of Michigan, D. Venkataraman structurally characterized the crystal structure from a hexakis(phenylacetylene) macrocycle bearing six hydrogen bonding phenolic groups on its perimeter.²⁸ Interestingly, these solids possessed

wide channels as a result of macrocycle stacking. In collaboration with Professor Paul Bohn at the University of Illinois, we found that these macrocyclic frameworks could be site-specifically functionalized to produce novel amphiphilic structures that formed well-behaved monolayers at the air–water interface, allowing the fabrication of monolayer films on various substrates.²⁹ Finally, molecular turnstile **25** was designed with the intention of producing a system that exhibited conformational bista-

(26) Shetty, A. S.; Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 1019.

(27) Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1994**, *116*, 2657.

(28) Venkataraman, D.; Lee, S.; Zhang, J.; Moore, J. S. *Nature* **1994**, *371*, 591.

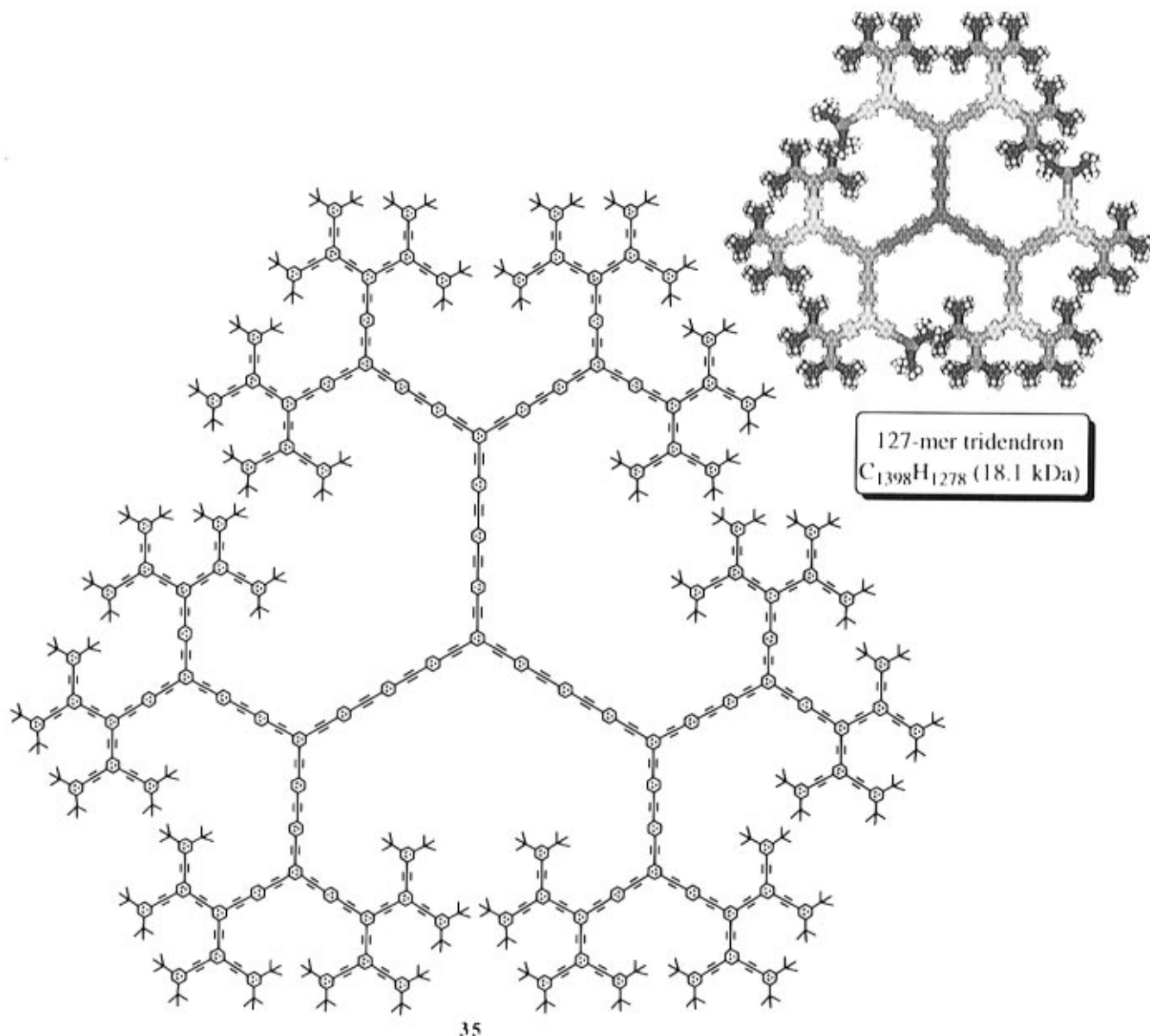


FIGURE 2. Chemical structure of a tridendron constructed from a series of monomers which increased in size with each generation. The space-filling model shown in the upper right-hand corner spans over 125 Å. Color rendering indicates the different building blocks used in the synthesis. This coloring scheme is also consistent with the behavior of this molecule to function as an energy funnel for electronic excitations.

bility. Interestingly, Tom Bedard found that rotation of the disubstituted spindle of **25** about its para axis is slow on the NMR time scale at subambient temperatures, but this motion becomes rapid at elevated temperatures.²³

New Dendritic Architectures, Improved Syntheses, and Accelerated Growth

The availability of repetitive synthetic methods that proceeded with high fidelity for constructing phenylacetylene oligomers significantly impacted our dendritic research program, since we now had complementary protecting groups for each partner of the cross-coupling reaction. Substantial improvements in our convergent dendrimer synthesis were realized simply by switching from dibromo monomer **1** used in Scheme 1 to diethynyl monomer **33** shown in Scheme 7.³⁰ By starting from monodendron **31**, the repetitive chemistry involved triazene to iodide transformation followed by palladium

catalyzed cross-coupling with **33**. Using a slight excess of the iodo-terminated monodendrons, postdoctoral associate P. Bharathi showed that the oxidative dimerization side reaction that hampered our early dendrimer syntheses (Scheme 1) could essentially be eliminated. The dramatic improvement in yield offered by Scheme 7 can be seen in Table 1. Thus, with this chemistry it was possible to prepare multigram quantities of our dendrimers even beyond the fifth generation.

The versatility of this chemistry made it possible to prepare new dendritic architectures such as **35** shown in Figure 2.³¹ This open dendrimer spans 125 Å in its planar conformation. The synthesis of **35** was facilitated by our repetitive methods which made it possible to easily prepare monomer and core building blocks that system-

(29) Shetty, A. S.; Fischer, P. R.; Stork, K. F.; Bohn, P. W.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 9409.

(30) Bharathi, P.; Patel, U.; Kawaguchi, T.; Pesak, D. J.; Moore, J. S. *Macromolecules* **1995**, *28*, 5955.

