Cyclization in Hyperbranched Polymer Syntheses: Characterization by MALDI-TOF Mass Spectrometry

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Abstract: Matrix-assisted laser desorption/ionization (MALDI)-time-of-flight (TOF) mass spectrometry allowed direct determination of the extent of macrocycle formation that occurred during the polymerization and copolymerization of A_2B and A_4B monomers. Cyclization in hyperbranched pentafluorophenyl-terminated poly(benzyl ether)s was indicated by the presence of ions 20 Da less than the masses of acyclic species, owing to the loss of the HF chain ends during polymerization. This loss occurs by *intramolecular* nucleophilic aromatic substitution of the benzyl oxide focal point functionality upon a pentafluorophenyl chain end. Homopolymerizations and copolymerization of A_2B and A_4B monomers gave cyclic products in all cases, and the extent of cyclization depended on counterion, reaction time, and reaction temperature. In the copolymerization, product distributions revealed that larger proportions of A_2B repeat units in the product led to increased amounts of cyclic products.

Introduction

Highly branched polymers have attracted considerable attention as materials that possess unusual properties in comparison to linear polymers.[1] Dendritic macromolecules are prepared by stepwise methodologies, involving polymerization of A_xB monomers with controlled growth occurring selectively at either the A chain ends (divergent growth strategy) or at the B focal point site (convergent growth strategy). In contrast, the preparation of the less highly branched and polydisperse hyperbranched polymers is achieved by the one-step polymerization of A_xB monomers, involving reaction of the A and B functionalities with each other. As with the condensation polymerization of AB monomers, reaction may occur intermolecularly to give polymer growth, or it may occur intramolecularly to give a macrocyclic species. However, unlike linear polymerizations, where cyclization gives termination of growth by removal of the two reactive chain ends, the hyperbranched macrocyclic species bear a large number of remaining A chain end functionalities ($\#A = (x - 1)DP_n$) that are available for further polymer growth. The formation of a macrocycle during hyperbranched polymerizations consumes the one unique B focal point functional group, but only when all B functionalities are consumed will polymerization no longer proceed. Therefore, macrocyclic species should continue to grow throughout the polymerization, and hyperbranched polymers containing a macrocyclic unit should exist at each degree of polymerization. Detection of these macrocyclic units by non-mass-spectrometric methods is not trivial, because the chemical linkage constituting the macrocycle is the same as those units forming the polymer backbone linkages, which result from intermolecular reactions, and the molecular weight is not affected to a large extent by ring formation.

The possibility for macrocycle formation has been discussed in several reports[2] of hyperbranching polymerizations, and although cyclization has often been considered to be negligible, it was the focus of a recent theoretical study.[3] The extent of cyclization may depend on the synthetic techniques employed and should affect the structure/property relationships of the end products.[4] Comparison of the hyperbranched polymer molecular weight calculated from end group analysis with the absolute molecular weight gives an indication of the extent of cyclization,[2c,d] where increased amounts of cyclized products correspond to decreased concentrations of the B focal point group and increased apparent molecular weight values by end group analysis. In one case,[2c] unique ^1H NMR resonances for macrocyclic and acyclic end groups allowed the overall extent of cyclization in the polyetherification of flexible A_2B monomer units containing phenolic and alkyl bromide functional groups to be determined. Isolation of the cyclized monomer was possible through a combination of precipitation and chromatography. However, the extent of cyclization that occurs at each degree of polymerization during the preparation of hyperbranched polymers has not been determined quantitatively, and thus, it remains as an important but experimentally unanswered question.[5] Herein, we demonstrate the matrix-assisted laser desorption/ionization (MALDI)-time-of-flight (TOF) mass spectrometric evaluation of cyclization of hyperbranched polymers, including the direct detection of acyclic and cyclic species

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[1] Hawker, C. J.; Malmström, E. E.; Frank, C. W.; Kampf, J. P. *J. Am. Chem. Soc.* **1997**, *119*, 9903−4.

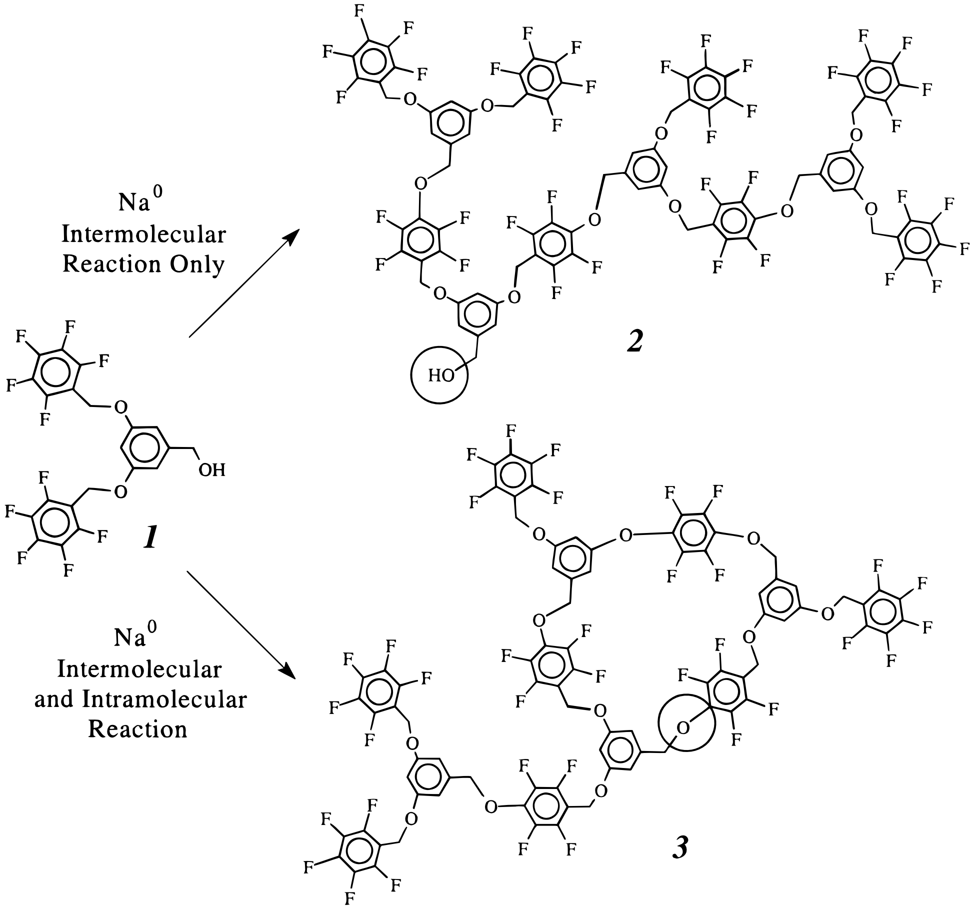
[2] (a) Flory, P. J. *Principles of Polymer Chemistry*; Cornell University Press: Ithaca, NY, 1953; pp 368, 370. (b) Miller, T. M.; Neenan, T. X.; Kwock, E. W.; Stein, S. M. *J. Am. Chem. Soc.* **1993**, *115*, 356−7. (c) Percec, V.; Chu, P.; Kawasumi, M. *Macromolecules* **1994**, *27*, 4441−53. (d) Chu, F.; Hawker, C. J.; Pomery, P. J.; Hill, D. J. T. *J. Polym. Sci. A: Polym. Chem.* **1997**, *35*, 1627−33. (e) Matyjaszewski, K.; Gaynor, S. G.; Kulfan, A.; Podwika, M. *Macromolecules* **1997**, *30*, 5192−4. (f) Hölter, D.; Burgath, A.; Frey, H. *Acta Polym.* **1997**, *48*, 30−5. (g) Beginn, U.; Drohmann, C.; Möller, M. *Macromolecules* **1997**, *30*, 4112−6.

