# Inimer Mediated Synthesis of Hyperbranched Polyglycerol via Self-Condensing Ring-Opening Polymerization

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# Inimer Mediated Synthesis of Hyperbranched Polyglycerol via Self-Condensing Ring-Opening Polymerization

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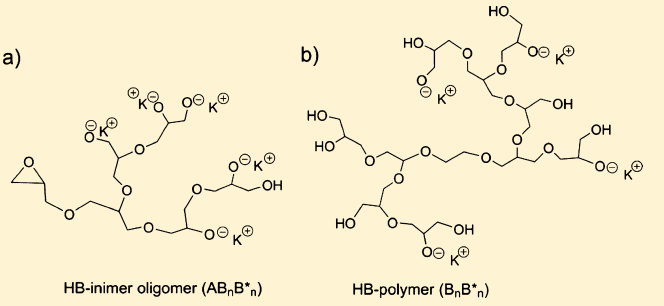
Supporting Information

**ABSTRACT:** A series of hyperbranched polyglycerols (HPGs) have been synthesized using glycol as an initiator in the presence of potassium counterion ($[K^+]_0/[-OH]_0 = 0.75$) and employing batch monomer addition (BMA) to obtain insight into the kinetics of the polymerization. The first-order time−conversion plots show that the polymerization is fast up to ∼200 min, and the rate decreases substantially with increasing reaction time. Size exclusion chromatography of the HPGs during the polymerization indicates the presence of two living species in the reaction: a large fraction that grows into oligomers (<3000 g/mol) and becomes stabilized at higher conversion and a small fraction, growing faster and able to sustain a larger degree of polymerization (>140 000 g/mol). $^{13}C$ NMR of the oligomer HPG shows signals corresponding to epoxy ring headgroup at 45.1 and 52.0 ppm and confirms the formation of epoxy anion, an inimer, via intermolecular proton transfer from glycidol. Self-condensing ring-opening polymerization of epoxy inimer produces ill-defined hyperbranched inimer−oligomers in high yield along with a small fraction of high molecular weight HPG that propagates without significant transfer to glycidol. The differential scanning calorimetry analysis shows the HPG exhibited two distinct $T_g$s (<−50 and >−20 °C) indicating the oligomer and high molecular weight fractions are immiscible, which is attributed to conformational constraint of two different types of branching. A mechanism of the formation of HPGs is proposed involving inimer-mediated equilibrium between oligomers and high molecular weight HPGs. The slow monomer addition (SMA) protocol was employed to reveal the existence of inimers during the reaction, supporting the proposed mechanism.




## INTRODUCTION

Hyperbranched polymerization has been the focus of extensive studies in order to find a simple "one pot" synthesis of multifunctional dendrimer-like macromolecules.[1−3] The desire for highly branched macromolecules stems from the unique properties of dendrimers including their globular shape, lack of entanglement, a large number of modifiable surface-functional groups and internal cavities.[2,4−6] Unlike dendrimers, which are well-defined structures that contain uniform branching evolving from rigorous multistep reactions and purification procedures, hyperbranched polymers possess irregular branching with distinct topological properties that resemble dendrimers.[2,7,8] On the other hand, hyperbranched polymers present the advantage of quick and convenient synthesis at a cost of controlled branching.[7,9−11]

Hyperbranched polymers are generally synthesized using $AB_x$-type monomers via (1) condensation polymerization, (2) self-condensing vinyl polymerization (SCVP), and (3) ring-opening multibranch polymerization. The latter two techniques require either vinyl or cyclic monomers that possess an initiating functionality for hyperbranching.[2,6,12] Generally, these techniques produce polymers whose molecular weight and molecular weight distribution (MWD) are difficult to control. Glycidol is a cyclic, latent $AB_2$-type monomer as its primary hydroxyl group can be activated after opening the epoxide ring via proton transfer in anionic polymerization. The anionic ring-opening polymerization of ethylene oxide and other epoxide containing monomers is typically carried out in polar solvents in the presence of countercations such as sodium, potassium, or cesium to suppress the aggregation of propagating alkoxide active center. Polymers derived from glycidol in linear and hyperbranched forms have attracted special attention because of their biocompatibility, showing no toxicity in cell culture, making them excellent candidates for numerous biomedical applications.[10,13−15]

Anionic ring-opening polymerization of glycidol was first reported by Vandenberg using KOH as an initiator.[16,17] Vandenberg obtained branched polyglycerol oligomers and attributed the failure to produce high molecular weight polymer to a slow propagation and competing proton transfer from glycidol. The tendency of alkoxide anion to form aggregated species even with potassium as the counterion in polar solvent is very high that contributes for slow propagation. In the case of anionic polymerization of glycidol, the possibility of aggregation

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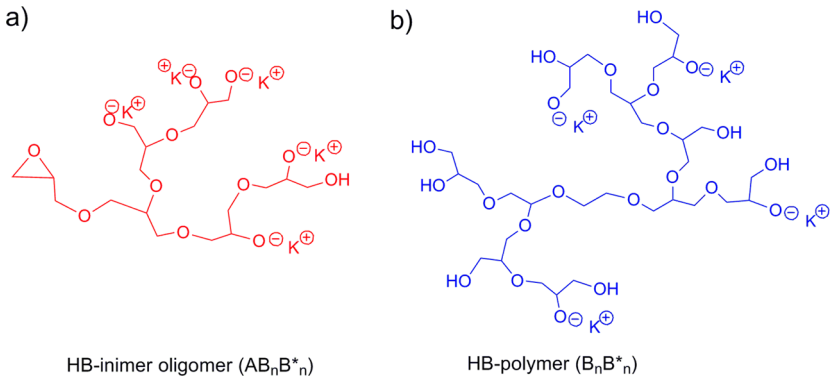
**Scheme 1. Hyperbranched Polyglycerols (HPGs) in Batch Monomer Addition Anionic Polymerization Using Glycol as Initiator in the Presence of Potassium Counterion ($[K^+]_0/[-OH]_0 = 0.75$): (a) Inimer−Oligomer of HPG and (b) Regular HPG without Transfer to Monomer**




