

Design of Branched and Chiral Solvatochromic Probes: Toward Quantifying Polarity Gradients in Dendritic Macromolecules

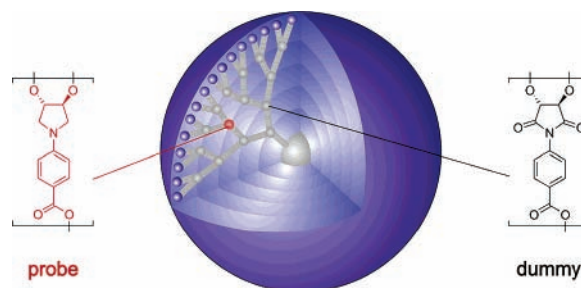
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ABSTRACT



A pair of chiral, branched monomer building blocks, consisting of a solvatochromic probe and a spectroscopically inactive volume dummy, has been developed. The probe can selectively be excited, and its fluorescence characteristics provide information about local polarity. Incorporation of these monomers into high-generation polyester dendrimers should enable a detailed investigation of the polarity/density profile in dendritic architectures and ultimately allow for the realization of energy gradients from *one* chromophore building block only.

Since the discovery of dendrimers representing a unique class of perfectly branched macromolecules,¹ research interest shifted toward controlled functionalization of the individual dendritic compartments. To tune molecular properties, a better understanding of the complex and dynamic three-dimensional dendritic structure and its relation to internal functionalization² is essential. In particular, the question concerning the radial density profile of dendrimers, i.e., dense shell vs dense core,³ raises a long-standing controversy among researchers in the field.

Our aim is to synthesize dendrimers equipped with generation-specific solvatochromic probes (Figure 1) and to elucidate their respective local environment, thereby gaining information about internal solvation and hence density distribution throughout the structure.⁴ Consequently, this approach should allow the construction of gradient architectures⁵ from *one* monomer building block to realize

(1) (a) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendritic Molecules: Concepts, Synthesis, Perspectives*; Wiley-VCH: Weinheim, 2001. (b) Fréchet, J. M. J.; Tomalia, D. *Dendrimers and Other Dendritic Polymers*; Wiley: Chichester, 2001.

(2) Hecht, S. *J. Polym. Sci., Part A: Polym. Chem.* **2003**, *41*, 1047–1058.

(3) Ballauff, M.; Likos, C. N. *Angew. Chem., Int. Ed.* **2004**, *43*, 2998–3020 and references therein.

(4) The original approach by Schlüter, Rettig, and co-workers is based on large pyrene-derived building blocks. Thus far only low-generation dendrons and dendrimers have been synthesized: (a) Modrakowski, C.; Flores, S. C.; Beinhoff, M.; Schlüter, A. D. *Synthesis* **2001**, 2143–2155. For pyrene-based probes: (b) Beinhoff, M.; Weigel, W.; Jurczok, M.; Rettig, W.; Modrakowski, C.; Brüdgam, I.; Hartl, H.; Schlüter, A. D. *Eur. J. Org. Chem.* **2001**, 3819–3829. (c) Weigel, W.; Rettig, W.; Dekhtyar, M.; Modrakowski, C.; Beinhoff, M.; Schlüter, A. D. *J. Phys. Chem. A* **2003**, *107*, 5941–5947. (d) Von Seggern, D.; Modrakowski, C.; Spitz, C.; Schlüter, A. D.; Menzel, R. *Chem. Phys.* **2004**, *302*, 193–202. (e) Beinhoff, M.; Weigel, W.; Rettig, W.; Brüdgam, I.; Hartl, H.; Schlüter, A. D. *J. Org. Chem.* **2005**, *70*, 6583–6591.

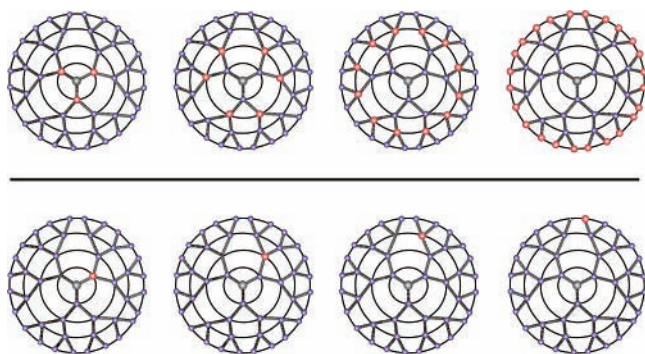


Figure 1. Investigating conformational dynamics in dendrimers by utilizing generation-specific solvatochromic probes. Dendrimer series consisting of generations entirely labeled with probes (top) or exact regioisomers containing a single generation-specific probe (bottom) are targeted. Probes are shown in red.