[3] Cameron, C.; Fawcett, A. H.; Hetherington, C. R.; Mee, R. A. W.; McBride, F. C. *ACS Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1997**, *38* (1), 56−7.

[4] For example, an acyclic hexamer composed of A_2B repeat units and containing branching sites at 50% of the repeat units when cyclized gives a calculated decrease to 33% degree of branching.

S0002-7863(97)03954-1 CCC: $15.00

Scheme 1[a]



[a] Reaction of the A_2B monomer **1** via intermolecular reactions gives the acyclic tetramer **2**, containing five A groups and one B group. Reaction of **1** via an intramolecular reaction consumes the B functionality and gives the cyclic tetramer **3**, containing only four A groups.

produced during hyperbranching polymerizations of A_2B and A_4B monomers. Additionally, we report the use of MALDI mass spectrometry for the determination of copolymer product distributions in hyperbranched copolymerizations.

Results and Discussion

To investigate the formation of macrocycles during hyperbranched polymerizations, pentafluorophenyl-terminated hyperbranched poly(benzyl ether)s[6] were prepared. The reaction of the A_2B monomer, 3,5-dipentafluorobenzyloxybenzyl alcohol (**1**) proceeds via intermolecular nucleophilic aromatic substitution reactions upon the para positions of the pentafluorophenyl groups to give a hyperbranched polymer (Scheme 1, shown only as tetramer **2**). The hyperbranched polymer has increasing numbers of pentafluorophenyl chain ends ($\#A = DP_n + 1$) as the polymerization degree (DP) increases but maintains a single benzylic alcohol at the focal point. Competing with polymerization is intramolecular attack of the benzyl oxide upon the para position of a pentafluorophenyl chain end group to yield the hyperbranched cyclophane polymer (shown as the tetramer **3** in Scheme 1). Unlike linear polymerizations, where cyclization gives termination of growth by removal of the two reactive chain ends, the hyperbranched macrocyclic species bear a large number of pentafluorophenyl (A) functionalities ($\#A = DP_n$) that remain available for further polymer growth; only when all benzyl oxide (B) functionalities are consumed will polymerization no longer proceed. It is important to note that because the benzyl−ether bond in the macrocycle is similar to those formed upon intermolecular polymerization, it is indistinguishable by spectroscopic techniques, such as IR and NMR.

An alternate structural tool is MALDI-TOF mass spectrometry, which has been developed[7] for the direct analysis of polymer molecular weights,[8] molecular weight distributions,[9] and end group compositions.[10] One issue with MALDI of

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(5) Cyclization of the chain ends of poly(propyleneimine) dendrimers has recently been reported by an elegant electrospray mass spectrometry study. This cyclization was by a side reaction of nitrile chain ends during hydrogenation and not a condensation reaction between focal point and chain end during hyperbranched polymer growth: Hummelen, J. C.; van Dongen, J. L. J.; Meijer, E. W. *Chem. Eur. J.* **1997**, *3* (9), 1489−93.

(6) (a) Mueller, A.; Wooley, K. L. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1997**, *38* (1), 58-9. (b) Mueller, A.; Kowalewski, T.; Wooley, K. L. *Polym. Mater. Sci. Eng.* **1997**, *77*, 89−90. (c) Mueller, A.; Kowalewski, T.; Wooley, K. L. *Macromolecules* **1998**, *31*, 776−86.

(7) (a) Schriemer, D. C.; Li, L. *Anal. Chem.* **1997**, *69*, 4169−75. (b) Schriemer, D. C.; Li, L. *Anal. Chem.* **1997**, *69*, 4176−83.

(8) (a) Tanaka, K.; Waki, H.; Ido, Y.; Akita, S.; Yoshida, Y.; Yoshida, T. *Rapid Commun. Mass Spectrom.* **1988**, *2* (8), 151−3. (b) Belu, A. M.; DeSimone, J. M.; Linton, R. W.; Lange, G. W.; Friedman, R. M. *J. Am. Soc. Mass Spectrom.* **1996**, *7*, 11−24.

(9) (a) Bahr, U.; Deppe, A.; Karas, M.; Hillenkamp, F.; Giessmann, U. *Anal. Chem.* **1992**, *64*, 2866−9. (b) Räder, H. J.; Spickermann, J.; Kreyenschmidt, M.; Müllen, K. *Macromol. Chem. Phys.* **1996**, *197*, 3285−96. (c) Vitalini, D.; Mineo, P.; Scamporrino, E. *Macromolecules* **1997**, *30*, 5285−9.

(10) (a) Danis, P. O.; Karr, D. E.; Westmoreland, D. G.; Piton, M. C.; Christie, D. I.; Clay, P. A.; Kable, S. H.; Gilbert, R. G. *Macromolecules* **1993**, *26*, 6684−5. (b) Montaudo, G.; Garozzo, D.; Montaudo, M. S.; Puglisi, C.; Samperi, F. *Macromolecules* **1995**, *28*, 7983−9. (c) Lee, S.; Winnik, M. A.; Whittal, R. M.; Li, L. *Macromolecules* **1996**, *29*, 3060−72. (d) Weidner, St.; Kühn, G. *Rapid Commun. Mass Spectrom.* **1996**, *10*, 942−6. (e) Pasch, H. *Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.)* **1996**, *37* (1), 319−20. (f) Zammit, M. D.; Davis, T. P.; Haddleton, D. M.; Suddaby, K. G. *Macromolecules* **1997**, *30*, 1915−20.