via both inter- and intramolecular association is considerably high. In 1999, Frey and co-workers demonstrated a controlled ring-opening polymerization of glycidol using a slow monomer addition (SMA) protocol and produced hyperbranched polyglycerol (HPG) up to molecular weights of <6000 g/mol with moderate MWDs ($M_w/M_n < 1.3$).[12] More recently, they described a two-step method for the synthesis of controlled molecular weight HPG up to 24 000 g/mol using oligomers as macroinitiators.[2] However, the obtained HPG exhibited broad MWDs ($1.3 < M_w/M_n < 1.8$). The SMA protocol and an efficient mixing were assumed to suppress the side reactions. Brooks and co-workers introduced the use of dioxane, an emulsifying agent, to reduce the viscosity of the reaction medium and obtained uncontrolled molecular weights up to 700 000 g/mol with narrow MWDs ($1.1 < M_w/M_n < 1.4$).[7,2] The limitation for the molecular weight control and for the broadening of MWD was attributed to inter- and intramolecular monomer-transfer reactions.[12,15,18,19]

The SMA protocol with the use of a low-concentration of alkoxide active center is recommended for the synthesis of controlled molecular weight HPG. It is important to note that anionic ring-opening polymerization of glycidol using conventional batch monomer addition (BMA) produces only oligomers due to the presence of intramolecular cyclization.[2,12,15] Although, such a loop formation has been identified in $AB_2$-type polycondensation and self-condensing vinyl polymerization (SCVP), it is not found to deter the growth of molecular weight.[15] Thus, the limited molecular weight control obtained for HPGs in the SMA protocol is not yet thoroughly understood.

In this paper, we investigate the kinetics of the anionic polymerization of glycidol using the BMA protocol. We compare the molecular growth and properties of HPG with the polymer synthesized using the SMA protocol. The side product consisting of self-condensing inimer has been identified in both the SMA and the BMA protocols. High molecular weight HPGs have been synthesized in batch polymerization at a prolonged duration of the reaction, which shed light on the mechanism of the polymerization. The formation of high molecular weight HPGs was attributed to a kinetic discrimination arising from aggregation and solvation of different species in the reaction medium (Scheme 1). The control of the molecular weight in the SMA protocol is a result of a stepwise inimer−oligomer formation and its addition into propagating alkoxide chain ends of HPG. The topology of the resulting polymers was characterized and discussed in accordance with previously reported results in the literature.

## EXPERIMENTAL SECTION

**Materials.** Ultrahigh purity (UHP) $N_2$ gas (Airgas) was bubbled through a toluene solution of oligostyryllithium anion to ensure the purity. Dioxane (Fischer Scientific) was dried over $CaH_2$ and vacuum distilled into a round-bottom flask and placed under $N_2$ at −20 °C. The glycidol monomer (Fischer Scientific) was fractionated using vacuum distillation and stored under $N_2$ at −20 °C. The precursor initiator (ethylene glycol, Fischer Scientific), proton transfer agent (potassium methoxide, Fischer Scientific), and internal standard (diphenyl ether, Fischer Scientific) were all used as received and purged with UHP-$N_2$ moments before the use.

**Polymerization.** The polymerization was carried out under a pure nitrogen atmosphere in a flame-dried single-neck round-bottom flask capped with a rubber septum, containing a stopcock side arm for vacuum and $N_2$ control. Ethylene glycol and potassium methoxide solutions were bubbled with $N_2$ and transferred by syringe into the reactor and allowed to react for 30 min. The reactor was then slightly heated and vacuum was applied for an hour to remove residual methanol emerging from the potassium methoxide reaction with ethylene glycol. An appropriate volume of dioxane, based on the monomer volume, and internal standard (when needed for kinetic analysis) were added into the reactor via cannula or syringe and subsequently heated to 90 °C. Glycidol was then added to the reaction mixture drop by drop for 10 h via a dosage syringe pump in the SMA delivery method or instantaneous for the BMA delivery method. The polymerization was left to proceed for a predetermined amount of time and quenched using a methanol/hydrochloric acid solution. The final product, HPG, was dissolved in an excess methanol and passed through a cation exchange column and precipitated in acetone. The precipitated polymer was dried overnight in a vacuum oven.

**Measurements.** Characterization of the HPG was carried out using size exclusion chromatography (SEC) consisting of a Waters model 510 pump and a Waters model R401 differential refractometer with a set of four columns: Polymer Standards Services, Suprema, 8 × 300 mm (10 μm); 100, 3000, and 10 000 Å along with a 8 × 50 μm guard. Data was collected and analyzed using Polymer Laboratories Cirrus software using monodisperse poly(ethylene oxide)s as calibration standard. Water containing 0.02% $NaN_3$ was used as the mobile phase at a flow rate of 1 mL $min^{-1}$ at 30 °C. $^{13}C$ NMR and $^1H$ NMR spectra were recorded in DMSO-$d_6$ on a Bruker 400 MHz spectrometer. A TA Instruments Q-1000 differential scanning calorimeter (DSC) was used from −100 to 20 °C at a heating rate of 10 °C/min with a 2 min isotherm at the maximum and minimum temperatures. Glass transition temperature was measured in second heating scan.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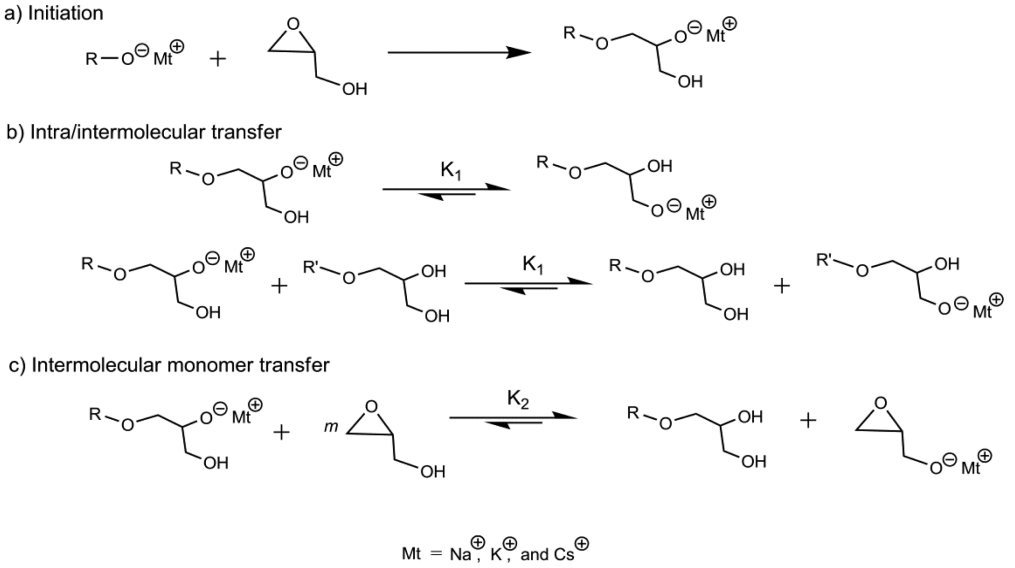
**Scheme 2. Anionic Polymerization of Glycidol: (a) Initiation, (b) Proton Abstraction of Propagating Alkoxide Anions, and (c) Proton Abstraction from Monomer**