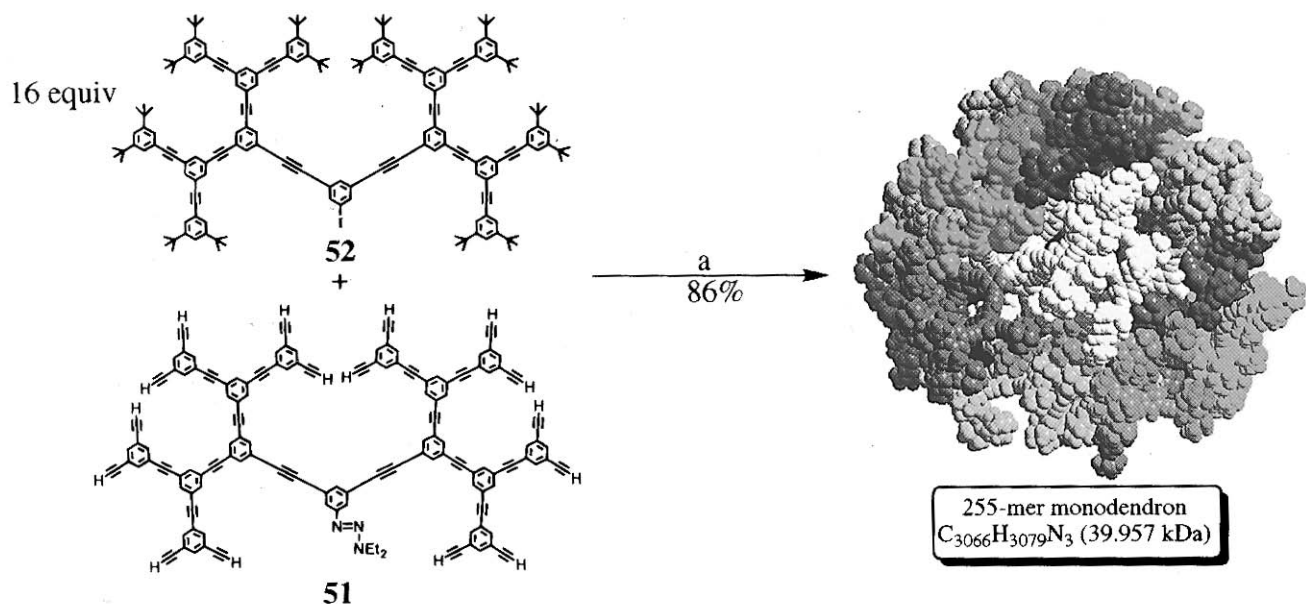


FIGURE 3. Final coupling step in the preparation of a 255-mer monodendron by double-exponential dendrimer growth involves the reaction of 16 monodendrons bearing iodo groups at their focal points (**52**) to ethynyl-terminated monodendron **51**. The space-filling model shows the 255-mer with the core (**51**) in white and each of the 16 periphery monodendrons (**52**) colored individually. The MALDI-TOF mass spectrum shows that the major product is the expected 39.9 kDa monodendron. Conditions: (a) $[Pd_2(dba)_3]/CuI/PPh_3/Et_3N/60\text{ }^\circ\text{C}/7\text{ d}$.

atically increased in size (Scheme 8). For example, AB_2 monomers **37** and **40** are expanded versions of **1**. Likewise, triiodo core **43** is an enlarged version of triiodobenzene (**7**). These large-size building blocks were synthesized by the same repetitive methods used in our oligomer construction. An interesting feature of **35** is the way in which segments of extended conjugation are spatially arranged. The longest string of para-connected phenylacetylene units (i.e., the