

Exact Linear Analogs of Dendritic Polyether Macromolecules: Design, Synthesis, and Unique Properties

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The study of dendritic macromolecules has progressed at such a rapid pace in recent years that these novel materials are becoming major areas of interest from both an industrial and academic standpoint.¹ Much of this research is based on the assumption that dendrimers are inherently different from linear macromolecules and it is this inherent difference that leads to many of the observed changes in physical properties.² Unfortunately, this comparison is not valid since the dendritic macromolecules are compared with polydisperse linear polymers of significantly different structure. For example, the unique melt viscosity behavior of dendritic polyethers was compared with linear polystyrene and not with monodisperse linear analogs containing the same number of polyether repeat units based on 3,5-dihydroxybenzyl alcohol.³ In this report, we describe a novel synthetic approach to monodisperse linear analogs of dendritic macromolecules and the use of this strategy for the preparation of the exact linear derivatives of the well-studied polyether dendrimers **1**.⁴

In designing the synthesis of the linear analogs it became immediately apparent that a traditional exponential growth strategy⁵ involving the synthesis of dimers, tetramers, octamers, etc. would not be applicable since the number of internal repeat units of the dendrimers increased in a different numerical sequence. For example, both the exact linear analog of the fourth-generation polyether dendrimer **2** and the actual dendrimer **1** must have 15 ($2^4 - 1$) internal repeat units which is not consistent with an exponential (2^n) approach (Figure 1). A strategy for the accelerated synthesis of linear polymers with 1, 3, 7, 15, 31, ($2^n - 1$) repeat units was therefore developed. The basic strategy, outlined in Schemes 1 and 2 involves a converging dual exponential growth strategy in which two series of linear macromolecules, one with 2^n repeat units and the other with $2^n - 1$ repeat units, are prepared and then coupled to give the desired linear analogs. To obtain the exact linear analogs, the deprotected monophenolic derivatives (i.e., **9** or **14**) are coupled at each generation step with the linear oligomer containing $2^n - 1$ repeat units and a single benzyl ether chain end (i.e., **11** or **13**). For example, reaction of the first-generation bromide **11** with the monophenol **9** leads to the exact linear analog **12** of the second-generation dendritic alcohol. Bromination of **12** gives the linear [G-2]-Br derivative **13** which can then be coupled with the next generation linear monophenolic derivative **14** to give the exact linear analog of the third generation alcohol **15** which contains seven repeat units, eight benzyl ether groups, and a single hydroxymethyl chain end.

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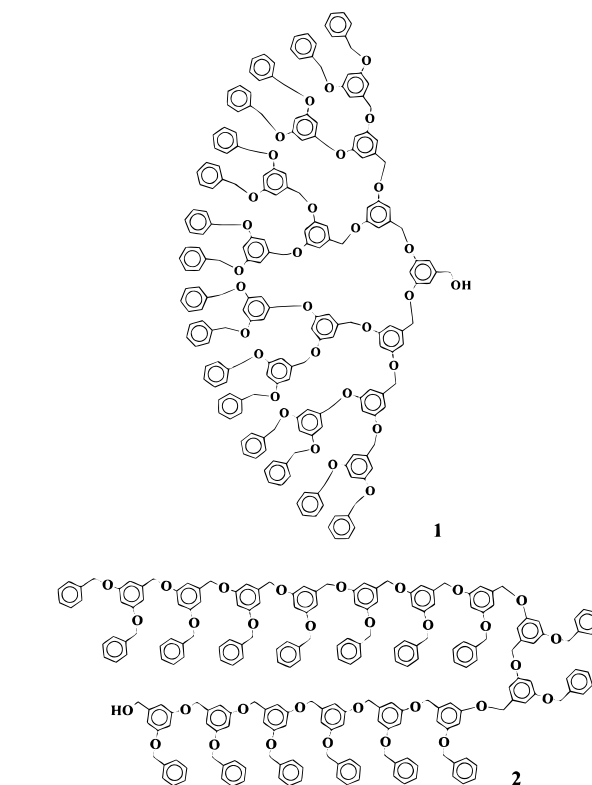


Figure 1. Comparative structures of the fourth-generation dendritic alcohol **1** and its exact linear analog **2**.