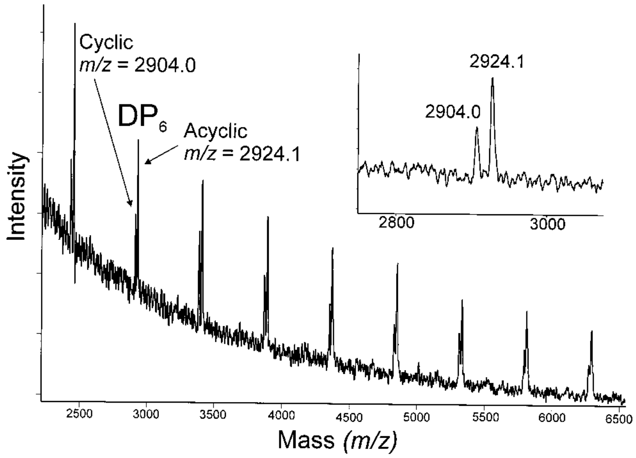

Figure 1. MALDI-TOF mass spectrum of **4**, in a dithranol matrix. The cationization is from adventitious sodium ions present in the matrix, on the sample plate, or in the sample. The cyclized products were cleanly resolved from the oligomers (see inset).

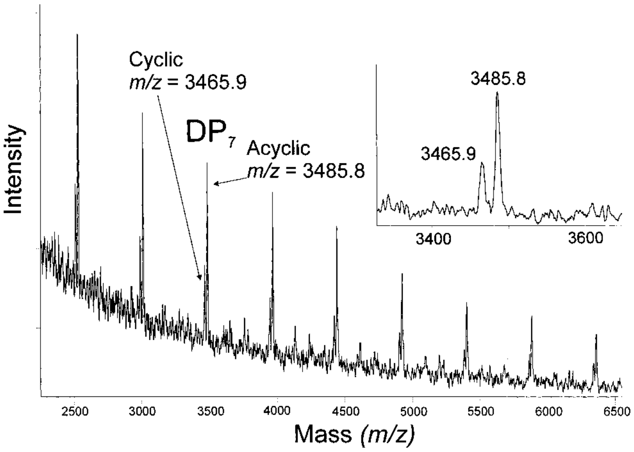

Figure 2. MALDI-TOF mass spectrum of **4**, cationized with silver in *trans*-3-indoleacrylic acid matrix. Degrees of polymerization from 5 to 13 are included, and the cyclized products are observed as resolved ion peaks at −20 m/z units from their acyclic analogues (see inset).

synthetic polymers is choice of matrix. Dithranol was one of the chosen matrixes, because it is commonly used for this class of compounds. The MALDI-TOF spectrum (Figure 1) of hyperbranched polymer **4** from polymerization of **1** is composed of peaks that correspond to Na$^+$-cationized oligomers. The cyclized products are clearly observable as ions that are 20 m/z units less than the masses of each main ion, owing to the loss of HF (from one A plus B chain ends) upon cyclization. For three oligomers with masses in a range where the mass resolving power is sufficient to give baseline separation, the peaks corresponding to HF loss were 47% of the area of the peak corresponding to the acyclic oligomer. The standard deviation ($N = 30$) was 11% (absolute) for a product isolated after 11 h of reaction time, indicating reasonable reproducibility.

There is a question of whether the loss of HF took place during the synthesis or as a consequence of the mass spectral ionization. To rule out a cyclization caused by mass spectrometry, the laser power was increased by 40%, with the expectation that the percent cyclization would remain constant. The new areas of the peaks corresponding to loss of HF were 50% with a standard deviation of 8% (absolute). The two percentages, 47 and 50%, are not significantly different at the 99% confidence level as determined by the standard t test.

To obtain further confidence in the percent cyclization value and in the conclusion that the loss of HF occurs in the synthesis, additional MALDI experiments were conducted with the matrix 4-phenyl-α-cyanocinnamic acid (PCC). PCC is a matrix that we had developed previously for detection of DNA bases that had been modified with polycyclic aromatic hydrocarbons,[11] and it was chosen because it resembles the repeat unit of the oligomer. The appearance and the signal-to-noise ratio of the MALDI mass spectrum of the oligomer mixture were nearly identical to those obtained with dithranol. The percent cyclization was determined to be 56% with a standard deviation of 9% (absolute), which is slightly greater (at 99% confidence) than the 46% cyclization value reported above.

A third matrix that we used is *trans*-3-indoleacrylic acid, a matrix that has found use for aromatic polyether dendrimers.[12] Sensitivity comparable to that found with the other two matrixes was achieved by spiking with silver trifluoroacetate, which led to desorption of silver-cationized oligomers. With this matrix and a single experiment, we found 45% average cyclization after 11 h (Figure 2), which compares favorably with the results reported above. After a shorter reaction time (8 h) under the same reaction conditions,[13] the percent cyclization was 25%.

The effects of branching upon the extent of cyclization were investigated from the polymerization of an A_4B monomer unit **5** (Chart 1),[14] which is a second-generation dendrimer that has an ideally branched layer built into each of the repeat units. Two MALDI-TOF spectra (Figure 3) of samples of **6**, obtained from homopolymerizations of **5**, demonstrate that the extent of cyclization is affected by the reaction conditions, suggesting again that cyclization occurs during polymerization and not during sample preparation or in the mass spectrometer. The product-size distributions also suggest that sample fractionation or fragmentation is not significant during the mass spectrometry experiment.

Although cyclization was observed for each of the oligomeric products that are composed of **4** and **6**, macrocyclic products of the monomers **1** and **5** were not observed. The enthalpies of cyclization, which were determined from semiempirical AM1 calculations, showed that cyclization is disfavored for **1** by 109 kJ/mol, favored for **5** by 15 kJ/mol, and favored for the dimer of **5** by 46 kJ/mol (Table 1). Considering also the entropic contributions (the product of entropy and temperature, ~-17 to -26 kJ/mol at 298 K),[15] only the dimer of **5** is expected to form a stable macrocycle.

We might expect that the same trends for cyclization would occur if the various monomers and oligomers were subjected to mass spectrometric conditions that lead to postsource decompositions (PSD) and collisionally activated decompositions (CAD). We were able to do a PSD/CAD experiment only for the A_4B monomer **5** but were unable to observe loss of HF even under forcing conditions of high laser power and introduction of argon gas in the collision cell. These results are consistent with those observed for **5** in solution and also suggest that the elimination of HF by a mass spectrometric process is unlikely.

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[11] George, M.; Wellemans, J. M. Y.; Cerny, R. L.; Gross, M. L.; Li, K.; Cavalieri, E. L. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 1021.

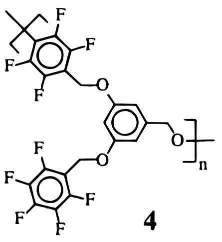
[12] Leon, J. W.; Fréchet, J. M. J. *Polym. Bull.* **1995**, *35*, 449−55.

[13] The polymerization conditions included reaction of **1** as a 0.5 M solution in tetrahydrofuran heated at reflux in the presence of sodium for 8 h, followed by purification by precipitation into water and then flash chromatography.

[14] Stefanescu, A. D.; Wooley, K. L. *Polym. Mater. Sci. Eng.* **1997**, *77*, 218−9.

