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Long-Chain Alkyl Epoxides and Glycidyl Ethers: An Underrated Class of Monomers

Patrick Verkoyen and Holger Frey*

Long-chain epoxides and specifically alkyl glycidyl ethers represent a class of highly hydrophobic monomers for anionic ring-opening polymerization (AROP), resulting in apolar aliphatic polyethers. In contrast, poly(ethylene glycol) is known for its high solubility in water. The combination of hydrophobic and hydrophilic monomers in block and statistical copolymerization reactions enables the synthesis of amphiphilic polyethers for a wide range of purposes, utilizing micellar interactions in aqueous solutions, e.g., viscosity enhancement of aqueous solutions, formation of supramolecular hydrogels, or for polymeric surfactants. Controlled polymerization of these highly hydrophobic long-chain epoxide monomers via different synthesis strategies, AROP, monomer-activated anionic ring-opening polymerization, catalytic polymerization, or via postmodification, enables precise control of the hydrophilic/lipophilic balance. This renders amphiphilic polymers highly interesting candidates for specialized applications, e.g., as co-surfactants in microemulsion systems. Amphiphilic polyethers based on propylene oxide and ethylene oxide, such as poloxamers are already utilized in many established applications due to the high biocompatibility of the polyether backbone. Long alkyl chain epoxides add an interesting perspective to this area and permit structural tailoring. This review gives an overview of the recent developments regarding the synthesis of amphiphilic polyethers bearing long alkyl chains and their applications.

1. Introduction

In current macromolecular chemistry, the introduction of functional groups at polymer backbones represents one of the major directions aiming at the development of smart and (multi)responsive materials. However, the importance of hydrophobic interactions is often neglected. Without hydrophobic interactions, the unique conformations of proteins and the controlled formation of cell membranes, which are essential for life, would not be possible.[1–3] Inspired by nature, these interactions can also be transferred to synthetic polymers, where the introduction of a defined amount of long alkyl chains at polymer backbones offers control over the behavior of polymers in aqueous solution and therefore permits to tune the physical properties of aqueous solutions. Already in 1957, Rogers and Mandelkern reported on the polymerization of *n*-alkyl methacrylates and investigated the thermal properties of the synthesized materials.[4] The highly hydrophobic character of *n*-alkyl methacrylates can be exploited in oil-absorptive fibers for cleaning of wastewater.[5] The combination of highly hydrophobic monomers and hydrophilic monomers conveniently leads to amphiphilic polymers with tunable solubility in aqueous solutions.

In the area of amphiphilic polyethers, poloxamers, also known as Pluronics, commercialized by BASF, represent a widely applied group of amphiphilic polyethers. Due to the polyether backbone composed of poly(ethylene glycol) (PEG) and poly(propylene glycol), combined to ABA triblock copolymers and the chemically inert structure, poloxamers show low toxicity and are widely used in various medical applications and as surfactants.[6] Additionally, poloxamers show thermoresponsive lower critical solution (LCST) behavior in aqueous solutions, rendering them highly interesting candidates for drug carrier systems with an inherent temperature triggered release mechanism.[6–8]

PEG is well-known for its low toxicity, antigenicity, and immunogenicity and is widely used in a vast variety of biomedical applications,[9] rendering PEG the "gold standard" in pharmaceutical applications. One main application in biomedical research and therapeutics is the so-called "PEGylation." In this approach, PEG is coupled to peptides or pharmaceutically active drugs enhancing the blood circulation time and therefore increasing the efficiency of the active agent.[10–13]

There is a significant and growing interest in amphiphilic polyethers motivated by the superior properties of the polyether backbone concerning its established biocompatibility. For instance, poloxamers are widely used in cosmetics, as pharmaceutical ingredients and in tissue engineering. Several poloxamers are already approved by the US Food and Drug Administration (FDA) and the Environmental Protection Agency

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(EPA).[6–8,13–16] PEG is the classical building block for nonionic surfactants and is produced on annual megaton-scale due to its high water solubility and biocompatibility. From a synthetic point of view, the synthesis of amphiphilic polyethers relies on a widely established one-pot (two-step) chemistry, whereas the synthesis of amphiphilic poly((meth)acrylates) demands increased synthetic effort if a narrow molar mass distribution is required and with regard to the selection of the hydrophilic (meth)acrylate monomer. In this short review article, different strategies for the synthesis of long-chain alkyl glycidyl ethers and long-chain alkyl epoxides and their controlled polymerization will be discussed. Since amphiphilic polyethers containing propylene oxide (PO) and 1,2-epoxy butane (BO) are well-known and have been discussed in numerous articles,[8,13,17–19] this overview focuses on the polymerization of less explored epoxides and glycidyl ethers bearing long alkyl chains with more than 4 carbon atoms. By increasing the alkyl chain length, the material properties, such as the glass transition temperature (T_g) can be adjusted. In contrast to poly(propylene oxide) (PPO), also crystalline polyethers can be generated, due to side-chain crystallization. The melting temperatures (T_m) can be adjusted by variation of the alkyl chain length, with melting temperatures above room temperature at 12 carbon atoms. Additionally, the tacticity of the polyethers plays a crucial role, which has been explored to a very limited extent to date. The increased hydrophobic character of the long alkyl chains enables the preparation of amphiphilic polyethers even at a low degree of polymerization (DP).