vectorial energy and electron-transfer processes, essential to efficient light harvesting and charge separation, respectively.⁶ An alternative approach to probe each internal dendritic layer has recently been reported by Thayumanavan and co-workers, who measured the accessibility of generation-specific anthracene probes within convergently grown Fréchet-type dendrons⁷ by fluorescence quenching using a small molecule quencher.⁸

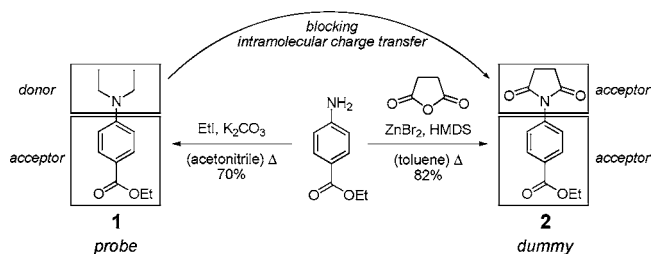
Here, we disclose both synthesis and photophysical properties of a pair of chiral, branched monomer building blocks, one of them serving as solvatochromic probe and the other as volume dummy, i.e., closely resembling the probe's structure yet being spectroscopically inactive. The described monomers should allow for the synthesis of high-generation dendrimers since the compact chromophore is directly incorporated, not appended,^{4,8} into the structure at a given branch point.

The probe has to fulfill several key requirements: it should be a compact and branched chromophore, which can be selectively excited in the presence (of a large excess) of the dummy and thereby exhibits significantly altered emission response toward a changing environment (solvatochromicity). Large solvatochromicity can be realized in donor–acceptor systems that display dual fluorescence from locally excited (LE) as well as twisted intramolecular charge transfer (TICT) states.⁹ In higher generation dendrimers the emission characteristics might in addition be influenced by steric effects due to the reorganization accompanying TICT state formation.

Although different probe/dummy model systems have been prepared and spectroscopically studied, the most promising

results were obtained using the pair of a *p*-aminobenzoate probe and a *p*-imidobenzoate dummy (Scheme 1). Our idea

Scheme 1. Concept and Synthesis of Model Compounds



is based on replacing the amino donor group in model probe **1** with an imido acceptor unit in model dummy **2**, thereby rendering the dummy optically inactive yet conserving chemical connectivity and structure.

The absorption spectra of the model probe/dummy pair show both required features: (1) selective excitation of **1** due to batho- and hyperchromically shifted absorption maxima (as compared to **2**) rather independent of solvent and (2) strong solvatochromic response of **1** (Figure 2). The

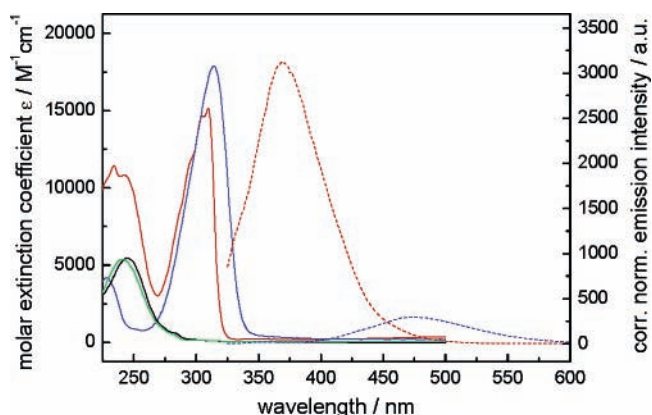


Figure 2. Absorption and emission spectra of model compounds. Probe **1** in cyclohexane: absorption (solid red line), emission (dashed red line). Probe **1** in acetonitrile: absorption (solid blue line), emission (dashed blue line). Absorption of dummy **2** in cyclohexane (green line) and acetonitrile (black line). All spectra at 25 °C; for emission spectra $\lambda_{\text{exc}} = 315$ nm was used.

