JOC Article

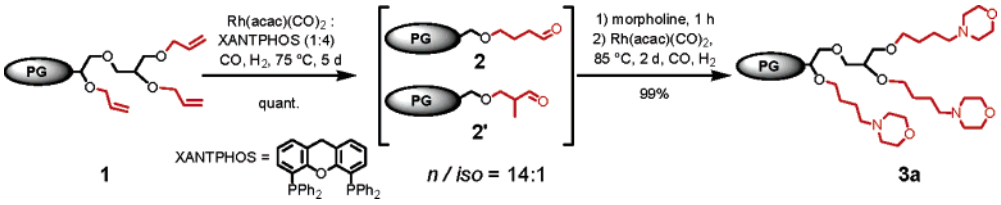
Highly Regioselective Synthesis of Amino-Functionalized Dendritic Polyglycerols by a One-Pot Hydroformylation/Reductive Amination Sequence

Fikret Koç, Monika Wyszogrodzka, Peter Eilbracht,* and Rainer Haag*

Organische Chemie, Universität Dortmund, Otto-Hahn-Str. 6, 44227 Dortmund, Germany

peter.eilbracht@udo.edu; rainer.haag@uni-dortmund.de

Received October 22, 2004



Dendritic architectures with neutral core structures and amines groups in the shell are a synthetic challenge, and there is a need for an efficient access. In this paper, highly selective Rh-catalysts are used for sequential hydroformylation/reductive amination of dendritic perallylated polyglycerols **1** with various amines in a one-pot procedure to give dendritic polyamines **3a**−**e** in high yields (73−99%). In all cases, complete conversion of the allyl ether and aldehyde intermediate has been observed. Furthermore, the use of protected amines provides reactive core−shell-type architectures after deprotection. These soluble but membrane filterable multifunctional dendritic polyamines are of high interest as reagents in synthesis or as supports in homogeneous catalysis as well as nonviral vectors for DNA-transfection.

Dendritic polyamines are an interesting class of compounds with respect to a number of applications[1] including DNA delivery and as antimicrobial agents as well as carriers for drugs and catalysts. Typically, polyamine dendrimers are prepared by a multistep procedure (two steps per generation) which is limited to lower generations (G1−G4).[2] However, for biomedical applications[1a,b] (i.e., DNA delivery[3]) typically larger nanoparticles (higher generations: G6−G8, 12−16 steps) are needed to observe the desired effects. A major problem in this application is the high cytotoxicity of the polycationic core molecules. Therefore, dendritic architectures with neutral core structures and amines only in the shell are a synthetic challenge and might overcome this biological problem. In contrast to polyamine dendrimers, dendritic polyglycerols offer a biocompatible core, which might reduce the cytotoxcicity of these compounds.[4]

Since the physicochemical properties of dendritic molecules are mostly determined by the terminal groups, the "shell", we wanted to use a modular approach based on an easily available hyperbranched polyglycerol core[5] as scaffold and an efficient method providing easy access to various amino shell functionalities. In addition, such a process would generate dendritic nanoparticles large enough to be separated by simple membrane separation techniques, avoiding lengthy column chromatography.

Initial investigations to generate amino-functionalized polyglycerols have been reported by the activation−substitution pathway; however, limited conversions (<75%) have been observed.[6,7] In addition, no gain of molecular weight of the polymer backbone can be achieved. First experiments to modify polyglycidol-polyallylglycidol copolymers with amine end groups via a hydroformylation sequence and to increase the molecular weight of the core were carried out by Sunder and Türk et al.[8] They demonstrated in a three-step reaction sequence of hydro

(1) (a) Haag, R. *Angew. Chem., Int. Ed.* **2004**, *43*, 278. (b) Stiriba, S.-E.; Frey, H.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *41*, 1329. (b) Astruc, D.; Chardac, F. *Chem. Rev.* **2001**, *101*, 2991. (c) Kreiter, R.; Kleij, A. W.; Gebbink, R. J. M. K.; Koten, G. v. *Top. Curr. Chem.* **2001**, *217*, 163. (d) Oosterom, G. E.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M. *Angew. Chem., Int. Ed.* **2001**, *40*, 1828. (e) Baars, M. W. P. L.; Meijer, E. W. *Top. Curr. Chem.* **2000**, *210*, 131.