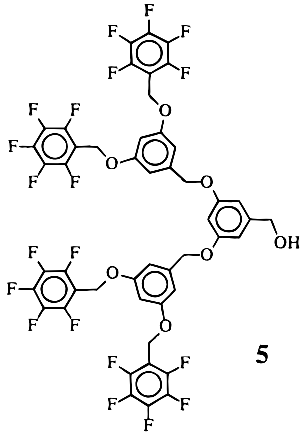
[15] The lower limit of 17 kJ/mol is characteristic for the cyclization of six- to eight-membered alkanes, whereas the 26 kJ/mol upper limit is obtained from simulations using the rotational isomeric state model (RIS) cf: Winnik, M. A. *Chem. Rev.* **1981**, *81*, 491.

Chart 1



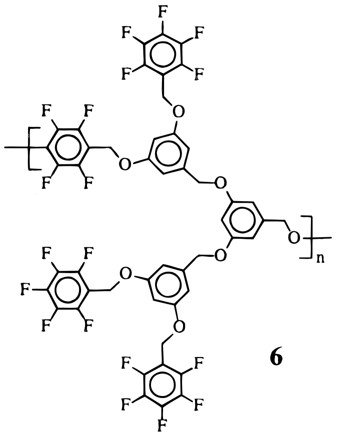
4

[$C_{21}H_9O_3F_9$, 480.28 Da]$_n$+ HF (acyclic)
Hyperbranched Polymer
Repeat Unit from **1** (A_2B)



5

$C_{49}H_{24}O_7F_{20}$, 1104.7 Da



6

[$C_{49}H_{23}O_7F_{19}$, 1084.7 Da]$_n$+ HF (acyclic)
Hyperbranched Polymer
Repeat Unit from **5** (A_4B)

Copolymerization of the A_2B (**1**) and A_4B (**5**) monomers allowed for evaluation of the behavior of competing polymerization/cyclization reactions during the preparation of copolymer **7**. The copolymer product distributions (relative abundances of **1** and **5**) agree with the statistically expected distribution for incorporation of **1** and **5**. For example, the series that results from a combined degree of polymerization of six (labeled in Figure 4), contained mass peaks of relative intensities ≤0.1, 0.39, 0.62, 0.43, and ≤0.1 for oligomers composed of $(A_2B)_5(A_4B)_1$, $(A_2B)_4(A_4B)_2$, $(A_2B)_3(A_4B)_3$, $(A_2B)_2(A_4B)_4$, and $(A_2B)_1(A_4B)_5$, respectively.

Under the polymerization conditions used, the main products were the cyclized hyperbranched polymers (Figure 4). The relative amounts of **1** and **5** within the copolymer also affect the amounts of cyclized products, in which cyclization is more prevalent with increasing content of **1**. The effects of comonomer content were evaluated as a function of both the degree of polymerization and the total number of pentafluorophenyl (A) groups present within the structure. For the pentamer series, $(A_2B)_3(A_4B)_2$ gave a ratio of cyclic:acyclic = 2.1:1, whereas $(A_2B)_2(A_4B)_3$ gave a lower ratio of cyclic:acyclic = 1.6:1. The heptamer $(A_2B)_4(A_4B)_3$ and the pentamer $(A_2B)_1(A_4B)_4$ both contain 14 pentafluorophenyl groups; however, ratios of cyclic to acyclic structures were 3.2:1 and 1.9:1, respectively. Similar data were found for other combinations throughout the MALDI-TOF spectrum (Table 2).

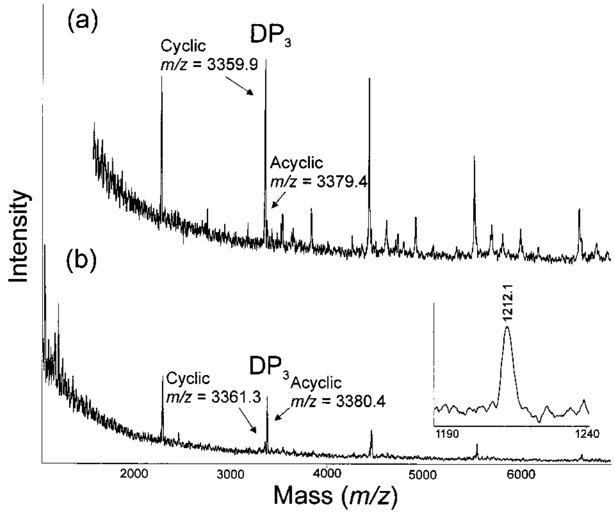


Figure 3. MALDI-TOF mass spectra of **6**, prepared under different polymerization conditions to result in different extents of cyclization: (a) 90% cyclized from polymerization of **5** at 0.3 M concentration in THF using sodium suspension (particle size <1 mm, 2.9 M in 1:3 toluene/THF) and heating at 55 °C for 0.5 h; (b) 15% cyclized from polymerization of **5** at 0.3 M concentration in THF using neat NaK at 25 °C for 25 h. The cyclized products are observed as resolved ion peaks at −20 *m*/*z* units from their acyclic analogues. As shown in the inset, the monomer **5** does not cyclize and is observed as the silver complex at 1212.1 Da.

Conclusions

The insight from MALDI-TOF MS analysis of hyperbranched polymers will lead to a better understanding of the effects of polymer structure upon the physical properties. For example, although macrocycles occupy smaller hydrodynamic volumes than their linear counterparts, it is not clear how these differences will be manifested, if at all, in a comparison of hyperbranched vs hyperbranched macrocyclic structures. Further investigations of the extent of cyclization under different reaction conditions and postpolymerization treatment are in progress.

Experimental Section

General Procedures. The MALDI-TOF experiments were carried out on a PerSeptive Biosystems, Inc., Voyager-DE RP mass spectrometer (Cambridge, MA). A nitrogen laser (337-nm, 20-kW peak laser power, 2-ns pulse width) was used to desorb the sample ions. The instrument was operated in linear delayed-extraction mode with an accelerating potential of 25 kV. Raw data were acquired with a Tektronix 520A digitizing oscilloscope before being transferred to a personal computer equipped with GRAMS/386 software (Galactic Industries). Peak areas were measured with the GRAMS software.

When necessary, the laser power was varied by controlling an iris in the beam path. The PSD experiments were conducted as previously described.[16] CAD experiments were conducted under the same conditions as PSD except argon gas was introduced to an indicated pressure (measured on Bayard-Alpert gauge) of 9×10^{-6} Torr in a collision cell that is located after the ion source. Results from approximately 80 laser shots were signal averaged to give one spectrum.

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[16] Gooden, J. K.; Byun, J.; Chen, L.; Rogan, E. G.; Cavalieri, E. L.; Gross, M. L. *Int. J. Mass Spectrom. Ion Processes* **1997**, *169*/*170*, 241−9.

