Hyperbranched Aliphatic Polyether Polyols

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ABSTRACT: Hyperbranched polymers, dendritic macromolecules with branch-on-branch structures, have become an important polymer class since the early 1990s. They combine several advantages of the perfectly branched dendrimers with easy accessibility, typically in a one-step synthesis. Hyperbranched polyethers are a particularly interesting class of chemically stable and often biocompatible materials. Multifunctional hyperbranched polyethers with controllable molar mass and comparably low polydispersities can been prepared using hydroxyl-functional epoxides or oxetanes for polymerization via anionic and cationic polymerization mechanisms. Here, we review the progress in the preparation, characterization, and application of these uniquely versatile aliphatic polyether polyols. Their unusual mechanical, thermal, and solution properties render them useful for a variety of applications, for example, as building blocks for various complex macromolecular architectures or in biomedical applications. © 2012 Wiley Periodicals, Inc. J. Polym. Sci., Part A: Polym. Chem. **2013**, *51*, 995–1019

KEYWORDS: hyperbranched; poly(3-ethyl-3-(hydroxymethyl)-oxetane); polyether; polyglycerol; polyol; ring-opening polymerization

INTRODUCTION Aliphatic hyperbranched polyether–polyols are one of the most intensely studied classes of dendritic polymers in recent years. In contrast to their perfectly branched analogs (dendrons and dendrimers), hyperbranched polymers can usually be synthesized in one reaction step, however, at the expense of a certain polydispersity. Representing multifunctional and highly branched building blocks, they are a promising alternative to the synthetically challenging dendrimers. In addition, it has been shown that hyperbranched polymers also possess some of the properties exhibited by dendrimers, such as low viscosity, good solubility, and multifunctionality.[1–11] Their high number of hydroxyl end groups offers various further functionalization opportunities. Their physical properties such as solubility in different solvents or glass transition temperature can be easily tailored by chemical modification of the functional end groups. In contrast to hyperbranched polyesters,[12] they are much more stable against acidic or basic hydrolysis. Thus, in the last two decades, hyperbranched polymers have attracted increasing attention from both an academic and industrial point of view, because of their high potential for advanced nanomaterials, novel biomaterials, and as rheology modifiers.

This highlight article focuses on the development of aliphatic, hyperbranched polyethers with a special emphasis on synthesis and structural modification of the dendritic structure. Although polyether dendrimers have been known since 1987,[13] synthesis and application options for dendrimers will not be covered in this highlight.[11,14–23] Also, star-shaped aliphatic polymers[24,25] will not be discussed, as we will focus only on branch-on branch type polymer structures. We will also summarize the use of these hyperbranched polymers to build up novel macromolecular architectures, for protein- or cell-resistant surfaces, as branched polyelectrolytes or for drug and dye delivery.

SUITABLE MONOMERS

Hyperbranched polyethers are mainly synthesized through ionic ring-opening polymerization (ROP) of cyclic "inimers" (initiator-monomers), either of hydroxyl-functional epoxides, such as glycidol or hydroxymethyl oxetane derivatives like 3-ethyl-3-(hydroxymethyl)oxetane, 3-methyl-3-(hydroxymethyl)oxetane, and 3,3-bis(hydroxymethyl)oxetane (BHMO).

Epoxides

Epoxides (or oxiranes) can be conveniently polymerized via ROP due to the high ring strain of the three-membered ring.[26] Glycidol is commercially available and synthesized by epoxidation of allyl alcohol (Fig. 1).

Glycidol is considered as a latent AB_2 monomer, because upon ring-opening it releases a second hydroxyl group that leads to the branching reaction. Each glycidol monomer adds exactly one additional hydroxyl group to the overall number of end groups in the polymers. To introduce further functionalities (besides the hydroxyl groups), copolymerization with other epoxides is possible.[27–29]

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Christoph Schüll studied Biomedical Chemistry at the University of Massachusetts Amherst (USA) and the Johannes Gutenberg-University of Mainz, where he received his diploma degree in 2010. Currently, he is working on his PhD thesis at the University of Mainz in the group of Prof. Holger Frey as a fellow of the Graduate School of Excellence "Material Science in Mainz." His research interests focus on the synthesis of complex polymer architectures containing hyperbranched polyether building blocks.

Holger Frey studied Chemistry at the University of Freiburg. Following a stay at Carnegie Mellon-University in Pittsburgh (Kris Matyjaszewski), he obtained the PhD for research on polysilane copolymers at the University of Twente (NL) in the group of Martin Moeller (1993). After his Habilitation at the University of Freiburg (1998) on polycarbosilanes, he moved to the Johannes Gutenberg-University (JGU) at Mainz in 2001. Since 2003, he holds a Full Professorship in Organic and Macromolecular Chemistry at JGU. His research interests are directed at novel linear and branched functional polymer structures with unusual topology and biomedically relevant materials in general. He has published 240 peer-reviewed original contributions and reviews and is a co-inventor of 13 patents.

Oxetanes

Hydroxy-functional oxetanes represent the second class of monomers used to prepare hyperbranched polyethers. A number of compounds can be used for the polymerization of hyperbranched polyether polyols. 3-Ethyl-3-(hydroxymethyl) oxetane, 3-methyl-3-(hydroxymethyl)oxetane, and BHMO can be synthesized from the corresponding polyols 1,1,1-trimethylol propane (TMP), 1,1,1-trimethylol ethane (TME), and pentaerythritol (PEA) via an addition-decarboxylation reaction with diethylene carbonate (Fig. 3).[30]

Multiols

TMP, TME, and PEA can be synthesized on industrial scale from butyraldehyde, propionaldehyde, or acetaldehyde, respectively, with formaldehyde via a crossed Cannizzaro reaction (Fig. 2).[31] Besides their use as substrate for the synthesis of the hydroxymethyl oxetanes, the multiols can be used for the preparation of hyperbranched polyethers via step-growth polycondensation.

POLYMERIZATION STRATEGIES

Anionic Ring-Opening Multibranching Polymerization

The ring-opening multibranching polymerization (ROMBP) mechanisms (anionic and cationic) have their seeds in the classical ROP mechanism, which results in linear polymers, especially polyethers and polyesters. Typical monomers used for anionic ROP are unsubstituted epoxides (ethylene oxide) or substituted epoxides [like propylene oxide (PO) or glycidol and its derivatives]. To achieve multibranching, at least one compound in a comonomer mixture has to possess an AB_2 or a "latent" AB_2 structure. Because of the fast proton exchange in epoxide polymerization reactions between (secondary and primary) alkoxides all chain ends can grow simultaneously, resulting in a branched structure. Figure 4 exemplifies this principle in the proposed reaction mechanism for the ROMBP of glycidol.

The polymerization is initiated by an alkali-metal alkoxide. Nucleophilic attack (generally at the unsubstituted ring position of the epoxide) leads to opening of the ring, and the subsequent attack at another monomer molecule causes propagation of the chain. The role of the counter ion during anionic epoxide polymerization has been intensively studied: Li^+ cations usually terminate the polymerization, because

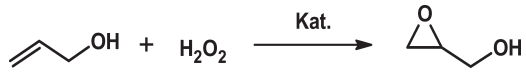

FIGURE 1 Synthesis of glycidol from allyl alcohol.

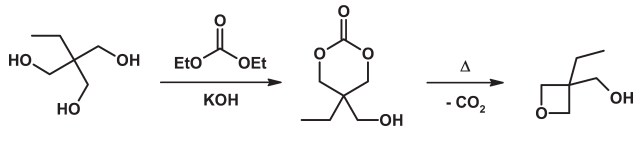

FIGURE 2 Synthesis of 3-ethyl-3-(hydroxymethyl)oxetane (EHO) from trimethylolpropane (TMP).

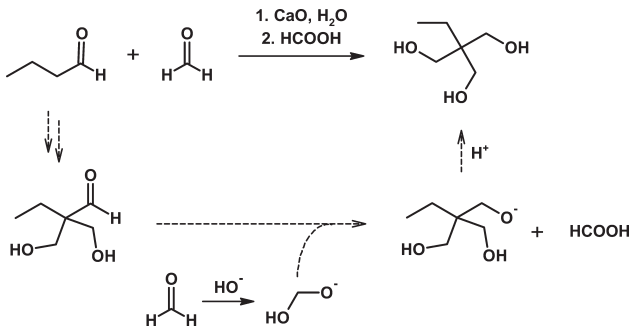

FIGURE 3 Synthesis of 1,1,1-trimethylolpropane (TMP) from butyraldehyde and formaldehyde via aldol addition and crossed Cannizzaro reaction.

the strong Li—O interaction prevents insertion of the oxiranes at the chain end.[33–35] However, in the presence of a phosphazene base,[36,37] which acts like a chelating ligand, polymerization can take place. For the other alkaline metals, the polymerization rate increases with increasing size of the counter ion ($Na^+ < K^+ < Cs^+$).[38] Most commonly, potassium is applied, due to reasonable polymerization results and lower cost in comparison with cesium. In some cases of substituted oxiranes, such as PO[39,40] or ethoxy ethyl glycidyl ether (EEGE),[41] cesium is preferred, as it reduces the occurrence of chain transfer reactions to the monomer that results in undesired, new unsaturated initiating species.

Cationic Ring-Opening Polymerization

Penczek and coworkers[42] and Dworak et al.[43] reported the cationic ROP of glycidol, leading to polyglycerol. The contribution of two polymerization mechanisms was confirmed by NMR spectroscopy, resulting in hyperbranched aliphatic polyethers. Several years later, the groups of Hult[44] and Penczek[45] described independently the cationic ROP of 3-ethyl-3-(hydroxymethyl)oxetane leading to poly(3-ethyl-3-(hydroxymethyl)oxetane) (PEHO) with a degree of branching (DB) of about 41%. One year later, Yan et al. published the successful polymerization of 3-methyl-3-(hydroxymethyl)oxetane with DBs up to 33%.[46]

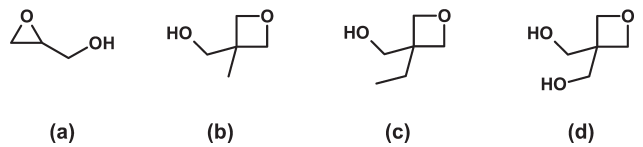

FIGURE 5 Cyclic ethers that can be polymerized via cationic ring-opening polymerization: (a) glycidol, (b) 3-methyl-3-(hydroxymethyl)oxetane, (c) 3-ethyl-3-(hydroxymethyl)oxetane, and (d) 3,3-bis(hydroxymethyl)oxetane.

Two different polymerization mechanisms are discussed for the cationic ROP (Fig. 6). The active chain end mechanism (ACE) involves the nucleophilic attack of an oxygen atom of the monomer at the carbon atom in α-position to the tertiary oxonium ion at the growing chain end. Because of the presence of an oxonium ion at the chain end, back-biting is a common side reaction leading to the formation of oligomeric or polymeric cycles.

The second mechanism described is the activated monomer mechanism (AM), which is possible in the presence of hydroxyl group containing compounds (alcohol, diol, and water). It involves a nucleophilic attack of an oxygen atom of the hydroxyl group (at the electrically neutral polymer chain) on the α-carbon atom of an oxonium ion (the protonated monomer). If this mechanism prevails, the polymer chain is formed by successive addition of protonated ("activated") monomer to the terminal hydroxyl group of the growing chain end. When the hydroxyl end group of the polymer is more nucleophilic than the monomer itself, this mechanism can dominate over the ACE mechanism.[48] This is desirable because side reactions (cyclization) can be avoided.

Both mechanisms may contribute to the propagation in the cationic polymerization of monomers containing both functions (e.g., cyclic ether group and hydroxyl groups) within the same molecule. Branching results from reactions involving hydroxyl groups (the protonated monomer can react with any hydroxyl group in the system, either at the chain end or in a linear repeating unit), whereas ACE-type propagation leads to a linear structure.

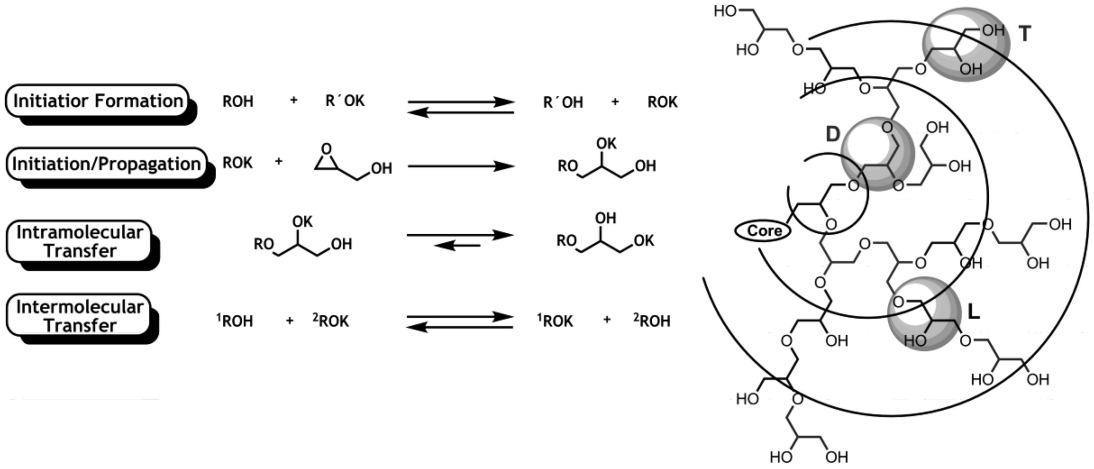

FIGURE 4 Mechanistic pathway of the anionic ring-opening multibranching polymerization of glycidol (Reproduced from Ref. 32).

