Hydroxyalkylation of Barbituric Acid. III. Product Analysis and Reaction Pathway

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ABSTRACT: Polyetherols containing a thermally stable pyrimidine ring were obtained upon the reaction of hydroxymethyl derivatives of barbituric acid with an excess of ethylene or propylene oxide. The reaction was monitored by ^{1}H-NMR and IR spectroscopy for the systems with variable starting molar ratios of reagents. We found that formaldehyde rearranged from *N*-hydroxymethyl and oxymethylene bridges into the end of the polyetherol chain during the reaction. Simultaneously, the *O*-hydroxymethyl groups underwent blocking by oxirane. The structures of the polyetherols was deduced on the basis of the course of the reaction and the analytical data. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 112: 1601–1606, 2009

Key words: addition polymerization; FTIR; heteroatom-containing polymers; NMR; oligomers

INTRODUCTION

Hydroxymethyl derivatives of barbituric acid (HMBAs) are a new class of compounds,[1] which react with an excess of oxiranes such as ethylene oxide (EO) and propylene oxide (PO) to give tetrafunctional polyetherols with a thermally stable pyrimidine ring incorporated into the polymer:[2]
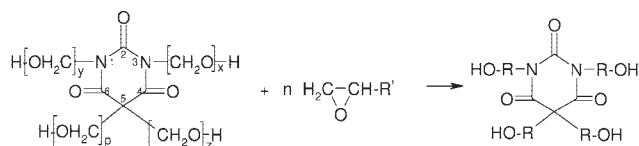
where R' is —H, —CH₃ and R is a short oxyalkylene chain containing the following subunits:
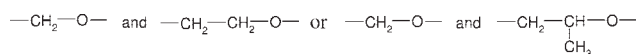
In the reversible reaction of 1 mol of barbituric acid (BA) with 6 mol of formaldehyde, a resinlike product is obtainable, which upon addition of 5% w/w of water leads to a product miscible with oxiranes and reacting with them at elevated temperatures (65–70°C) in the presence of triethylamine (TEA) as a catalyst with the formation of the mentioned polyetherols. Previously, we established the conditions for the reaction of 1 mol of BA with 6 mol of formaldehyde.[2] We found that, upon the reaction of that semiproduct with oxiranes, the obtained polyetherols were useful candidates for the fabrication of thermally stable polyurethane foams. Some of those polyetherols had unstable hemiacetal groups (*O*-hydroxymethyl) at the end of the polyetherol chain. These groups are unfavorable for the formation of polyurethane foams because of the release of formaldehyde during foaming and the mechanical destruction of the foams. Therefore, it is desirable to block all or almost all hemiacetal groups with the oxyalkyl groups that form upon the decomposition of the oxirane ring. Here, we explain the reaction of additional oxiranes (EO or PO) with HMBA, which resulted in the formation of polyetherols, with particular control of unstably bonded formaldehyde (UBF) as hemiacetal groups.

EXPERIMENTAL

Syntheses

Synthesis of HMBA

HMBA was obtained as a BA : HCHO 1 : 6 system, as described in ref. 2.

Reaction of HMBA with the oxiranes

To a thick-glass, high-pressure reactor of 250-cm³ capacity, 10.43 g of HMBA solution in dimethylsulfoxide (DMSO; 6.95 g or 0.025 mol of HMBA; with DMSO distilled and stored over molecular sieves) was introduced, and then, 1 cm³ of TEA and EO or

PO were added to obtain HMBA : oxirane molar ratios equal to 1 : 1–1 : 4, l : 6, 1 : 8, 1 : 10, 1 : 12, and 1 : 18. The reaction mixture was heated to 40–45°C (in the systems with EO) or 45–50°C (in the systems with PO), and this temperature was retained until the end of the process.
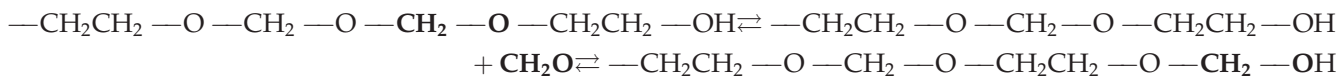
Analytical methods