(2)) (a) Newkome, G. R.; Moorefield, C. N.; Vögtle, F. *Dendritic Molecules: Concepts, Syntheses, Perspectives*, 2nd ed.; Wiley-VCH: Weinheim, 2001. (b) Tomalia, D., Fréchet, J. M. J., Eds. *Dendrimers and other Dendritic Polymers*; John Wiley & Co.: London, 2001.

(3)) Denning, J.; Duncan, E. *Rev. Mol. Biotech.* **2002**, *90*, 339.

(4)) Frey, H.; Haag, R. *Rev. Mol. Biotech.* **2002**, *90*, 257.

(5)) (a) Sunder, A.; Hanselmann, R.; Frey, H.; Mülhaupt, R. *Macromolecules* **1999**, *32*, 4240. (b) Sunder, A.; Mülhaupt, R.; Haag, R.; Frey, H. *Macromolecules* **2000**, *33*, 253.

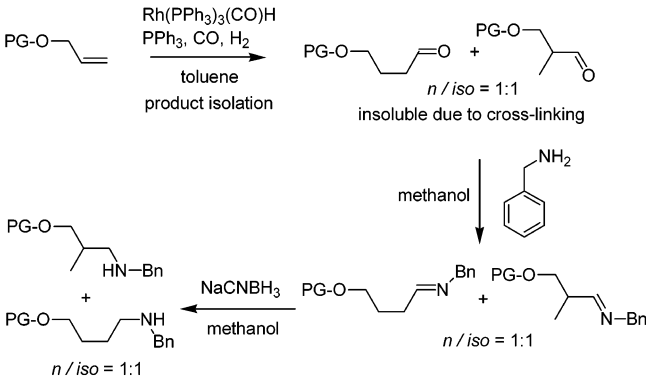
(6)) Salazar, R.; Fomina, L.; Fomine, S. *Polymer Bull.* **2001**, *47*, 151.

(7)) Roller, S.; Zhou, H.; Haag, R. *Mol. Diversity* **2005**, in press.

(8) Sunder, A.; Türk, H.; Haag, R.; Frey, H. *Macromolecules* **2000**, *33*, 7682.

10.1021/jo0481304 CCC: $30.25
Published on Web 02/16/2005

SCHEME 1. Initial Experiments for the Formation of Benzylamino Polyglycidol -poly(allylglycidol) Copolymers from Ref 8



formylation, imine formation, and reductive amination that this sequence can be applied to polyallyl ethers (Scheme 1). In this case, the hydroformylation of the polyallyl ether was achieved in the presence of Wilkinson's catalyst and no regiocontrol was obtained. Due to the incomplete allylation, hemiacetal formation occurs, leading to cross-linked products. Isolation of the insoluble aldehyde and addition of benzylamine forms the imine as a crude product, which was then reduced with $NaBH_3$-CN (Scheme 1).[9] The main drawbacks of this route are the poor regioselectivity (1:1) of the hydroformylation step and the required isolation of the instable aldehyde intermediate due to a solvent change.

Clearly a regioselective hydroaminomethylation or a hydroformylation combined with a subsequent reductive amination in one pot is of significant importance for synthetic dendrimer chemistry and would provide easy access to a wide range of different shell-modified dendritic polyamine architectures.

Herein we present a simple and efficient approach to dendritic polyamines via a catalytic hydroaminomethylation procedure starting from readily available dendritic polyallyl ethers **1**.[10] The synthetic concept involves a regioselective hydroformylation of the polyglycerol allyl ether (**1**) with XANTPHOS[11] as an *n*-selective directing phosphin ligand and $Rh(acac)(CO)_2$ as catalyst[12] followed by a reductive amination with various amines to generate amino-terminated polyglycerols[3a–e] using the same catalytic system. This simple one-pot protocol has been used to generate a number of dendritic polyglycerol architectures with a polyether core and different amino functionalities in the periphery.

Results and Discussion

Recently, efficient methods for the regiocontrolled hydroaminomethylation have been developed.[13,14] To test this method for the generation of dendritic polyamines we have prepared the dendritic polyallyl ether **1** on a multigram scale by allylation of hyperbranched polyglycerol (M_n = 5000 g/mol) using a simple phase-transfer protocol.[10] Our first approach was the direct domino hydroaminomethylation of **1** with morpholin in the presence of $Rh(acac)(CO)_2$ and XANTPHOS as ligand. However, the direct version of the hydroaminomethylation which was reported for relatively simple compounds[13] is not selective in this case; even the use of higher amounts of ligand had no influence. We obtained the morpholin-modified polyglycerol **3a/3a′** in 97% yield and an *n* to iso ratio of 1:1 (Scheme 2).