2. Synthesis of Long-Chain Alkyl Epoxides and Glycidyl Ethers

Generally, epoxides can be accessed via various synthetic strategies. The most prominent epoxide, ethylene oxide (EO), is typically synthesized via catalytic epoxidation of ethene with an annual production of 34.5 million metric tons in 2016.[20] Propylene oxide is typically obtained via four industrial processes: i) via the chlorohydrin process, ii) via hydroperoxide routes (e.g., the hydrogen peroxide to propylene oxide (HPPO) process), iii) via coproduct routes with undesired coproducts, such as styrene or *tert*-butyl alcohol, and iv) via gas-phase epoxidation.[21] For propylene oxide, the current annual production has been reported to exceed 10 million metric tons.[22] For the epoxidation of longer unsaturated alkyl chains via the well-known Prileschajew reaction,[23,24] *meta*-chloroperoxybenzoic acid is utilized as epoxidation reagent with generally high yields in the range of 90%.[25,26] However, it is important to note that oxidation via the Prileschajew reaction results in full epoxidation of all available double bonds, which is prohibitive for the introduction of a single epoxide functionality in case of polyunsaturated alkyl chains, e.g., biobased long chain alcohols of this type.

For the synthesis of long-chain alkyl glycidyl ethers, a general two-step one-pot synthesis protocol introduced by Mouzin et al. in 1983 can be employed using epichlorohydrin, the respective alkyl alcohol, and a basic component, such as aqueous sodium hydroxide solution (**Figure 1**).[27]

The procedure relies on the following steps: i) Under basic conditions, the alcohol is deprotonated, followed by a nucleophilic ring-opening reaction of the alkoxide and the epoxide.

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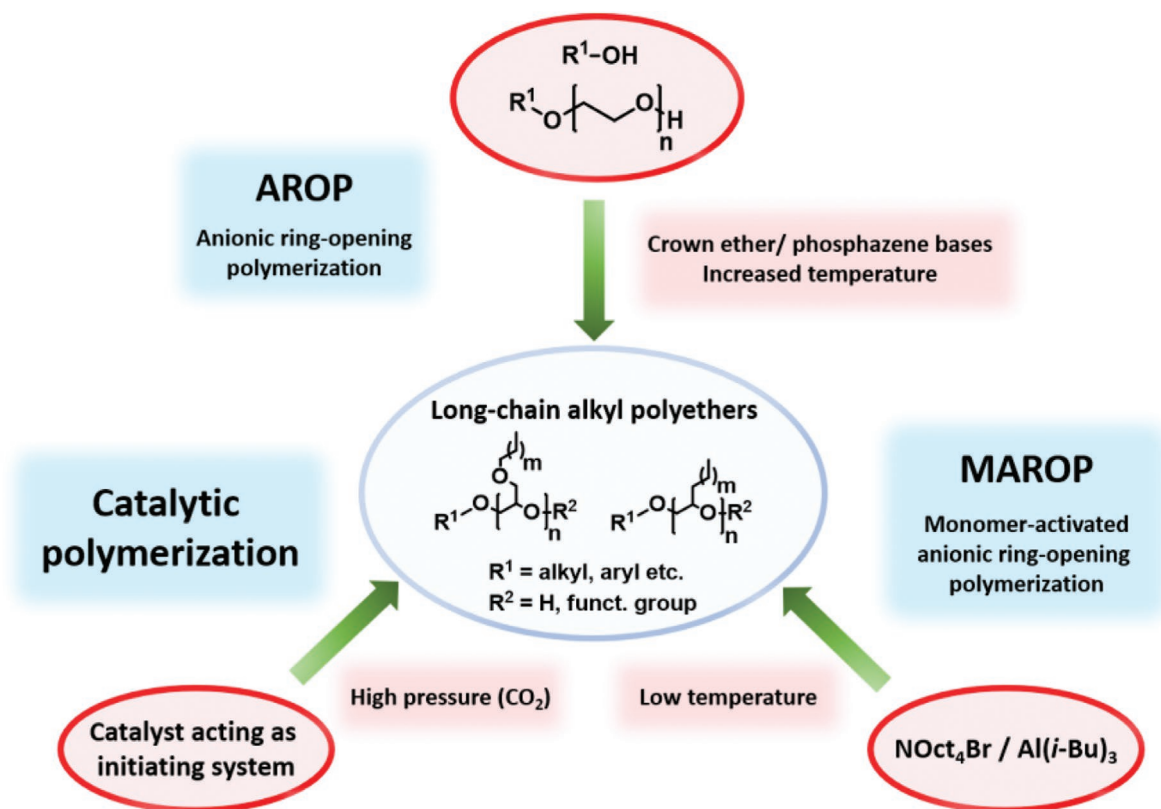
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ii) The subsequent intramolecular nucleophilic ring-closing reaction of this intermediate yields the desired glycidyl ether, while the formation of the respective halide (chloride, bromide) salt drives the reaction. Since epichlorohydrin and water are immiscible, the transformation is carried out utilizing phase-transfer catalysts, such as tetrabutyl ammonium bromide or tetrabutyl ammonium hydrogen sulfate.[28–30] In addition, apolar solvents, such as hexane or benzene, can be added to lower the concentration in the organic phase. Various modifications of this general synthesis protocol, such as the use of potassium hydroxide pellets and organic solvents in a heterogeneous
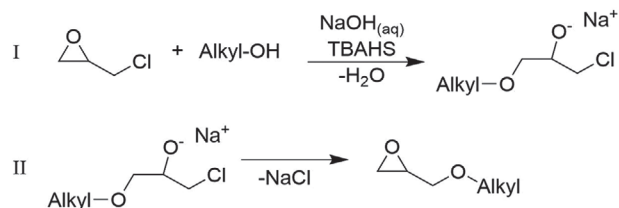
Figure 1. General synthesis: two-step, one-pot synthesis of glycidyl ethers. I) Deprotonation and subsequent nucleophilic attack of the alkyl alkoxide at the epoxide, leading to a ring-opening reaction catalyzed by the phase-transfer catalyst tetrabutylammonium hydrogen sulfate (TBAHS); II) nucleophilic-substitution of the chloride by the alkoxide leading to ring-closure, formation of the alkyl glycidyl ether, and sodium chloride formation.