strong solvatochromicity of the probe **1** is most likely the result of vastly different solvation along the $^1\text{L}_a$ excited-state surface leading to emission from either the LE state in the case of nonpolar solvents (cyclohexane) or the TICT state in the case of polar solvents (acetonitrile).⁹

To further test the suitability of this system, a 1:44 mixture of **1** and **2** resembling the relative ratio of both components in a G-4 dendrimer carrying a single probe unit (Figure 1, bottom) was investigated. In this “pseudo G-4 scenario”, selective excitation of **1** could be achieved at $\lambda_{\text{exc}} = 315$ nm

(5) A unique example of a gradient architecture is given by: Devadoss, C.; Bharathi, P.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 9635–9644.

(6) Adronov, A.; Fréchet, J. M. J. *J. Chem. Commun.* **2000**, 1701–1710.

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(9) (a) Grabowski, Z. R.; Rotkiewicz, K.; Rettig, W. *Chem. Rev.* **2003**, *103*, 3899–4031. (b) Rettig, W. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 971–988.

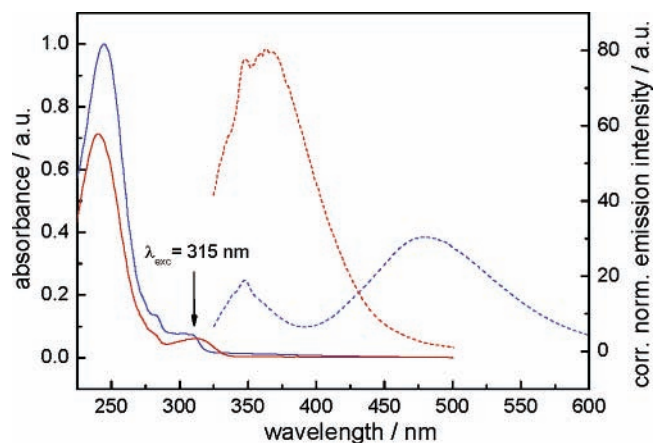


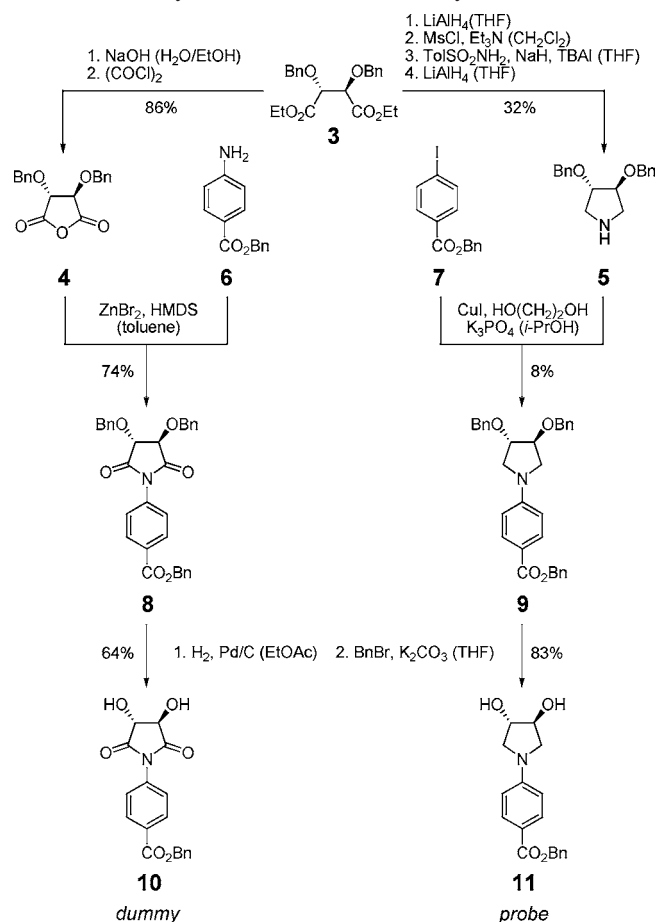
Figure 3. Absorption and emission spectra of the probe/dummy model pair in 1:44 ratio resembling a G-4 dendrimer as depicted in the bottom of Figure 1. Absorption at 25 °C in cyclohexane (solid red line) and acetonitrile (solid blue line). Emission at 25 °C in cyclohexane (dashed red line) and acetonitrile (dashed blue line) using $\lambda_{\text{exc}} = 315$ nm.

and the probe exhibited strongly solvent-dependent fluorescence emission featuring a large bathochromic shift ($\Delta\lambda_{\text{abs}} = 105$ nm) and a somewhat decreased intensity when comparing cyclohexane with acetonitrile solutions (Figure 3). A separate experiment analyzing the individual contributions in the mixture is provided in Supporting Information.

