Chiral Hyperbranched Dendron Analogues

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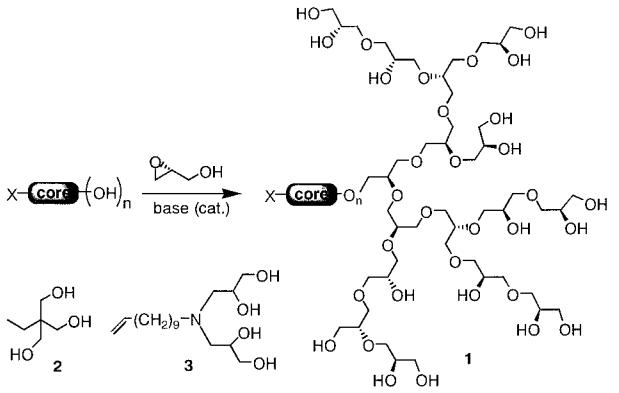
Dendrimers are perfectly cascade-branched macromolecules based on AB_m type structural units, possessing a large number of end groups.[1] Dendrons are dendrimer "wedges", which are characterized by the presence of *precisely one* functional group at the core, which is different from the B end groups in the periphery of the structure. Recently, dendron structures have been used widely as versatile modules for the preparation of "dendronized" polymers.[2] In most examples of dendrons used as supramolecular building blocks, dendritic polybenzyl ethers based on convergent reactions developed by Hawker and Fréchet have been employed.[3] Generally, due to their tapered or conical shape, dendrons are useful to create shape-controlled nanostructures and nanoobjects.[4] An important issue in dendrimer chemistry is the incorporation of chiral units into cascade-branched structures. This may be realized either by suitable end group functionalization[5] or by the use of chiral building blocks.[6,7] However, hitherto only a few examples of chiral dendrons have been reported.[8,9]

In contrast to the tediously constructed dendrimers, hyperbranched polymers are cascade-branched structures prepared by a one-pot synthesis of AB_m- or latent AB_m-type monomers.[10] Thus, their architecture is less perfectly branched; i.e., linear, dendritic, and terminal units are incorporated randomly. In contrast to dendrimers, hyperbranched polymers do not possess a gradient of structural density. So far, hyperbranched polymers have been regarded as poorly defined because of their commonly broad polydispersities and the lack of control over the core incorporation.[10] Recently, we reported the preparation of highly defined hyperbranched polyglycerols, based on the ring-opening multibranching polymerization of glycidol (ROMBP).[11] Due to the chain-growth nature of this process, these macromolecules possess the initiator employed as core unit and can be prepared in a molecular weight range between 1000 and 10 000, with narrow polydispersities M_w/M_n < 1.5 (mostly <1.3). Molecular weights are controlled by the monomer/initiator ratio.

In this Communication we report the first synthesis of chiral hyperbranched polymers and chiral hyperbranched dendron analogues **1**, based on the polymerization of both commercially available enantiomers of glycidol (Scheme 1). Incorporation of precisely one functional group at the core was achieved via an initiator bearing a functional group, i.e., a terminal double bond. Chiral polyglycerols in general may be suitable in the separation of enantiomers, in chiral catalysis, or for biochemical applications. The single double bond attached to the focal unit in the dendron-like structure is accessible for a variety of further functionalization methods by common olefin reactions,

Scheme 1



e.g., hydrosilylation, radical thiol addition, metathesis, or ene reactions. This renders the hyperbranched dendron analogues interesting materials for specific surface modification, novel polymeric supports, building blocks in supramolecular chemistry, and solubilizing agents, e.g., for ligands. Detailed investigations concerning these reactions and applications will be the subject of forthcoming publications.

As shown in Scheme 1, we applied trimethylolpropane (TMP), **2**, as well as bis(2,3-dihydroxypropyl)-10-undecenylamine[12] as initiators for the base-catalyzed ROMBP of the two enantiomeric glycidols. Compound **3** was prepared by reaction of 10-undecenylamine[13] with 2 equiv of glycidol. Polymerization and characterization were achieved by the methods described previously.[11] All experiments were carried out on a 20 g scale. The characterization data of several chiral polyglycerols are summarized in Table 1.