From earlier investigations it was known that amines can coordinate with the catalyst and decrease the regioselectivity of the hydroaminomethylation.[13,14] For this reason the regioselective hydroformylation was carried out in the presence of the ligand and absence of amine. Thus, we performed first the hydroformylation of **1** in the presence of XANTPHOS and $Rh(acac)(CO)_2$. In this case, the hydroformylation can be achieved with very high *n*-selectivity (14:1) to obtain the aldehyde **2** with quantitative conversion. The spectrum of the aldehyde did not show any remaining allyl signals, and no cross-linking was observed in this case.[15] In addition, no hydrogenation occurred during the in situ hydroformylation as compared by integration of the ^1H NMR spectra of **1** and **2** (see the Supporting Information). The addition of amine (Scheme 2 and Table 1) to the preformed polyaldehyde **2**, respectively, **2′** results in an enamine or imine which can be reduced in the autoclave to afford the dendritic polyamine **3a** with the same rhodium catalyst. By using this improved sequential but one-pot procedure the high regioselectivity of the hydroformylation is not reduced and isolation of the sensitive polyaldehyde is not required. This leads to highly regioselective dendritic polyamines which can be isolated in pure form after simple dialysis[16] (Figure 1). An analogue method was investigated by one of us to form macroheterocycles.[17]

To demonstrate the generality of this method we performed this reaction sequence with different aliphatic and aromatic amines. All employed amines (Table 1) could be converted to the corresponding dendritic polyamines **3a**–**e** in high to excellent isolated yields and high regioselectivity after simple purification by dialysis.

These investigations also include the modification of **1** with different protected amines in order to generate dendritic polyamines containing reactive primary and secondary amino end groups. The mono-Boc protected

(9)) Borch, R. F.; Bernstein, M. D.; Durst, H. D. *J. Am. Chem. Soc.* **1971**, *93*, 2897.
(10) (a) Haag, R.; Sunder, A.; Stumbé, J.-F. *J. Am. Chem. Soc.* **2000**, *122*, 2954. (b) A. Garcia-Bernabé, M. Krämer, B. Olah, R. Haag, *Chem. Eur. J.* **2004**, *10*, 2822.
(11) (a) van der Veen, L. A.; Keeven, P. H.; Schoemaker, G. C.; Reek, J. N. H.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Lutz, M.; Spek, A. L. *Organometallics* **2000**, *19*, 872. (b) Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Franje, J. *Organometallics* **1995**, *14*, 3081.
(12) (a) Müller, T. E.; Beller, M. *Chem. Rev.* **1998**, *98*, 675. (b) Landis, C. R.; Uddin, J. *J. Chem. Soc., Dalton Trans.* **2002**, 729. (c) Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Acc. Chem. Res.* **2001**, *34*, 895. (d) Carbó, J. J.; Maseras, F.; Bo, C.; van Leeuwen *J. Am. Chem. Soc.* **2001**, *123*, 7630.
(13) Ahmed, M.; Seayad, A. M.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc.* **2003**, *125*, 10311.
(14) Eilbracht, P.; Kranemann, C. L.; Bärfacker, L. *Eur. J.Org. Chem.* **1999**, 1907.
(15) The polyaldehyde is stable in solution under argon for several days and can be stored at temperatures below −20 °C for several weeks.
(16) Haag, R.; Sunder, A.; Hebel, A.; Roller, S. *J. Comb. Chem.* **2002**, *4*, 112.
(17) Angelovski, G.; Eilbracht, P. *Tetrahedron* **2003**, *59*, 8265.