Table 1. Results of the Molecular Mechanics (MMFF) and Quantum Semiempirical (AM1) Calculations (Values in kJ/mol)

						dimer of **5**	
calculation method	energy	**1**	**1** cyclic	**5**	**5** cyclic	acyclic	cyclic
MMFF	stretch	1.55	2.44	4.52	4.14	9.33	8.45
	bend	13.64	11.96	51.00	46.78	110.62	106.90
	torsion	12.05	82.10	11.80	46.02	26.15	65.98
	VdW	−28.07	−32.01	−4.73	−36.65	−12.26	−79.91
	out of plane	0.062	5.91	0.010	0.53	0.054	0.30
	total (strain)	−0.72	70.37	62.58	60.84	133.89	101.71
AM1	ΔH_f	−1968.0	−1548.7	−3853.9	−3558.5	−7437.9	−7173.5
	$\Delta\Delta H_f$	−419.3		−295.4		−264.4	
	$\Delta H_r = \Delta\Delta H_f - 310.6$	+108.7		−15.2		−46.2	

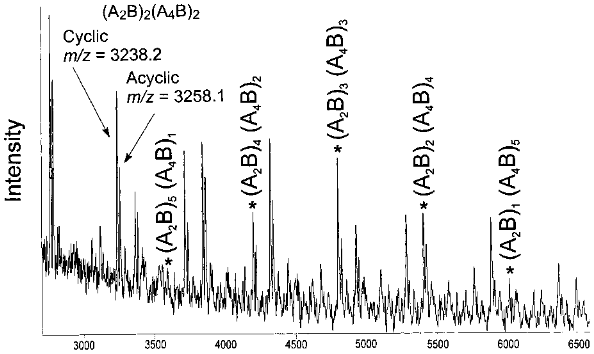

Figure 4. MALDI-TOF mass spectrum of **7**. The compositions of each of the oligomers were assigned; for example, the series of hexamers constructed from differing numbers of A_2B (**1**) and A_4B (**5**) monomer *m/z* units is labeled (∗). The cyclized products are observed as resolved ion peaks at −20 Da from their acyclic analogues.

Table 2. MALDI-TOF *m/z* and Relative Intensity Values for a Sample of the Copolymer **7**, Composed of Different Combined Numbers of **4** and **6** and at Different Overall Degrees of Polymerization

	DP$_n$		[cyclic species·Ag]$^+$			[acyclic species·Ag]+		
			m/z			*m/z*		
species	**4**	**6**	calcd	found	intens	calcd	found	intens
dimers	0	2	2276.1	2277.4	0.73	2296.1	2296.9	0.67
trimers	2	1	2152.6	2153.4	0.47	2172.6	2172.8	0.52
	1	2	2756.4	2757.1	1.00	2776.4	2777.0	0.72
	0	3	3360.2	3361.7	0.43	3380.2	3381.6	0.32
tetramers	3	1	2632.9	2633.6	0.37	2652.9	2652.8	0.29
	2	2	3236.7	3237.6	0.84	3256.7	3257.4	0.45
	1	3	3840.5	3841.4	0.70	3860.5	3861.2	0.53
	0	4	4444.3	4445.1	0.18	4464.3	4464.8	≤0.1
pentamers	4	1	3113.2	3113.5	0.19	3133.2	3134.0	≤0.1
	3	2	3717.0	3717.7	0.65	3737.0	3737.0	0.30
	2	3	4320.8	4321.7	0.73	4340.8	4341.5	0.44
	1	4	4924.6	4925.0	0.32	4944.6	4945.3	0.17
hexamers	5	1	3593.5	3593.7	≤0.1	3613.5	3612.3	≤0.1
	4	2	4197.3	4197.5	0.39	4217.3	4217.4	0.24
	3	3	4801.1	4801.6	0.62	4821.1	4822.1	0.26
	2	4	5404.9	5404.9	0.43	5424.9	5425.7	0.30
	1	5	6008.7	6009.5	≤0.1	6028.7	6030.0	≤0.1
heptamers	5	2	4677.6	4677.8	0.15	4697.6	4696.3	≤0.1
	4	3	5281.4	5281.4	0.43	5301.4	5301.7	0.13
	3	4	5885.2	5885.8	0.43	5905.2	5906.4	0.14
	2	5	6489.0	6489.4	0.15	6509.0	6510.5	≤0.1
octamers	5	3	5761.7	5761.6	0.21	5781.7	5781.2	≤0.1
	4	4	6365.5	6365.3	0.22	6385.5	6385.8	≤0.1
	3	5	6969.3	6969.0	≤0.1	6989.3		

Three MALDI matrixes, dithranol,[17] *trans*-3-indoleacrylic acid (IAA), and 4-phenyl-α-cyanocinnamic acid (PCC), were used. The former two were purchased from Aldrich (Milwaukee, WI), and the latter was synthesized as previously reported.[12]

Analytes were dissolved in tetrahydrofuran (THF) at 10 mg/mL, and a small volume (e.g., 10 μL) of that solution was added to an equal volume of a saturated solution of the matrix in THF. An aliquot of the resulting solution (1 μL) was deposited on the sample plate surface and allowed to air-dry. Silver-doped samples were prepared by using silver trifluoroacetate in THF to give a concentration of 2−7 mM in the matrix/analyte solution.

Size exclusion chromatography (SEC) was conducted on a Hewlett-Packard series 1050 HPLC pump with a Hewlett-Packard 1047A refractive index detector; data analysis was done by Viscotek (Houston, TX) Trisec SEC Software, v. 3.0. Two 5-μm Polymer Laboratories PLgel columns (300 × 7.7 mm) connected in series in order of increasing pore size (500 Å, mixed bed C) were used with THF (distilled from CaH_2) as solvent. The M_w and M_w/M_n values for the samples **4**, **6**, and **7** were calculated from SEC results, based upon calibration with PS standards.

IR spectra were obtained on a Mattson Polaris spectrometer as thin films on NaCl disks. ^1H NMR spectra were recorded on solutions in $CDCl_3$ or toluene-d_8 on a Varian Unity 300-MHz spectrometer with the solvent proton signal as standard. ^{13}C NMR spectra were recorded at 75 MHz on solutions in $CDCl_3$ or toluene-d_8 on a Varian Unity 300 spectrometer or at 125 MHz on a Varian 500 spectrometer, with the solvent carbon signal as standard. ^{19}F NMR spectra were recorded at 282 MHz on solutions in $CDCl_3$ or toluene-d_8 on a Varian Unity 300 spectrometer with external $CFCl_3$ as standard.