Molecular weights of the dendron analogues range between 1300 and 4800, being well-controlled by the monomer/initiator ratio ([M]/[I]; cf. Table 1), representing a degree of polymerization of 20−60 glycidol units per polymer. The degree of branching was in the range 0.53−0.57, similar as in the case of the racemic polyglycerol.[11] SEC shows that all samples exhibited narrow molecular weight distributions (M_w/M_n < 1.5). ^{1}H NMR clearly evidences incorporation of the initiator applied. However, to clarify whether the initiator was incorporated in all species present in the molecular weight distribution, MALDI-TOF mass spectrometry was employed. Figure 1 shows representatively the spectrum of sample PG5. All peaks can be assigned unambiguously to polyglycerols bearing the undecenylamine unit. For instance, the peak at m/z = 1433.5 is explained by the mass of the counterion (Li, M = 6.9), plus the initiator (bis(2,3-dihydroxypropyl)-10-undecenylamine, M = 317.5) and 15 (chiral) glycidol units (M = 74.1). A weak subdistribution is observed, caused by polymers detected without lithium ions. Hence, the peak left to m/z = 1433.5 appears at m/z = 1427.5. Another effect typical of such amine-containing polyglycerols is that only a certain fraction of the molecular weight distribution is detected. Whereas the MALDI-TOF spectrum suggests a molar mass of around 2000 g/mol, NMR calculations and SEC results clearly point to a molar mass of 3400 g/mol.

All samples were characterized concerning their optical rotation power in methanol solution. For comparison,

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Table 1. Characterization Data for Chiral Polyglycerols with 2 and 3 Applied as Initiators

sample	initiator	[M]/[I][a]	DP_n[b]	M_n[b]	M_w/M_n[c]	$[\alpha]_D^{20°}$[d] (deg)
(+)-PG1	TMP (**2**)	20 (+)	16	1300	1.5	+5.7
(+)-PG2	TMP (**2**)	45 (+)	46	3500	1.3	+5.5
(+)-PG3	TMP (**2**)	60 (+)	63	4800	1.4	+5.1
(+)-PG4	C11 (**3**)	60 (+)	57	4600	1.3	+2.0
(−)-PG5	C11 (**3**)	40 (−)	42	3400	1.3	− 2.3
(±)-PG6	C11 (**3**)	90 (±)	89	6900	1.4	0

[a] Monomer/initiator ratio (optical rotation of monomer). [b] Calculated from ^{13}C NMR,[11] measured in d_4-methanol. [c] Determined by SEC, performed in DMF at 45 °C using poly(propylene oxide) standards. [d] Measured in 5% methanol solution.

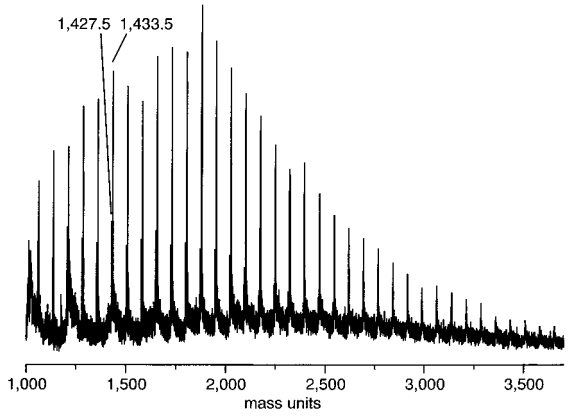
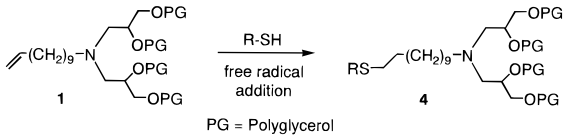


Figure 1. MALDI-TOF MS spectrum of sample (−)-PG5. α-Cyano-4-hydroxycinnamon acid was used as matrix, and LiCl was added.

the racemic sample PG6 has also been prepared and characterized. As listed in the last column of Table 1, all samples exhibit the same specific optical rotation [α] as the monomor used for polymerization. This is in accordance with the expectation that in anionic epoxide polymerization nucleophilic attack occurs at the least substituted end of the epoxide ring,[14] in this case leaving the chiral center unaffected. Since each monomer unit adds one chiral center to the polymer, [α] is independent of the degree of polymerization. An interaction of the chiral centers leading to a molar mass dependent increase of [α] is not observed. This may be attributed to the highly flexible polyether structure and the fact that all chiral centers are separated by one oxygen and at least one carbon atom. The values of [α] observed for the TMP **3** initiated samples (PG1, PG2, PG3) are very similar. The absolute values are in good agreement with literature values for chiral glycerol ethers, e.g., glycerol−monomethyl ether[15] $[\alpha]_D^{20°} = 5.4°$ and linear poly-*R*-(1,3-glycidol), $[\alpha]_D^{20°} = 5.5°$.[16] When **3** is applied as initiator (PG4, PG5), the value of [α] is significantly lower, probably due to the higher achiral fraction of the polymer. This is obviously related to the different initiator used for the preparation of these polymers, which does not possess an asymmetric carbon and exhibits a lower substitution density. CD spectra of the samples did not provide additional information.

The double bond attached to the focal unit of PG4, PG5, and PG6 is accessible to further functionalization. Exposing one of the polymers to an excess of a thiol (e.g., cysteamine hydrochloride) in the presence of free radicals (generated by AIBN and heating) led to quantitative addition of the thiol to the double bond (Scheme 2) to obtain compound **4**.[17] The reaction was monitored by NMR and MALDI-TOF mass spectrometry.