SCHEME 2. Hydroaminomethylation and Highly Regioselective One-Pot Hydroformylation/Reductive Amination Sequence of Polyallyl Ether 1 to the Corresponding Dendritic Amino Polyglycerols 3a–e (cf. Table 1). Insert: ^{1}H NMR Trace of Aldehyde Signals of 2

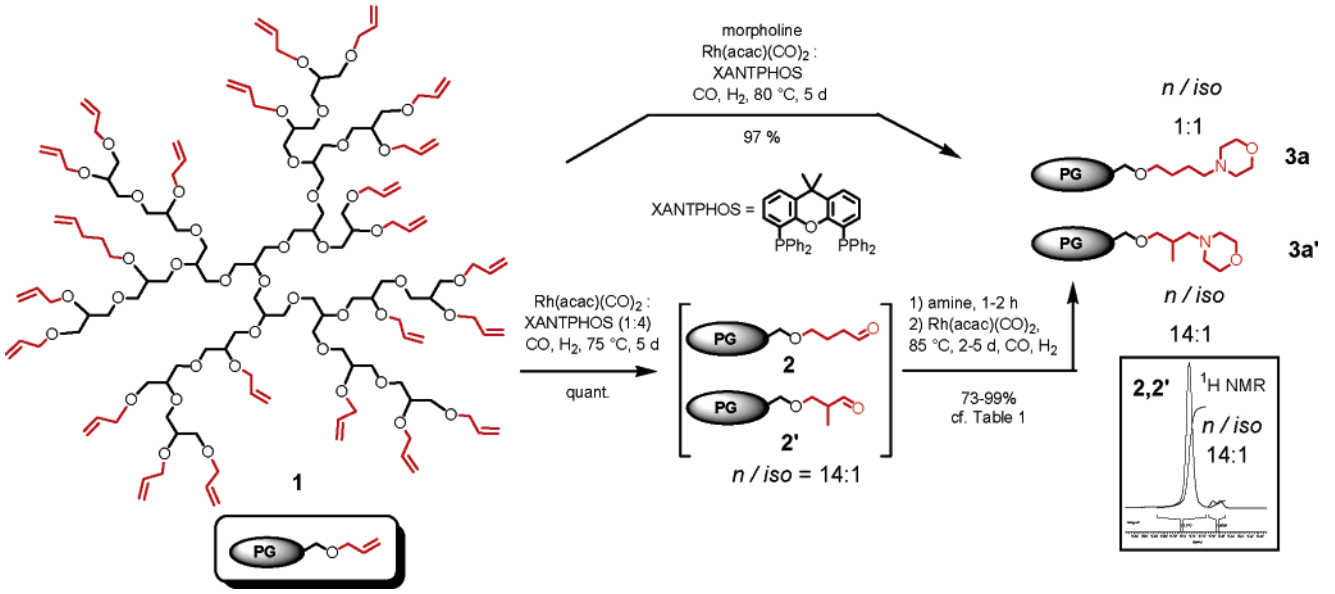
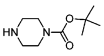
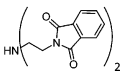


TABLE 1. Sequential One-Pot Reaction of Different Functional Amines with Dendritic Polyallyl ether 1[18]

Entry	Amine	t [h]	Dialysis [h][16]	Prod	M_n [g/mol]	Yield [%]
1		48	48	**3a**	14600	99
2		48	24	**3b**	15900	79
3		96	48	**3c**	15000	73
4		120	48	**3d**	21200	78
5		120	36	**3e**	33200	99

piperazine[19] was reacted with **2** in very good yields to the protected polyamine **3d** (Table 1, entry 4). A second reaction was performed with bis-[2-(*N*-phthalimidyl)-ethyl]amine[20] and the preformed polyaldehyde **2**, respectively, **2′** resulting in nearly quantitative yields of the highest molecular weight (M_n = 33 200) dendritic polyamine **3e** in this series (Table 1, entry 5).

For the deprotection of these dendritic polyamines **3d**,**e** different methods were investigated. The deprotection of **3d** can be performed under standard Boc-deprotection conditions with HCl to form the secondary amine modified dendritic polyglycerol **4** (M_n = 14 500 g/mol) according to Scheme 3. The use of TFA for deprotection of **3d** was not successful.

(18) All reactions are done under synthesis gas atmosphere (60 bar H_2, 10 bar CO) and 85 °C.

(19) (a) Boschi, D.; Di Stilo, A.; Fruttero, R.; Medana, C.; Sorba, G.; Gasco, A. *Arch. Pharm. (Weinheim)* **1994**, *327*, 661. (b) Angelovski, G.; Costisella, B.; Kolarić, B.; Engelhard, M.; Eilbracht, P. *J. Org. Chem.* **2004**, *69*, 5290.

(20)) Yuen, Ng. C.; Motekaitis, R. J.; Martell, A. E. *Inorg. Chem.* **1979**, *18*, 2982.