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Figure 2. Overview of different polymerization strategies for the synthesis of polyethers bearing long alkyl chains.

reaction, as well as temperature variation and different reaction times can be found in literature.[31–33]

Additionally, other synthetic strategies, such as the reaction of the respective long-chain alcohol with allyl bromide, followed by epoxidation via *meta*-chloroperoxybenzoic acid for the synthesis of long-chain alkyl glycidyl ethers have been reported.[34] Following these strategies, both the synthesis and polymerization of several long-chain epoxides and alkyl glycidyl ethers have been reported (**Table 1**).

3. Polymerization of Long-Chain Alkyl Glycidyl Ethers and Epoxides

For the polymerization of long-chain alkyl epoxides and glycidyl ethers, different synthesis strategies, such as the conventional anionic ring-opening polymerization (AROP), the monomer-activated anionic ring-opening polymerization (MAROP), or the AROP in combination with phosphazene bases, can be utilized (**Figure 2**).[35] Furthermore, catalytic polymerization capitalizing on different catalysts, such as the industrially highly relevant double metal cyanide (DMC) catalyst,[36,37] the Vandenberg catalyst,[30] calcium amide-alkoxide catalysts, as well as nonmetallic catalysts, such as *N*-heterocyclic carbenes and *N*-heterocyclic olefins, can generally be used for polyether synthesis, but to date these catalysts have not been employed for long-chain epoxide monomers.[38–41]

The conventional anionic ring-opening polymerization technique yields well-defined polyethers with narrow molecular weight distributions suitable for biomedical applications. Due to the living character of the anionic ring-opening polymerization, good control over the polymerization reaction can be achieved, enabling the introduction of a defined end group. However, chain-transfer reactions limit the accessible molecular weight of the polymers. In order to suppress these side-reactions, in seminal work Allgaier et al. reported the block copolymerization of EO with 1,2-butylene oxide (BO), 1,2-hexene oxide (HO), and 1,2-octylene oxide (OO) using different counter ions and crown ethers to generate amphiphilic block copolymers with high molecular weights.[42] Further developing this strategy, our group reported the homo-, and block copolymerization of dodecyl- and hexadecyl glycidyl ether with bifunctional PEG macroinitiators.[34] In contrast to the polymerization of alkyl epoxides, no chain-transfer reactions could be observed for the alkyl glycidyl ethers. This can be explained by the +M-effect of the additional oxygen atom in β-position to the epoxide, decreasing the acidic character of the protons in α-position of the epoxide moiety. Concerning the copolymerization of long-chain alkyl epoxide monomers, distinct reactivity ratios for the monomer pair BO/EO of $r_{BO} = 0.15$ and $r_{EO} = 6.46$ were determined, implying the formation of gradient copolymers with significantly increased incorporation of BO at the polyether terminus.[43] Concerning the copolymerization of glycidyl ethers, to the best of our knowledge, no reactivity ratios have been determined until today.