## RESULTS AND DISCUSSION

The propagating center in anionic ring-opening polymerization of epoxide monomers (ethylene oxide, propylene oxide, etc.) is an alkoxide anion, which exists in equilibrium with aggregated species. In order to control the polymerization, the reaction is conducted in polar solvent in the presence of bulky alkali metal counterion.[7] In general, the concentration of counterion is kept lower than the initiator alcohol as the propagation rate constant ($k_p$) is considerably lower than the proton exchange rate constant ($k_{ex}$), between dormant alcohol and propagating alkoxide anion, thus providing ideal control for molecular weight and narrow MWD.[20−23] In the anionic polymerization of glycidol, the nucleophilic attack on the epoxide ring generates a reactive propagating secondary alkoxide anion which tends to undergo proton abstraction either intra/intermolecularly with propagating chain or with a monomer to generate primary alkoxide anion (Scheme 2). As the proton exchange rate is higher for secondary alkoxide anion as compared to primary alkoxide, the synthesis of controlled HPG via anionic ring-opening polymerization is affected by the competing proton transfer from monomer vs polymer.

**Kinetics of Batch Monomer Addition (BMA) Polymerization.** Kinetic investigation of the anionic polymerization of glycidol was performed by adding the total monomer at the beginning of the polymerization. As expected, the probability for the formation of epoxy anion via intermolecular proton transfer from monomer to initiator is very high in BMA method due to high monomer concentration (Scheme 2c). The reaction was monitored by withdrawing samples at regular intervals. The analysis was performed using $^1$H NMR to monitor the monomer (epoxide, 2.70 ppm) conversion using phenyl ether (7.55 ppm) as an internal standard. Three reactions were performed with increasing concentration of glycol ([I]). In all instances, the potassium counterion concentration was kept constant, $[K^+]_0/[-OH]_0 = 0.75$.

The first-order time−conversion plots show that the polymerization follows two distinct phases, a fast and a slow, depending on the initiator concentration (Figure 1). At moderate initiator concentrations, the apparent rate constant, $k_{app}$, decreases significantly after 200 min. However, the reaction continues slowly even after 1500 min. The decrease in $k_{app}$ could be due to increased aggregation of the active centers. However, at the beginning, the polymerization is very fast with more than half of the monomer converted into HPG within 2 h of the reaction. In the case of high concentration of the initiator, $[I]_0 = 11.2 \times 10^{-2}$ mol/L, 100% monomer conversion is achieved within 4 h. The $k_{app}$ of the polymerization was determined using the initial slope of the first-order time−conversion plots, which increases with increasing initiator concentration (Table 1).

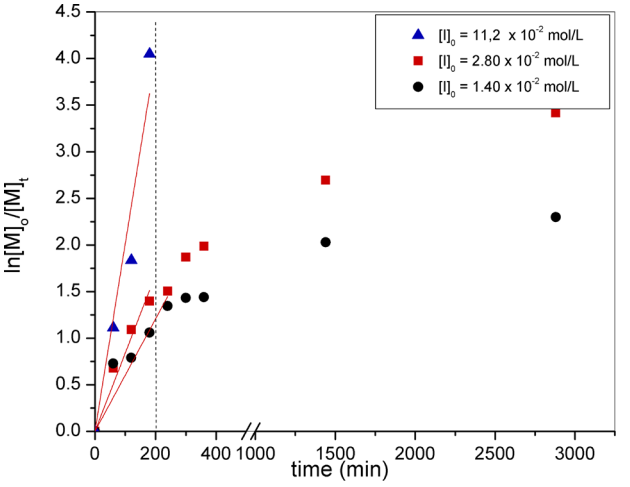



**Figure 1.** First-order time−conversion plots of batch anionic polymerization of glycidol using glycol as initiator with potassium counterion, $[K]_0/[-OH]_0 = 0.75$ in dioxane at 90 °C (Table 1, runs B1, B2, and B7).

Interestingly, the SEC of the HPGs during the polymerization showed a growth of two distinct populations (Figure 2 and Supporting Information). On the basis of the earlier work of Vandenberg, we attribute the peak corresponding to the higher elution volume at ∼29 mL to HPG oligomer resulting from inimer via SCROP.[16,17,24] The HPG inimer−oligomer carrying an epoxy head group gradually shifts to higher elution volume during the polymerization. This indicates that the HPG