On the basis of these encouraging results, we engaged in the synthesis of the dendritic probe and dummy monomers. To enable efficient and modular dendrimer growth allowing for generation-specific labeling, convergent polyesters prepared from acid-diol-type AB_2 monomers were targeted.^{9,10} While a benzoic acid functionality was already present, a tartrate-based building block was utilized to incorporate the diol unit into the monomers. In addition to providing both hydroxyl groups necessary for branching multiplicity, the tartrate also introduces chirality into the system and the resulting dendrimers.¹¹

The convergent synthesis of both monomers involved preparation of benzyl-protected tartrate-based building blocks, which were joined with the respective *p*-substituted benzoate moieties (Scheme 2). Whereas the dummy precursor **8** was prepared in good yields via imide formation between bis-benzylated tartaric acid anhydride **4** and benzyl 4-aminobenzoate **6** utilizing chemistry pioneered by Vorbrüggen,¹² the probe precursor **9** was accessed in rather sluggish yields by Cu-catalyzed amination¹³ of 4-iodobenzoate **7** with bis-benzylated pyrrolidine **5**. Initially anticipated direct conver-

Scheme 2. Synthesis of Dendritic Dummy/Probe Monomers



sion **8** → **9** by chemoselective reduction¹⁴ was not successful. The fully benzylated precursors **8** and **9** were converted into the respective monomers **10** and **11** via complete hydrogenolysis followed by chemoselective rebenzylation of the focal carboxylates.

To verify the key optical requirements of the synthesized probe and dummy monomers, their absorption and emission characteristics in various solvents were investigated in a similar fashion as described for the model system (Figure 4). While the dummy **10** was not affected as compared to the model **2**, the probe's (**11**) absorption and emission characteristics were somewhat altered upon introduction of the cyclic constraint, i.e., diethylamino group → pyrrolidino group, as compared to model **1**. Both the large Stoke's shift of the emission arising from the LE state was diminished, i.e., $\Delta\lambda_{\text{max}} = 22$ nm for **11** instead of $\Delta\lambda_{\text{max}} = 45$ nm for **1** in chloroform, and the emission was less dramatically altered in response to changing solvent. Compared to model **1**, the emission shifted hypsochromically in cyclohexane ($\lambda_{\text{em}} = 330$ nm) and showed two emission bands in acetonitrile ($\lambda_{\text{em}} = 347$ and 485 nm). This suggests that rigidification of the donor moiety in **11** leads to dual fluorescence emission from both LE and TICT states.⁹

(10) Efficient convergent synthesis of high-generation polyester dendrimers based on 2,2-bis(hydroxymethyl)propionic acid has been reported in: (a) Ihre, H.; Hult, A.; Soederlind, E. *J. Am. Chem. Soc.* **1996**, *118*, 6388–6395. (b) Ihre, H.; Hult, A.; Fréchet, J. M. J. *Macromolecules* **1998**, *31*, 4061–4068.

(11) For a review on chiral dendrimers, consult: Ramagnoli, B.; Hayes, W. J. *Mater. Chem.* **2002**, *12*, 767–799 and references therein.

(12) Vorbrüggen, H. *Acc. Chem. Res.* **1995**, *28*, 509–520.

(13) For a review, consult: Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400–5449 and references therein.

(14) Merkel, W.; Mania, D.; Bormann, D. *Liebigs Ann. Chem.* **1979**, 461–468.