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Table 1. Overview of different long-chain epoxides and alkyl glycidyl ethers.

Monomer structure	Polymerization technique	Name and peculiarities	Refs.
	AROP, MAROP, Microwave-assisted polymerization, copolymerization with CO_2	Hexylene oxide (HO)	[42,50–54]
	AROP, copolymerization with CO_2	Octylene oxide (OO)	[42,53]
	MAROP	Octadecylene oxide (ODO)	[54]
	Copolymerization with CO_2	Hexyl glycidyl ether (HGE)	[55]
	MAROP	2,4-hexadien-1-yl glycidyl ether (HDEGE) Functionalization via triazolinediones, Diels–Alder-ene reactions	[28]
	AROP	Citronellyl glycidyl ether (CitroGE) Functionalization via triazolinediones, Alder-ene-reactions	[28]
	Vandenberg catalyst, copolymerization with CO_2	Octyl glycidyl ether (OGE)	[30,55]
	Phosphazene bases	Decyl glycidyl ether (DGE)	[56–59]
	Phosphazene bases	Dec-9-enyl glycidyl ether (DEGE) Introduction of terminal hydroxyl groups	[57]
	AROP (DDGE, HDGE), Vandenberg catalyst, copolymerization with CO_2 (DDGE)	Dodecyl glycidyl ether (DDGE) Hexadecyl glycidyl ether (HDGE) Docosyl glycidyl ether (DOGE)	[30,34,60]
	Calcium amide-alkoxide catalyst	Dodecyl-, Tetradecyl glycidyl ether mixture (DDGE, TDGE), Oligo ethylene glycol alkyl glycidyl ethers (Brij72GE, Brij76GE)	[61]
	AROP, Vandenberg catalyst	1,3-dioctyloxy-2-glycidyl-glycerol (DOGG) 1,3-didodecyloxy-2-glycidyl-glycerol (DDGG) 1,3-dihexadecyloxy-2-glycidyl-glycerol (DHGG)	[30,49]

However, very recent investigations on the copolymerization of dodecyl glycidyl ether and EO indicate a random copolymerization of the monomer pair with reactivity ratios close to one,[44,45] which is in line with other copolymerization reactions of glycidyl ethers and EO.[46–48] The distinct reactivity ratios of alkyl epoxides compared to alkyl glycidyl ethers offer intriguing opportunities to control the polymer architecture in statistical (one-pot) copolymerization reactions. While copolymerization of alkyl epoxides with EO leads to gradient copolymers bearing a hydrophobic and a hydrophilic part, the copolymerization of

alkyl glycidyl ethers with EO enables the synthesis of amphiphilic polyethers with randomly distributed alkyl chains along the polyether backbone.

To further increase the hydrocarbon/monomer ratio, Tsvetanov and co-workers reported the block copolymerization of double chain alkyl glycidyl ethers, such as 1,3-didodecyloxy-2-glycidyl-glycerol (DDGG) and EO to yield amphiphilic polyether structures utilizing the anionic ring-opening polymerization.[49] It is noteworthy that the high molar masses of the polymerized alkyl epoxides and alkyl glycidyl ethers caused by the long alkyl chains (e.g., M (hexadecyl glycidyl ether) = 298.5 g mol^{-1}) result in significantly higher molecular weights of the resulting polyethers, even at low degrees of polymerization. However, even a low degree of polymerization results in a highly hydrophobic character, due to the long alkyl chains.

As an important variation of the conventional AROP technique, Satoh et al. reported the polymerization of long-chain alkyl glycidyl ethers using phosphazene bases for deprotonation of the initiator. Due to their capability of charge delocalization, protonated phosphazene bases are able to increase the distance between charges in ion pairs, which directly results in higher propagation rates of the polymer chains.[62,63] On the other hand, due to the cytotoxicity of phosphazene bases and their residues in the polymers, purification of the amphiphilic polyethers for use in biomedical applications remains challenging.[64] Using this approach, Satoh and co-workers reported the synthesis of complex star, ring, and bases figure-eight-shaped structures by block copolymerization of decyl glycidyl ether (DGE) and 2-(2-(2-methoxethoxy)ethoxy)ethyl glycidyl ether as hydrophobic and hydrophilic monomer, respectively.[56,58] Additionally, the block copolymerization of DGE and dec-9-enyl glycidyl ether (DEGE) with controlled tacticity of the two blocks was reported. For this purpose, racemic and optically pure monomers were polymerized yielding atactic and isotactic blocks, respectively. Subsequent postmodification of the terminal double bond of the PDEGE-block yielded terminal hydroxyl groups and resulted in a poly(10-hydroxyl decyl glycidyl ether)-block (PHoxDGE) with increased polarity compared to the PDGE block.[57]