segment of highest conjugation length) is found at the core of **35**. Heading outward from the core, the length of these para-connected segments decreases. Thus, the molecule possess an electronic energy gradient that decreases from the perimeter to the core. In a collaboration with Professor Raoul Kopelman at the University of Michigan and my postdoctoral associate Chelladurai Devadoss, the efficiency of energy

transduction in these molecular energy funnels has been investigated and found to be extremely high.^{32–34} In other words, these dendritic architectures function as convergent and directional antenna.

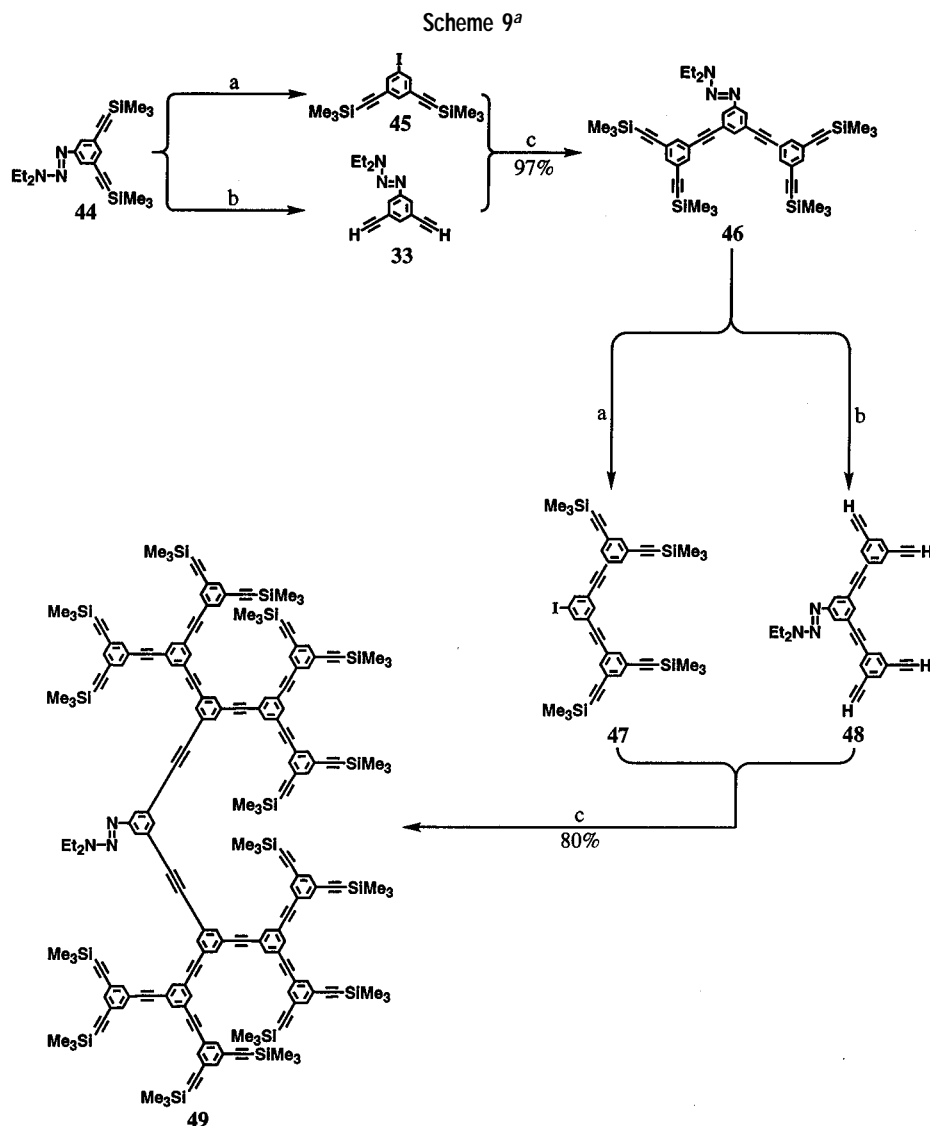
Accelerated schemes to make large-size dendrimers in as few synthetic steps as possible are highly attractive. By generalizing the repetitive methods described above for synthesizing straight-chain oligomeric sequences of “AB” monomers, visiting scientist Tohru Kawaguchi developed an exponentially accelerated dendrimer growth process.³⁵ These methods were used to prepare the 39 kDa 255-mer monodendron shown in Figure 3. We called this method