A_2B Monomer, 3,5-Bis(pentafluorobenzyloxy)benzyl Alcohol (1). To a solution of 3,5-dihydroxybenzyl alcohol (22.98 g, 0.1640 mol) and 2,3,4,5,6-pentafluorobenzyl bromide (90.13 g, 0.3453 mol) in dry THF (200 mL) were added potassium carbonate (49.82 g, 0.361 mol) and 18-crown-6 (4.33 g, 0.0164 mol). The reaction mixture was heated to 55 °C and allowed to stir under dry argon for 4 days. After cooling to room temperature, most of the THF was removed at reduced pressure leaving a pale yellow paste that was partitioned between CH_2Cl_2 (100 mL) and water (100 mL). The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL). The organic layers were combined, dried over $MgSO_4$, and evaporated to dryness. The product was then purified by flash chromatography on silica gel, eluting with 50% hexane/CH_2Cl_2 and gradually increasing to CH_2Cl_2 to give **1** as a white crystalline solid: yield 58.42 g (71%); T_g −0.5 °C; mp 94−95 °C; IR 3600−3100, 3100−2850, 1660, 1595, 1528, 1512, 1458, 1433, 1382, 1307, 1288, 1161, 1062, 973, 942, 830, 770, 685 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.96 (t, 1H, J = 6 Hz, $ArCH_2OH$), 4.64 (d, 2H, J = 6 Hz, $ArCH_2OH$), 5.08 (s, 4H, $C_6F_5CH_2OAr$), 6.47 (t, 1H, J = 2 Hz, ArH), 6.64 (d, 2H, J =

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(17) Juhasz, P.; Costello, C. W. *Rapid Commun. Mass Spectrom.* **1993**, *7*, 343−51.

2 Hz, Ar*H*); ^{13}C NMR (CDCl$_3$) δ 57.5 (C$_6$F$_5$*C*H$_2$O), 64.9 (Ar*C*H$_2$OH), 101.3, 106.3 (Ar*C*H), 109.9 (m, C$_6$F$_5$ ipso *C*), 137.6 (d of m, $^1J_{C-F} = 249$ Hz, Ar*C*F), 141.8 (d of m, $^1J_{C-F} = 256$ Hz, Ar*C*F), 144.0 (Ar ipso *C*), 145.7 (d of m, $^1J_{C-F} = 249$ Hz, Ar*C*F), 159.4 (Ar ipso *C*); ^{19}F NMR (CDCl$_3$) δ −142.5 (m, 4F, *o-F*), −152.7 (t, 2F, $J = 21$ Hz, *p-F*), −161.7 (m, 4F, *m-F*). Anal. Calcd for $C_{21}H_{10}F_{10}O_3$ (500.29): C, 50.42; H, 2.01; F, 37.97. Found: C, 50.40; H, 2.23; F, 38.12.

3,5-Bis(pentafluorobenzyloxy)benzyl Bromide (8). Carbon tetrabromide (13.32 g, 39.9 mmol) in dry THF (10 mL) was quickly poured into a stirred solution of **1** (10.05 g, 20.08 mmol) and triphenylphosphine (10.51 g, 40.1 mmol) in dry THF (50 mL) cooled to 0 °C (ice bath). The mixture was then allowed to stir, maintaining the cooling, under an atmosphere of dry argon for 2 min, after which time it became milky. Water (50 mL) was immediately added together with CH$_2$Cl$_2$ (100 mL). The organic layer was separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 50 mL). The organic extracts were combined and washed three times with water (50 mL) before being dried (MgSO$_4$) and evaporated to dryness. The product was then purified by flash chromatography on silica gel, eluting with 50% hexane/CH$_2$Cl$_2$, and increasing to 15% hexane/CH$_2$Cl$_2$ to give **8** as a white crystalline solid: yield 9.53 g (85%); T_g −13 °C; mp 112−113 °C; IR 3100−2850, 1659, 1595, 1525, 1508, 1462, 1434, 1382, 1308, 1290, 1169, 1062, 973, 940, 835, 770, 685 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.41 (s, 2H, ArC*H*$_2$Br), 5.10 (s, 4H, C$_6$F$_5$C*H*$_2$O), 6.49 (t, 1H, $J = 2$ Hz, Ar*H*), 6.67 (d, 2H, $J = 2$ Hz, Ar*H*); ^{13}C NMR (CDCl$_3$) δ 32.9 (Ar*C*H$_2$Br), 57.5 (C$_6$F$_5$*C*H$_2$O), 102.1, 108.7 (Ar*C*H), 109.7 (m, C$_6$F$_5$ ipso *C*), 137.6 (d of m, $^1J_{C-F} = 251$ Hz, Ar*C*F), 140.3 (Ar ipso *C*), 142.0 (d of m, $^1J_{C-F} = 254$ Hz, Ar*C*F), 145.8 (d of m, $^1J_{C-F} = 246$ Hz, Ar*C*F), 159.2 (Ar ipso *C*); ^{19}F NMR (CDCl$_3$) δ −143.3 (m, 4F, *o-F*), −153.4 (t, 2F, $J = 20$ Hz, *p-F*), −162.4 (m, 4F, *m-F*). Anal. Calcd for $C_{21}H_9F_{10}BrO_2$ (563.18): C, 44.79; H, 1.61; F, 33.73; Br, 14.19. Found: C, 44.72; H, 1.61; F, 33.56; Br, 14.00. *m/z* 562.3, 564.3 [M]$^+$, 483.3 ([M]$^+$ − Br), 181.0 [C$_7$H$_2$F$_5$]$^+$.

A$_4$B Monomer, 3,5-Bis[3,5-bis(pentafluorobenzyloxy)benzyloxy]benzyl Alcohol (5). To a solution of 3,5-dihydroxybenzyl alcohol (0.18 g, 1.3 mmol) and **8** (1.53 g, 2.71 mmol) in dry acetone (10 mL) were added potassium carbonate (0.39 g, 2.8 mmol) and 18-crown-6 (0.034 g, 0.12 mmol). The mixture was heated at 55 °C with vigorous stirring under dry argon for 30 h. Most of the acetone was then removed on a rotary evaporator, leaving a pale yellow paste. Water (50 mL) and CH$_2$Cl$_2$ (50 mL) were added. The organic layer was separated, and the aqueous layer was extracted with CH$_2$Cl$_2$ (3 × 50 mL). The organic extracts were combined, dried over MgSO$_4$, and evaporated to dryness. Flash chromatography using 10% hexane/CH$_2$Cl$_2$ and increasing to CH$_2$Cl$_2$ as eluent gave **5** as a white solid: yield 0.99 g (69%); T_g 30 °C; IR 3600−3200, 3100−2850, 1658, 1595, 1526, 1504, 1457, 1375, 1308, 1294, 1164, 1062, 970, 942, 836, 740, 685 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 1.81 (t, 1H, $J = 6$ Hz, ArCH$_2$O*H*), 4.66 (d, 2H, $J = 6$ Hz, ArC*H*$_2$OH), 4.99 (s, 4H, ArC*H*$_2$O), 5.11 (s, 8H, C$_6$F$_5$C*H*$_2$O), 6.52 (t, 2H, $J = 2$ Hz, Ar*H*), 6.53 (t, 1H, $J = 2$ Hz, Ar*H*), 6.62 (d, 2H, $J = 2$ Hz, Ar*H*), 6.71 (d, 4H, $J = 2$ Hz, Ar*H*); ^{13}C NMR (CDCl$_3$) δ 57.5 (C$_6$F$_5$*C*H$_2$O), 65.2 (Ar*C*H$_2$OH), 69.5 (Ar*C*H$_2$O), 101.4, 101.5, 105.7, 106.7 (Ar*C*H), 109.9 (m, C$_6$F$_5$ ipso *C*), 137.6 (d of m, $^1J_{C-F} = 246$ Hz, Ar*C*F), 139.8 (Ar ipso *C*), 141.7 (d of m, $^1J_{C-F} = 268$ Hz, Ar*C*F), 143.6 (Ar ipso *C*), 145.8 (d of m, $^1J_{C-F} = 250$ Hz, Ar*C*F), 159.3, 159.9 (Ar ipso *C*); ^{19}F NMR (CDCl$_3$) δ −142.4 (m, 8F, *o-F*), −152.6 (t, 4F, $J = 18$ Hz, *p-F*), −161.6 (m, 8F, *m-F*). Anal. Calcd for $C_{49}H_{24}F_{20}O_7$ (1104.7): C, 53.28; H, 2.19; F, 34.39. Found: C, 53.12; H, 2.32; F, 34.73.