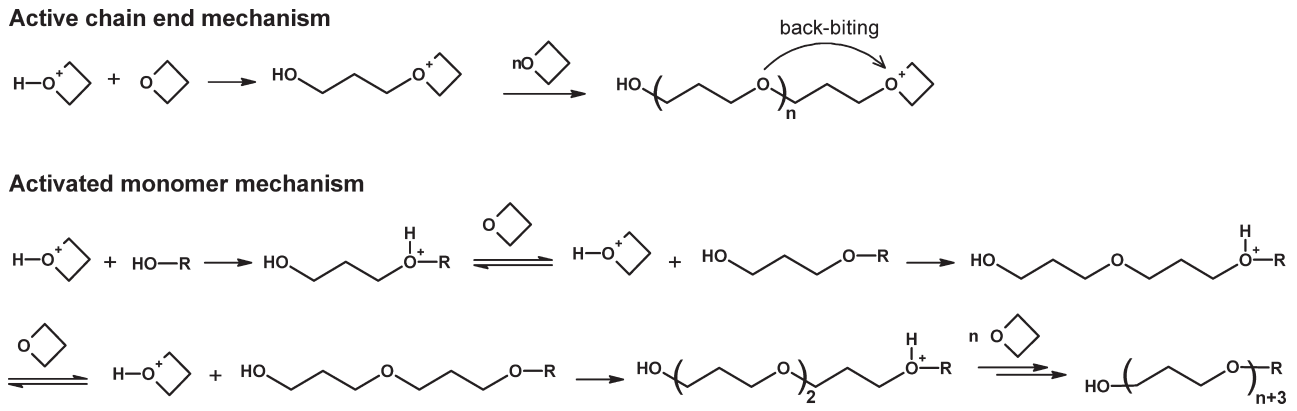

FIGURE 6 Active chain end mechanism (ACE) and activated monomer mechanism (AM) for the cationic ring-opening polymerization of cyclic ethers, exemplified for oxetane (Modified from Ref. 47).

Dworak et al. described a dependence of the AM contribution on the type of initiator applied.[43] To quantify the contribution of both mechanisms is difficult, because the concentration of hydroxyl groups of the monomer molecules and in the polymer changes in the course of the reaction. Both types of hydroxyl groups may have different reactivity; thus, the relative contribution of both mechanisms may change during the polymerization.[47] Magnusson and Malmstrom[49] observed that the content of branched units increases with increasing monomer conversion. An increasing contribution of the AM mechanism in the course of the polymerization can be deduced.

Proton-Transfer Polymerization

In 1999, Fréchet and coworkers introduced a new polymerization process termed "proton-transfer polymerization" and its use in producing epoxy or hydroxyl functionalized hyperbranched polymers (Fig. 7). The first implementation of this proton-transfer polymerization was achieved with the base-initiated polymerization of phenolic bis-epoxide yielding an aromatic hyperbranched polyether.[50] Some months later, they successfully transferred this concept to the synthesis of an aliphatic hyperbranched polyether using two monomers with A_2 and B_3 structure, like 1,2,7,8-diepoxyoctane (as A_2 monomer) and 1,1,1-tris(hydroxymethyl)ethane (TME, as B_3 monomer).[51] According to the authors, the practical advantage of the $A_2 + B_3$ approach is the commercial availability of bi- and tri-functional monomers that precludes the need for an AB_n monomer synthesis. A key feature of this new polymerization method is that each propagation step involves a proton transfer for the activation of the nucleophile used in epoxide opening.

Using the nucleophilic catalyst *tetra-n*-butylammonium chloride, the initiation occurs by the nucleophilic attack of the chloride anion at the epoxide at the less sterically hindered carbon to give a secondary alkoxide. Through rapid proton exchange, the primary alkoxide of the triol is formed in an equilibrium reaction. Propagation from secondary alkoxides is expected to occur as well, especially at the later stages of the reaction but it is less favored due to steric hindrance and the slightly higher acidity of a primary over a secondary alcohol.[50]

The preparation of aliphatic hyperbranched polymers using AB_2, AB_3, and A_2 and B_3 approaches was shown by the same group one year later.[52] These aliphatic epoxide monomers were prepared in one step from commercially available starting materials and were polymerized with Bu_4NCl catalysis to

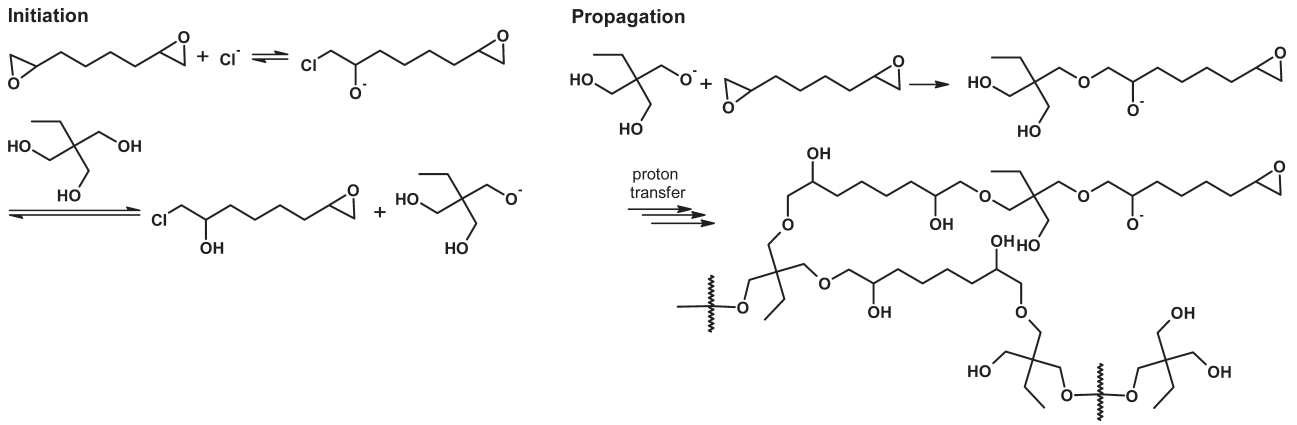

FIGURE 7 Reaction mechanism of the proton transfer polymerization of a bis-epoxide and a triol to generate a hyperbranched polyether.[50]

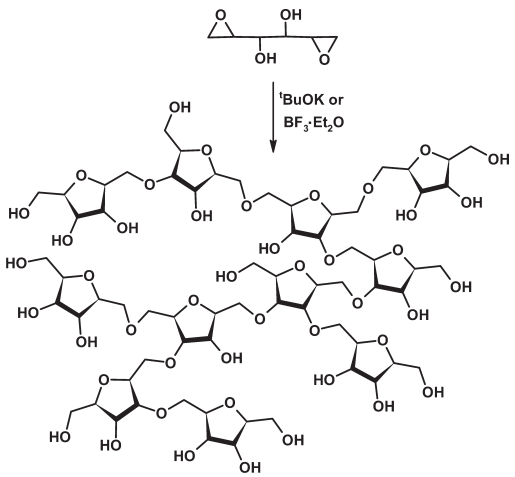

FIGURE 8 Reaction scheme of the proton transfer polymerization with epoxide and hydroxyl functionalities in one molecule.[53]

give aliphatic polyethers with epoxide chain end substituents.

Also hyperbranched carbohydrate polymers made from anhydrocarbohydrate monomers have been synthesized via cationic polymerization with proton-transfer mechanism (Fig. 8).[53,54]

DEGREE OF BRANCHING

Hyperbranched polymers based on a branching multiplicity of 2 (AB_2-systems) possess three types of structural units: dendritic units as fully branched AB_2 monomer structures (D), linear units with one unreacted B group (L), and terminal groups with two unreacted B groups (T). In contrast, perfectly branched dendrimers consist only of dendritic and terminal units. For those maximum branched structures, DB is normalized to 100%, whereas it is 0% for linear polymers. Thus, hyperbranched polymers exhibit an intermediate DB between 0 and 100%. The DB is one of the important characteristics and globally describes the branching structure of hyperbranched polymers. Fréchet and coworkers[55] defined the term "DB" as

$$\mathrm{DB} = \frac{D + T}{D + T + L} \tag{1}$$

where *D*, *T*, and *L* are the fraction of dendritic, terminal, and linear units, respectively.

Using eq 1, for small or little-branched molecules leads to an overestimation of DB due to the relatively high amount of terminal units in the structure. Hölter and Frey developed a modified eq 2,[56] based on a systematic approach:

$$\mathrm{DB} = \frac{2D}{2D + L} \tag{2}$$

Equation 2 leads to reliable DB values, particularly for small hyperbranched molecules, and does not require the determination of *T*. However, if one considers large hyperbranched molecules, eqs 1 and 2 give approximately the same result. The DB is commonly calculated on the base of data obtained from NMR spectra.

The DB is determined by the polymerization statistics, and for one-pot polymerizations of AB_2 monomers a DB value of 50% is obtained, if both B units possess the same reactivity.[56] By using a dilution/slow addition process, the DB can be increased up to 67% for AB_2 systems, which is considerably higher than in the case of a random one-pot polymerization of AB_2 monomers.[56,58]

Thus, the DB is a measure of the dendritic character of a structure. Linear units are treated as defects. The DB can be enhanced up to values close or equal to 100% by using concepts like the postsynthetic modification.[57,59–62] To systematically lower the DB, the branching monomer can be copolymerized with a linear comonomer.[62–65] The implications of this approach will be discussed later in this article.

IMPORTANT HYPERBRANCHED POLYETHER STRUCTURES

Polyglycerol

Hyperbranched polyglycerol (*hb*PG) has become one of the essential hyperbranched polymers, which can be polymerized with control over molecular weight and polydispersity by anionic ROMBP of the latent AB_2 monomer glycidol.[66] Already in the 1930s, Rider and Hill briefly described the first polymerization of glycidol in the presence of pyridine to a "water soluble black tar," when investigating the synthesis of glycidol and its storage stability.[67] Later, Sandler and Berg studied the polymerization of glycidol in the presence of various bases at room temperature. They aimed at a linear topology, but the hydroxyl groups lead to termination and transfer reactions.[68] At this point, the authors did not see the potential to generate branched polymer topologies. In the mid-1980s, Vandenberg performed detailed studies of the anionic polymerization of glycidol in the presence of several bases.[69] He was able to assign different repeat units by ^{13}C NMR spectroscopy and mainly described the formation of low molecular weight oligomers by self-initiation of glycidol, which he could explain by detailed reaction mechanisms. In other works, the polymerization of 3-oxetanol in the presence of acids was observed, which would also lead to a branched polyglycerol structure.[70] Vandenberg et al. also investigated the cationic polymerization of protected 3-oxetanol, resulting in a linear polyglycerol-type structure.[71] In the mid-1990s, Dworak and coworkers studied the cationic polymerization of glycidol, assigning different repeat units by NMR spectroscopy and constituting the branched structure to different polymerization mechanisms (cf. section on "Cationic Ring-Opening Polymerization").[42,43]

Significant progress in this area was made by Frey, Sunder, and Mülhaupt, who established the slow monomer addition (SMA) technique for the anionic ROMBP of glycidol in 1999, leading to hyperbranched polyglycerols with controlled molecular weights (M_n = 1100–6500 g mol^{-1}), moderate to narrow molecular weight distributions ($M_w/M_n < 1.5$, mostly

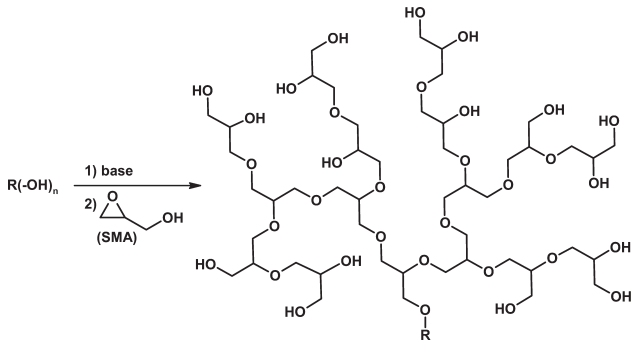

FIGURE 9 Synthesis of hyperbranched polyglycerol (*hb*PG) via anionic ring-opening polymerization using the slow monomer-addition technique (SMA).

<1.3) and controlled degree of branching (DB = 0.53–0.59) (Fig. 9).[58,66]

To overcome the molecular weight limitations of the first works on *hb*PG, Wilms et al. introduced the use of *hb*PG of low molecular weight as macroinitiator for the synthesis of *hb*PG. Here, controlled molecular weights up to 24 kg mol^{-1} with moderate polydispersities ($M_w/M_n < 1.8$) were achieved.[72] In a very interesting work in this area, Brooks and coworkers added dioxane as an emulsifier in the established SMA procedure, obtaining extremely high molecular weight *hb*PG (M_n up to 700 kg mol^{-1}).[73]

These materials exhibit the highest molecular weights obtained for synthetic hyperbranched polymers reported to date. To facilitate the synthesis of *hb*PG for industrial processing, microreactor technology[74] can be used to obtain polymers with molecular weights up to 1500 g mol^{-1}.[75] In this approach, an efficient continuous process is used, which results in significantly reduced experimental effort. Besides the use of glycidol, the environmentally benign monomer glycerol carbonate (4-hydroxymethyl-1,3-dioxolan-2-one) was also used in ROMBP to generate *hb*PG (M_n = 800–1100 g mol^{-1}, $M_w/M_n < 1.3$), which is formed under decarboxylation.[76] In another work, the microwave-assisted polymerization of glycerol carbonate only led to the formation of PG oligomers.[77]

To sum up, almost 90 years after the first reported "polymerization" of glycidol, the synthesis of *hb*PG by ROMBP using the slow monomer-addition (SMA) technique and other methods has become a versatile method for the synthesis of these hyperbranched polyether polyols with control over molecular weight, polydispersity, and DB. *hb*PG has become an essential material to further explore the potential of hyperbranched polymers in the synthesis of complex polymer architecture, for fundamental work aiming at the understanding of structure–property relationships or for various potential applications, ranging from biomedicine to catalysis.[32,78]

Poly(3-ethyl-3-(hydroxymethyl)oxetane)

PEHO is obtained from 3-ethyl-3-(hydroxymethyl)oxetane (EHO) by cationic or anionic ROMBP (Fig. 10). In 1999, Hult and coworkers[79] and Penczek and coworkers[80] published their independent studies on the cationic ROMBP of 3-ethyl-3-(hydroxymethyl)oxetane by using the sulfonium salt initiator 1-benzyltetrahydrothiophen-1-ium hexafluoroantimonate or boron trifluoride diethyletherate and trifluoromethanesulfonic acid. Surprisingly, narrow molecular weight distributions (M_w/M_n around 1.5) and molecular weights up to 5000 g mol^{-1} were found with degrees of branching up to 41%. A correlation between the DB and the monomer conversion could be found. When EHO was polymerized by slow addition of monomer to a core molecule, a lower DB was obtained, compared with the one-step synthesis with full conversion of the monomer. The polydispersity was generally slightly lower when a core molecule was used compared with the one-step homopolymerization.[49]

Detailed mechanistic investigations led to the conclusion that the polymerization proceeds with participation of both the ACE and the AM mechanism.[81]

An interesting finding is that M_n does not increase with monomer conversion and that there seems to be an upper limit of achievable molecular weights, regardless of the reaction conditions.[47] Both molar mass and DB depend only to a low extent on the polymerization conditions, because significant chain transfer and the coexistence of two propagation mechanisms limit the growth of the polymer.[82] In MALDI-TOF MS spectra only cyclic polymer structures are found. A possible explanation are intramolecular chain transfer reactions of hydroxyl groups. With increasing number of hydroxyl groups of the polymer, the probability of intramolecular chain transfer increases. Thus, after reaching a certain degree of polymerization ($DP_n \approx 12$), cyclization occurs and polymer growth is strongly impeded (Fig. 11). This observation is explained by strong hydrogen bonding between multiple hydroxyl groups of the polymer.[82]

By carrying out the polymerization in ionic liquids, Biedron et al. tried to reduce the interfering influence of the hydroxyl groups.[83] However, despite higher yields, the molecular weight of the polymers could not be increased.