(31) Xu, Z.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1354.

(32) Xu, Z.; Moore, J. S. *Acta Polym.* **1994**, *45*, 83.

(33) Devadoss, C.; Bharathi, P.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 9635.

(34) Kopelman, R.; Shortreed, M.; Shi, Z. Y.; Tan, W.; Xu, Z.; Moore, J.; Bar-Haim, A.; Klafter, J. *Phys. Rev. Lett.* **1997**, *78*, 1239.



double-exponential dendrimer growth, since the degree of polymerization depends on the generation number n , raised to a power, raised to a power (eq 2). From a purely

$$dp = 2^{2^n} - 1 \quad (2)$$

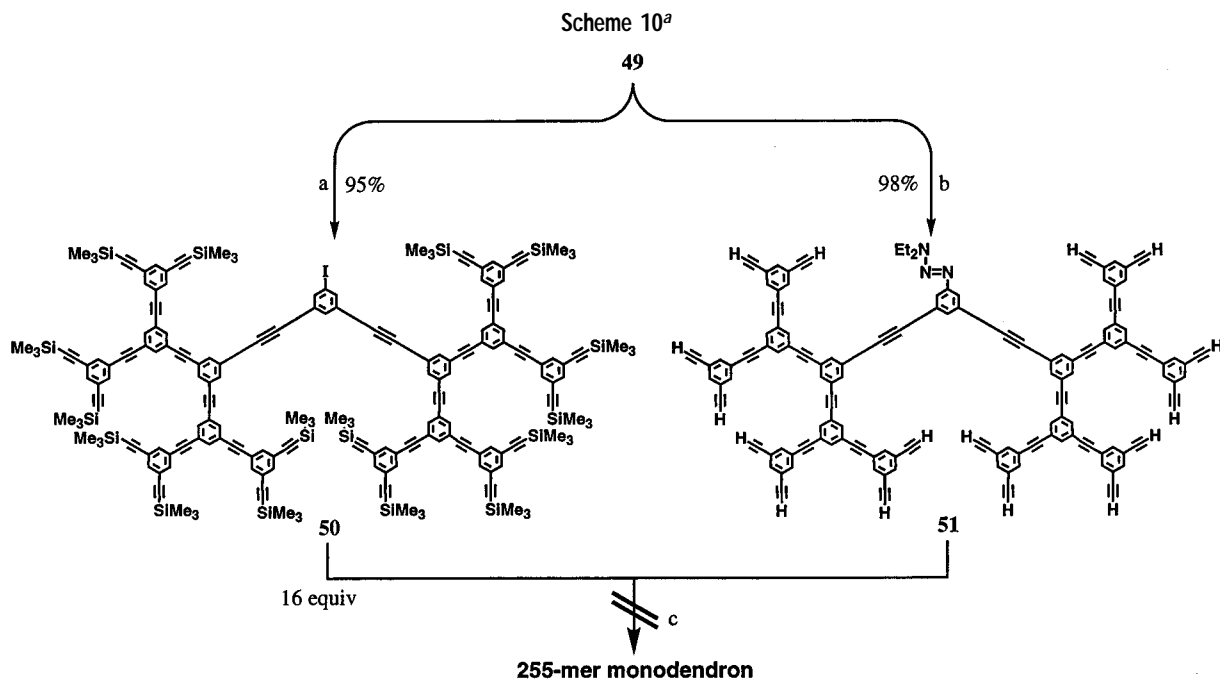
mathematical point of view, this represents one of the most powerful combinatorial engines for preparing dendritic molecules. Starting from diprotected monomer **44**, a set of three reactions are used in repetition, as Scheme 9 shows for the first two generations of growth. Intermediates **33** and **45** are first prepared in a 1:2 ratio by deprotection of **44**. Coupling of these two intermediates produces **46**, which is functionalized just like **44** except that there are four peripheral ethynyl groups per focal point. Repeating these steps again in a 4:1 ratio from monodendron **46** gives the second-generation product **49**, a 15-mer with 16 peripheral ethynyl groups. Scheme 10 shows our attempt at carrying out this reaction sequence through one additional generation. Each of the deprotection steps on **49** worked well, although **51** exhibited poor solubility and was rather unstable. Coupling 16