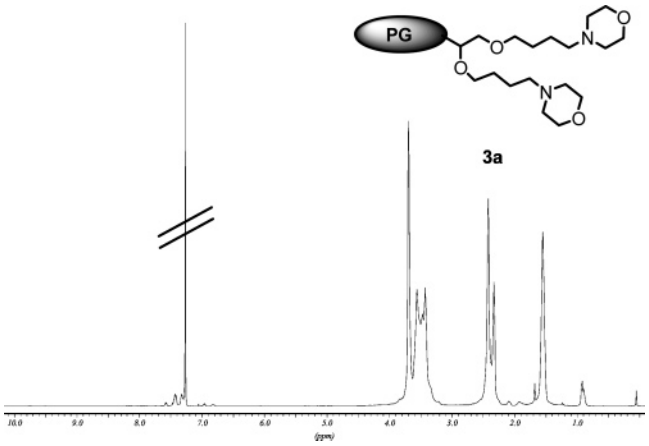


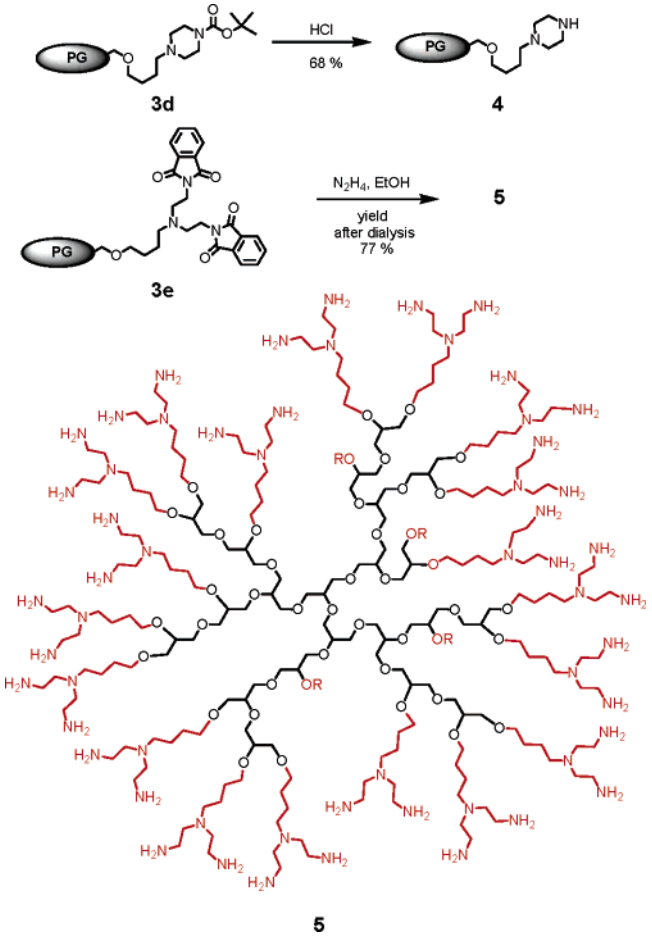
FIGURE 1. ^{1}H NMR of polymorpolino-terminated polyglycerol **3a** in $CDCl_3$.

The phthalimide derivative **3e** was deprotected to form the dendritic polyamine **5** (M_n = 15 600 g/mol). This was achieved by treatment with hydrazine in ethanol for 72 h liberating all primary amine functionalities in one step. At this point, the dendritic polyglycerol with an amino shell **5** (Scheme 3) has a new, well-defined branching point, from where a divergent synthesis of a dendritic polyamine shells can be started by means of hydroaminomethylation according to procedures reported previously.[21]

Finally, it had to be clarified whether the regioselectivity was a statistical median for the whole macromolecule **1** or a median of very different regioselectivities of the outer allylic groups and the internal allylic groups of the hyperbrached polyglycerols. For this reason, we performed a hydroformylation experiment with a shell-protected hyperbranched polyglycerol **6** (Scheme 4). This investigation was carried out under similar conditions as with **1**. In this approach, all terminal 1,2-diols of the

(21) Koc, F.; Eilbracht, P. *Tetrahedron* **2004**, *60*, 8465.