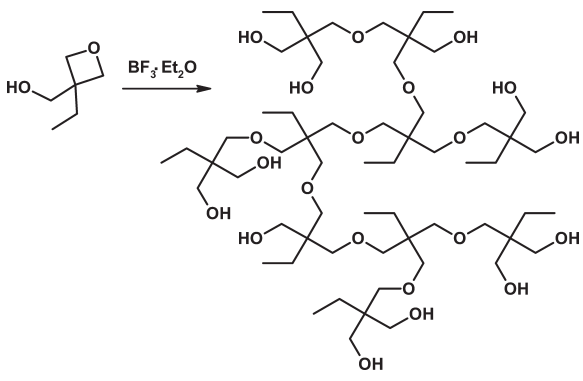

FIGURE 10 Reaction scheme of the cationic ring-opening polymerization of (3-ethyl-3-(hydroxymethyl)oxetane).

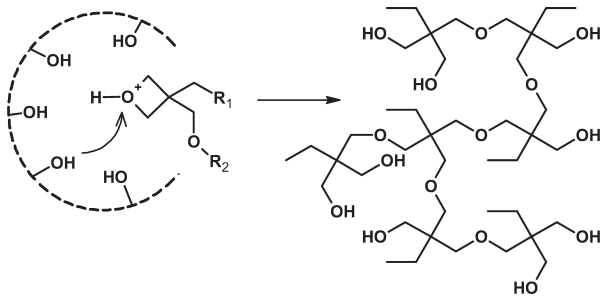

FIGURE 11 Intramolecular chain transfer reactions of hydroxyl groups limit growth of the polymer.[81]

Although M_n cannot be controlled by varying the polymerization conditions, Mai et al. made the discovery that DB seems to depend on the reaction temperature.[84] PEHO samples with various DBs were obtained at −50 to +30 °C. It was found that the DB increases with increasing reaction temperature. This is explained by preferential addition of monomer to terminal groups at low temperatures to generate mainly linear polymer chains. At higher temperatures, the addition reaction becomes a random process resulting in hyperbranched polymers. Only a small change of the DB value can be observed when the reaction temperature exceeds 20 °C, which might explain why this effect was not observed by other groups.[49]

The limitation of the molecular weight could partly be overcome by copolymerization of EHO with the dihydroxy-substituted dioxetane comonomer (diHO-diOX), yielding polymers with M_n close to 7000 g mol^{-1}.[85] However, in the copolymerization, EHO is consumed first, and consequently, the process is not a true copolymerization, but can be rather described as coupling of PEHO macromolecules formed at the first stage by the difunctional monomer as a coupling agent. This artificial increase of molecular weight does not lead to an increased DB.

To increase the branching probability, EHO can be copolymerized with the bishydroxy substituted oxetane (BHMO). The availability of more hydroxyl groups leads to copolymers with higher DB.[86]

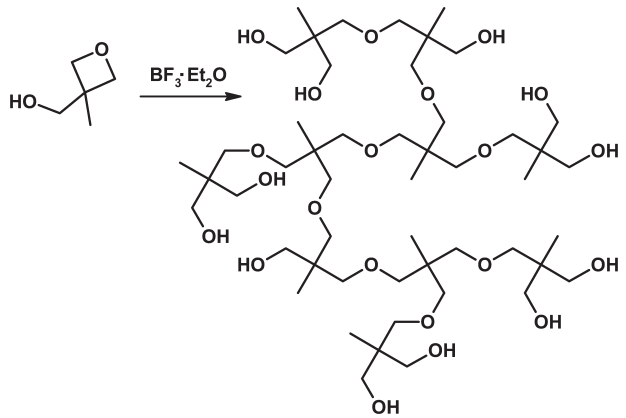

FIGURE 12 Synthesis of hyperbranched poly(3-methyl-3-(hydroxymethyl)oxetane) (PMHO) via cationic ring-opening polymerization.[90]

Anionic polymerization of oxetanes is commonly difficult. 3-Ethyl-3-(hydroxymethyl)oxetane was polymerized anionically using NaH with the coinitiators benzyl alcohol or trimethylol propane (TMP).[87] Slow addition of monomer to both mono- and tri-functional initiators resulted in hyperbranched polymers. Pendant hydroxyls facilitate the multibranching reaction. NMR spectroscopy confirmed the presence of linear, dendritic, and terminal repeat units, but MALDI-TOF MS showed quite low molecular weights (around 500 g mol^{-1}) and revealed the presence of both cyclic oxetane end groups or macrocyclic species besides the TMP end groups.

Nishikubo and coworkers could improve the anionic polymerization of EHO by using potassium *tert*-butoxide in the presence of 18-crown-6 for the initiation.[88,89] They obtained polymers with molecular weights up to 4100 g mol^{-1} in good yields, but with broad polydispersities (M_w/M_n = 4.0–5.5). The DB was comparatively low with values between 16% and 27%.

Poly(3-methyl-3-(hydroxymethyl)oxetane)

Poly(3-methyl-3-(hydroxymethyl)oxetane) (PMHO) can be synthesized in the same manner as PEHO (Fig. 12). The monomer 3-methyl-3-(hydroxymethyl)oxetane undergoes ring-opening under acidic conditions and results in hyperbranched polyether polyols comparable with PEHO. Interestingly, Yan et al. could show a dependency of the DB on the catalyst to monomer ratio. A low ratio of catalyst to monomer results in mainly linear or slightly branched polymers and high catalyst to monomer ratios lead to a hyperbranched polymer. This hyperbranched polyether is amorphous, and the essentially linear version obtained is partially crystalline. Consequently, the DB and the degree of crystallization of the resulting polymers are dependent on the catalyst to monomer ratio.[46]

To increase the number of hydroxyl end groups, MHO can be copolymerized cationically with glycidol to obtain hyperbranched poly[glycerol-*co*-3-methyl-3-(hydroxymethyl)oxetane]s with low cytotoxicity and thermoresponsive behavior.[91] This was the first copolymerization of oxirane and oxetane monomers. Here, molecular weights up to 8000 g mol^{-1} with low polydispersity indexes (PDIs) (<1.4) were obtained. However, the influence of the different reactivities

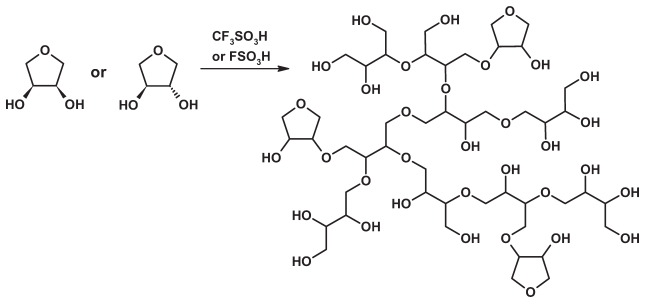

FIGURE 13 Synthesis of hyperbranched carbohydrate polymers consisting mainly of erythritol and L-threitol units via cationic ring-opening polymerization.[93]

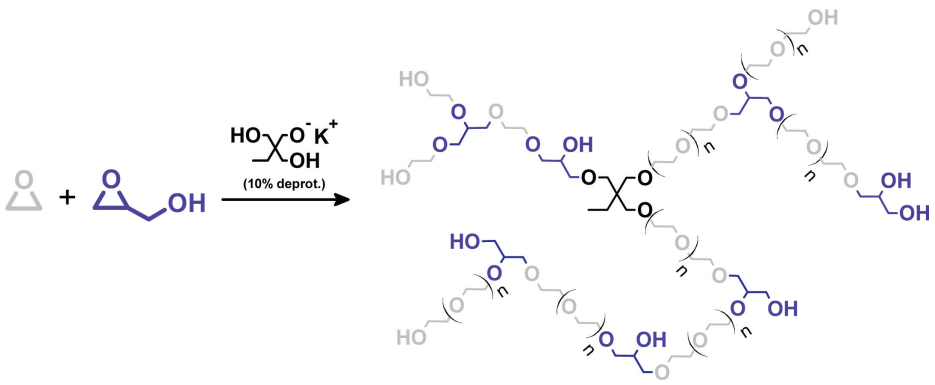

FIGURE 14 Synthesis scheme for hyperbranched poly(ethylene glycol) (hbPEG) by anionic copolymerization of ethylene oxide and glycidol.[102]

of the two types of monomers on the resulting polymer structure has not yet been investigated.

Poly(3,3-bis(hydroxymethyl)oxetane)

BHMO [Fig. 5(d)] as a cyclic oxetane monomer with latent AB_3-character can also be used for cationic ROMBP. In 1989, Vandenberg et al. reported that cationic polymerization of BHMO leads to branched polymers, but no detailed investigation of the reaction was carried out, because the work targeted the synthesis of linear polymers.[92]

The polymerization of BHMO gives the possibility to obtain hyperbranched polyethers with increased number of hydroxyl groups compared with PEHO, because each monomer unit contains two hydroxyl groups and the probability of branching should be increased at the same time. BHMO polymerizes easily by a cationic mechanism. However, characterization of the polymers is limited by the strong aggregation of the highly hydroxyl-substituted polymers and their resulting low solubility in common solvents.[86]

Copolymerization of BHMO and EHO gives access to branched copolyethers with varying DB and number of end groups, depending on the composition. The use of an equimolar comonomer ratio resulted in soluble copolymers with molecular weights similar to those of the PEHO homopolymer. ^{13}C NMR analysis demonstrated that DB is considerably higher compared with PEHO homopolymers. Nevertheless, there is no possibility to control the molecular weight of the polymers.[86]

Hyperbranched Polymers from Five-Membered Cyclic Ethers

The first five-membered cyclic ethers that have been polymerized to hyperbranched structures were hydroxyl-substituted anhydrosugars. Hyperbranched carbohydrate polyethers were obtained by cationic polymerization of two isomers of dihydroxytetrahydrofuran, that is, 1,4-anhydroerythritol and 1,4-anhydro-L-threitol (Fig. 13),[93] and 1,2:5,6-dianhydro-D-mannitol[53] or 1,6-anhydro-β-D-mannopyranose[94] (a bicyclic system) with M_n up to 2.7 $\times$ 10^6 g mol^{-1}. The authors observed that the molecular weights increased with increasing temperature. Several other anhydrosugars have been polymerized in the following years.[53,54,93–98]

Anhydrosugars containing a tetrahydrofuran scaffold are rather expensive monomers. Therefore, the group of Bednarek and Kubisa focused on the polymerization of tetrahydrofurans substituted with hydroxyl groups, mainly 2-(hydroxymethyl)tetrahydrofuran, but also 3-hydroxytetrahydrofuran and 3,4-dihydroxytetrahydrofuran.[99] Cationic bulk polymerization of 2-(hydroxymethyl)tetrahydrofuran was performed at different temperatures, but only low molecular weight products up to 3000 g mol^{-1} were obtained, independent of the polymerization conditions. MALDI-TOF analysis revealed elimination of water in the course of the polymerization as a side reaction, and thus, the resulting polymer contains fewer hydroxyl groups than expected from the number of monomer units.

In summary, it has been shown that five-membered cyclic ethers substituted with hydroxyl groups may be polymerized by cationic ROP, although yields and molecular weights remain limited.[81]

CHARACTERISTIC PROPERTIES OF HYPERBRANCHED POLYETHERS

Hyperbranched polymers exhibit a unique topology and, therefore, possess interesting physical and chemical properties. Especially, the influence of the DB on rheological and thermal behavior, as well as on solution or optoelectronic properties, and encapsulation and biomedical applications have been summarized for hyperbranched polymers in general by Yan and coworkers.[1,100] In the following, the key properties of hyperbranched aliphatic polyethers will be discussed.

Thermal Behavior

The number of branching junctions, the content and chemical nature of the end-groups, and the compactness of the hyperbranched structure may have an influence on the glass transition temperature (T_g) of hyperbranched polymers. Their T_g can differ drastically from the corresponding linear polymers.

