

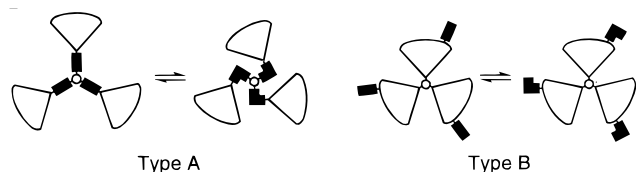
## Effect of Macromolecular Isomerism on the Photomodulation of Dendrimer Properties

Sheng Li and Dominic V. McGrath\*

Department of Chemistry, University of Arizona  
Tucson, Arizona 85721

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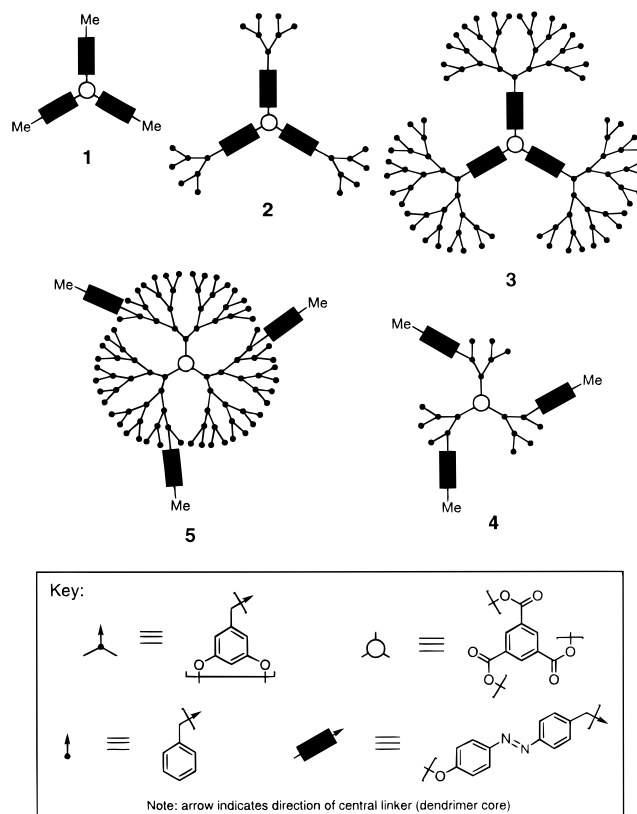
Proteins use stimuli-responsive groups that are sensitive to photons,<sup>1</sup> redox,<sup>2</sup> and ligand interactions<sup>3</sup> to alter their conformation and, in turn, their activity within living systems. Similar effects have been demonstrated in synthetically altered biomolecules.<sup>4</sup> The precise placement of stimuli-responsive groups within a structure is crucial to the effectiveness of the responsive behavior. Dendrimers, intrinsically globular synthetic macromolecules, include among their diverse structural types stimuli-responsive materials.<sup>5</sup> Intense interest in the application of dendrimers warrants a need for investigations of dendrimer structure–property relationships. Previous studies have compared dendrimers of varying generation, dendrimers with their linear analogues, and dendrimers of different structural classes.<sup>6</sup> However, no study has been made of external modulation of dendrimer properties as a function of subunit placement within the structure. Previously, we have reported photoresponsive benzyl aryl dendrimers with azobenzene-containing cores.<sup>7–9</sup> When three azobenzenes are incorporated into the center of these dendrimers (type A), four discrete states are observed depending on the *E/Z*



configuration of the individual azobenzenes (*EEE*, *EEZ*, *EZZ*, and *ZZZ*).<sup>8</sup> Herein we compare the properties of these materials to macromolecular isomeric<sup>10</sup> dendrimers containing photochromic groups at the periphery (type B). In doing so we provide the first