SCHEME 3. Deprotection of 3d,e To Form the Free Secondary and Primary Amines 4 and 5, Respectively, on the Dendritic Polyamine Structure (R = Further Amino Functionalizations)

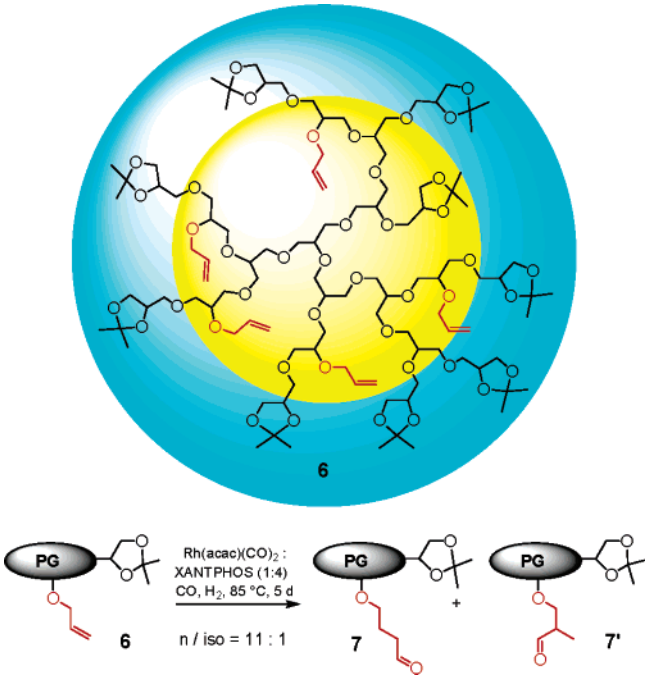


shell are protected as acetals and allylation only occurred at the internal OH-groups. This allows us to differentiate between regioselectivities on the outside and the inside of the dendritic polyglycerol structure after hydroformylation.

In fact, these experiments result in an only slightly lower *n*-/iso-selectivity of 11:1. This indicates that the regioselectivity of **1** was really a statistical median through the whole macromolecule and not a sum of different regioselectivities of outer and internal allyl group hydroformylation. This initial experiment using hydroaminomethylation provides also the possibility to build macromolecules with core−shell-type architectures, with amine functionalities in the core and a hydrophilic shell after deacetalization at the outer spheres.

In conclusion, we have shown that the use of a hydroformylation/reductive amination sequence on dendritic polyallyl ethers results in high to excellent yields in the shell-modified dendritic polyamines. This methodology significantly increases the applicability and flexibility of the new shell-modified polyamine dendrimers. Furthermore, the modification of hyperbranched polyglycerols with protected amines is possible. The main advantage can be seen in the high molecular weight (M_n = 15 600 g mol^{-1}) dendritic aminoterminated polyglycerol **5**, which was synthesized in two steps with an overall yield of 76%. The molecular weight increases drastically (triples) and makes these nanoparticles (5−10 nm) attractive for separation by membrane filtration techniques and biological applications.[22] The obtained dendritic polyamines are also in a perfect size regime for DNA delivery and still have a high degree of flexibility due to their polyether core.[23] Gene transfection experiments to study DNA complexation and transport are currently in progress and will be reported in due course. In addition, amino groups located in the core of the dendritic architecture, such as in products derived from compound **7** are interesting precursors for water-soluble nanocarriers for drug delivery.

SCHEME 4. Hydroformylation of 6 To Form Aldehyde 7



Experimental Section

General Remarks. Hyperbranched polyglycerol was prepared according to a published procedure[5] with a molecular weight of 5000 g mol^{-1} and analyzed by NMR and GPC. All other molecular weights are based on this M_n considering the conversion and degree of functionalization of the respective product. The dendritic polyallyl ether **1** was prepared according to a procedure we have reported previously.[10]

Preparation of Hydroaminomethylated Hyperbranched PG-Dendrimers. PG-Allyl, Rh(acac)(CO)$_2$, and Xantphos were dissolved in dry toluene and placed in the autoclave. The autoclave was pressurized with 30 bar of CO/H$_2$ (1:1) and heated at 70 °C for 5 days. After cooling, the amine was added to the crude PG-aldehyde (^{1}H NMR was used to confirm full conversion) and stirred for 1−2 h. After stirring, Rh(acac)(CO)$_2$ was added and the autoclave was pressurized with 70 bar of CO/H$_2$ (1:6) and heated at 85 °C for 2−5 days. After cooling, the solvent was removed in a rotary evaporator and the crude mixture was purified by dialysis (benzoylated cellulose tubing) to give the respective dendritic polyamine. Dialysis was performed in 2 L beaker charged with chloroform and stored over 24 h, and after this time solvent was exchanged.