Frey and coworkers compared the T_gs of hyperbranched polyglycerols and their derivatives esterified with long alkyl chains. They demonstrated a strong influence of the chemical

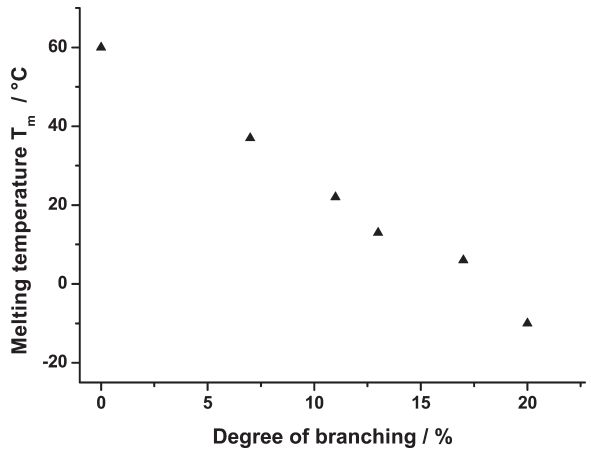

FIGURE 15 Dependency of the melting temperature (T_m) on the degree of branching (DB) for hyperbranched poly(ethylene glycol).[102]

nature of the end group on the T_g of the polymer and found a dependence of the T_g on the tendency of the substituents to form higher ordered structures.[101]

Recently, the synthesis of hyperbranched poly(ethylene glycol) (hbPEG) was established in our group to generate polyether polyols with adjustable DB and end group functionality that are mainly based on ethylene oxide (EO) as a readily available monomer (Fig. 14). Linear PEG is a highly crystalline material with a melting temperature of 66°C. By introducing glycerol branching units via copolymerization of EO and glycidol, the polyether structure changes to a branched architecture with adjustable DB just by varying the glycerol content. Remarkably, a glycerol fraction as low as 3 mol % is sufficient to decrease the melting point by 30 °C compared with a linear PEG homopolymer of comparable molecular weight (Fig. 15). A further increase of the glycerol fraction leads to a continuous decrease of melting temperature and enthalpy, until the melting peak eventually vanishes at around 15% glycerol units. As it is expected, the higher is the DB, the lower is the degree of crystallization, because with increasing number of branching points and constant molecular weight the mean distance between branching points decreases. This lowers the ability to crystallize to an increasing extent. If a minimum average length of a linear segment is undercut, the hyperbranched polymer cannot crystallize anymore. For hbPEG, the glass transition temperature remains constant at values around −60 °C, independent of the DB.

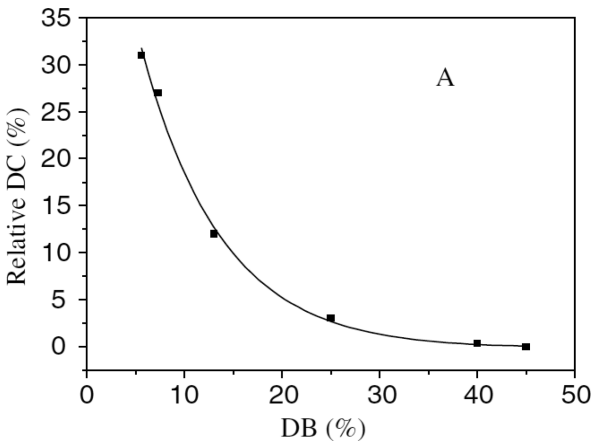

FIGURE 16 Plot of relative degree of crystallization (DC) versus degree of branching (DB) of PEHO (Reproduced from Ref. 104).

Yan and coworkers found a way to synthesize hyperbranched PMHO samples with varying DB dependent on the catalyst to monomer ratio. Low concentrations of catalyst result in only slightly branched polymers, whereas high amounts of catalyst lead to hyperbranched structures.[46] They found a simple relationship between the DB and the degree of crystallization, too. Studies of PEHO by Magnusson et al.[103] indicated that depending on the DB, the material can be either amorphous with a glass-transition temperature around 40 °C (for high DB $>$ 0.40) or semicrystalline with a melting temperature between 100 °C and 130 °C (with low DB $\approx$ 0.11–0.32). The authors observed an increased crystallinity with decreasing DB. Mai et al. could investigate the dependence of the crystallinity of PEHO on the DB by determining the degree of crystallization with XRD measurements, where a quantitative relationship was found (Fig. 16).[104]

Zhu et al. studied the influence of the DB on the T_g of polyethers exemplarily by comparing PEHO and PMHO polymers with different branching structure, synthesized by varying the polymerization temperature (Fig. 17).[84,105]

For amorphous samples, T_g first increases with DB, then passes through a maximum at intermediate DB, and decreases sharply with higher DBs. The authors explain this by the competition between the branch point density in the polymer backbone, which renders the polymer quite compact and rigid and thus explains the increase of the DB, and on the other hand, the increasing free volume of the end groups with increasing DB, which supports the overall mobility of

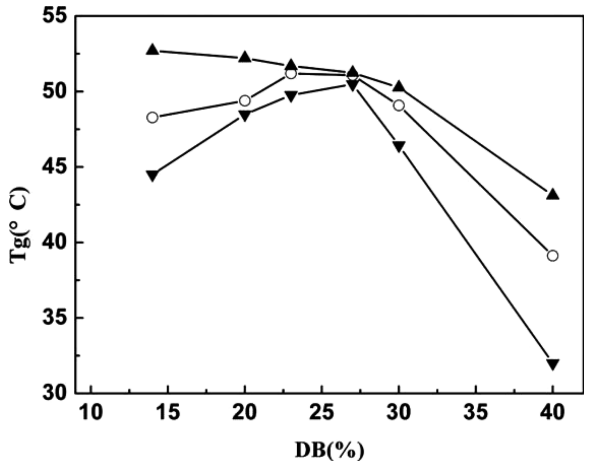

FIGURE 17 The relation between glass transition temperature (T_g) and the degree of branching (DB) of PEHOs with different thermal treatments (▲, amorphous samples; O, isothermally crystallized at 90 °C for 24 h; ▼, isothermally crystallized at 90 °C for 72 h) (Reproduced from Ref. 105).

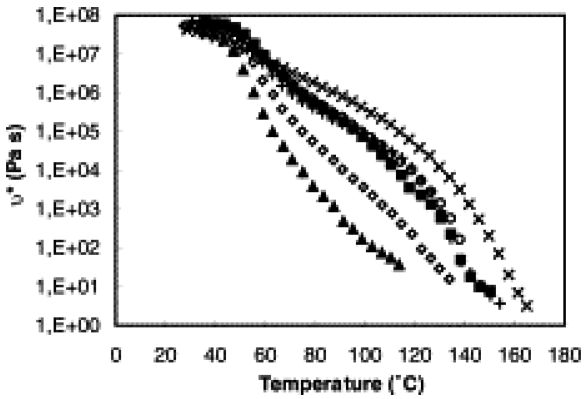

FIGURE 18 Complex dynamic viscosity versus temperature for polyethers with different DBs: 0.43 (▲); 0.40 (+); 0.36 (■); 0.38 (◇); 0.30 (○) (Reproduced from Ref. 103).

the molecule. In contrast to this finding for amorphous samples, the T_g decreases monotonically with DB for PEHO samples after isothermal crystallization.[105]

Mechanical and Rheological Properties

In close connection to the thermal properties of hyperbranched polyethers are their melt rheological properties, as they also depend strongly on the DB. Johansson and coworkers[103] investigated a series of hyperbranched PEHO samples, comparing the rheological curves of complex dynamic viscosity versus temperature for different DBs (Fig. 18).

The sample with the highest DB (DB = 0.41) exhibited a completely amorphous structure with rapidly decreasing viscosity above the T_g. No rubbery plateau is observed, suggesting the absence of chain entanglement. In contrast, the semicrystalline samples with low DB exhibited only a small drop in viscosity at the T_g, together with the presence of a rubbery plateau before the viscosity drops at the melting temperature. This indicates the presence of a crystalline phase or entanglements. As the molecular weight is well below the critical entanglement molecular weight, the latter is not very probable. Whereas for PEHO no entanglement was found, Tonhauser et al.[106] investigated hyperbranched polyglycerols over a broad molecular weight range (600–106,000 g mol^{-1}) with constant DB (≈60%) and—for the first time for hyperbranched polymers—found entanglements at elevated molecular weights (Fig. 19). A plateau-like area is found between 3000 and 10,000 g mol^{-1}, which results from a "dendrimer-like" behavior of the polymers. Thus, no increasing viscosity with molecular weights is observed in this molecular weight range. Above a critical mass of ≈20,000 g mol^{-1}, the viscosity increases considerably. This can be understood as a consequence of entangled star-like polymers with a densely packed core region.

Solution Properties

Molecular self-assembly of amphiphilic hyperbranched polyethers in solution can create extraordinary structures, despite their randomly branched structure. Yan et al.[107] synthesized PEHO-*star*-PEO copolymers with hydrophobic PEHO core and hydrophilic PEO arms. In acetone, these copolymers assemble to macroscopic multiwalled tubes with centimeters in length (Fig. 20). The thickness of the tube walls approaches 400 nm, and the walls have an alternating structure between ordered hydrophilic domains and amorphous, partly irregular hydrophobic domains. According to the authors, the formation of hydrogen bonds in both core and arm lamellae strengthens the self-assembled tubes and drives the molecular self-assembly process.

In water, the PEHO-*star*-PEO copolymers assemble to form giant polymer vesicles (>100 μm) with hydrophilic fractions (>60%).[108] Cheng et al.[109] synthesized PEHO-*star*-PEO copolymers with varying DB of the PEHO core. The solution self-assembly behavior of the obtained polymer samples was carefully evaluated and different aggregate structures, like vesicles, wormlike micelles and spherical micelles were found, depending on the DB of the PEHO core.

Another interesting phenomenon for polyethers in solution can be observed, when the hydrophobic PEHO core of the star polymers above is replaced with highly hydrophilic PG. Kojima et al. obtained OEG-Suc-HPGs by coupling oligo(ethylene glycol) chains to hyperbranched PG with succinic anhydride.[110] These copolymers underwent a temperature-dependent solubility change. By increasing the temperature, the polymers became less soluble in water and subsequently aggregated. This so-called "lower critical solution temperature" (LCST) depends on the structure and composition of the polyether. The phase transition temperature was dependent on the length of oligo(ethylene glycol) chains and the terminal group. Cheng et al.[111] found a relationship of the LCST phase transition with DB of the core polymer.

To date, two different strategies have been used to prepare thermoresponsive hyperbranched polymers. One is the modification with temperature-responsive functional groups or oligomers.[110–114] The other is the combination of hydrophobic and hydrophilic functionalities into a highly branched polymer. Here, the temperature sensitivity is caused by a peculiar balance of hydrophilic and hydrophobic moieties. These backbone-thermoresponsive hyperbranched polymers

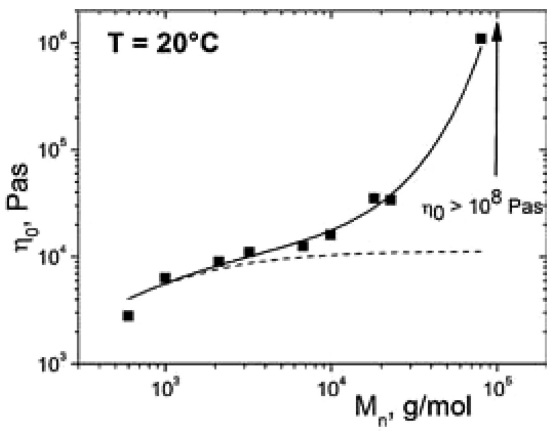

FIGURE 19 Zero shear viscosity at 20 °C versus molecular weight for hyperbranched PG (Reproduced from Ref. 106).

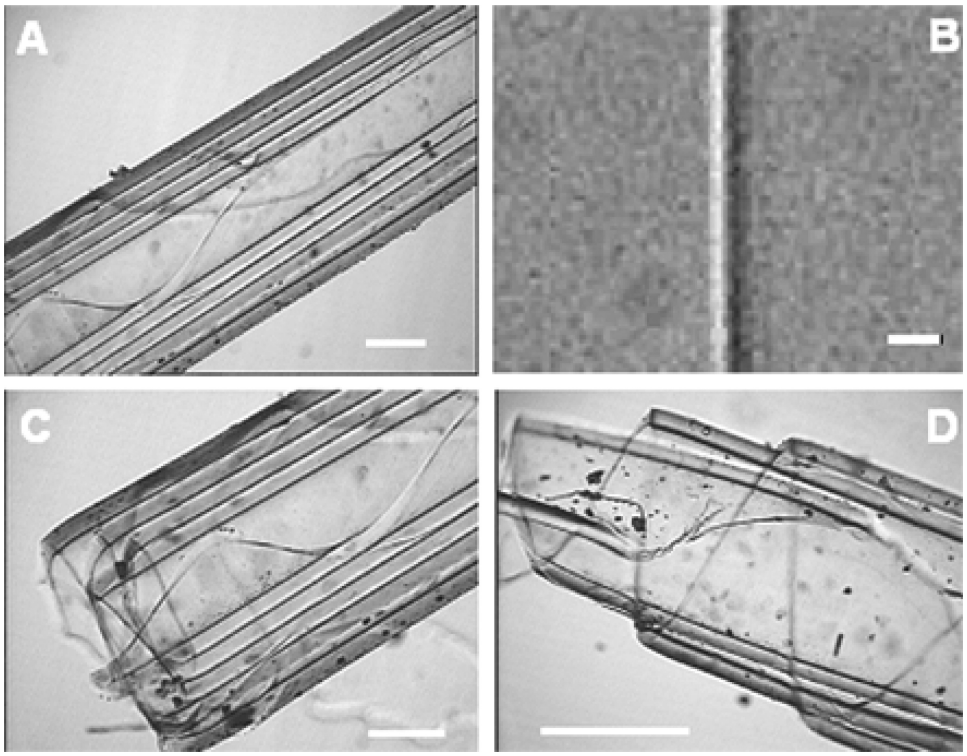

FIGURE 20 Optical microscopy images of the PEHO-*star*-PEO copolymer tubes in acetone. A: A penta walled self-assembly tube. One of the dark lines shows a single wall, and the space between two lines is vacant. B: Image of a single wall. C: An internal (left-hand) screw end of the self-assembly tube. D: An external (right-hand) screw end of the self-assembly tube. Scale bars, 300 μm (A), (C), and (D), and 1 μm (B) (Reproduced from Ref. 107).

have been less investigated. Recently, some examples, prepared through proton transfer polymerization of diglycidyl ethers[115,116] or cationic polymerization,[91] were reported.

We have recently investigated the LCST behavior of a new hyperbranched polymer mainly based on poly(propylene oxide) (PPO).[65] PPO as traditional water-insoluble polyether was modified by anionic copolymerization of PO with a minor fraction of glycidol (Fig. 21). The resulting hyperbranched copolymers consist of PPO segments connected by glycerol branching units. Because each glycerol unit adds exactly one additional hydroxyl end group, the copolymers become more polar with increasing glycerol content, and the LCST can be adjusted by varying the ratio of hydrophobic and hydrophilic comonomer (Fig. 22).