As an alternative synthesis strategy to the direct polymerization, postmodification reactions can be utilized, enabling the functionalization of designated polymer structures via different modification reactions. However, postmodification reactions generally lead to additional reaction steps, and full conversion of the postmodification reaction cannot always be achieved. Utilizing the well-known thiol-ene coupling reaction as a postmodification strategy, Murakami et al. reported the synthesis of amphiphilic ABA triblock copolymers bearing different alkyl chain lengths in the hydrophobic A-block. For this purpose, the authors performed the polymerization of allyl glycidyl ether (AGE) and EO using bifunctional PEG macroinitiators. Subsequent postmodification of the polyethers via thiol-ene coupling of various long-chain alkyl thiols to the allylic double bond resulted in amphiphilic ABA triblock copolymers.[65]

Since the accessible molecular weights in the synthesis of polyethers are mainly limited by side-reactions at the chain-end,[42,66–68] mainly proton transfer, other polymerization techniques have to be utilized for the synthesis of higher molecular weights. The monomer-activated anionic ring-opening polymerization (MAROP) enables the synthesis of high molecular weight polyethers, relying on activation of the epoxide and the suppression of chain-transfer reactions.[62,69–71] For this purpose, triisobutylaluminium is commonly used as Lewis acid coordinating to the epoxide, thereby increasing its reactivity to nucleophilic ring-opening reactions.[69] It is noteworthy that for polymerization of alkyl glycidyl ethers, increased amounts of the coordinating species (4.5 equiv.) are used to achieve successful polymerization, compared to alkyl epoxide monomers (1.25 to 2 equiv.) for comparable alkyl chain lengths (2,4-hexadien-1-yl glycidyl ether (HDEGE) vs 1,2-hexylene oxide (HO)).[28,50,54] However, side-reactions of the activating Lewis acid can lead to β-hydride elimination and initiation of polymerization resulting in undefined end groups of the resulting polyethers.[72]

Utilizing this technique, Pispas and co-workers reported the synthesis of diblock copolymers using monomethoxy poly(ethylene glycol) (mPEG) and HO.[50] To introduce additional functionality at inert long-chain alkyl glycidyl ethers, Johann et al. introduced the synthesis and statistical copolymerization of olefinic alkyl glycidyl ethers, such as 2,4-hexadien-1-yl glycidyl ether (HDEGE) with EO, PO, and EEGE utilizing the MAROP technique.[28] Furthermore, block copolymerization of citronellyl glycidyl ether (CitroGE) via the conventional AROP technique with mono-, and bi-functional PEG macroinitiators was described as well in this work.

In addition to the anionic ring-opening polymerization techniques, catalytic polymerization of epoxides can be carried out. Utilizing the Vandenberg catalyst, Francois and co-workers reported the synthesis of comb-like polyether structures. In block and statistical copolymerization reactions of EO and various long-chain alkyl glycidyl ethers (AlkGE), such as octyl glycidyl ether (OGE), dodecyl glycidyl ether (DDGE), hexadecyl glycidyl ether (HDGE), and docosyl glycidyl ether (DoGE), various amphiphilic structures with high molecular weights in the range from 10 000 to 100 000 g mol^{-1} have been synthesized. Unfortunately, no molecular weight distributions have been reported. Additionally, the polymerization of dialkyl glycidyl ethers (DAlkGE), such as di(octyloxymethyl)propyl glycidyl ether, di(dodecyloxymethyl)-propyl glycidyl ether, and di(hexadecyloxymethyl)propyl glycidyl ether, has been described.[30] The bimetallic nature of the Vandenberg catalyst based on trialkylaluminium and acetylacetone generally enables the synthesis of isotactic enriched high molecular weight polyethers with moderate size distributions (Đ) (e.g., M_n (PPO) = 930 000 g mol^{-1}, Đ = 2.4). Besides the polymerization of epoxides, aldehydes, lactones, and carbonates can be polymerized.[73,74] Compared to the conventional AROP, additional reaction steps for the preparation of the catalyst with a defined stoichiometry are needed.