equiv of 15-mer **50** with 1 equiv of the 15-mer core **51** was expected to produce a 50 kDa monodendron with a degree of polymerization of 255 in only nine synthetic steps from **44**. Although the coupling reaction yielded a high molecular weight product of narrow polydispersity, MALDI mass spectrometry showed that it was a four-component mixture containing none of the expected 255-mer. Instead, the observed products had masses corresponding to the 240-mer, 225-mer, 210-mer, and 190-mer which result from incomplete coupling (i.e., the addition of 15, 14, 13, and 12 equiv, respectively, of **50** to core **51**). Molecular models suggested that the 255-mer is highly congested, and so we decided to try the coupling procedure again using the 15-mer monodendron **52**, which has dimensions that are slightly smaller than **50** (Figure 3). After extensive experimentation, conditions were found which yielded the 255-mer in essentially pure form as determined by MALDI-MS.³⁵

Future Directions

We now have in hand repetitive synthetic methods for making a variety of architectures covering a range of sizes on the nanometer scale, all from simple monomers. An

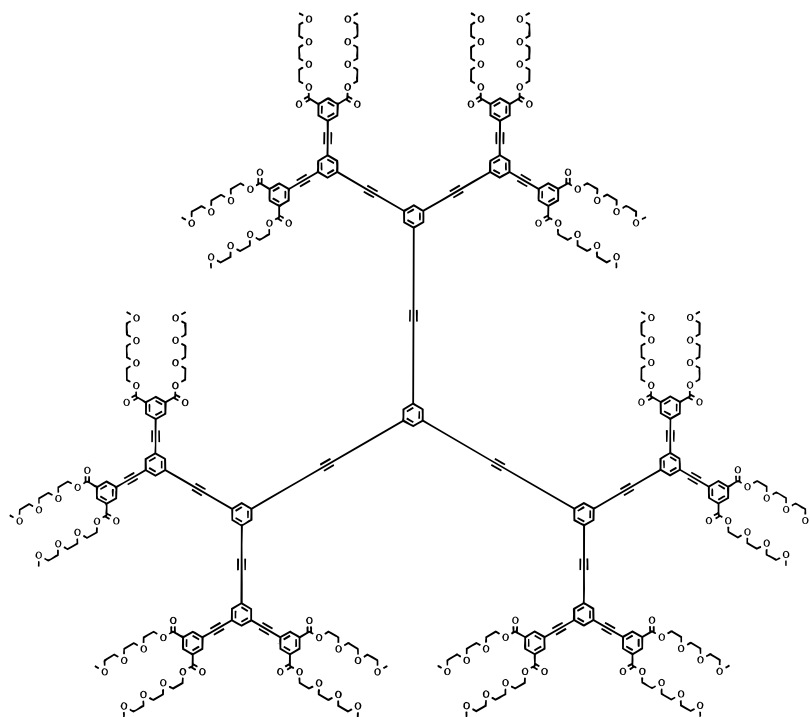
(35) Kawaguchi, T.; Walker, K. L.; Wilkins, C. L.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 2159.