(22) Tzschucke, C.-C.; Markert, C.; Bannwarth, W.; Roller, S.; Hebel, A.; Haag, R. *Angew. Chem., Int. Ed.* **2002**, *114*, 3964.
(23)) Krämer, M.; Stumbé, J.-F.; Grimm, G.; Krüger, U.; Kaufmann, B.; Weber, M.; Haag, R. *ChemBioChem* **2004**, *8*, 1081.

PG-Aldehyde (2, 2′). PG-allyl (2.00 g, 14 mmol), Rh(acac)-$(CO)_2$ (10 mg, 0.28 mol %), and Xantphos (100 mg, 1.23 mol %) in 100 mL of dry toluene. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.81−1.13 (m), 1.72−1.95 (m), 2.32−2.63 (m), 3.18−3.95 (m), 9.67 (d, J = 7.5 Hz), 9.73 (s) ppm.

PG with Morpholin Shell (**3a**). As described above, PG-aldehyde (**2**, **2′**) (0.60 g, 3.85 mmol), Rh(acac)$(CO)_2$ (2 mg, 0.22 mol %), and morpholin (3.35 g, 38.50 mmol) in 100 mL of dry toluene afforded crude **3a**, which was purified by dialysis in chloroform for 48 h to give product (913 mg, 99%). This product still contains traces of Xantphos. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45−1.65 (m), 2.20−2.65 (m). 3.10−3.63 (m), 3.63−3.85 (m), ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.0, 27.6, 28.1, 53.5, 58.9, 66.7, 70.3, 71.5, 72.0, 78.0 ppm. IR (KBr plate): ν 1118 (vs), 1401 (w), 1457 (m), 1558 (w), 1653 (w), 2854 (s), 2924 (s) cm^{-1}.

PG with Benzylamin Shell (**3b**). As described above, PG-aldehyde (**2**, **2′**) (0.50 g, 3.50 mmol), Rh(acac)$(CO)_2$ (5 mg, 0.55 mol %), and benzylamine (3.75 g, 35.00 mmol) in 100 mL of dry toluene afforded crude **3b**, which was purified by dialysis in chloroform for 24 h to give product (642 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45−1.65 (m), 2.55−2.65 (m), 3.15−3.65 (m), 3.65−3.87 (m), 7.13−7.36 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.3, 26.8, 48.4, 52.2, 53.6, 54.5, 69.5, 70.3, 71.3, 76.1, 126.8, 128.1, 128.3, 140.5 ppm. IR (KBr plate): ν 1114 (vs), 1359 (w), 1454 (m), 1603 (w), 2864 (s), 3026 (w) cm^{-1}.

PG with Anilin Shell (**3c**). As described above, PG-aldehyde (**2**, **2′**) (0.50 g, 3.50 mmol), Rh(acac)$(CO)_2$ (3 mg, 0.22 mol %), and benzylamine (1.70 g, 18.30 mmol) in 100 mL of dry toluene afforded crude **3c**, which was purified by dialysis in chloroform for 48 h to give product (561 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.14−1.95 (m), 2.85−3.15 (m), 3.15−4.25 (m), 6.50−7.25 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 15.3, 25.9, 29.8, 43.5, 47.8, 69.3, 71.4, 78.4, 112.6, 117.0, 129.1, 148.4 ppm. IR (KBr plate): ν 1110 (vb), 1260 (m), 1322 (m), 1507 (m), 1602 (s), 2865 (s) cm^{-1}.

PG with Boc-piperazine Shell (**3d**). As described above, PG-aldehyde (**2**, **2′**) (0.50 g, 3.50 mmol), Rh(acac)$(CO)_2$, (5 mg, 0.55 mol-%), and Boc-piperazine (0.93 g, 5.00 mmol) in 100 mL of dry toluene afforded crude **3d**, which was purified by dialysis in chloroform for 48 h to give product (855 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.45 (s), 1.48−1.61 (m), 2.25−2.49 (m), 3.25−3.85 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 22.0, 28.0, 28.7, 42.3, 43.5, 52.3, 58.0, 70.7, 71.3, 79.3, 80.2, 155.0 ppm. IR (KBr plate): ν 1005 (w), 1125 (s), 1171 (s), 1247 (m), 1287 (w), 1365 (m), 1419 (s), 1457 (m), 1698 (vs), 2931 (s) cm^{-1}.