Scheme 2



We are confident that the versatile and well-controlled approach to hyperbranched chiral polyglycerol dendron analogues provides access to novel molecular entities suitable for applications that have been thought to be exclusively fulfilled by dendrons constructed in a stepwise synthetic fashion.

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References and Notes

(1) (a) Tomalia, D. A.; Naylor, A. M.; Goddard III, W. A. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 119. (b) Tomalia, D. A.; Durst, H. D. *Top. Curr. Chem.* **1993**, *165*, 193. (c) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendritic Macromolecules: Concepts, Syntheses, Perspectives*; VCH: Weinheim, Germany, 1996. (d) Fréchet, J. M. J.; Hawker, C. J. *React. Funct. Polym.* **1995**, *26*, 127. (e) Matthias, O. A.; Shipway, A. N.; Fraser-Stoddart, J. F. *Prog. Polym. Sci.* **1998**, *23*, 1. (f) Frey, H.; Lach, C.; Lorenz, K. *Adv. Mater.* **1998**, *10*, 279. (g) Vögtle, F. Dendrimers, *Top. Curr. Chem.* **1998**, *197*. (h) Fischer, M.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1999**, *38* (7), 885.

(2) (a) Schlüter, A.-D. In *Dendrimers*; Vögtle, F., Ed.; Springer: Berlin, 1998; pp 165. (b) Frey, H. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2193.

(3) Hawker, C. J.; Fréchet, J. M. J. *J. Am. Chem. Soc.* **1990**, *112*, 7638.

(4) (a) Balagurusamy, V. S. K.; Ungar, G.; Percec, V.; Johansson, G. *J. Am. Chem. Soc.* **1997**, *119*, 1539. (b) Hudson, S. D.; Jung, H.-T.; Percec, V.; Cho, W. D.; Johansson, G.; Ungar, G.; Balagurusamy, V. S. K. *Science* **1997**, *278*, 449. (c) Percec, V.; Ahn, C.-H.; Ungar, G.; Yeardley, D. J. P.; Möller, M.; Sheiko, S. S. *Nature* **1998**, *391*, 161.

(5) Peerlings, H. W. I.; Meijer, E. W. *Chem. Eur. J.* **1997**, *3*, 1563.

(6) (a) Chang, H.-T.; Chen, C.-T.; Kondo, T.; Siuzdak, G.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 182. (b) Seebach, D.; Rheiner, P. B.; Greiveldinger, G.; Butz, T.; Sellner, H. In *Dendrimers*; Vögtle, F., Ed.; Springer: Berlin, 1998; pp 125 and references therein.

(7) Chow, H.-F.; Mak, C. C. *Pure Appl. Chem.* **1997**, *69*, 483.

(8) Murer, P. K.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1995**, *107*, 2297.

(9) Chapman, T. M.; Hillyer, G. L.; Mahan, E. J.; Shaffer, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 11195.

(10) Kim, Y. H. *J. Polym. Sci., Polym. Chem. Ed.* **1998**, *36*, 1685.

(11) Sunder, A.; Hanselmann, R.; Frey, H.; Mülhaupt, R. *Macromolecules* **1999**, *32*, 4240.

(12) Bis(2,3-dihydroxy)-10-undecenylamine was prepared by slowly adding 2 equiv of glycidol to 10-undecenylamine at 100 °C in bulk. The product was not isolated prior to polymerization.

(13) 10-Undecenylamine was prepared from 10-undecenol by first chlorination using SO_2Cl_2 and subsequent amination by Gabriel synthesis. Reactions were carried out in a 100 g scale.

(14) Bailey, F. E.; Koleske, J. V. Alkylene Oxides and their Polymers. In *Surface Science Series*; Schick, M. J., Fowkes, F. M., Eds.; Marcel Dekker: New York, 1990; Vol. 35.

(15) Goldstein, I. J.; Hamilton, J. K.; Smith, F. *J. Am. Chem. Soc.* **1957**, *79*, 1190.

(16) (a) Vandenberg, E. J. *J. Macromol. Sci.* **1985**, *A22*, 619. (b) Taton, D.; Leborgne, A.; Sepulchre, M.; Spassky, N. *Macromol. Chem. Phys.* **1994**, *195*, 139.

(17) Free radical addition of cysteamine hydrochloride onto polyvinyl-substituted polyethers has been reported by: (a) Cammas, S.; Nagasaki, Y.; Kataoka, K. *Bioconjugate Chem.* **1995**, *6*, 226. (b) Kieburg, C.; Dubber, M.; Lindhorst, T. K. *Synlett* **1997**, *12*, 1447.

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