Biocompatibility

Among the wide range of hyperbranched polyethers polyglycerol offers the unique advantage of a controlled synthesis permitting to obtain hyperbranched materials with defined molecular weight and narrow polydispersity. As this is a key criterion for possible biomedical application, the biocompatibility has been extensively evaluated in both *in vitro* and *in vivo* studies. In contrast to the many studies on polyglycerol, so far no data concerning the biocompatibility of polyoxetanes is available. All known polyoxetanes are insoluble in

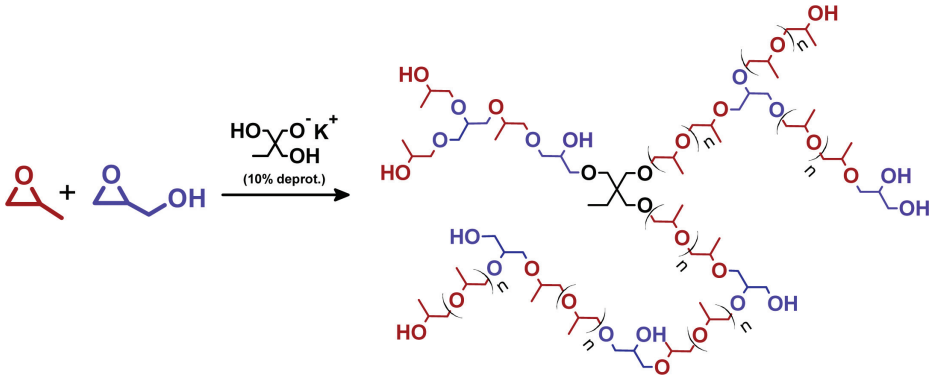

FIGURE 21 Synthesis scheme for the anionic ring-opening multibranching copolymerization of propylene oxide and glycidol.[65]

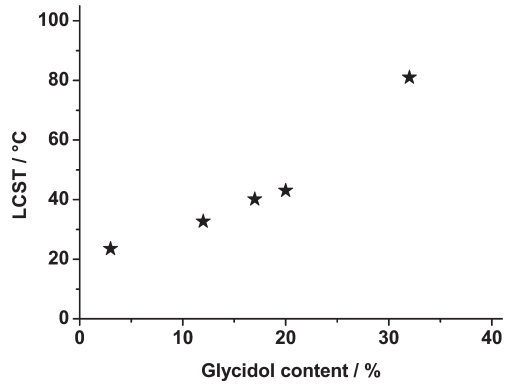

FIGURE 22 Effect of glycidol content on LCST (Reproduced from Ref. 65) for hyperbranched copolymers of glycidol and propylene oxide.

water, and thus, their applicability for biomedical applications is limited.

Brooks and coworkers reported several toxicity studies with different PG architectures. For both linear and hyperbranched PG (with $M_n = 6400$ g mol^{-1}), biocompatibility is similar or even better compared with the established PEG and hetastarch (polymers commonly used in a variety of clinical applications) (Fig. 23). The topology of the polymers was found to have no effect. *In vivo* studies conducted on mice revealed no sign of toxicity after i.v. injection at a dose of 1 g kg^{-1}.[117]

Also very high molecular weight hyperbranched PG (up to 700 kDa) appears to have little effect on the biocompatibility *in vitro* for blood compatibility, viscosity, complement activation, platelet activation, plasma protein precipitation, and cytotoxicity.[118] Although the biocompatibility of polymers in general is a function of molecular weight, the inherently compact hyperbranched structure appears to remove many of the disadvantages associated with the exposure of high molecular weight linear polymers to blood and cells: in solution, *hb*PG s behave more like proteins than linear polymers. The plasma circulation half-life of *hb*PG in mice was found to be between 32 h for a molecular weight of 106 kDa and 58 h for polymers with 540 kDa. This shows that high molecular weight *hb*PG is a potential candidate for drug delivery and imaging applications, where long circulation times are needed. Urinary excretion is very low due to the molecular size of the polymers. The average hydrodynamic radius of *hb*PG with 540 kDa is about 6.8 nm, which is well above the glomerular filtration threshold of the human kidney. Linear polymers are able to pass through pores smaller than their hydrodynamic radius due to their high flexibility. Proteins or dendritic polymers are less deformable and, therefore, restricted to broader pores. It has been reported that the equivalent pore radius of the glomerular filter in terms of the hydrodynamic radius is higher for a linear polymer, such as dextran, compared with branched polymers such as Ficoll® or proteins.[119] A detailed tissue distribution profile of these polymers as a function of molecular weight was described by Kainthan and Brooks.[120] Tissue accumulation was found to decrease with time in the kidney, lung, and heart. However, the nonexcreted *hb*PG is accumulated in the liver and spleen for at least 30 days due to the limited urinary excretion and the nondegradability of the polyether structure.

Also *hb*PG synthesized by cationic ROP with the typical broad molecular weight distribution was tested regarding its biocompatibility by Sharma and coworkers.[121] They separated two fractions, that is, the high and low molecular weight fraction of one sample and investigated the cell viability with human peripheral blood mononuclear cells and tumor derived human B cell line. The cationic synthesis mechanism of *hb*PG seems to have no influence, and comparable toxicity of these structures with PEG was found.

In 2010, Khandare et al. investigated the structure–biocompatibility relationship of hyperbranched polyglycerol derivatives possessing neutral, cationic (with amine end groups), and anionic charges (with sulfate end groups) at different pH values. The cell compatibility results show that the *hb*PGs are as safe as linear PEG polymers or dextran, which indicates the suitability of *hb*PG derivatives in delivering therapeutic agents systemically.[122]

In an interesting work, Haag and coworkers have recently observed a molecular mass and size-dependent cellular uptake of *hb*PG, indicating a molecular weight/size optimum around 200 kDa/12 nm.[123] Their data suggest that the

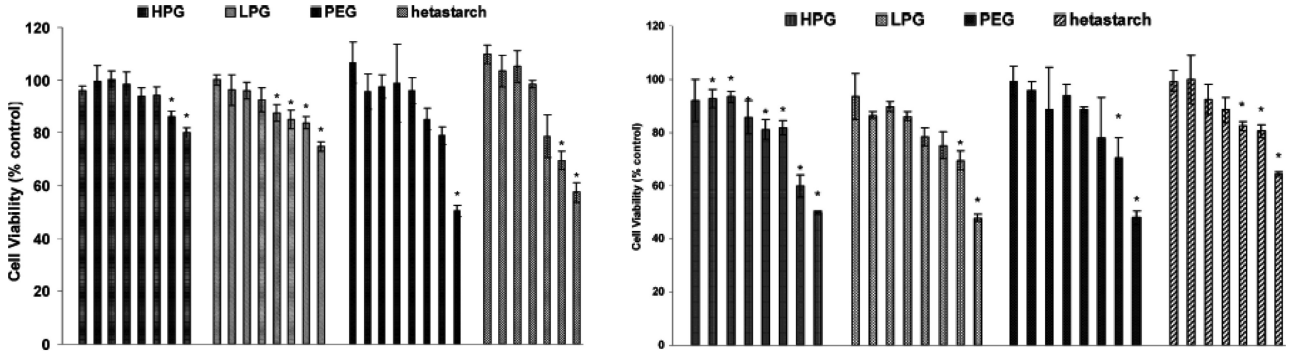

FIGURE 23 Cytotoxicity of linear and hyperbranched polyglycerol against L-929 (left) and HUVEC (right) cells at increasing concentrations from left to right: 0.0001, 0.001, 0.01, 0.1, 0.5, 1, 5, 10 mg/mL compared with PEG and hetastarch (Reproduced from Ref. 117).

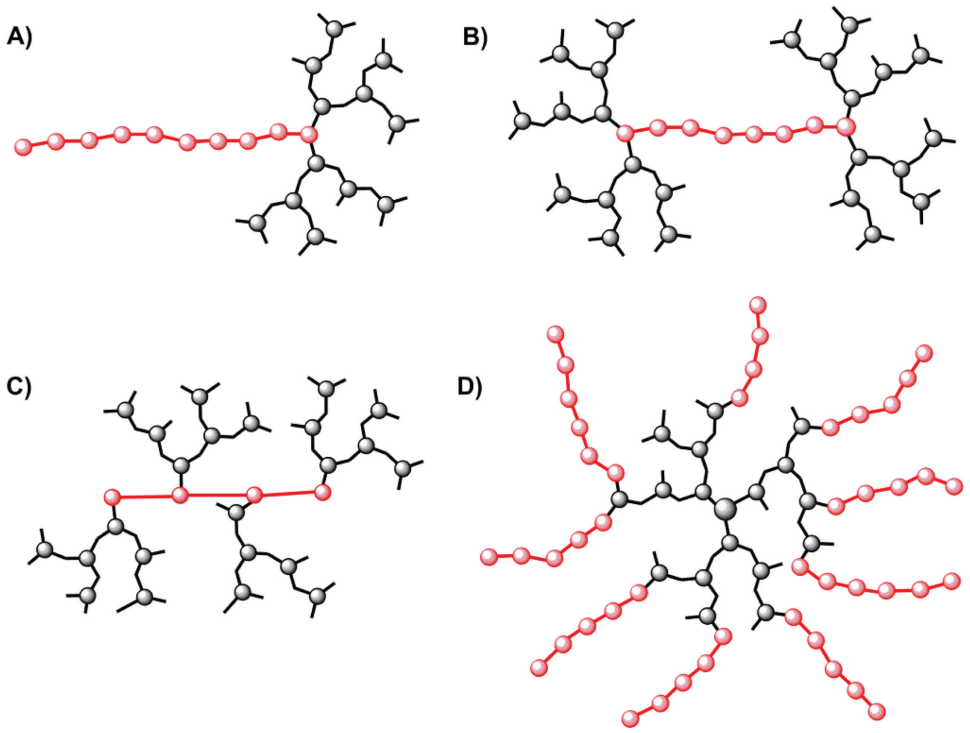

FIGURE 24 Linear-hyperbranched copolymer topologies: (A) and (B) linear-hyperbranched block copolymers (LHBCs); (C) linear-hyperbranched graft-copolymers (LHGCs); (D) multiarm star-polymers with hyperbranched core.

higher molecular weight *hb*PGs (40–870 kDa) predominantly accumulate in the cytoplasm and that endocytotic uptake can be suppressed for lower molecular weights (2–20 kDa).

HYPERBRANCHED POLYETHERS AS BUILDING BLOCKS FOR COMPLEX MACROMOLECULAR ARCHITECTURES

Due to their multifunctionality and their interesting properties, hyperbranched polyether polyols are useful building blocks for the synthesis of complex macromolecular architectures. Recently, the combination of linear and hyperbranched building blocks has afforded novel classes of block copolymers. By combining linear and hyperbranched blocks, various key copolymer topologies can be obtained (Fig. 24): linear-hyperbranched block-copolymers (LHBCs), linear-hyperbranched graft-copolymers (LHGCs), and multiarm star-polymers with hyperbranched cores.

Linear-Hyperbranched Block Copolymers

LHBCs have gained increasing attention during the last decade. Due to their facile synthesis and interesting properties both in bulk and solution—caused by the highly branched topology and the multiple end groups of the hyperbranched block—these polymers are interesting for many potential applications ranging from drug delivery and biomineralization to electrochemistry and catalysis. Particularly, the availability of advanced polymerization techniques for the controlled synthesis of hyperbranched polymers has paved the path for further structure–property investigations in this emerging field, especially in comparison to similar structures with perfectly branched dendrimer blocks. Hyperbranched polyether polyols are of special interest in this context, because some systems fulfill the required synthetic criteria regarding the control of the molecular structure. This area of research, including general synthetic strategies, properties in bulk and solution as well as potential applications have been covered in detailed recent reviews by our group and others.[124,125] Therefore, this sub-chapter will only describe some selected examples of LHBCs with respect to synthesis as well as peculiar properties and applications focusing on hyperbranched polyether polyol building blocks.

Following pioneering works by Kricheldorf and Stukenbrock,[126] Frey et al. described the first controlled synthesis of amphiphilic LHBCs consisting of a linear poly(propylene oxide)-*co*-poly(ethylene oxide) (PPO-*co*-PEO) and a *hb*PG block in 2003.[127] Here, a commercially available Jeffamine® was bisglycidolized and used as a macroinitiator for the ROMBP of glycidol. This concept was further improved according to theoretical works on the ROMBP process, which showed that an enhanced number of initiator groups lead to better control over the polymerization and lower polydispersities.[58] The use of linear macroinitiators with several hydroxyl groups applicable for the ROMBP of glycidol has become an efficient method for the preparation of LHBCs with control over molecular weight, DB, and polydispersity. Based on a linear polystyrene-*block*-polybutadiene copolymer and subsequent hydroboration, the resulting hydroxyl groups were used for the hypergrafting of glycidol to give amphiphilic LHBCs consisting of a linear polystyrene and a *hb*PG block.[128]

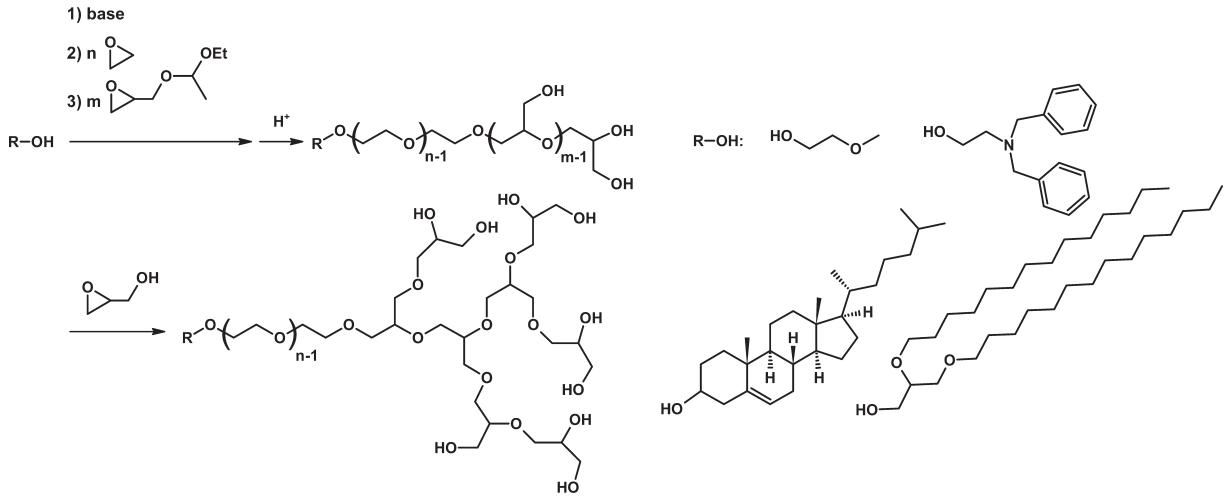

FIGURE 25 Synthesis of LHBCs based on PEG and *hb*PG with variable structural parameters and single functional end groups using specific initiators.[129–131]

Particularly, the combination of PEG as a linear block and *hb*PG as a hyperbranched block has led to an interesting toolbox in the synthesis of LHBCs. The resulting polyether-based materials are interesting candidates for various applications, for instance in the field of polymer therapeutics, due to the excellent biocompatibility of PEG and PG, as described above. Following, the ROP of ethylene oxide from a functional initiator to give the linear PEG block, a short block of an acetal-protected glycerol derivative (e.g., EEGE), and subsequent, acidic cleavage of the protective groups leads to a linear PEG macroinitiator with several linear polyglycerol (*lin*PG) repeat units (PEG-*b*-*lin*PG). The multiple hydroxyl groups are suitable for the ROMBP of glycidol to synthesize the *hb*PG block after the formation of the alkoxide salt (Fig. 25).[129] The resulting LHBCs PEG-*b*-*hb*PG exhibit narrow molecular weight distributions and overall molecular weights from 13,100 to 17,700 g mol^{-1}.

