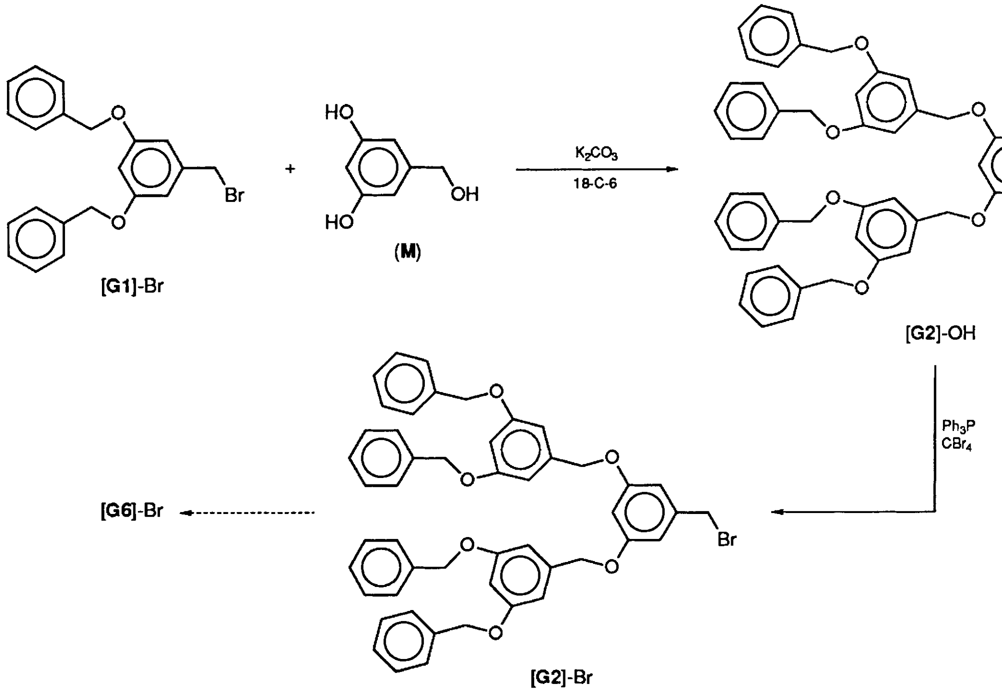
A New Convergent Approach to Monodisperse Dendritic Macromolecules

Craig Hawker and Jean M. J. Fréchet*

Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301, USA

A novel convergent approach for the synthesis of dendritic macromolecules is presented and its scope and versatility demonstrated with the synthesis of a series of monodisperse dendritic polyether macromolecules based on 3,5-dihydroxybenzyl alcohol as the monomer unit up to a molecular weight of 40 689.

Highly branched polymers have received considerable synthetic[1—4] and theoretical[5—8] attention recently. Perhaps the earliest relevant examples of such highly branched structures are the 'cascade' molecules of Vögtle[1] which had relatively low molecular weights. Later, and almost simultaneous work by Tomalia[2] and Newkome[3] produced truly macromolecular hyperbranched polymers, such as the 'starburst' polymers. The interest in these macromolecules is due to their novel, highly branched, globular structure that is reminiscent of many important biological molecules. The



Scheme 1

discovery of new phenomena or new properties may be expected from the study of these uniquely shaped and non-entangled macromolecules.

Previous synthetic work[2—4] had primarily been directed towards the synthesis of dendritic macromolecules by a divergent methodology. In these cases, growth occurs from a central core by successive stepwise addition and activation steps which multiply the number of branches. A significant feature of this methodology is the rapid increase in the number of reactive groups at the periphery of the growing macromolecule. Potential problems which may arise as growth is pursued include incomplete reaction of these terminal groups, which would lead to imperfections in the next generation, or the large excesses of reagents that are required to force reactions to completion. This, in turn, presents difficulties in purification. We report a new approach and methodology for the synthesis of dendritic macromolecules which overcomes these problems and may be used for different families of structures.

Using the symmetrical nature of these molecules to advantage we start construction of the macromolecule at what will become the extremities of the chains or 'periphery' of the spheroidal molecules using a convergent approach. Each successive generation is then synthesized in step-wise fashion producing a new dendritic molecule in which a single reactive group located at the focal point of all branches is used in further growth. The final reaction involves the attachment of a complete dendritic 'wedge' to a polyfunctional core molecule to afford a spheroidal dendritic macromolecule.