In order to synthesize amphiphilic high-molecular weight polyethers, in seminal work, Tsvetanov and co-workers introduced the synthesis of diblock copolymers utilizing the industrial calcium amide-alkoxide initiating system. With this catalyst initiating system, high-molecular weight polyethers can be achieved. However, additional steps for the preparation of the initiating systems are needed. In sequential block copolymerization reactions, EO and long-chain alkyl glycidyl ethers, such as dodecyl glycidyl ether, tetradecyl glycidyl ether, and

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long-chain alkyl glycidyl ethers bearing oxyethylene spacers between the terminal alkyl chain and the epoxy group, have been polymerized to yield amphiphilic block copolymers with molecular weights in the range of 130 000–160 000 g mol^{-1} and relatively broad molecular weight distributions (Đ) from Đ = 4.9 to 8.4.[61] Due to the high molar masses and outstanding hydrophobic character of long-chain alkyl glycidyl ethers and alkyl epoxides, low degrees of polymerization result in relatively high molecular weight polyethers. For the catalytic polymerization reactions, the amount of hydrophobic monomers lie in the range of 1 mol% (for the Vandenberg catalyst)[30] and between 1.2 and 1.5 wt% for the calcium amide-alkoxide initiating system.[61] Interestingly, the relatively low degree of incorporation at the hydrophilic polyether backbone was reported to be sufficient for successful preparation of amphiphilic polyethers that show hydrophobic association in aqueous solution.

In a different approach, Glatter and co-workers as well as Trathnigg and co-workers reported the block copolymerization of hexylene oxide by PEG macroinitiators, utilizing microwave assisted polymerization to yield amphiphilic block copolymers.[51,52]

Besides copolymerization of long-chain alkyl glycidyl ethers with other epoxides, aliphatic epoxide monomers can also be copolymerized with CO_2 to yield polycarbonates. For this purpose, Thorat et al. reported the copolymerization of hexylene oxide and 1,2 octene oxide (OO) with CO_2 and further investigated the thermal properties of the synthesized materials.[53] Furthermore, Grinstaff and co-workers reported the copolymerization of butyl glycidyl ether, octyl glycidyl ether, and stearyl glycidyl ether with CO_2 to provide crystalline aliphatic polycarbonates,[55] whereas Kunze et al. described the copolymerization of dodecyl glycidyl ether, PO, and CO_2.[60] However, for the synthesis of poly(carbonates), high pressure around 50 bar is needed. Furthermore, side-reactions lead to cyclic byproducts, which have to be separated after the polymerization reaction.

4. Application of Polyethers Bearing Long Alkyl Chains

Due to their outstanding hydrophobic character, long-chain alkyl epoxides and alkyl glycidyl ethers, as well as long-chain alkyl halides are widely used as end-functionalization agents for the synthesis of ionic or nonionic surfactants, using the epoxide moiety for coupling (no polymerization).[75–84] They are commercially available as mixtures of different alkyl chain lengths ($C_{12/14}$, $C_{13/15}$) under the trade name Grilonit and find use as nonvolatile additives for epoxy resins for the control of the resin viscosity.[85] In contrast to the end-functionalization approach, facile variation of the hydrophilic/lipophilic balance (HLB)[86] in the polyether can be achieved by utilizing the controlled anionic ring-opening polymerization technique. Concerning the differences in the reactivity ratios of alkyl epoxides and alkyl glycidyl ethers with EO, statistical copolymers bearing randomly distributed alkyl chains at the polyether backbone can easily be synthesized utilizing the respective alkyl glycidyl ethers. In contrast, statistical (i.e., one-pot) copolymerization of alkyl epoxide monomers with EO yields

gradient block copolymers, due to the distinct reactivity ratios. For synthesis of block copolymers, both, alkyl glycidyl ethers and alkyl epoxides can be utilized.

By variation of the polymer architecture from diblock copolymers to ABA triblock or statistical copolymers, not only the formation of micelles or aggregates,[56,58,59] but also the generation of intermolecular crosslinked structures based on the self-association in aqueous solution can be achieved (**Figure 3**).

While statistical P(EO-co-AlkGE) copolymers (comb-like copolymers) have been reported to act as thickening agents due to formation of intra- and intermolecular crosslinked micelles or aggregates in aqueous solution, ABA triblock copolymers with telechelic hydrophobic blocks further increase the viscosity in aqueous solution, due to the exclusive formation of intermolecular crosslinked structures and flower-like micelles similar to hydrophobically modified urethane-ethoxylate (HEUR) thickeners.[30,84,87] This underlines the importance of the polymer architecture for the aggregation and the resulting enhancement of the viscosity in aqueous solutions. Furthermore, gelation of aqueous solutions can be achieved by increasing the hydrophobic blocks in ABA triblock copolymers yielding noncovalently crosslinked hydrogels, based solely on hydrophobic interaction and crystallization for longer n-alkyl chains.[34,65] To the best of our knowledge, no lower critical solution temperatures for the statistical or block copolymers has been reported, which distinguishes this type of amphiphilic polyethers from the well-known class of poloxamers. This can be attributed to the highly hydrophobic character of the long-chain epoxides and glycidyl ethers compared to propylene oxide. Due to the long alkyl chains, a low degree of polymerization in block or statistical copolymers sufficiently increases the hydrophilic–lipophilic balance in the polyethers, resulting in viscous aqueous solutions or gelation ("thickening"), caused by the formation of micellar structures or aggregates. Recently we demonstrated that the polymerization of long-chain AlkGE with tunable melting temperatures above room temperature results in thermoresponsive hydrogels with hydrophobic crystalline domains, rendering these hydrogels interesting candidates for thermoresponsive drug delivery systems or implants for long-term dosing applications of hydrophobic drugs.[34]