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**Table 1. Kinetic Results for the Polymerizations of Glycidol (M) Using Ethylene Glycol As the Initiator (I) in the Presence of Potassium Methoxide in Dioxane at 90 °C**

| | | | | | | HPG | | | inimer−oligomer by SCROP | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| run[a] | $[I]^b \times 10^2$ (mol/L) | [M] (mol/L) | $t_{max}{}^c$ (h) | $x_p{}^d$ (%) | $k_{app}{}^e \times 10^3$ ($min^{-1}$) | $M_{w,sec}{}^f \times 10^{-3}$ (g/mol) | $M_w/M_n{}^f$ | yield[g] (%) | $M_{w,sec}{}^f \times 10^{-3}$ (g/mol) | $M_w/M_n{}^f$ | yield[g] (%) |
| B1 | 1.40 | 6.06 | 48 | 89.9 | 6.52 | 141 | 1.54 | 8.7 | 2.82 | 1.31 | 91.3 |
| B2 | 2.80 | 6.06 | 48 | 96.7 | 8.78 | 309 | 1.39 | 49.7 | 2.23 | 1.43 | 50.3 |
| B3 | 2.80 | 6.06 | 0.75 | 40.7 | –[h] | 17.7 | 1.08 | 3.3 | 0.82 | 1.30 | 96.7 |
| B5 | 5.60 | 6.06 | 2 | 86.5 | 17.6 | 324 | 1.06 | 1.0 | 1.49 | 1.76 | 99.0 |
| B6 | 2.54 | 2.75 | 120 | –[h] | –[h] | 570 | 1.53 | 98.3 | 1.41 | 1.92 | 0.70 |
| B7 | 11.2 | 6.06 | 48 | 98.6 | 20.2 | 21.4 | 1.04 | 0.4 | 1.32 | 1.66 | 99.6 |
| S1 | 1.12 | 6.06 | 48 | – | – | 122 | 1.35 | 99.1 | 1.56 | 1.04 | 0.90 |

[a]B denotes reactions performed using the BMA method, and S denotes reaction performed using the SMA method. [b]Ethylene glycol concentration and the ratio of potassium methoxide to [I] was 1.5:1 for all reactions. [c]Maximum reaction time at termination. [d]Monomer conversion calculated using $^1$H NMR. [e]Apparent rate constant determined using initial slope up to 200 min. [f]Weight-average molecular weight determined using SEC calibrated with PEO standards in water. [g]Calculated gravimetrically. [h]Not determined.

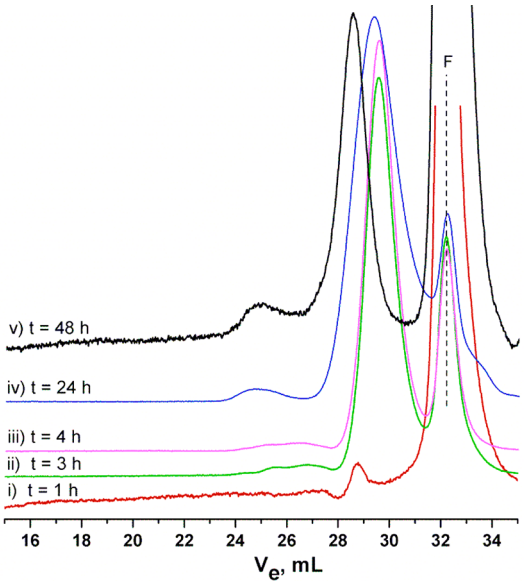


**Figure 2.** SEC traces of HPG during the batch anionic polymerization of glycidol using glycol as initiator in the presence of potassium counterion in dioxane at 90 °C. $[I]_0 = 1.40 \times 10^{-2}$ mol/L, $[M]_0 = 6.06$ mol/L (Table 1, run B1).

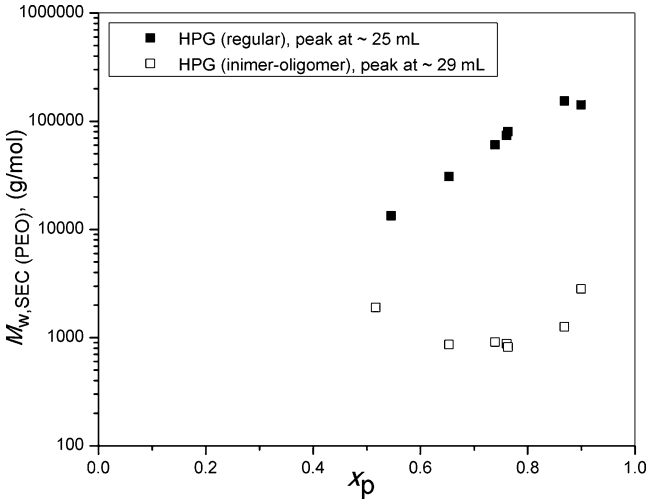


**Figure 3.** Plot of $M_{w,SEC}$ vs monomer conversion ($x_p$) in the batch anionic polymerization of glycidol.

inimer−oligomer is growing slowly (2800 g/mol, $M_w/M_n$ = 1.31) and not self-terminated via cyclization side reaction. In reactions with moderate initiator concentration (Table 1, runs B1 and B2), there is a new multimodal, broad high molecular weight peak appears after 2 h of the polymerization, which tends to grow gradually over time. The fraction of high molecular weight peak appears to increase with increasing concentration of $[I]_0$. The SEC data clearly indicate the presence of two living species in the reaction; one that grows quickly to a relatively low molecular weight (at 29 mL, <3000 g/mol) and becomes stabilized at higher conversion and a second, a small fraction, growing faster and able to sustain a larger degree of polymerization throughout the polymerization (at 25−26 mL), shown in Figure 3. Similar results showing two distinct populations were obtained in reaction B2 (Supporting Information).

Reaction carried out for a shorter reaction time (B3 and B5) gave a higher fraction of inimer−oligomer with broad MWD, which contains a small fraction of HPG exhibiting narrow MWD. A well-resolved peak in SEC with narrow MWD suggests that this small fraction of HPG is formed via linear propagation with exclusively ring-opening mechanism without undergoing transfer to pendant hydroxyl groups at early stages of the polymerization. The obtained weight-average molecular weight ($M_{w,SEC}$) for high molecular weight fraction is very high in the range of 140 000−324 000 g/mol with broad MWD (Table 1, also Supporting Information).