By using functional initiators (which must be suitable both for application in anionic ROP and acidic cleavage of the acetal protective groups of EEGE), interesting α,ω_n-telechelics with tailored properties can be obtained. Because of the excellent control in the ROMBP of glycidol, the number of end-groups and the molecular weight of the hyperbranched block can be tailored for specific purposes.

The use of a benzyl protected amino-functional initiator gives double-hydrophilic α,ω_n-telechelics, which were used for noncovalent bioconjugation of avidin, using the deprotected focal α-amino group for the coupling to biotin.[130] By covalent attachment of a pyrene anchor to the focal amine, LHBCs based on PEG and *hb*PG have also been used to solubilize carbon nanotubes.[132] The use of cholesterol or other aliphatic glyceryl ethers as initiator resulted in unusual linear-hyperbranched lipids, which are suitable for liposome preparation and drug-delivery applications.[131] Moreover, it could be shown that the focal cholesterol moiety supports the formation of monolayers and the cholesterol moiety is able to crystallize.[133] In an extension of this concept, other complex lipids could be obtained by polymerizing different glycidyl ethers from aliphatic, hydrophobic initiators and the attachment of a dye at the polyether polyol block opens the path for detection of the liposomes *in vivo*.[134]

In a different synthetic approach, Yan and coworkers recently described the elegant synthesis of linear-hyperbranched amphiphiles using supramolecular assembly of adamantyl-functionalized alkyl chains (AD-C$_n$, n = 12, 18, 30) and *hb*PG grafted from β-cyclodextrin (CD-*g*-*hb*PG, M_n = 5900 g mol^{-1}) by specific AD/CD host-guest interactions.[135] Such amphiphiles self-assemble in water to vesicles and show high stability even after storage for several months.

Besides linear-hyperbranched diblock copolymers, several examples of hyperbranched-linear-hyperbranched triblock copolymers with aliphatic polyethers as terminal hyperbranched block have also been reported (Table 1).

Dworak and coworkers used bishydroxy-endfunctional PEG as an initiator for the ROMBP of glycidol, which led to difficulties due to the presence of only two initiating hydroxyl groups. The introduction of additional hydroxyl groups by glycidyl ethers and subsequent polymerization of ethylene oxide gave a suitable macroinitiator for the hypergrafting of glycidol.[137] This method was further developed by Wurm et al. by direct grafting of glycidol from a linear multihydroxy-functional PEG macroinitiator with short *lin*PG

TABLE 1 Overview on Hyperbranched-Linear-Hyperbranched Triblock Copolymers

Hyperbranched Block	Linear Block	References
Poly(3-ethyl-3-(hydroxymethyl)oxetane)	Poly(ethylene glycol)	136
Polyglycerol	Poly(ethylene glycol)	137
Polyglycerol	Poly(ethylene glycol)	138
Polyglycerol	Poly(tetrahydrofuran)	139

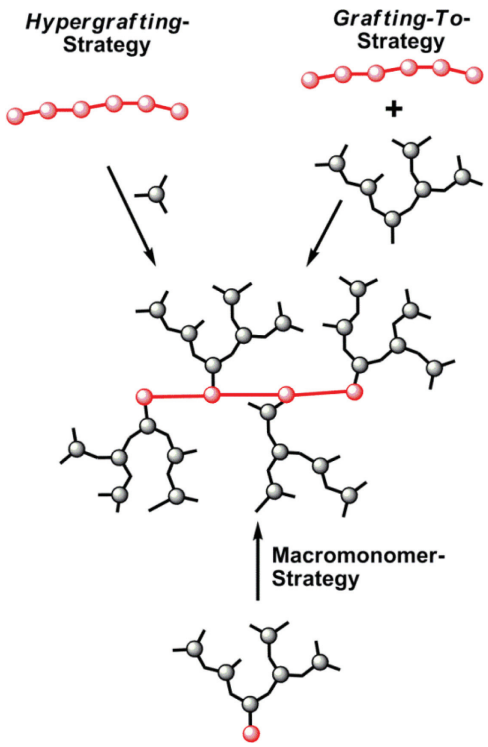

FIGURE 26 Three basic strategies for the synthesis of linear-hyperbranched graft-copolymers (LHGCs).

segments at both PEG ends (*lin*PG-*b*-PEG-*b*-*lin*PG). These materials are available over a broad range of molecular weights and with up to 300 end groups.[138] Moreover, some other triblock copolymers with hyperbranched PEHO and linear PEG blocks,[136] or linear poly(tetrahydrofuran) (PTHF) and *hb*PG were described.[139]

In summary, the use of aliphatic polyether polyols, especially hyperbranched polyglycerol as building blocks for the synthesis of LHBCs with controlled molecular weights and tailored molecular architecture, is advantageous. One may envision other synthetic strategies like coupling linear and hyperbranched dendron analogs, or the grafting from hyperbranched macroinitiators with a focal initiator group, which might allow for the synthesis of more LHBCs with novel interesting properties. This is essential to further explore the potential of hyperbranched aliphatic polyether polyols as building blocks for linear-hyperbranched copolymers and to investigate their structure–property relationships.

Linear-Hyperbranched Graft Copolymers

When hyperbranched macromolecules are being attached to a linear polymer backbone as side chains, LHGCs are obtained. Such macromolecules could also be perceived as chain-analogs of hyperbranched polymers or as hyperbranched brush-type polymers. The analogous dendronized polymers (DenPols) consisting of a linear backbone and perfectly branched dendritic side chains represent a well-established class of macromolecules.[140,141] The sterically demanding, perfectly branched dendritic side chains force the linear backbone of these polymers into an extended conformation and can lead to the formation of molecular objects in the nanometer range.[142,143] It remains an intriguing question, if LHGCs are also able to show this behavior and if they could be used for similar applications as DenPols, which range from biomedicine to catalysis. The major distinction of LHGCs compared with DenPols is their facile synthesis. For the synthesis of DenPols—independent of the synthetic strategy—perfectly branched dendritic building blocks have to be synthesized in challenging multistep protocols, especially for high molecular weight DenPols. In analogy to synthetic routes toward DenPols, three basic synthesis strategies (and combinations thereof) can be applied for LHGCs: hypergrafting (grafting-from) and grafting-to strategy as well as the macroinitiator (grafting-through) approach (Fig. 26).

*hb*PG is a particularly valuable building block for the synthesis of the hyperbranched side chains, because molecular weight and polydispersity can be controlled using anionic ROMBP and the slow monomer-addition technique (SMA). The hypergrafting-strategy (grafting-from) has already been

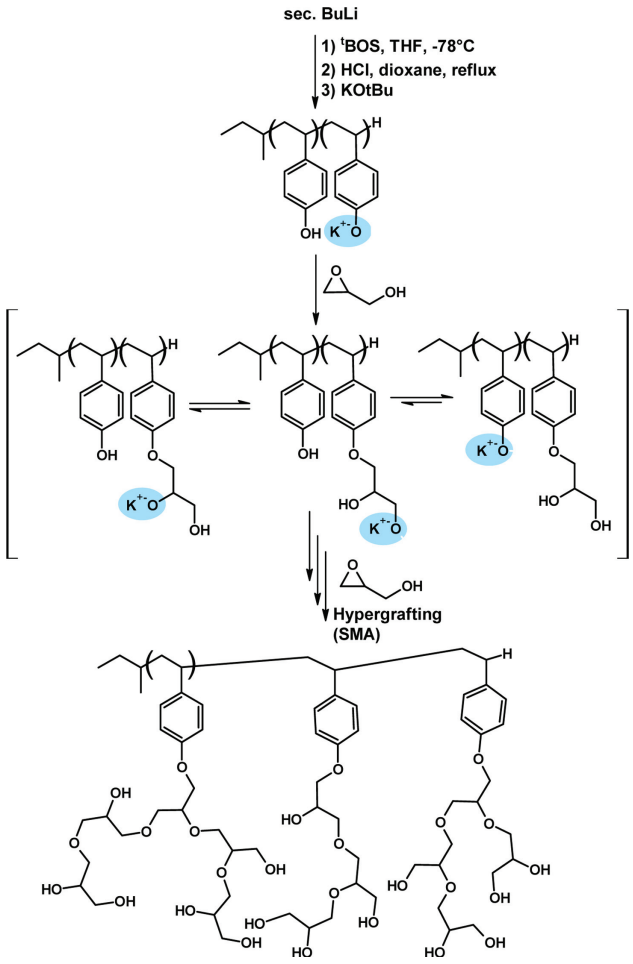

FIGURE 27 Synthesis of polyether-based LHGCs with high side chain density by hypergrafting of glycidol from poly(4-hydroxy styrene) (PHOS). The rapid proton transfer between PHOS and the growing side chains is supported by the slow monomer-addition technique.

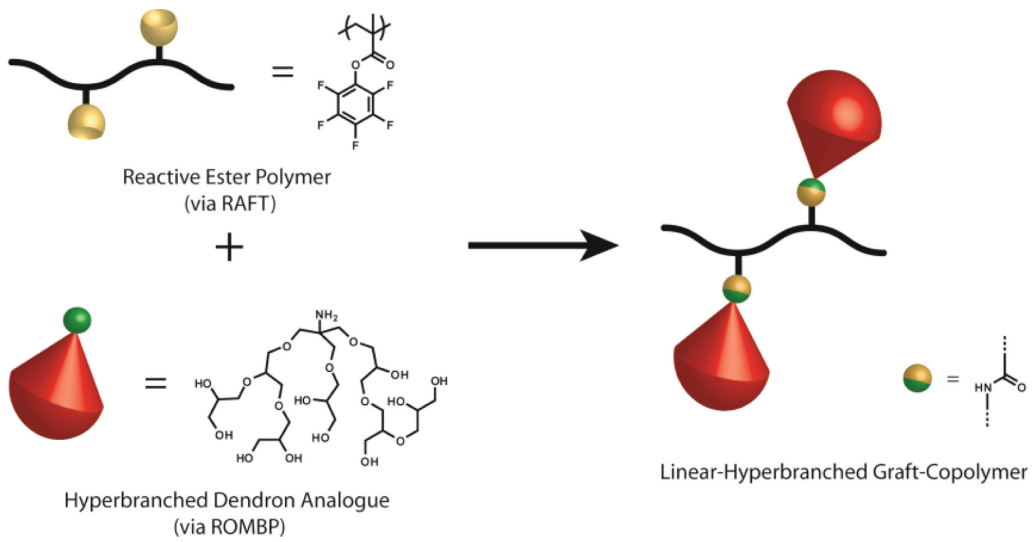

FIGURE 28 Synthesis of LHGCs by grafting-to strategy using hyperbranched polyglycerol dendron analogs and reactive ester polymers (Reproduced from Ref. 145).

used in several works by our group for the synthesis of linear-hyperbranched block copolymers (LHBCs, vide supra), where usually short linear "macroinitiator blocks" are used to build up the hyperbranched block. In a recent work by our group, the hypergrafting strategy was applied to synthesize LHGCs with a high side chains density, using poly(4-hydroxy styrene) (PHOS) as a linear macroinitiator (Fig. 27).[144]

Two linear macroinitiators with low polydispersities ($M_w/M_n < 1.2$) were synthesized by carbanionic polymerization of *tert*-butoxy styrene and subsequential acidic removal of the protective groups. Because of the higher acidity of the phenolic hydroxyl groups of PHOS compared with the aliphatic hydroxyl groups of the growing *hb*PG chains, rapid proton transfer in the reaction system supported by the slow monomer-addition technique favors the growth of the side chains at the PHOS repeat units over the polymerization of the *hb*PG side chains. This happens despite the fact that only 10% of the PHOS repeat units were deprotonated to initiate the ROMBP of glycidol to ensure solubility of the macroinitiator in the reaction solvent. The high grafting density was proven by ^{13}C NMR spectroscopy. The quantitative functionalization of each PHOS repeat unit is advantageous for the potential formation of cylindrical objects, due to high sterical repulsion of the highly branched side chains. Moreover, it could be shown that the molecular weight of the LHGCs (M_n = 10–31 kg mol^{-1}, $M_w/M_n < 1.4$) and the side chains as well as the thermal properties can be tailored ($T_g = -13$ °C to -36 °C).