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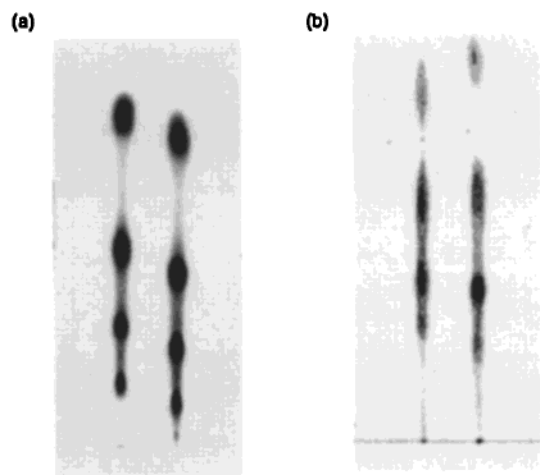
Chart 1



demonstration that precise relative placement of stimuli-responsive subunits within a dendrimer structure is necessary for maximizing their effect on the modulation of dendrimer properties. This direct comparison of isomeric, stimuli-responsive dendritic structures directly probes the nature of dendritic architectures.

Second and fourth generation dendrimers of types A and B were prepared for this study (Chart 1). The preparation of dendrimers of type A (1–3) has been previously reported.<sup>8</sup> Compound 1 serves as the smallest member of both dendrimer types A and B. To access type B dendrimers 4<sup>11</sup> and 5, it was necessary to prepare dendrons with a single functional group on the periphery and then attach them to the central core. Since the standard convergent method for dendrimer synthesis only provides dendrons with identical peripheral subunits,<sup>12</sup> a protection/half wedge generation/deprotection/whole generation synthetic strategy was applied. Similar extended strategies have been used in the past.<sup>13</sup> We note that second generation dendrimers 2 (C<sub>195</sub>H<sub>162</sub>N<sub>6</sub>O<sub>27</sub>) and 4 (C<sub>177</sub>H<sub>150</sub>N<sub>6</sub>O<sub>27</sub>) and fourth generation dendrimers 3 (C<sub>699</sub>H<sub>594</sub>N<sub>6</sub>O<sub>99</sub>) and 5 (C<sub>681</sub>H<sub>582</sub>N<sub>6</sub>O<sub>99</sub>) are not exact structural isomers of each other. However, the relative placement of the azobenzene subunits in the center and on the periphery makes them effectively macromolecular isomers.<sup>10,14</sup> Dendrimers 4 and 5 exhibit photochromic behavior essentially identical with dendrimers 1–3<sup>8</sup> that is characteristic of azobenzene-containing materials.<sup>15</sup>

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- (14) Satisfactory characterization data (<sup>1</sup>H and <sup>13</sup>C NMR spectroscopy, GPC, and MALDI mass spectrometry) were obtained and found to be consistent with the assigned structure of all new compounds reported.



**Figure 1.** Thin-layer chromatography (TLC) of second generation dendrimers **2** and **4** and fourth generation dendrimers **3** and **5** on SiO<sub>2</sub>-coated plates: (a) **2** (left) and **4** (right) with 1:24 ether–methylene chloride as eluent; (b) **3** (left) and **5** (right) with 3:90:7 ether–methylene chloride–hexane as eluent. Samples were irradiated with 350 nm light in acetone solution for approximately 1 min prior to experiment.

The effect of the relative placement of azobenzene subunits within the architecture of dendrimers **1–5** on their physical properties was initially studied by absorption chromatography. Since *Z*-azobenzene is more polar than *E*,<sup>15</sup> the azobenzene subunits in these dendrimers serve as probes of the accessibility of regions of the dendrimer to the outside environment. We had previously reported that the chromatographic retention times of the individual diastereomeric states of **1–3** (*EEE*, *EEZ*, *EZZ*, and *ZZZ*) increase with increasing *Z* content of the trisazo core.<sup>8</sup> Similarly, monitoring the distribution of the isomers of **4** and **5** as a function of irradiation time was also possible. We directly compared the chromatographic behavior of second generation dendrimers **2** and **4**, dendrimers that differ only in the placement of azobenzenes within the dendritic architecture (Figure 1). After irradiation with 350 nm light, four spots were observed for both compounds which represent the four isomers (*EEE*, *EEZ*, *EZZ*, and *ZZZ*). Despite a small difference in the absolute *R<sub>F</sub>* values of the individual isomers, the range of *R<sub>F</sub>* values for the isomers of both compounds is identical. This indicates that the effect of the azobenzene on the polarity properties of both dendrimers is similar (by TLC), even though their structures are significantly different. Even the chromatographic behavior of fourth generation dendrimers **3** and **5** exhibits a remarkable similarity in the observed *R<sub>F</sub>* values of the corresponding configurational isomers. Indeed, the range of *R<sub>F</sub>* values for the isomers of **3**, with interior azobenzenes, is somewhat smaller than the corresponding range for the isomers of dendrimer **5**, with exterior azobenzenes. Yet overall, we find that photomodulation of dendrimer polarity is insensitive to the relative placement of the responsive groups within the structure. Presumably the flexibility of the benzyl aryl ether dendrons<sup>16–18</sup> as well as a lack of secondary interactions between the end groups<sup>19</sup> precludes these dendrimers from adopting a fully insulating core–shell morphology,<sup>20,21</sup> at least to the fourth generation.