In contrast to the chemically inert aliphatic long-chain alkyl epoxides and glycidyl ethers, unsaturated glycidyl ethers, such as HDEGE and CitroGE, can further be modified via postmodification reactions. In this context, Johann et al. demonstrated the successful postmodification of polyethers bearing multiple double bonds, utilizing highly reactive triazolinediones (TADs) in Diels–Alder and Alder-ene reactions. Furthermore, the authors demonstrated the rapid functionalization of PHDEGE-b-PEG-b-PHDEGE triblock copolymers with bifunctional TADs to yield covalently crosslinked organogels.[28]

Besides the beneficial feature concerning the tunability of the hydrophobic character of the long-chain epoxides and glycidyl ethers, the melting temperatures of the alkyl chains can easily be tuned by controlled variation of the alkyl chain length beyond a threshold of ≈10 carbon atoms in the alkyl chains. Utilizing the high crystallinity of polyethers bearing long alkyl chains, Satoh and co-workers investigated the thermal properties and morphologies of PDGE-b-PDEGE diblock copolymers with different tacticities.[57] Furthermore, these authors
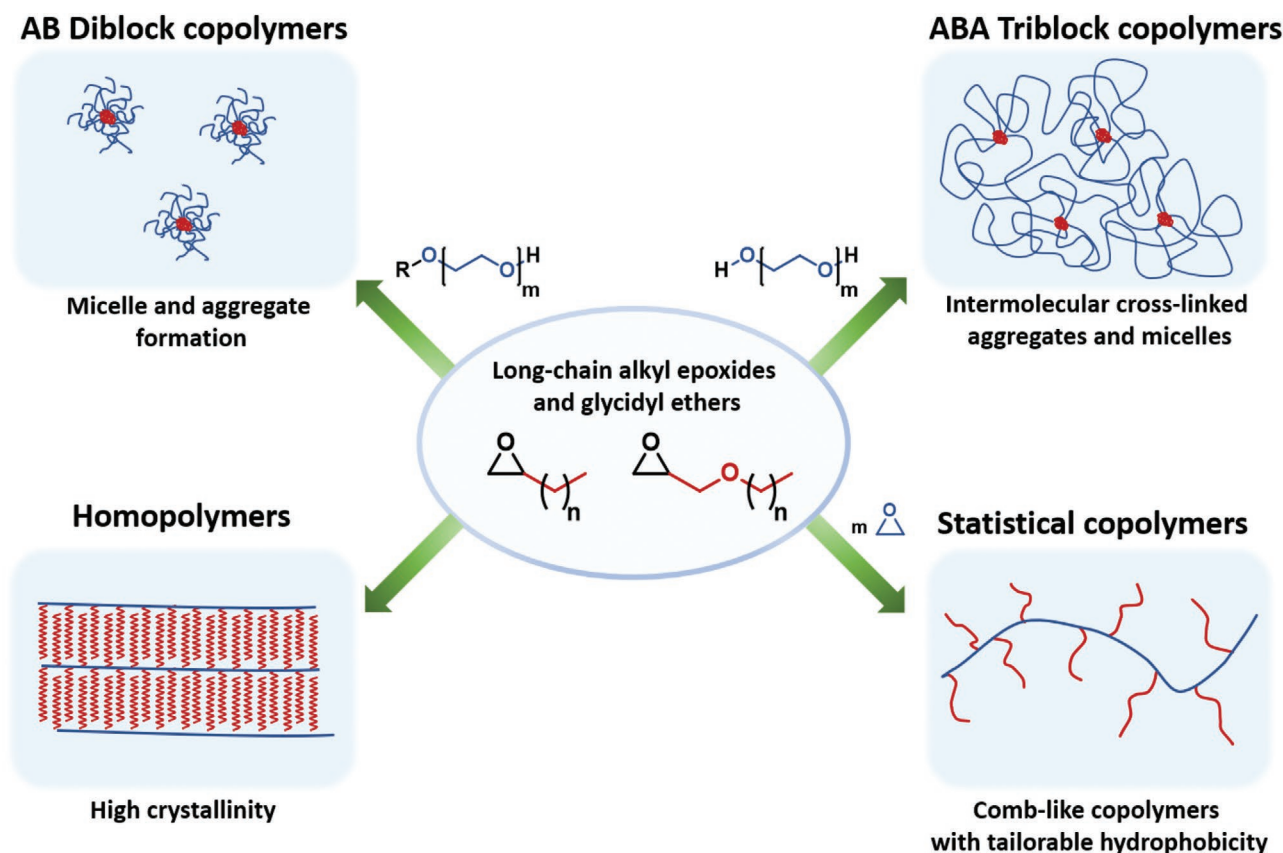
Figure 3. Overview of different applications for long-chain alkyl epoxides and glycidyl ethers by homo-, block-, and statistical copolymerization, resulting in highly crystalline homopolymers or amphiphilic block copolymers that show association in aqueous solution.