In order to identify the chemical structure of these fractions, a batch polymerization was performed, and the reaction was terminated at 45 min (Table 1, run B3). The $^{13}$C NMR of the HPGs obtained at 45 min reaction showed several signals that indicated the structure of the HPG is distinctly different than the HPG synthesized by SMA protocol (Figure 4). The characteristic signals—linear 1,3 (L13), linear 1,4 (L14), dendritic (D), and terminal (T)—arise from the well-defined HPGs synthesized by SMA protocol (Figure 7a).[6,12,25] Comparing the HPG synthesis using the slow monomer addition, we find there are additional signals at 45.1, 52.0, 61.5, 69.6, 73.4, and 77.4 ppm. The signals at 45.1 and 52.0 ppm correspond to epoxy ring end group of the HPG resulting from SCROP of the epoxy anion inimer. Other additional signals are very complex and difficult to assign accurately. However, they are all located adjacent to linear (L13 and L14) structural units, indicating that they correspond to random pendant hydroxyl groups of the irregular hyperbranched inimer−oligomers. This


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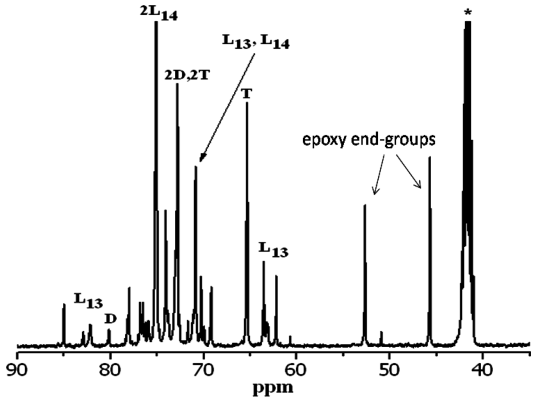


**Figure 4.** $^{13}$C NMR of inimer−oligomer HPG recovered at 0.75 h, indicating presence of epoxy ring end group (Table 1, run B3).

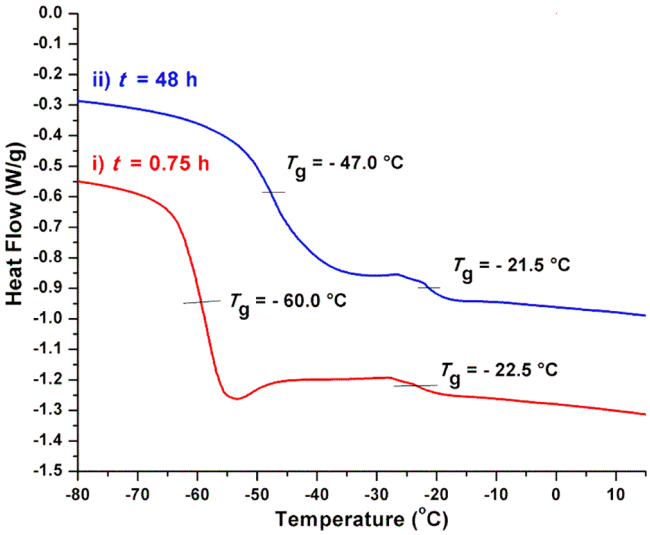


**Figure 5.** DSC of HPGs synthesized via batch anionic polymerization (SCVP) at different reaction times: (i) 0.75 h and (ii) 48 h.

confirms that the first population eluting at ∼29 mL in SEC is the product of SCROP of the epoxy anion inimer.

The HPGs recovered from these reactions were analyzed using DSC to determine the effect of $T_g$ on the topology of HPGs and compared to the polymers obtained via the slow monomer addition method (Table 2). The DSC of the HPGs synthesized via batch monomer addition for 0.75 and 48 h reactions showed clearly two distinct $T_g$s, indicating there are two immiscible polymers formed in the reaction (Figure 5). The glass transition at −22 °C is similar to the HPGs synthesized using the SMA (−16 °C, $T_g$ < −26 °C); in addition, there is a second transition around −60 °C for the reaction continued for 0.75 h (Figure 5i). The lower $T_g$ at −60 °C confirms the existence of more mobile, fewer densely branched chains. We attribute this transition to the inimer−oligomer HPG fraction. The reaction carried out for 48 h (Table 2, run B2), which had an equal percentage of the low to the high molecular weight species (Supporting Information), showed two $T_g$s: one at −21.5 °C and another at −47 °C (Figure 5ii). The presence of low-$T_g$ material may correspond to the inimer−oligomer HPG fraction. A high $T_g$ of the second fraction shows that this HPG product has a more regular branching and fewer numbers of internal end groups similar to the product obtained from SMA. The mechanism for the formation of this product can be explained by considering the presence of two different types of propagating centers that are propagating at different rates.

Hyperbranching of glycidol via inimer-mediated SCROP produces branched oligomers with high concentration of potassium counterion, [K$^+$]/[−OH]. Intermolecular reaction of epoxy anion will add more counterion during the propagation, which will lead to aggregation. The propagation rate is perturbed due to extensive aggregation, and this leads to an ill-defined self-condensation and irregular branching. On the other hand, a small fraction of initiator propagates via regular hyperbranching to yield HPG with fewer defects, similar to the ones obtained in the SMA protocol (Table 1, run S1). Observation of two $T_g$s in the same sample of HPG confirms that the HPG synthesized by BMA consists of two immiscible HPGs (Figure 5). Immiscibility arising from PS stars with two different branch density is known in the literature.[26] A partial immiscibility of products in a polymerization must be originated from conformational constraints of two different branching structures. The DSC results support the presence of two distinctly branched HBG materials: one with nearly well-defined branching and another irregular branching (Scheme 3 and Figure 5).