To demonstrate this new 'convergent-growth' methodology we describe the synthesis of a number of dendritic polyether macromolecules based on 3,5-dihydroxybenzyl alcohol as the monomer unit [structure (M), Scheme 1]. Synthesis of the polyether macromolecules involves a repetitive two-step process. Reaction of the known[9] benzylic bromide [**G1**]-Br, which is our first generation dendrimer, with the monomer unit (**M**) in the presence of potassium carbonate and 18-crown-6 gives the next generation alcohol [**G2**]-OH, as a crystalline solid with m.p. 110—111 °C in 91% yield. This second generation alcohol can be converted to the corresponding bromide, [**G2**]-Br, by reaction with carbon tetrabromide/triphenylphosphine. Once again the bromide obtained in 93% yield is crystalline with m.p. 129—130.5 °C and can therefore be purified readily by recrystallization. Repetition of the two step process leads to successive generations up to the sixth generation bromide [**G6**]-Br having the nominal molecular formula $C_{889}H_{763}BrO_{126}$ corresponding to a mass† of 13 542. High yields are obtained throughout the process and while the early generation materials were crystalline, all materials from generation three on were amorphous or glassy materials which were easily purified by standard flash chromatography.

Attachment to a polyfunctional core, in this case 1,1,1-tris(4′-hydroxyphenyl)ethane {structure [C]-$(OH)_3$, Scheme 2} was by a similar alkylation reaction to that employed above. Reaction of the appropriate bromide, for example the fourth generation [**G4**]-Br, with the core gives the tri-alkylated derivative such as [**G4**]$_3$-[C] ($C_{671}H_{576}O_{93}$, nominal *M* 10 127) in 84% yield after chromatographic purification. This reaction was carried out with each generation dendritic bromide such that a series of spheroidal polyether macromolecules of increasing molecular size was obtained. For example, reaction of [**G6**]-Br with core [C]-$(OH)_3$ afforded a macromolecule of molecular formula $C_{2687}H_{2304}O_{381}$ with nominal molecular weight 40 689.

All compounds were fully characterized by standard spectroscopic methods. The purities of the various products could also be monitored by chromatographic techniques. Size exclusion chromatography (SEC) was particularly useful since molecular sizes changed drastically at each growth step.

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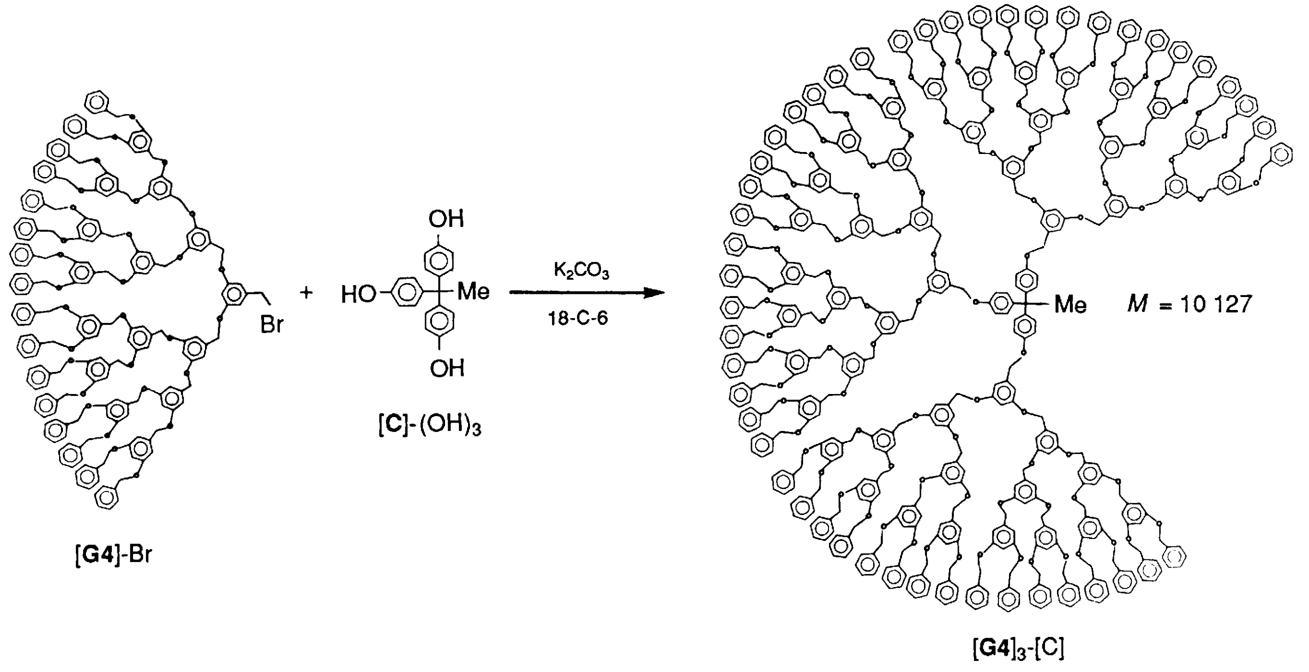
† Calculated on the basis of C 12.01, H 1.008, O 16.00.