PG with Bis[2-(*N*-phthalimidyl)ethylamine Shell (**3e**). As described above, PG-aldehyde (**2**, **2′**) (0.50 g, 3.50 mmol), Rh-(acac)$(CO)_2$, (3 mg, 0.33 mol %), and Bis-[2-(*N*-phthalimidyl)-ethylamine (1.82 g, 5.00 mmol) in 100 mL of dry toluene afforded crude **3e**, which was purified by dialysis in chloroform for 36 h to give product (1.70 g, 99%). This product still contains traces of Xantphos. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.13−1.51 (m), 2.35−2.60 (m), 2.60−2.87 (m), 3.15−4.25 (m), 7.55−7.90 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.8, 28.4, 35.7, 51.4, 53.7, 62.4, 70.3, 72.4, 77.2, 123.1, 132.1, 133.8, 168.0 ppm. IR (KBr plate): ν1028 (m), 1088 (s), 1089 (w), 1397 (s), 1434 (m), (1468 (w), 1615 (w), 1710 (vs), 1772 (s), 2939 (m) cm^{-1}.

PG with Piperazine Shell (4). Compound **3d** (100 mg, 0,009 mmol) was dissolved in dioxane (15 mL), and 3 M HCl (4 mL) was added. The reaction was stirred at room temperature for 3 h, and then the solvents were evaporated. The residue was stirred for 3 h at room temperature in methanol and acidic ionic exchange resin Lewatit K 1131, filtered, and concentrated in a vacuum. The crude mixture was purified by dialysis in MeOH for 24 h to give **4** (46 mg, 67.5%). ^{1}H NMR (400 MHz, CD_3OD): δ 1.43−1.74 (m), 2.25−2.65 (m), 2.76−2.97 (m), 3.34−3.97 (m) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.1, 28.9, 46.2, 54.9, 60.2, 68.4, 71.3, 72.4 ppm. IR (KBr plate): ν 1115 (s), 1136 (s), 1205 (s), 1457 (m), 1699 (vs), 2806 (s), 2866 (s), 2933 (s), 3437 (m) cm^{-1}.

PG with *N*-(2-Aminoethyl)ethane-1,2-diamino Shell (5). Compound **3e** (282 mg, 0.0085 mmol) was dissolved in absolute ethanol (35 mL), and a large excess of hydrazine (5 mL) was added. The reaction was stirred under reflux for 72 h and then was partially concentrated. The white suspension was filtered, and the solvent was evaporated. The crude mixture was purified by dialysis in methanol for 48 h to give the dendritic polyamine **5** (102 mg, 77%). ^{1}H NMR (400 MHz, CD_3OD): δ 1.46−1.65 (m), 2.41−2.65 (m), 2.65−2.81 (m), 3.38−3.81 (m) ppm. ^{13}C NMR (100 MHz, CD_3OD): δ 24.8, 28.8, 40.1, 55.6, 62.7, 71.4, 72.6, 79.3 ppm. IR (KBr plate): ν 1121 (s),-1384 (s), 1457 (w), 1653 (w), 2939 (m), 3675 (w) cm^{-1}.

PG-aldehyde (7, 7′). PG-allyl (**6**) (0.96 g, 4.11 mmol), Rh-(acac)$(CO)_2$ (7 mg, 0.66 mol %), and Xantphos (70 mg, 2.94 mol %) in 100 mL of absolute toluene. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.20−1.45 (m), 1.73−2.10 (m), 2.38−2.66 (m), 3.03−3.85 (m), 3.87−4.39 (m), 9.66−9.69 (m), 9.74 (s) ppm.

Acknowledgment. We thank the Fonds der chemischen Industrie and the Deutsche Forschungsgemeinschaft for financial support. Holger Türk is kindly acknowledged for providing hyperbranched polyglycerol.

Supporting Information Available: ^{1}H NMR spectra of compounds **3a**−**e**, **4**, **5**, and **7**. CH-correlation spectra of **3a**−**e**. ^{13}C NMR of compound **4** and **5**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO0481304