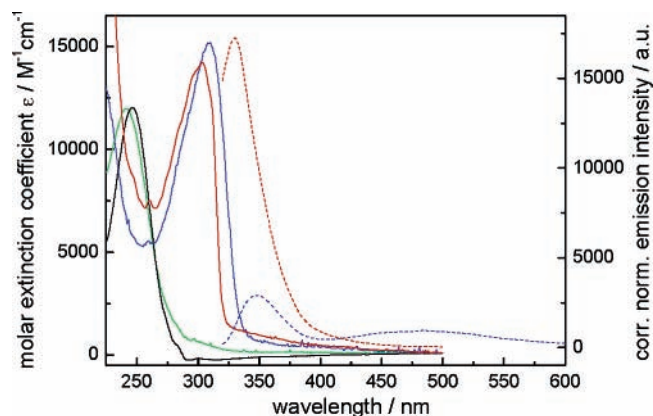


Figure 4. Absorption and emission spectra of branched probe and dummy monomers. Probe **11** in cyclohexane: absorption (solid red line), emission (dashed red line). Probe **11** in acetonitrile: absorption (solid blue line), emission (dashed blue line). Absorption of dummy **10** in cyclohexane (green line) and acetonitrile (black line). All spectra at 25 °C; for emission spectra $\lambda_{\text{exc}} = 315$ nm was used.

Monomers **10** and **11** still exhibit the necessary requirements for successful design of dendrimers carrying generation-specific probes. Selective excitation can be achieved and

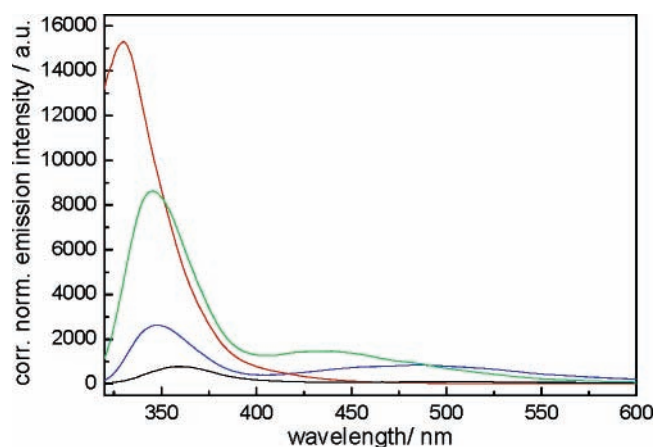


Figure 5. Emission spectra of branched probe monomer in various solvents. Probe **11** in cyclohexane (red line), acetonitrile (blue line), methylene chloride (green line), and methanol (black line). All spectra at 25 °C with $\lambda_{\text{exc}} = 315$ nm.

emission from the dummy monomer **10** is negligible at $\lambda_{\text{exc}} = 315$ nm (see Supporting Information). Furthermore, the

probe monomer **11** displays a significant solvatochromic response of its emission characteristics (Figure 5). Increasing solvent polarity seems to stabilize the TICT state relative to the LE state, and dual fluorescence can be observed. Both emission maxima and relative intensities seem to correlate well with solvent polarity, in particular with Reichardt's solvent parameter $E_{\text{T}}(30)^{15}$ (Table 1). In addition to solvent

Table 1. Solvatochromic Response of Probe Monomer **11**

	solvent			
	C ₆ H ₁₂	CH ₂ Cl ₂	CH ₃ CN	CH ₃ OH
$\lambda_{\text{max}}^{\text{LE}}$ (nm)	330	344	347	359
$\lambda_{\text{max}}^{\text{TICT}}$ (nm)	no ^a	439 ^b	484 ^b	488 ^b
$I_{\text{rel}}(\text{LE})^c$	1	0.56	0.17	0.05
$I_{\text{rel}}(\text{TICT})^c$	no ^a	1	0.58	0.07
$E_{\text{T}}(30)^d$	31.2	40.7	45.6	55.4

^a Not observed. ^b Broad maximum. ^c Relative intensity. ^d Reichardt's solvent parameter.¹⁵

polarity, solvent acidity seems to contribute to the observed effects, as illustrated by the use of methanol.

In conclusion, we have synthesized a pair of sterically similar, yet optically contrasting, branched chiral monomers, i.e., dummy **10** and probe **11**. These building blocks should enable the preparation of high-generation, convergent polyester dendrimers equipped with single or multiple generation-specific solvatochromic probes (see Figure 1) and thereby allow for a quantitative evaluation of the internal solvation profile. In addition to providing valuable insight into the density distribution throughout dendritic architectures, the building blocks described herein should facilitate the design of gradient systems based on *one* monomer unit only. Furthermore, the effect of chirality on these parameters can conveniently be studied.

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Supporting Information Available: Description of all experimental procedures including synthesis, characterization data, and additional optical spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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