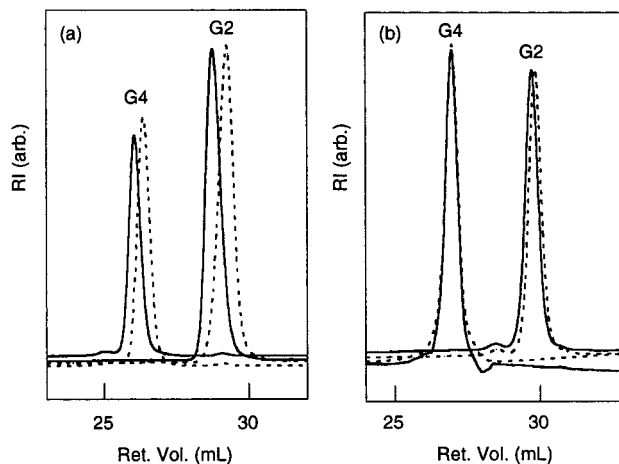
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**Figure 2.** GPC traces for dendrimers (a) **2** and **3** and (b) **4** and **5** before (—) and after (---) irradiation with 350 nm light. Conditions: CH<sub>2</sub>Cl<sub>2</sub>; 1 mL/min; 500 Å, 1000 Å, 10 000 Å DVB (Jordi) columns (250 × 10 mm); ambient temperature.

The effect of azobenzene isomerism on the three-dimensional molecular size of dendrimers **1–5** was studied by gel permeation chromatography (GPC). All compounds exhibited an increase in GPC retention volume, indicating a decrease in hydrodynamic volume, following irradiation of the sample (Figure 2). For example, the peak retention volume of fourth generation type A dendrimer **3** was 26.06 mL before irradiation and 26.37 mL after.<sup>22</sup> However, a clear difference was observed between the change in hydrodynamic volume of the dendrimers before and after irradiation depending on the placement of the azobenzenes within the dendrimer. For type A dendrimers **2** and **3**, a marked decrease in hydrodynamic volume (29 and 16%, respectively) was observed after irradiation with 350 nm light to a photostationary state. However, for type B dendrimers **4** and **5**, a much smaller difference in hydrodynamic volume (6.1 and 0.5%, respectively) was observed under the same conditions. Overall, the photomodulation of dendrimer hydrodynamic volume is extremely sensitive to the relative placement of the responsive groups within the structure.

In conclusion, a comparison of benzyl aryl ether dendrimers containing photochromic azobenzenes constructed in two limiting isomeric forms reveals that the relative placement of responsive groups within the structure can dramatically alter their effect on the photomodulation of dendrimer properties. However, the magnitude of that alteration is markedly dependent on the property observed. Similar studies involving different photochromic units and dendrimers of different structural classes are underway.

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**Supporting Information Available:** Synthetic details and characterization data for **5** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(22) Although all four isomers of dendrimers **1–5** are present together in solution as confirmed by <sup>1</sup>H NMR, we did not observe individually resolved peaks in the GPC of equilibrium mixtures after different irradiation times. However, a reproducible limiting elution volume (±0.02 mL) was always observed for both dark incubated and extensively irradiated samples. Based on a photostationary state ratio of 1:9 *E/Z* for these experimental conditions, the isomer ratio for **1–5** after extended irradiation was approximately <0.1: 3:24:72 *EEE/EEZ/EZZ/ZZZ* and the reverse for a dark incubated sample.