Repetition of this strategy leads to higher generation linear analogs of the dendritic polyether macromolecules which have *exactly* the same number of repeat units and pseudo-chain ends as their dendritic equivalents. In essence they are macromolecular isomers of dendrimers and the synthesis has been continued up to the sixth-generation derivative. Using standard techniques developed for dendritic macromolecules,⁶ the structure of the exact linear analogs and associated precursor molecules could be confirmed using a combination of ¹H and ¹³C NMR spectroscopy, GPC, and MALDI mass spectrometry. As expected GPC analysis of the linear analogs showed a single peak (polydispersity less than 1.01), while MALDI mass spectrometry showed a single molecular ion corresponding to the expected molecular weight on the basis of the synthetic strategy.

The ability to prepare the exact linear analogs of the polyether dendrimers permits an unprecedented opportunity to study the actual difference between linear and dendritic macromolecules. Initially the three-dimensional molecular size of the linear and dendritic polymers were compared by gel permeation chromatography. Interestingly, a discontinuous relationship between the hydrodynamic volumes of the exact linear analogs and the corresponding dendrimers was observed. For generations four and below, the hydrodynamic volume of the linear and dendritic macromolecules were essentially the same. However, a marked increase in the hydrodynamic volume for the linear derivatives, compared to the dendritic equivalents, was observed on going to generation five and six. For example, both the fifth generation dendrimer [G-5]-OH, **16**, and the exact linear analog **17** with 31 repeat units have molecular formulas of C₄₄₁H₃₈₀O₆₃ and nominal molecular weights of 6680. While these materials show the same molecular ion by MALDI, the GPC traces show

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Scheme 1

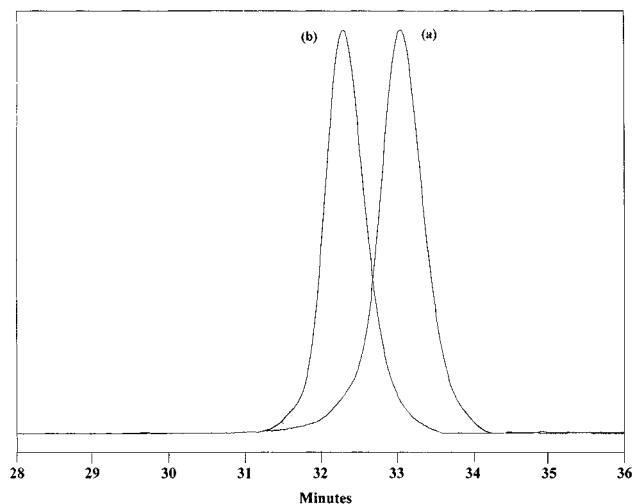
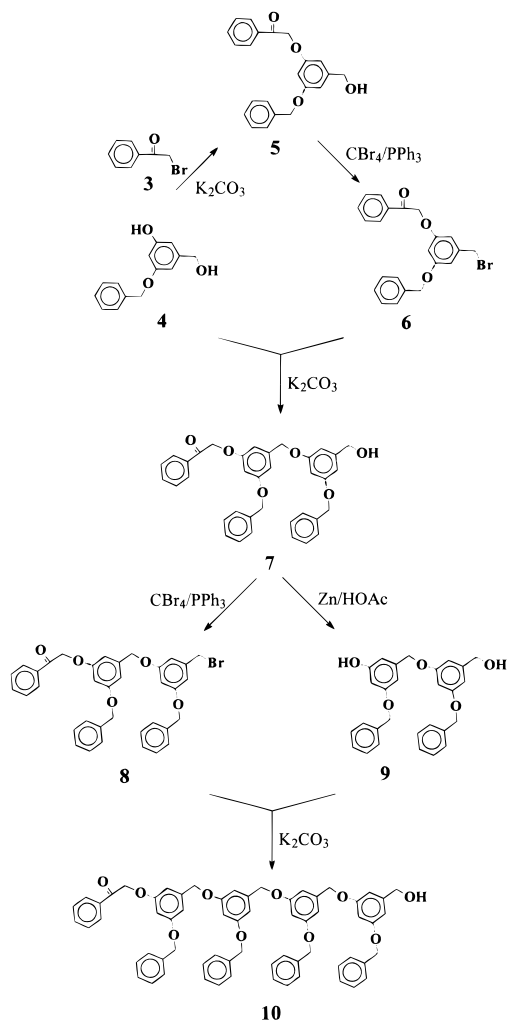
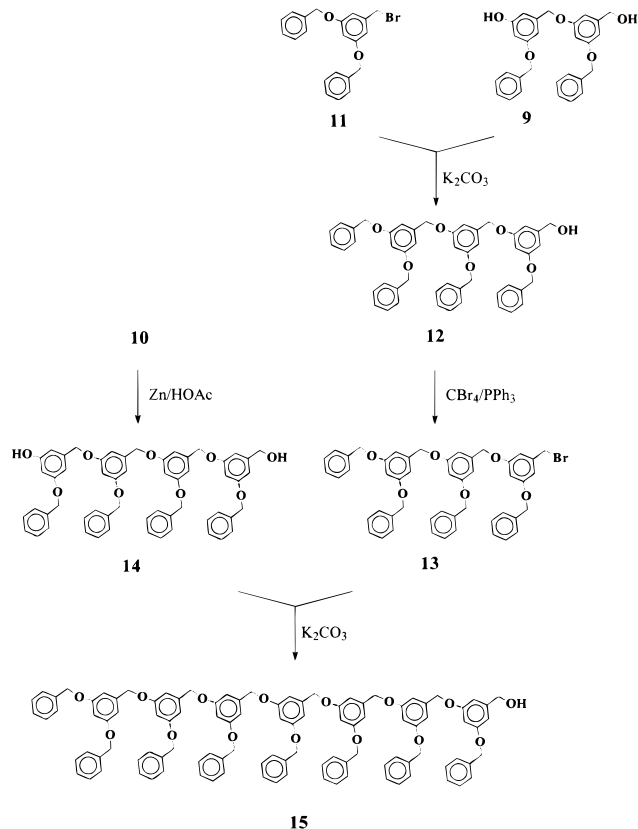