demonstrated the successful introduction of terminal hydroxyl groups via postmodification of the PDEGE blocks and the impact on the thermal properties and morphological structures. Interestingly, due to the introduction of the terminal hydroxyl groups, microphase separation of the polar poly(10-hydroxyl glycidyl ether) (PHoxDGE) and the apolar PDGE block were observed, resulting in the formation of horizontal lamellar structures. Additionally, a significant influence on the melting temperatures as a consequence of the tacticity of the PHoxDGE and PDGE blocks was found, resulting in microphase separation and separated melting temperatures of the two blocks. The presence of two separate melting temperatures has also been observed for other block copolymer systems with distinct polarities, such as PDDGE-*b*-PEG-*b*-PDDGE and PHDGE-*b*-PEG-*b*-PHDGE triblock copolymers.[34]

The effect of a tailor-made crystallinity depending on the length of the alkyl chains can also be utilized for copolymerization reactions of long-chain epoxides and glycidyl ethers with CO_2. In this regard, Grinstaff and co-workers as well as Kunze et al. reported the synthesis of semicrystalline polycarbonates using butyl, octyl, dodecyl, and stearyl glycidyl ether, and the dodecyl and stearyl glycidyl ether containing polymers exhibited melting temperatures of 14 and 55 °C, respectively. Due to the high thermal stability and high oxygen/carbon ratio, these structures represent promising candidates for solid polymer electrolytes.[55,60]

5. Conclusion and Outlook

Both amphiphilic block- and statistical polyether copolymers play an important role in manifold applications. While poloxamers based on PO and EO are widely used and have been commercialized for various applications long ago, long-chain alkyl epoxides and glycidyl ethers represent an underrated class of highly hydrophobic epoxide monomers. Due to the distinct reactivity ratios of alkyl epoxides and EO in statistical copolymerization reactions, gradient copolymers with an increased concentration of alkyl side-chains at the polymer terminus are obtained. In contrast, in copolymerization reactions of alkyl glycidyl ethers with EO, randomly distributed alkyl chains at the polyether backbone are obtained. This feature offers a powerful tool to control the polymer architecture of amphiphilic polyethers by choosing the respective monomer class to achieve either gradient or randomly distributed amphiphilic copolymers in one-pot reactions. Compared to their shorter counterparts, long-chain alkyl epoxides and glycidyl ethers possess highly hydrophobic character, enabling the synthesis of very hydrophobic blocks even at a low degree of polymerization. This greatly enhances the options for apolar polyether structures beyond the established poly(propylene oxide). Also, the introduction of unsaturated alkyl chains at the polyether backbone, enabling further functionalization of the hydrophobic block, has only scarcely been explored in the literature to date.

Based on unsaturated fatty acids, transformed to the respective glycidyl ethers via convenient reduction and reaction with epichlorohydrin, partially biobased long-chain alkyl glycidyl ethers can be established.

Besides the controlled variation of the hydrophilic/lipophilic balance in polyethers, polymerization of long-chain alkyl epoxides and glycidyl ethers offers the possibility for the introduction of tunable crystallization of the hydrophobic block. Utilizing these features, well-defined amphiphilic diblock polyethers can be synthesized that can be utilized as cosurfactants in microemulsion systems, reducing the amount of surfactant and improving the economic and ecological implications of industrial applications.[83] Furthermore, amphiphilic triblock copolymers bearing hydrophobic end-blocks play an important role in the field of viscosity control of aqueous solutions and the preparation of hydrogels.[30,84,87]

Tuning of the crystallization of the long alkyl chains in addition to the mere hydrophobic interaction offers the possibility to introduce thermoresponsiveness at physiological temperature. This renders these polyethers promising candidates for the design of thermoresponsive drug carrier systems for hydrophobic drugs. To sum up, the high hydrophobicity of long-chain alkyl epoxides and glycidyl ethers combined with tailoring of the crystallization behavior paves the way for a variety of biomedical applications, as well as for large-scale industrial applications as surfactants or as rheology modifiers.

Conflict of Interest

The authors declare no conflict of interest.

Keywords

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