A$_2$B Hyperbranched Polyfluorinated Poly(benzyl ether)s 4. To a 0.5 M solution of **1** (10.00 g, 19.99 mmol) in dry THF (40 mL) at room temperature under argon were added small pieces of sodium (0.51 g, 22.00 mmol, 1.1 equiv). The reaction was heated at reflux for 10.5 h and then quenched by precipitation of the polymer into water. The product was isolated by centrifugation and further purified by flash chromatography, eluting with 30% hexanes/CH$_2$Cl$_2$, and increasing to CH$_2$Cl$_2$ to give **4** as a transparent glass: yield 8.47 g (88%, SEC M_w = 7,900, M_w/M_n = 2.8); T_g 52 °C; IR 3100−2900, 1719, 1658, 1599, 1524, 1510, 1502, 1461, 1431, 1379, 1312, 1292, 1164, 1059, 1005, 977, 830, 770, 685 cm^{-1}; ^{1}H NMR (toluene-*d*$_8$) δ 4.5−4.8 (br, 4H, C$_6$F$_4$C*H*$_2$O and C$_6$F$_5$C*H*$_2$O), 4.8−5.0 (br, 2H, ArC*H*$_2$O), 6.5 (br, 1H, Ar*H*), 6.7 (br, 2H, Ar*H*); ^{13}C NMR (toluene-*d*$_8$) δ 57.3 (C$_6$F$_4$*C*H$_2$O), 57.6 (C$_6$F$_5$*C*H$_2$O), 75.9 (Ar*C*H$_2$O), 102.5, 107.5 (Ar*C*H), 109.3 (m, C$_6$F$_5$ ipso *C*), 110.1 (m, C$_6$F$_4$ ipso *C*CH$_2$O), 137.4 (d of m, $J = 250$ Hz, Ar*C*F), 137.8 (C$_6$F$_4$ ipso *C*OCH$_2$), 139.1 (m, Ar ipso *C*), 141.9 (d of m, $J = 250$ Hz, Ar*C*F), 145.9 (d of m, $J = 250$ Hz, Ar*C*F), 146.3 (d of m, $J = 250$ Hz, Ar*C*F), 160.0 and 160.1 (Ar ipso *C*), assignments confirmed by ^{19}F-decoupled ^{13}C NMR at 125 MHz; ^{19}F NMR (CDCl$_3$) δ −143.6 (2F, C$_6$F$_5$ *o-F*), −144.8 (2F, C$_6$F$_4$ *o-F*), −153.59 (1F, *p-F*), −156.94 (2F, C$_6$F$_4$ *m-F*), −162.62 (2F, C$_6$F$_5$ *m-F*); average of 45% cyclized by MALDI-TOF.

"Cyclized" A$_4$B Hyperbranched Polyfluorinated Poly(benzyl ether)s (6). A suspension of sodium (particle size <0.1 mm, 2.90 M) in 1:3 toluene/THF (0.070 mL, 0.20 mmol) was added under argon at room temperature to a stirred solution of **5** (0.110 g, 0.100 mmol) in dry THF (0.260 mL). The reaction mixture was heated to 55 °C for 0.5 h and then quenched by precipitation of the polymer into 10 mL of water. The product was centrifuged, dried, redissolved in THF/hexanes (2:3), and further purified by filtration through silica gel. After the evaporation of the combined eluents, **6** was obtained as a transparent glass: yield 0.071 g (65%, SEC M_w = 9,800, M_w/M_n = 2.0); T_g 55 °C; IR 3100−2880, 1657, 1597, 1523, 1506, 1457, 1434, 1379, 1312, 1295, 1162, 1058, 1007, 976, 836, 734, 690 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 4.7 (s, 2H (6%), ArC*H*$_2$OH), 5.0 (br, 4H, ArC*H*$_2$OAr), 5.1 (br, 8H, OC$_6$F$_4$C*H*$_2$O and C$_6$F$_5$C*H*$_2$O), 5.2 (br, 2H, (90%), ArC*H*$_2$OC$_6$F$_4$), 6.5 (br, 3H, Ar*H*), 6.7 (br, 6H, Ar*H*); ^{13}C NMR (CDCl$_3$) δ 57.5 (OC$_6$F$_4$*C*H$_2$O, C$_6$F$_5$*C*H$_2$O), 69.7 (Ar*C*H$_2$OAr), 76.0 (Ar*C*H$_2$OC$_6$F$_4$), 101.7, 102.3, 106.8 (Ar*C*H), 109.8, 109.9 (C$_6$F$_5$ ipso *C*, OC$_6$F$_4$ ipso *C*CH$_2$O), 137.5 ($J = 264$ Hz, O*C*$_6$F$_4$), 139.7 (Ar ipso *C*CH$_2$O), 159.3, 159.5, 159.9 (Ar ipso *C*O); ^{19}F NMR (CDCl$_3$) δ −142.7 (br, 2F (69%), C$_6$F$_5$ *o-F*), −144.6 (br, 2F (31%), C$_6$F$_4$ *o-F*), −153.0 (br, 1F (69%), C$_6$F$_5$ *p-F*), −156.5 (br, 2F (31%), C$_6$F$_4$ *m-F*), −162.0 (br, 2F (69%), C$_6$F$_5$ *m-F*). Calculated M_n: 4300 (^{19}F NMR); 9000 (^{1}H NMR, relative to peak at 5.2 ppm); 17 500 (^{1}H NMR, relative to peak at 4.7 ppm); average of 90% cyclized by MALDI-TOF.