In a different work, a grafting-to approach was used to synthesize LHGCs with molecular weights exceeding 126 kg mol^{-1} and narrow molecular weight distributions ($M_w/M_n < 1.3$).[145] In this work, hyperbranched polyglycerol dendron analogs with a single focal amino functionality (H_2N-*hb*PG) were attached to a reactive ester polymer (poly(pentafluorophenol methacrylate), PPFPMA) (Fig. 28). The dendron analogs were synthesized in a three-step synthesis using a benzyl protected amino-functional initiator for the ROMBP of glycidol and subsequent hydrogenation, whereas the defined linear backbones were synthesized by RAFT polymerization. This combination of controlled polymerization techniques ensures low polydispersities and high precision of the macromolecular architecture.

These unusual polymer topologies are especially valuable for biomedical applications, because after the attachment of H_2N-*hb*PG to the linear backbone, residual PPFPMA repeat units can further be functionalized with other amine containing molecules, like drugs or dyes.[146]

The macromonomer strategy has been applied for the synthesis of brush-type polymers with *lin*PG side chains, where the methacrylate or styrene functionalized hyperbranched macromonomers were polymerized by free radical[147] or atom transfer radical polymerization (ATRP).[148] Möller and coworkers extended this concept in a recent work, where *hb*PG oligomers with focal acrylate and methacrylate functions were copolymerized with hydrophobic monomers.[149] Moreover, Huck and coworkers described the grafting of polyglycerol macromonomers with different topologies from gold surfaces and found a strong dependence of the antifouling properties of the surface, depending on the brush architecture.[150]

Linear polymers with hyperbranched side chains can be synthesized using hypergrafting (grafting-from), grafting-to, or a macromonomer approach. Hyperbranched polyethers like hyperbranched polyglycerol are valuable building blocks, because they can be synthesized with control over molecular weight and polydispersity, leading to well-defined structures. LHGCs are promising candidates as a novel approach to cylindrical molecular objects besides the established DenPols with perfectly branched side chains. The conveniently prepared LHGCs could be used, for example, as templates for

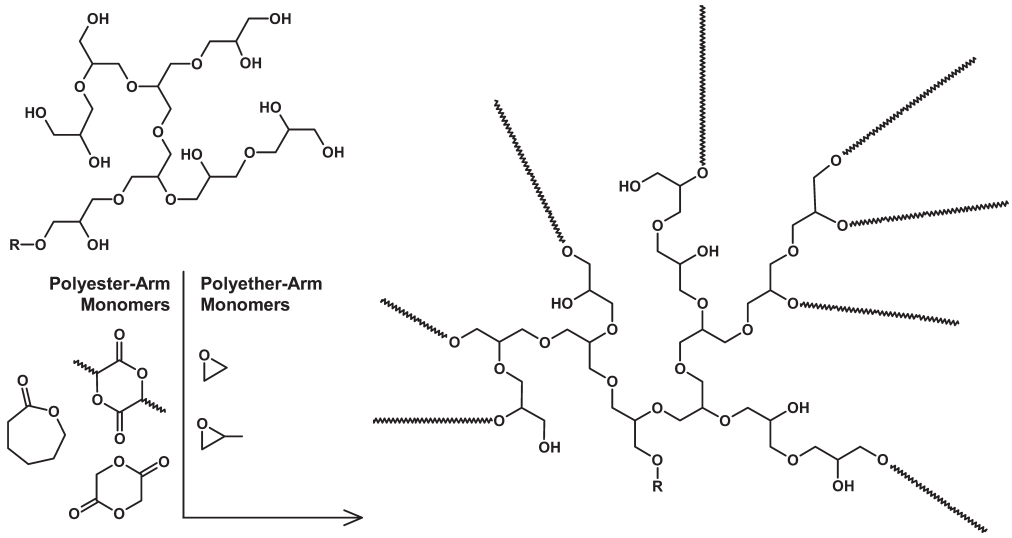

FIGURE 29 Synthesis of various MSPs using *hb*PG as macroinitiator core for the ring-opening polymerization of suitable monomers.

elongated organic or inorganic nanostructures. The use of *hb*PG as a building block also opens options for polymer therapeutics with unusual topologies, due to the excellent biocompatibility of *hb*PG.

Multiarm Star Copolymers with a Hyperbranched Core

Hyperbranched aliphatic polyethers are versatile core building blocks for the synthesis of multiarm star polymers (MSPs), especially due to their excellent applicability for chemical derivatization of the large number of hydroxyl groups and their chemical inertness and stability under various reaction conditions. MSPs consist of a branched core molecule to which multiple (several to hundreds) linear polymers are attached. One can distinguish between homoarms (one arm-type) and miktoarms (different arm-types). General strategies for the synthesis of MSPs have been covered in several excellent reviews.[18,151–153] The potential applications of the hyperbranched aliphatic polyethers and their corresponding MSPs, for example, as unimolecular containers, for molecular self-assembly and biomedical purposes have been covered in other reviews[154–156] and will be discussed with a special focus on hyperbranched aliphatic polyethers in different sections of this highlight article.

Especially, the "key polymers" hyperbranched PEHO and *hb*PG have been widely used as macroinitiator cores in the synthesis of MSPs.[32,107,157] Depending on the chemical structure of the arms, polarity, solubility, flexibility, and functionality of the hyperbranched core can be modified. By using well-controlled polymerization techniques, such as anionic and catalytic ring-opening (ROP), or controlled radical polymerizations such as ATRP or RAFT for the preparation of the arms, defined macromolecular architectures can be achieved. The hydroxyl groups of hyperbranched polyols are especially interesting as initiating groups for ROP. Here, arms of controlled length can be grafted directly from the multifunctional core in one-reaction step.

*hb*PG was used as a macroinitiator for the ROP of various monomers (Fig. 29). The use of ethylene oxide[158,159] and propylene oxide[160] changed the thermal properties of *hb*PG significantly as a consequence of the attachment of linear polyether arms. The ROP of L-lactide[161] or ε-caprolactone[162,163] leads to unimolecular micelles with biodegradable hydrophobic polyester arms. Polyglycolide became soluble in several organic solvents upon attachment as arms to a *hb*PG core.[164] Just recently, hbPEG,[102] which is somewhat related to *hb*PG, was also used as a macroinitiator for the ROP of L-lactide to yield MSPs with molecular weights up to 800 kg mol^{-1}.[165]

In addition, *hb*PG was functionalized with suitable initiator groups by esterification for controlled radical polymerization of the arms, for example, by ATRP.[166,167] Here, poly(methyl acrylate),[168] poly(methyl methacrylate),[169] and poly(2-hydroxyethyl methacrylate)[170] were grafted as homoarms from the *hb*PG core. Moreover, block copolymer arms were attached using the same ATRP strategy, for example, to polymerize polystyrene-*block*-poly(*tert* butyl acrylate) and polystyrene-*block*-poly(acrylic acid) arms[171] or polystyrene-*block*-poly(ethylene oxide) arms. In the latter case, poly(ethylene oxide) blocks were attached by a radical coupling reaction after the ATRP of styrene from the core[172] or by azide-alkyne click chemistry.[173] Reversible addition–fragmentation chain transfer polymerization (RAFT)[174,175] is another versatile controlled radical polymerization technique that can be used for the synthesis of MSPs after attachment of suitable functional groups to the *hb*PG core. For example, *hb*PG with poly(*N*-isopropylacrylamide) arms, that exhibits thermoresponsive properties, have been described.[176] By combination of RAFT and ATRP, the synthesis of interesting miktoarms (polystyrene and poly(*tert* butyl acrylate)) on a *hb*PG core could be realized.[177]

While *hb*PG represents a hydrophilic core for MSPs, the utilization of hyperbranched aliphatic polyethers based on 3-alkyl-3-(hydroxymethyl)oxetanes yields hydrophobic core

structures. Nevertheless, they possess a similar hyperbranched polyol structure compared with *hb*PG where the multiple hydroxyl groups can be used for attachment of homo- and mikto-arms. Therefore, they are very useful macroinitiators for the synthesis of MSPs, but with clearly different solubility behavior and other properties than *hb*PG. Yan and coworkers extensively studied MSPs based on PEHO with a certain focus on self-assembly and biomedical applications.[155] Especially, PEHOs with PEG arms show unique self-assembly behavior up to the formation of macroscopic visible fibers in acetone (see section "Solution Properties").[107,108,178]

In ongoing studies, it was found that the DB of PEHO has a significant effect on the aggregation behavior, as the MSPs can self-assemble into vesicles, wormlike micelles, and spherical micelles with a decrease in DB of the hyperbranched core, respectively.[109] Yan and coworkers also synthesized other PEHO-based MSPs, for example, with cationic amino-functional arms, that were the first reported example of self-assembled hyperbranched polymers.[179] By using poly(2-(dimethylamino)ethyl methacrylate) arms, thermoresponsive MSPs are obtained[180] that also self-assembled upon attachment of an additional fluorine containing block.[181] In an interesting work, MSPs with a PEHO core and PTHF arms were synthesized directly in a one-pot reaction by cationic ROP.[182]

MSPs with a hyperbranched core represent the so far most studied linear-hyperbranched copolymer topology. The facile synthesis of hyperbranched aliphatic polyethers with defined molecular weights and narrow molecular weight distribution makes them ideal building blocks for MSPs. Particularly, the multiple hydroxyl groups of the key polymers hyperbranched polyglycerol and PEHO can be directly used for ROP of suitable monomers, resulting in well-defined MSPs in convenient two-step syntheses. After attachment of suitable initiator functionalities, controlled radical polymerization techniques open options for an almost infinite variety of monomers for the arms. As MSPs based on hyperbranched aliphatic polyether polyols became a topic of interest in the field of polymer therapeutics and self-assembly, other potential applications, for example, in electronic or catalytic applications might also be of interest in the near future.

APPLICATION POTENTIAL

Since the origin of the term "hyperbranched polymer" in 1988,[183,184] these materials have gained strong attention. Because of their interesting properties in bulk or solution in combination with the facile synthesis aliphatic hyperbranched polyethers are interesting for many possible applications. Especially, the multitude of end groups, that can be used for further derivatization reactions, has led to a rapidly growing significance in biomedical applications ranging from drug delivery to surface coatings for the creation of protein-repellent surfaces. In addition, the highly branched and, therefore, noncrystalline structure makes them useful as polymer electrolytes in the seminal field of energy storage for consumer electronics or electric vehicles.

Biorepellent Surfaces

An area of major potential regarding biomedical application can be found in biorepellent surfaces for medical devices, because protein or unspecific cell adsorption marks a severe problem for polymer objects implanted in the human body, such as artificial joints or catheters. Currently, PEG is frequently used for anti-biofouling surface coatings,[185] but the relatively low stability toward oxidation limits its application in biological systems. Polyglycerol as a highly biocompatible aliphatic polyether shows higher stability toward oxidation,[186] and self-assembled monolayers (SAMs) presenting oligo- or polyglycerols exhibit excellent protein resistance.[187–189] Readily available PG has been modified with a surface-active disulfide or triethoxysilane linker, and subsequently, SAMs of these polymers on gold or glass surfaces were prepared (Fig. 30). The respective PG SAMs proved similar protein resistant as their linear PEG analogs.[190] However, in contrast to linear PEG, hyperbranched PG with its multiple hydroxyl groups offer the possibility of further derivatization in order to not only reduce nonspecific interactions with biofluids but also enhance specific interactions via the simultaneous presentation of specific ligands on the surface.

In contrast to the above described grafting-to strategies, Buchmeiser and coworkers[191] developed a grafting-from synthesis for PG on polystyrene (PS) and poly(ethylene terephthalate) surfaces after oxygen plasma-treatment to form thin hydrophilic films of PG without any additional initiator. A significant decrease of unspecific protein adsorption was evidenced by fluorescence microscopy.

Toward Biomedical Applications

The application of hyperbranched polyethers in medicine and pharmaceuticals is a rapidly advancing area. Special needs in this field are biocompatible and bioactive materials for transport applications and drug delivery. The use of *hb*PG for biomedical applications and in nanomedicine has been reviewed just recently by Caldéron[78] and Khandare.[192] Some aspects were also covered by Yan and coworkers[155] as part of their review on self-assembled hyperbranched polymers for biomedical applications. Therefore, we will only briefly illustrate selected recent developments in this field.

An interesting application for hyperbranched polyethers makes use of their high amount of hydroxyl end groups. Calderón and coworkers developed cleavable polymer-drug conjugates derived from *hb*PG and maleimide-bearing prodrugs of doxorubicin and methotrexate, that are cleaved enzymatically by cathepsin B (Fig. 31).[193] Both the synthesis and *in vitro* application of this new macromolecular nanocarrier has been studied. Cytotoxicity of the conjugates against human tumor cell lines showed that the activity of the drugs was primarily retained after the cleavage.