The growth of two distinct populations of HPGs in solution during the polymerization must have come from a kinetic discrimination resulting from the aggregation. The reactivity of inimer−oligomer with high concentration of potassium salts ([K$^+$]/[−OH]) is low compared to HPGs that are propagating without transfer to monomer. The SEC results indicated a very small fraction of the initiator contributes to the growth of HPG that propagates without transfer to monomer. Its reactivity must be high as it will be less aggregated and will have better solubility in the reaction medium. These two populations in the polymerization grow at different rates and remain in the system even at 90% monomer conversion that was achieved in 48 h

**Table 2. Glass Transition Temperature and Overall Degree of Branching of the HPG and SCROP Species of Various Slow and Bulk Monomer Addition Polymerizations**

| | | HPG | | inimer−oligomer by SCROP | | $^{13}$C NMR characterization | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| run[a] | $t_{max}$[b] (h) | $M_{p,SEC}$[c] × 10$^{-3}$(g/mol) | $T_g$[d] (°C) | $M_{p,SEC}$[c] × 10$^{-3}$(g/mol) | $T_g$[d] (°C) | T | D | $L_{1,3}$ | $L_{1,4}$ | DB[e] |
| B2 | 48 | 272 | −21.5 | 1.83 | −47.0 | 3.07 | 1.0 | 0.44 | 3.98 | 0.31 |
| B3 | 0.75 | 18 | −22.5 | 0.650 | −60.0 | 11.7 | 1.0 | 1.91 | 13.3 | 0.11 |
| B6 | 120 | 342 | –[f] | 1.10 | −50.1 | 5.03 | 1.0 | 0.90 | 4.3 | 0.28 |
| S1 | 48 | 127 | −34.0 | 1.03 | –[f] | 3.12 | 1.0 | 0.33 | 2.44 | 0.42 |

[a]B denotes reactions performed using the BMA method, and S denotes reaction performed using the SMA method. [b]Maximum reaction time at termination. [c]Apparent peak maximum molecular weight determined by SEC. [d]Glass transition temperature determined by DSC on second heating cycle. [e]Degree of branching calculated using $^{13}$C NMR integrations of terminal (T), dendrimeric (D), and linear (L) constituents. [f]Not determined.


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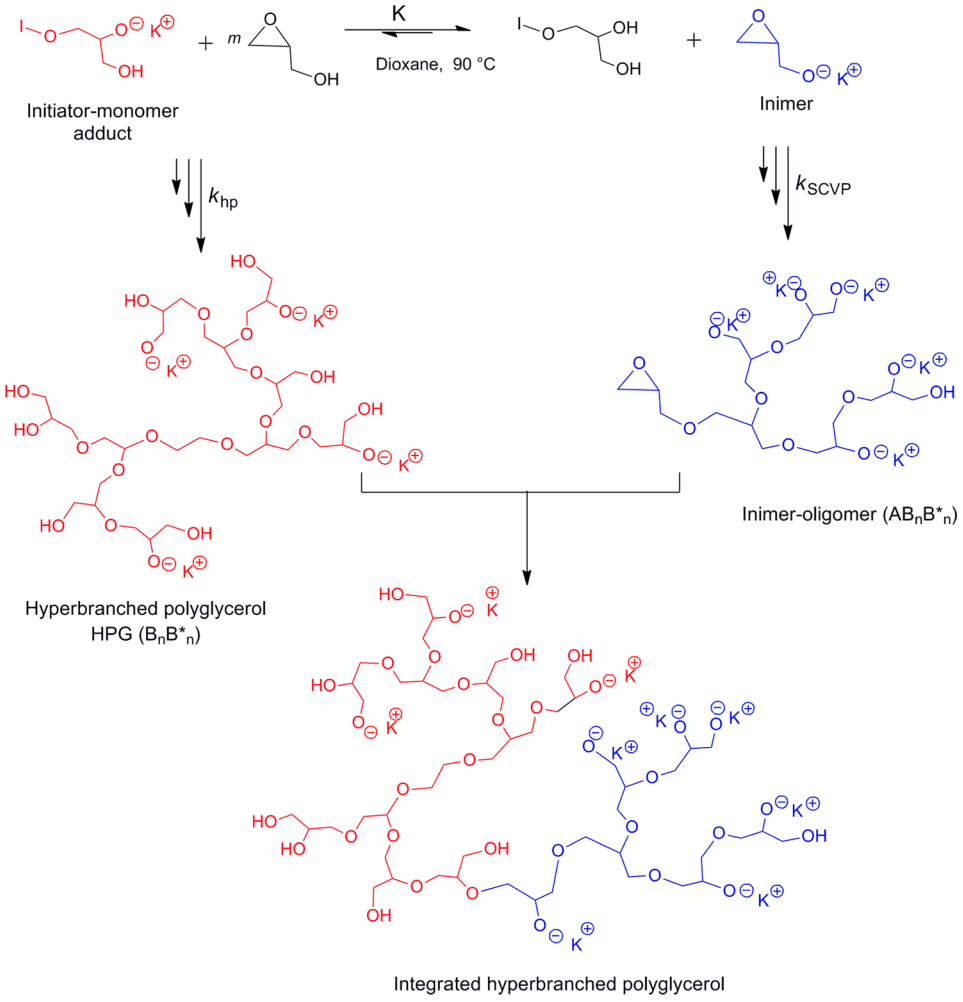
**Scheme 3. Proposed Mechanism for the Synthesis of HPG in BMA Method via Inimer-Mediated Oligomer Insertion**



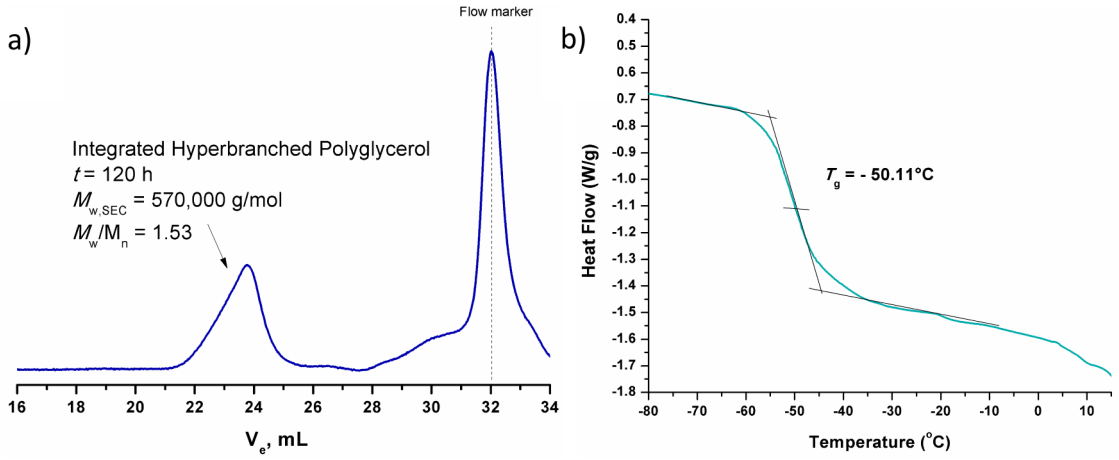




**Figure 6.** SCROP of glycidol at 90 °C for 120 h: (a) SEC trace of integrated HPG and (b) DSC of integrated HPG.

(Table 1, run B2). However, these populations should react and merge as the inimer−oligomer contains the epoxy monomer unit as a headgroup (Scheme 3). Absence of such an integration of these populations can be attributed to a high viscosity and a low reactivity induced by alkoxide aggregation. If sufficient time is given, they may intermolecularly react very slowly and form a single population.