Scheme 2

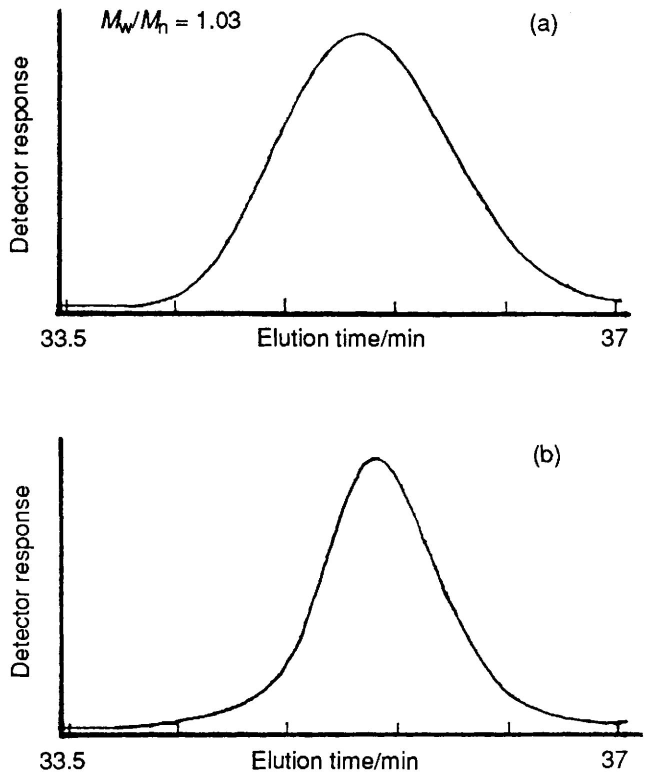


Figure 1. SEC chromatograms of a polystyrene standard (a) with polydispersity 1.03 and a dendritic polymer [G-5]$_3$-[C] (b), using tetrahydrofuran (THF) as eluent under similar conditions.

Similarly, both ^{1}H and ^{13}C NMR spectroscopy proved to be useful, as changes involving reactive groups are easily observed by ^{1}H NMR, and significant differences in the chemical shifts for successive layers are seen in the ^{13}C spectra.

In addition, the nominal molecular weights of the lower dendritic structures (<2000 amu) were confirmed by FAB MS. For example [G3]-OH, which has a nominal molecular weight of 1592, showed M^+ at 1592.6. In the case of the larger dendritic macromolecules, much useful information was obtained from experiments involving SEC coupled to low-angle laser light scattering (LALLS) measurements which provided confirmation of the nominal molecular weights within the experimental errors of the LALLS technique. For example, [G5]$_3$-[C] with a nominal molecular weight of 20 314 shows a LALLS M_w value of 21 300. SEC also provides insight into the internal structures of the polymers and their polydispersity. Figure 1 shows the elution characteristics of a narrow molecular weight distribution polystyrene standard‡ (upper curve) with a polydispersity of 1.03 as well as the elution characteristics of [G5]$_3$-[C] which has a LALLS molecular weight of 21 300. This comparison obtained from runs under identical conditions over a stable set of columns suggests clearly that [G5]$_3$-[C] has a very low polydispersity index. It is also interesting to note in Figure 1 that the elution volume of this polystyrene standard is approximately the same as that of our large dendritic macromolecule [G5]$_3$-[C], even though its LALLS weight average molecular weight (11 700) is much lower. This suggests that the dendritic polymer [G5]$_3$-[C] is a very dense and compact molecule as was observed earlier in the case of Tomalia's starburst polymers.[2,8]

In conclusion, we have demonstrated a new approach for the construction of dendritic macromolecules which possesses a number of distinguishing features when compared to the divergent 'starburst' methodology. The low number of possible side reactions and the easily controllable number of reactive groups required for generation growth associated with the convergent approach allows the synthesis of almost monodisperse dendritic molecules with a high degree of control. The extension of this to the synthesis of dendritic

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‡ Polystyrene standards were obtained from Polymer Laboratories, Amherst, MA, USA.

macromonomers or dendritic macromolecules in which selected 'outer' extremities of the dendritic chains carry reactive groups is being developed, as is the use of different monomer units.

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