Zimmerman and coworkers reported water-soluble polyglycerol-dendronized perylenediimides and demonstrated specific labeling of proteins on the surface of living bacterial and mammalian cells.[194] In contrast to these perfectly branched dendrons, alkyne-core *hb*PGs[195] were used for the

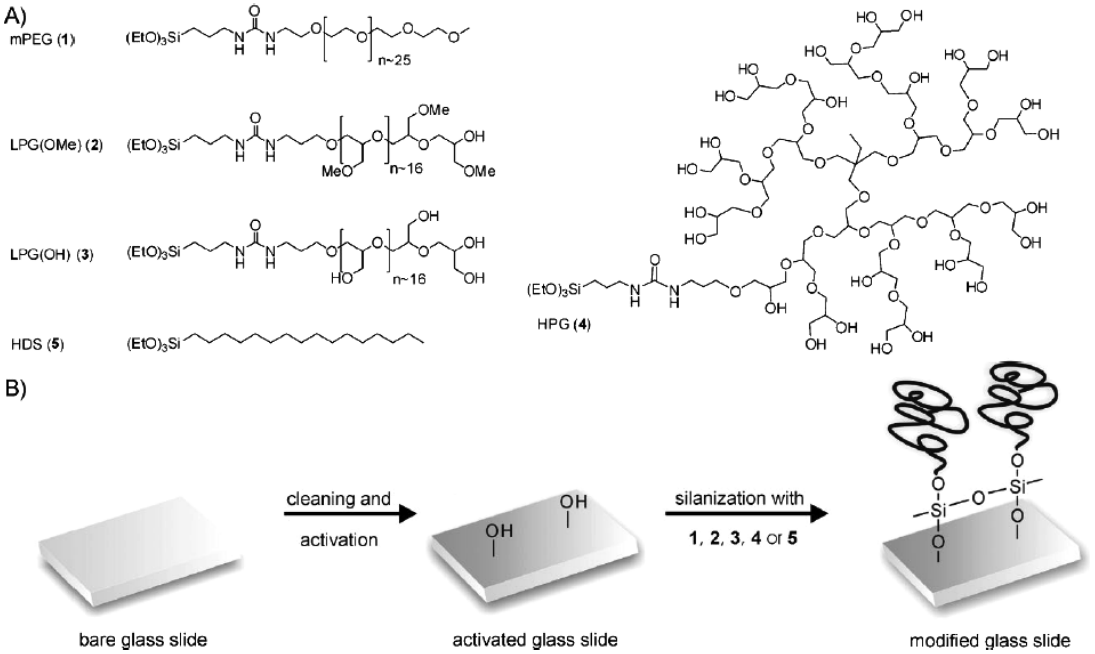

FIGURE 30 A: Chemical structure of triethoxysilane modified compounds 1, 2, 3, 4, and 5 and (B) sketch of monolayer formation on glass with these compounds (Reproduced from Ref. 190).

preparation of potential biological imaging agents, such as monofunctionalized fluorescein or biotin *hb*PG, for the stabilization of gold nanoparticles, and the synthesis of unimolecular acid-labile micelles that are capable of incorporating nonpolar guests.

Kainthan et al. developed a substitute for human serum albumin (HSA) based on hyperbranched polyglycerol as a synthetic plasma expander, that can replace not only the osmotic and volume expansion properties of HSA but also its binding and transport properties. Hyperbranched polyglycerols were derivatized with hydrophobic groups for binding fatty acids and other hydrophobic materials and short PEG chains to shield the polymer from host defense systems and to enhance the overall blood circulation time. Because of the hyperbranched structure, the polymers have only a small effect on plasma viscosity. *In vitro* and *in vivo* investigations showed no activation of the immune system or blood coagulating effects and a circulation half-life of 34 h in mice. The properties can be precisely controlled by manipulating the molecular weight and the degree of PEG derivatization.[196]

Just recently, the same group suggested the application of an *hb*PG derivative as tissue sealant and in the self-assembly of lipid nanostructures. *hb*PG functionalized with choline phosphate (CP) at the surface binds electrostatically to a variety of phosphatidylcholine (PC)-rich cell membranes and to PC-containing liposomes. Remarkably, a strong adhesion is produced by simple reversion of the head group orientation. The authors also showed that PC-rich membranes adsorb and rapidly internalize fluorescent *hb*PG–CPs, which paves the way to a potential use as drug-delivery agents.[197]

Dendritic core-double-shell architectures consisting of a hyperbranched polyglycerol core, a long aliphatic hydrophobic inner shell, and hyperbranched polyglycerol-based hydrophilic outer shell have been synthesized by Burakowska and Haag.[198] This unique architecture was inspired by the molecular mimicry of a liposome. The obtained, well-defined,

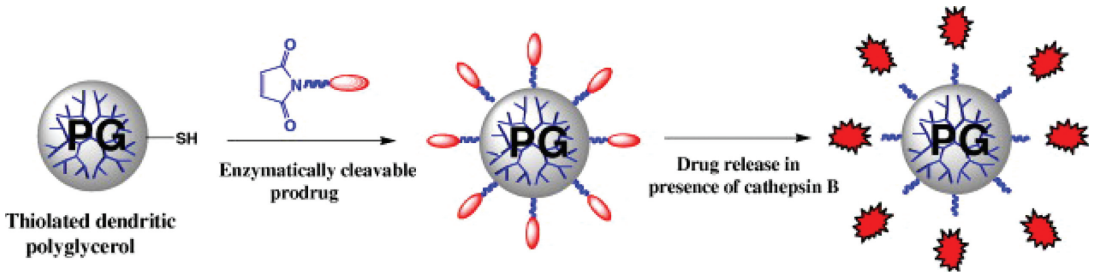

FIGURE 31 Hyperbranched polyglycerol as nanocarrier for enzymatically cleavable prodrugs like doxorubicin and methotrexate. (Reproduced from Ref. 193).

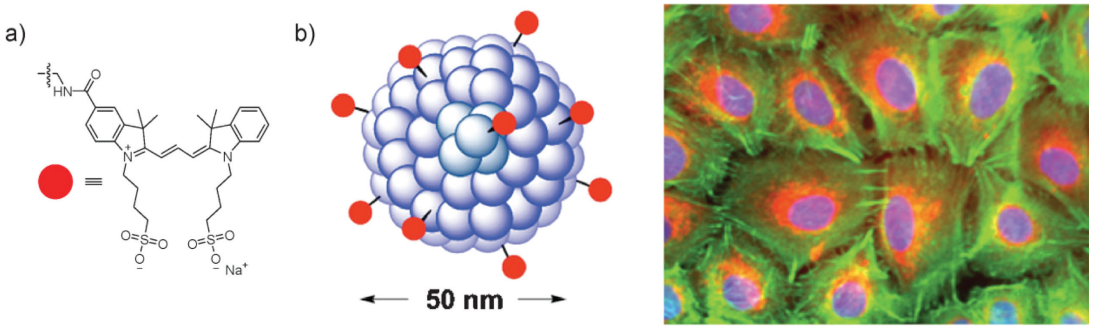

FIGURE 32 Fluorescence microscopy shows clear evidence for cellular uptake of fluorescently labeled PG-microgels via an endocytotic pathway: Culture of the human lung cancer cell line A549 incubated with ICC-labeled PG-microgel for 4 h at 37 °C. Actin cytoskeleton was stained with Alexa Fluor 488 phalloidin (green), nuclei stained with 4′,6-diamidino-2-phenylindole (DAPI, blue) (Reproduced from Ref. 78).

globular, nanometer-sized architectures possess the ability to encapsulate polar guest molecules, such as Rose Bengal and Congo Red, and water insoluble compounds, such as nimodipine, Nile red, and pyrene in the same nanocarrier. The nanoparticles assemble into highly stable supramolecular aggregates, which are responsible for their transport ability. The complexes of polymers and guest molecules showed long-term stability for several months.

Sisson et al. first developed a route to high molecular weight PG analogs by crosslinking of existing *hb*PG macromonomers using the nanoreactor template to control their size. Crosslinking was achieved by a "click"-type Huisgen alkyne/azide cycloaddition reaction in miniemulsion. Nanogels in the size range of 20–90 nm were obtained (Fig. 32).[199] Dye or drug molecules can be encapsulated in the nanoparticles either covalently or physically in the dispersed phase before the crosslinking polymerization. By using these miniemulsion polymerization techniques, polyglycerol nanogels on previously unavailable length scales can be obtained. The particles' size was tuned between 25 and 350 nm in diameter. Biodegradable polyglycerol-based nanogels can also be prepared by incorporating redox active disulfide branching points within the nanogel structure.[200] Cell culture studies proved high biocompatibility of these nanogels. Additionally, dye-labeled nanogels are shown by optical microscopy techniques to readily internalize into cells by endocytotic mechanisms.[201]

Lithium Ion Conducting Polyelectrolytes

Polymer electrolytes have been considered to be a suitable replacement of liquid electrolytes in Li ion battery applications, as long as their ion conductivity reaches the magnitude of 10^{-3} S cm^{-1}. The main difficulty encountered currently is how to efficiently increase the ion conductivity of polymer electrolytes, because the ion conductivity of the first generation of PEO–LiX-based polymer electrolytes (10^{-7} S cm^{-1}) does not meet the requirement of lithium ion batteries. Hyperbranched polymers show several advantages compared to their linear counterparts, for example, high solubility, good processability, less unfavorable interaction, and absent/low crystallization ability. Furthermore, benefiting from the existence of many terminal groups in the hyperbranched polymers, the properties can be easily adjusted by modifying the functional end groups or changing the intra- and intermolecular interactions. One possibility to improve the ion conductive performance of polymer electrolytes is to lower their glass transition temperature (T_g) or to increase the amorphous regions. As it is well known, the hyperbranched structure can suppress crystallization of a polymer and thereby enhance the amorphous phases as compared with linear polymers.

Hawker et al.[202] and Itoh et al.[203] reported a multistep synthetic pathway to hyperbranched polyesters consisting of oligo(ethylene glycol)s with aromatic branching units. However, because of the low mobility of the aromatic moieties, their ion conductivity was too low to match the practical standard for lithium ion batteries. To circumvent this drawback, Lin et al.[204] developed the novel cyclic ether monomer 3-{2-[2-(2-hydroxyethoxy)ethoxy]ethoxy-methyl}-3′-methyloxetane (HEMO) (prepared from the reaction of 3-hydroxymethyl-3′-methyloxetane tosylate with triethylene glycol). The conductivity of the corresponding hyperbranched polyether electrolyte (PHEMO) reaches 5.6×10^{-5} S cm^{-1} at room temperature and 6.3×10^{-4} S cm^{-1} at 80 °C after doping with LiTFSI ($LiN(CF_3SO_2)_2$) at a ratio of Li:O = 0.05, respectively. The performance of pure PHEMO could be improved by reaction with different diisocyanates to form a gel polymer electrolyte based on hyperbranched poly(ether urethane)[205] or by blending it with PVDF-HFP (poly(vinylidene fluoride-hexafluoropropylene) to form a new polymer matrix.[89,206,207]

A novel kind of hyperbranched polyether intended for the solid polymer electrolyte was synthesized via copolymerization of 3-{2-[2-(2-methoxyethoxy)ethoxy]-ethoxy}methyl-3′-methyloxetane (MEMO) and 3-hydroxymethyl-3′-methyloxetane (HMO). Herein, HMO was used to create the hyperbranched structure, whereas MEMO was responsible for the ion transport of the resulting copolymers. The ionic conductivity measurements showed a maximum ionic conductivity of 8.0×10^{-5} S cm^{-1} at 30 °C after doping with the lithium salt LiTFSI.[208] Hyperbranched polyglycerol as part of various copolymers[209,210] or blends[211] was reported to show moderate to low Li ion conductivity between 6.6×10^{-6} S cm^{-1} and 3.5×10^{-5} S cm^{-1} at 20 °C.

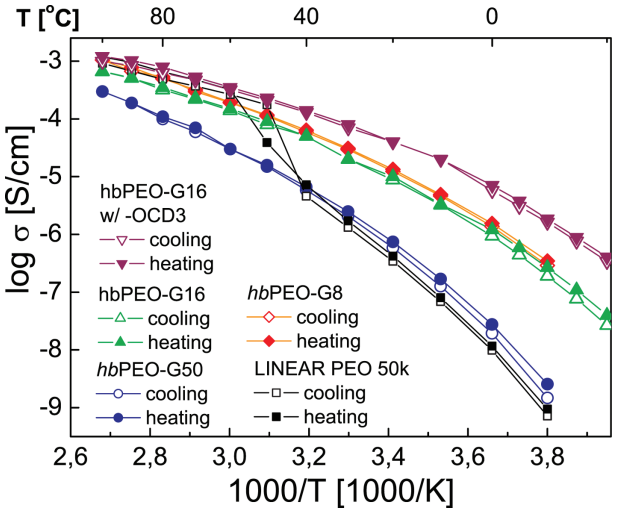

FIGURE 33 Temperature-dependent Li-ion conductivity for hyperbranched PEO samples with varying glycerol branching contents and permethylation, as compared with linear PEO, blended with LiTFSI salt in molar ratio O:Li of 25:1 (Reproduced from Ref. 212).

Recently, we published the first use of hyperbranched poly (ethylene oxide) (*hb*PEO), synthesized via one-step multibranching copolymerization of ethylene oxide and glycidol, as Li ion conducting polyelectrolyte (Fig. 33).[212] The resulting materials are highly viscous liquids, because the tendency of PEG to crystallize is successfully suppressed through the introduction of glycerol branching points.

The linear PEO shows a large, step-like change in Li ion conductivity near the melting point of the PEO crystallites. Such discontinuities in the conductivity are not observed for the hyperbranched samples, consistent with the absence of discernable crystallinity in these samples. The result is a ~100-fold increase in the Li-ion conductivity of the *hb*PEO systems over linear PEO below 50 °C. To evaluate the effects of the hydrogen-bonded network, we also investigated a permethylated version of the *hb*PEO with —OCD_3 end groups to break up the hydrogen bonds between the polymer termini. As expected, the permethylated sample shows a significant increase in the Li-ion conductivity as shown in Figure 33. The maximum room temperature conductivity of permethylated *hb*PEO is 6×10^{-5} S cm^{-1}.

CONCLUSIONS

Since their discovery in the 1990s, the interest in hyperbranched aliphatic polyethers based on polyglycerol and various polyoxetanes has constantly grown. Understanding and controlling the branching pattern as well as molecular weight and polydispersity are important issues. Thus, the respective anionic and cationic polymerization mechanisms have been widely studied. Particularly, the synthesis of hyperbranched polyglycerol has been developed further, giving access to molecular weights in the range of 500 to several hundred thousand g mol^{-1}, whereas polydispersities remain low ($M_w/M_n < 1.5$). The combination of the ROMBP of glycidol and different oxetane derivatives with the highly versatile ROP of epoxides or lactones and controlled radical polymerization gives access to complex macromolecular architectures with well-defined structures. Due to the unique topology of hyperbranched polyethers, their physical and chemical properties differ from the corresponding linear polymers. Thus, detailed elucidation of the structure–properties relationship is necessary to develop further applications of hyperbranched polymers. The multifunctionality of the polymers in combination with their bioinert scaffold has led to a rapidly growing significance in biomedical applications ranging from drug delivery to surface coatings. The highly branched, amorphous structure can contribute to applications in the seminal field of energy storage for consumer electronics or electric vehicles. Further research in this exciting area of polymer science will contribute to the development of hyperbranched polyether polyols with high promise for academic and commercial specialty purposes.

ACKNOWLEDGMENTS

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