In order to examine this possibility, we conducted a polymerization using BMA for 120 h (Table 1, run B5). The polymerization was kept at 90 °C for 5 days. The HBG obtained after 5 days showed a broad, high molecular weight peak in SEC, confirming integration of inimer−oligomer HBG with a regular HBG (Figure 6a). Depletion of inimer−oligomer HBG can be seen at ∼29 mL of the elution volume. The DSC showed that the HPG had only one $T_g$ at −50 °C. The free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volume and chain mobility are controlled by the branching architecture, which significantly affects the $T_g$ of the polymer. The integrated product obtained at prolonged reaction time is unique in architecture as it encompasses inimer−oligomer segments linked discretely in the regular HPG. The obtained low $T_g$ indicates a less dense HPG due to inimer−oligomer integration, which also confirms that the two populations had merged over a very long reaction time (Figure 6b).

**Polymerization Using Slow Monomer Addition (SMA) Protocol.** The successful synthesis of controlled molecular weight HPG with moderately narrow MWD in SMA protocol is mainly attributed to the absence of intermolecular proton transfer from monomer (Scheme 2c), thus preventing the formation of epoxy anion that can undergo oligomerization independently via self-condensing ring-opening polymerization (SCROP) with an epoxide group as a focal unit.[2,6,12] The SMA protocol gives controlled molecular weight of HPGs up to 24 000 g/mol with only ∼10 mol % of active centers. It is suggested that the propagation is controlled via proton transfer mechanism exclusive of monomer hydroxyl groups (Scheme 2b).[2,6,12] However, at a relatively low initiator concentration, the propagation rate is expected to decrease gradually over conversion, which does not favor for the nucleophilic attack on the epoxide ring over the proton abstraction at every step of the dropwise monomer addition. The previously suggested mechanism does not account for these issues in the synthesis of controlled molecular weight HPG.[2,6,12]

In order to understand the effect of SMA protocol, we performed the polymerization of glycidol using potassium counterion with glycol as an initiator. A high counterion concentration was used by converting 75% of the total hydroxyl groups of the initiator into potassium salt for the polymerization to promote a faster propagation. The polymerization was performed in dioxane via a slow addition of glycidol (0.5 mL/h) over 10 h under nitrogen at 90 °C. After 48 h, the reaction was diluted in methanol, passed through a cation exchange column, and precipitated in acetone. The analysis of the recovered product using $^{13}$C NMR and $^{1}$H NMR in DMSO-$d_6$ showed characteristic signals corresponding to HPG as reported in the literature (Figure 7a, Supporting Information). The degree of branching (DB) calculated using eqs 1 and 2 yielded 0.43, which is slightly lower than the values reported by Frey and co-workers (0.50 < DB < 0.60).

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

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

The apparent molecular weight of the HPG was determined using size exclusion chromatography (SEC) with respect to poly(ethylene oxide) standards in water. The number-average molecular weight ($M_{n,SEC}$) of HPG was 90 000 g/mol, which is higher than the theoretically expected molecular weight ($M_{n,th}$ = 60 000 g/mol) based on the feed ratio of monomer to initiator (Table 1). The results are in accordance with Brooks and co-workers, who used dioxane and diglyme as emulsifying agents for the polymerization.[7] On the other hand, extensive work of Frey and co-workers indicated that the number-average molecular weight ($M_n$) of HPG can be controlled under a limited molecular weight range ($M_n$ < 24 000 g/mol) using macroinitiator with two-step strategy.[2] The SEC of the HPG, obtained in this study, exhibited monomodal with MWD, $M_w$/