Figure 2. GPC traces for the (a) fifth generation dendritic alcohol 16, [G-5]-OH, and (b) the corresponding exact linear analog 17.

a significant difference in retention volume with the linear analog 17, having an approximately 40% larger hydrodynamic volume (Figure 2). This result is fully consistent with the more compact globular structure of the dendrimer in comparison to the random coil structure of its linear analog. It is of particular interest that similar property changes, or discontinuities, between generation four and fifth has been observed for a number of other dendrimer systems and suggests a fundamental difference between linear and dendritic macromolecules may only manifest itself in higher generation materials.⁷

Scheme 2



Significant differences were also found when the solubility and crystallinity of the linear and dendritic polyethers were compared. The fifth generation dendrimer 16 is completely amorphous and shows a glass transition temperature of 42 °C. In direct contrast, the exact linear analog 17 is highly crystalline and displays a strong melting transition at 150 °C. This high level of crystallinity was also observed for all other linear analogs and results in significantly different solubility behavior when compared to the amorphous dendrimers. In fact, the linear analogs can be crystallized from THF, acetone, or chloroform; solvents in which the dendrimers are extremely soluble.

In conclusion, a double-exponential growth strategy has been developed and successfully applied to the preparation of the linear analogs of the well-studied polyether dendrimers and the physical properties of the two series of macromolecular isomers compared. Significantly, it is observed that there is essentially no difference in hydrodynamic volume between the linear and dendritic polyethers up to generation four; however, a marked difference occurs for generation five and six with the linear macromolecule having a significantly larger hydrodynamic volume in tetrahydrofuran. It is also observed that the linear analogs are highly crystalline and have low solubilities which is in direct contrast to the amorphous and highly soluble dendrimers.

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Supporting Information Available: Experimental data for compounds discussed in this work (10 pages). See any current masthead page for ordering and Internet access instructions.

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