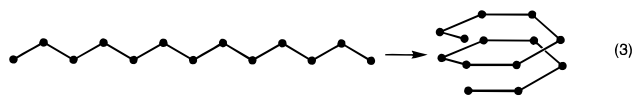
^a Conditions: (a) MeI/110 °C. (b) THF/KOH/0.5 h. (c) [Pd₂(dba)₃]/CuI/PPh₃/Et₃N.

appropriate question to ask is “What problems will benefit from the high level of molecular precision that we can build in nanoscale structures?” One answer may lie in the area of single-molecule electronic or photonic devices. It is interesting to note that, during the period that chemists have been successful in synthesizing large-size dendritic molecules, engineers have managed to carry out chemical reactions on solid substrates with spatial resolution well below 100 Å.³⁶ While there are clearly many unsolved problems associated with the merger of molecular chemistry to device fabrication at the single-molecule level, it is reasonable to expect that much progress will be made soon,³⁷ now that the “bottom-up” and “top-down” size scales have converged.

The field of supramolecular polymer chemistry is another area which may benefit from macromolecules of precise structure.^{38,39} As a consequence of large-area, information-rich molecular surfaces, covalent macromolecules offer special opportunities in supramolecular chemistry not available to small molecules.³⁹ At the same time, the complexity of these macromolecular systems presents major challenges in controlling noncovalent organization at both the intramolecular as well as intermolecular levels. Truly shape-persistent molecular objects may require that we understand how to “fold” nonbiological polymers into unique and stable conformations. Toward this end, we have recently initiated a project on the design of phenylacetylene oligomers that spontaneously organize into



helical conformations driven by solvophobic forces (eq 3).⁴⁰ With appropriate modification, the large, tubular



cavity defined by this helix could function as a receptor site for binding hydrophobic substrates.

At the level of intermolecular self-organization, large molecules hold considerable promise for molecularly engineered materials. For example, shape-persistent dendrimers may provide novel mesogens that could undergo nanophase segregation involving incompatible arms. Another unique possibility with dendritic mesogens would involve organizing donor and acceptor segments in concentric shells of a columnar structure. Such architectures may show unusual photoconducting properties (i.e., molecular coaxial cables). With these ideas in mind, Doug Pesak in my laboratory recently developed a new series of columnar liquid crystalline phenylacetylene dendrimers

- (36) Shen, T.-C.; Wang, C.; Abeln, G. C.; Tucker, J. R.; Lyding, J. W.; Avouris, P.; Walkup, R. E. *Science* **1995**, *268*, 1590.
 (37) Abeln, G. C.; Thompson, D. S.; Lee, S. Y.; Moore, J. S.; Lyding, J. W. *Appl. Phys. Lett.* **1997**, *70*, 2747–2749.
 (38) Balagurusamy, V. S. K.; Ungar, G.; Percec, V.; Johansson, G. *J. Am. Chem. Soc.* **1997**, *119*, 1539–1555.
 (39) Moore, J. S. *Curr. Opin. Solid State Mater. Sci.* **1996**, *1*, 798–805.
 (40) Nelson, J. C.; Saren, J. G.; Moore, J. S.; Wolynes, P. G. *Science*, **1997**, in press.
 (41) Pesak, D. J.; Moore, J. S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1636–1639.

(e.g., **53** on previous page).⁴¹ In great contrast to the *tert*-butyl-capped dendrimers such as **9** or **35**, which decompose without exhibiting a glass transition temperature, peripheral group modification as in **53** yields substances that are viscous, ordered fluids even at room temperature.

New developments in precisely defined macromolecular architectures will continue to enhance our fundamental understanding of molecular and structural chemistry, while offering the potential to impact technology on a number of fronts. For example, advances in the control of macroscopic order may be achieved through combinations of architecture, supramolecular chemistry, and induced organizations. For over 60 years, nearly all of the attention in the field of synthetic polymer chemistry has focused on substances that are mixtures. Perhaps now, the situation is changing. Even with the availability of dendritic syntheses and other repetitive methods, it must still be noted that a significant synthetic shortfall persists. In particular, the development of general methods for the preparation of nonbiological, sequence-specific heteropolymers that are hundreds of kilodaltons in size remains an unsolved problem in polymer chemistry. To fully capitalize on the possibilities that exist with macromolecular “products of known structure”, this remaining void will need to be filled.

This research was funded by the National Science Foundation.

AR950232G