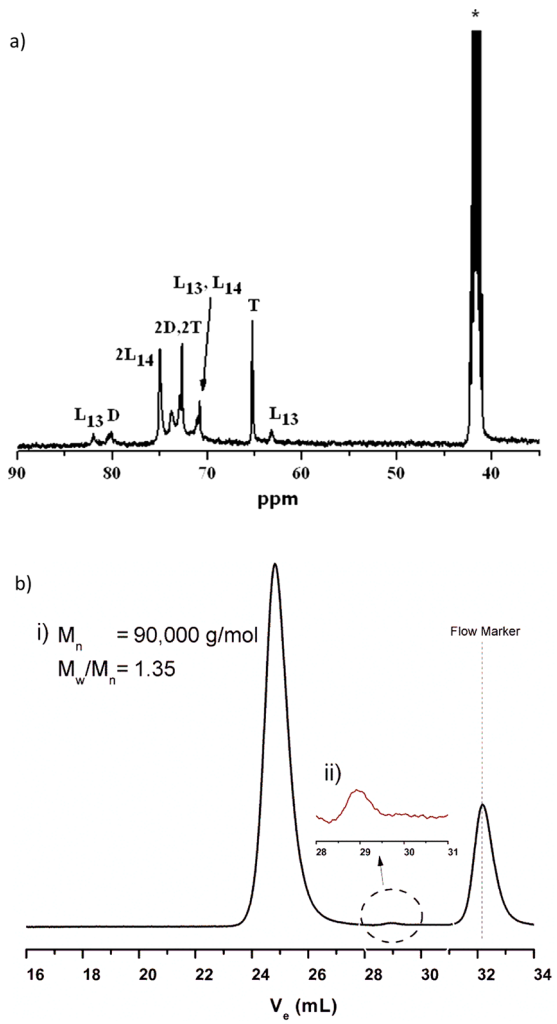


**Figure 7.** $^{13}$C NMR (a) and SEC (b) of HPG obtained via the SMA method.

$M_n$ = 1.35 (Figure 7b). Interestingly, there is a small peak at an elution volume of 29 mL, indicating the presence of a small fraction of oligomer (Figure 7b(ii)). This oligomer constitutes less than 1% of total concentration and its peak maximum molecular weight at one-tenth of the molecular weight of the main peak at ∼25 mL. Prior investigation has reported observing the low molecular weight oligomer formation being at least 10% of the total concentration.[2] This clearly indicates that the oligomer is either formed late in the polymerization or unable to grow further, considering that the polymerization was kept at 90 °C for 38 h after completion of the monomer addition. As the percentage is very low, it is difficult to fractionate this oligomer for ascertaining the chemical identity.

The formation of oligomers in the synthesis of HPG has been attributed to side reaction resulting from proton abstracted glycidol. As discussed above, the molecular weight control can only be obtained in SMA protocol, when the propagating alkoxide anion exchanges fast with both the primary and secondary hydroxyl groups of the polymer via inter- and intramolecular abstraction processes during the polymerization. Although the propagating alkoxide anions exist in equilibrium with aggregated anions in dioxane, the proton abstraction of potassium alkoxide will follow as given in Scheme 2, if the glycidol is not reacted at epoxide ring at a faster rate. It can be seen that in both the cases of intra- and intermolecular


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proton exchanges the forward reaction is faster than the backward reaction due to the stability of less hindered primary alkoxide anions and higher tendency for aggregation. Thus, the formation of epoxy anion via intermolecular monomer transfer is inevitable even in the SMA protocol, though the concentration can be minimized by controlling local monomer concentration. The reactivity differences of primary and secondary alkoxides make the formation of epoxy anion difficult to stop. It appears that a small percentage of epoxy anion formation is formed at every stage of the monomer addition in SMA protocol. The epoxy anion is an "inimer" and can propagate to form hyperbranched oligomer or polymer via SCROP.

The weak signal in SEC trace at 29 mL must be attributed to a product formed during the last stages of SMA via SCROP. As the concentration of potassium salt is high in such a SCROP product than the regular (or desired) HPG product, its reactivity is expected to be suppressed by extensive aggregation of alkoxide centers. High viscosity of the reaction prevents this oligomer, carrying the epoxy headgroup, to react with the regular HPG at high conversion. Recently, Weiss and co-workers have shown that the presence of oligomer and cyclic side product in the thermally initiated polymerization of glycidol using the SMA method.[27]

Theoretically, it has been shown that the concentration of potassium salt in the propagating regular HPG decreases during the polymerization in the SMA method.[2] With a low concentration of potassium counterion, the regular HPG will be less aggregated, highly solvated, and reactive as compared to the inimer−oligomeric product formed via SCROP. At every stage in SMA, a fraction of propagating alkoxide anions undergoes proton abstraction with monomer leading to inimer formation similar to BMA protocol. The inimer propagates via SCROP forming highly aggregated oligomers with the epoxide headgroup, which then reacts slowly with the growing HPG propagating chains (Scheme 3). Therefore, a drop-by-drop SMA method provides sufficient time for the inimer−oligomer to integrate with the growing HPG chain ends. The proposed mechanism provides control of molecular weight based on the feed ratio of monomer to the initiator as the initiator concentration is not changed in every stage of the process. The mechanism for the control of the molecular weight in SMA appears to be an inimer-mediated growth of HGP as proposed in Scheme 3.

The structural differences of the various HPGs can be assessed through their DB values (Table 2). In the case of SMA synthesis, the regular HPG exhibited very high DB value, 0.42, confirming its structural regularity. On the other hand, the HPG produced via BMA protocol consisted of mostly inimer−oligomer (45 min reaction product) and had a DB of 0.11. The HPG consisting of a mixture of both the regular and the inimer−oligomer (48 h reaction product) had a DB of 0.31. However, the HPG obtained after the merger of two populations (5 day reaction product) exhibited a slight increase in DB = 0.28. These DB values correlate nicely to the DSC results, showing an increase in $T_g$ of HPGs with increasing the DB values. The results suggest that the HPGs produced by SCROP in all stages have an ill-defined branching with random linear segments (1,3 and 1,4 units) in their branches.

## CONCLUSIONS

In summary, the polymerization of polyglycidol in bulk monomer addition method involves propagation via two distinct reaction centers: one that originates from glycidol proton transfer leading to epoxy anion inimer and a second, smaller fraction that undergoes hyperbranching without any transfer to monomer. Oligimerization of epoxy anion inimer is the major reaction in BMA, which produces ill-defined branched polymer via SCROP. SEC showed a large amount of oligomers and a small fraction of high molecular weight products present during the reaction. The kinetic study showed the slow evolution of the high molecular weight peak at the expense of oligomer inimer concentration as the reaction progressed. This led to high molecular weight, uniquely branched structures with different physical properties that were not miscible with their oligomer inimer counterparts.

DSC analysis of the HPG obtained by BMA showed the product exhibits two distinct $T_g$s changing over reaction time, confirming that they possess different conformation due to irregular branching and immisciblity. The two populations of HPGs merge into one via intermolecular reaction, if the reaction is performed for a longer time (120 h). The presence of a small fraction of oligomeric product was identified in the SMA method, as well. The propagation mechanism for hyperbranched polyglycidol involves participation of self-condensing epoxy anion inimer as intermediate depending on the monomer concentration in the polymerization. In the SMA method, monomer concentration is small during the polymerization, which prevents the formation of a large amount of inimer and provides a limited control for the polymerization.

## ASSOCIATED CONTENT

### Supporting Information

SEC of HPGs over time for reaction B2, a plot of molecular weight over time for reaction B1, a plot of MWD over time for reaction B1, $^{13}C$ NMR of HPG synthesized using the slow monomer addition (SMA) method. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

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