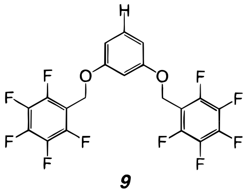
"Acyclic" A$_4$B Hyperbranched Polyfluorinated Poly(benzyl ether)s (6). To a stirred solution of **5** (0.386 g, 0.349 mmol) in dry THF (1.100 mL) was added a drop of Na−K alloy (21 mg, 0.210 mmol Na, 0.415 mmol K) under Ar at room temperature. After 25 h of stirring at room temperature, an aliquot of 0.050 mL was carefully quenched under argon at 0 °C in 0.5 mL of moist THF, and then the polymer was precipitated into 10 mL of water. After the usual workup, the polymer was separated as a transparent glass (SEC M_w = 2900, M_w/M_n = 1.4). Calculated M_n: 2400 (^{19}F NMR); 2900 (^{1}H

NMR, relative to peak at 5.2 ppm); 2700 (^{1}H NMR, relative to peak at 4.7 ppm); average of <15% cyclized by MALDI-TOF.

A_2B and A_4B Hyperbranched Polyfluorinated Copoly(benzyl ether) (7). A 0.290 M solution of sodium *tert*-butoxide in THF (0.364 mL, 0.106 mmol) was added under Ar at room temperature to a stirred solution of **1** (0.025 g, 0.050 mmol) and **5** (0.056 g, 0.050 mmol) in dry THF (0.136 mL). The reaction mixture was stirred at room temperature for 12 h, and then the polymer was separated by quenching the solution with water, followed by the usual workup, to yield copolymer **7** as a transparent glass: yield 0.075 g (95%, SEC $M_w = 14\,200$, $M_w/M_n = 2.7$); T_g 30 °C; ^{1}H NMR ($CDCl_3$) δ 4.66 (br d, J = 6 Hz, $ArCH_2OH$), 5.0 (br, $ArCH_2OAr$), 5.1 (br, $OC_6F_4CH_2O$ and $C_6F_5CH_2O$), 5.2 (br, $ArCH_2OC_6F_4$), 6.5 (br, Ar*H*), 6.7 (br, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 57.5 ($OC_6F_4CH_2O$, $C_6F_5CH_2O$), 67.7 ($C_6H_3CH_2OH$), 69.7 ($ArCH_2OAr$), 75.9, 76.2 ($ArCH_2OC_6F_4$), 101.7, 102.5, 105.8, 106.9, 107.4 (Ar*C*H), 109.9 (C_6F_5 ipso *C*, OC_6F_4 ipso CCH_2O), 137.5 (J = 253 Hz, OC_6F_4), 138.3 (t, J = 31 Hz, C_6F_4 ipso $COCH_2$) 139.7 (br, Ar ipso CCH_2), 159.3, 159.5, 159.9 (Ar ipso *C*O); ^{19}F NMR ($CDCl_3$) δ −142.7 (br, C_6F_5 *o-F*), −144.5 and −144.6 (br, C_6F_4 *o-F*), −152.9 (br, C_6F_5 *p-F*), −156.5 (br, C_6F_4 *m-F*), −162.0 (br, C_6F_5 *m-F*), ~2% *tert*-butoxide substitution upon the *p*-F positions detected by ^{1}H and ^{19}F NMR; average of 60% cyclized by MALDI-TOF.

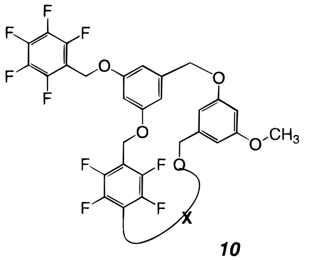
Molecular Modeling. Molecular mechanics (MMFF force field) and semiempirical (AM1 force field) calculations were performed with the Spartan version 5.0 software (Wavefunction, Inc., Irvine, CA). All structures were minimized in vacuo with the MMFF module, followed by geometry optimization and calculation of the heats of formation using the AM1 module. The AM1 calculations could not be performed on the dimer of **5** owing to the large number of atoms; therefore, only the cyclic and corresponding acyclic core fragments **11,c** (cyclized) and **11,a** (acyclized, where X = F and H) were used in the calculations. The remainders of the structures, consisting of the spectator side arms, were replaced by H atoms (hydrogenation). The formation energy of the entire dimer was derived from the heats of formation of the cyclic and acyclic core fragments (**11**) and detached side arms (**9**), and the corresponding heat of hydrogenation calculated from similar fragments from monomer **5**.

AM1 calculations of the heats of formation of the species **9**−**11** and those of HF (−310.6 kJ/mol) and H_2 (−21.7 kJ/mol) were used to derive, by thermochemical manipulation of the data, the final cyclization heats of reaction and the heats of formation corresponding to the cyclic and acyclic dimers of **5**.



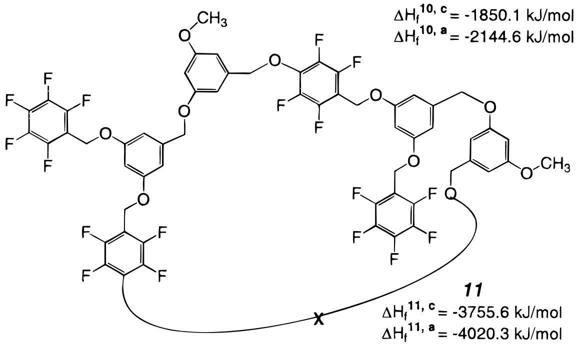
9

ΔH_f^{9} = -1744.2 kJ/mol



10

$\Delta H_f^{10,c}$ = -1850.1 kJ/mol
$\Delta H_f^{10,a}$ = -2144.6 kJ/mol



11

$\Delta H_f^{11,c}$ = -3755.6 kJ/mol
$\Delta H_f^{11,a}$ = -4020.3 kJ/mol

For the hydrogenation/fragmentation reaction of the cyclic species

$$\mathbf{5,c} + H_2 \rightarrow \mathbf{10,c} + \mathbf{9}$$

estimation of the hydrogenation heats was done by using the equation

$$\Delta\Delta H^{\text{hydrogenation,c}} = \Delta H_f^{\mathbf{9}} + \Delta H_f^{\mathbf{10,c}} - \Delta H_f^{H_2} - \Delta H_f^{\mathbf{5,c}} = -14.2 \text{ kJ/mol}$$

In a similar fashion, the hydrogenation heat of the corresponding acyclic species gave −13.3 kJ/mol.

An average hydrogenation heat $\Delta\Delta H^{\text{hydrogenation}} = -13.8$ kJ/mol was used in the calculation of the formation heat of the cyclic dimers of **5** according to the reaction

$$(\mathbf{5})_2\mathbf{,c} + 2H_2 \rightarrow \mathbf{11,c} + 2 \times \mathbf{9}$$

$$\Delta H_f^{\mathbf{5,c}} = 2\Delta H_f^{\mathbf{9}} + \Delta H_f^{\mathbf{11,c}} - 2\Delta\Delta H^{\text{hydrogenation}} - \Delta H_f^{H_2} = -7173.5 \text{ kJ/mol}$$

In a similar fashion, the formation heat of the acyclic dimer of **5** gave −7437.9 kJ/mol (see Table 1).

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