The reaction was monitored by the determination of the epoxide number with the hydrochloride-in-dioxane method.[3] The process was discontinued when the epoxide number was zero. In the solutions obtained in the reaction between HMBA and the oxiranes, the acidic number (AN) was also determined by alkacymetric titration, and the percentage of UBF as N—, C_5—, and O-hydroxymethyl groups was determined iodometrically.[4] The products were analyzed by ^{1}H-NMR spectroscopy (Tesla spectrometer type BS586A, 80 MHz, Prague, Czech Republic) in DMSO-d_6 after the removal of TEA under reduced pressure ($p = 20$ hPa; $t \leq 60°$C).
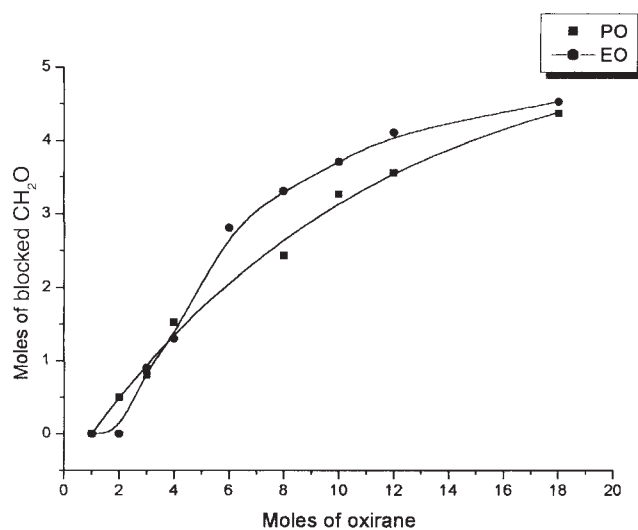
RESULTS AND DISCUSSION

Formaldehyde determination

The progress of the reaction was monitored for the HMBA substrate obtained from the BA : CH_2O 1 : 6 system (BA : CH_2O = 1 : 5.3 in the product), that is, for the sample used successfully for the synthesis of polyetherols.[2] The homogeneity of the system (anhydrous HMBA, oxirane, TEA) was achieved by the dissolution of the mixture in DMSO. The AN and percentage of UBF were determined at every step of added oxirane. The acidic character of the reaction mixture was due to release of formaldehyde from HMBA with the formation of CONHCO or C_5—H groups. From the analytical data, it follows that (Fig. 1):

• After the reaction of 1 and 2 mol of EO with HMBA, the percentage of UBF remained the same as it was before the starting process, whereas in the case of PO instead of EO, the percentage of UBF decreased (the percentage of blocked formaldehyde accrued).

Figure 1 Number of moles of blocked formaldehyde in the reaction of HMBA with oxiranes.

• Further addition of EO resulted in a continuous decrease of UBF.
• The blocking of 85% of the starting amount of formaldehyde occurred upon the addition of 18 mol of oxirane. This was previously revealed as a limiting condition to the production of stable polyurethane foam from the polyetherol.

Further observation indicated some relevant details on the route of the analyzed reaction. Thus, the first 2 mol of EO did not block the hydroxymethyl groups or block them in an unstable manner. The 3rd mol of EO did block almost 1 mol of hydroxymethyl groups. The 4th, 5th, and 6th mol of EO blocked about 0.7 mol of formaldehyde each, whereas next moles of EO caused the blocking of 0.3–0.4 mol of formaldehyde. In the systems, with PO the first moles of oxirane blocked 0.5–0.7 mol of formaldehyde, whereas the next ones blocked only 0.2–0.3 mol (Fig. 1). From this analysis, the conclusion was drawn that formaldehyde was able to split from the oxymethylene bridges and rearrange into the end of the chain. This behavior was observed previously and was studied in detail for the reaction between hydroxymethyl derivatives of isocyanuric acid and melamine; in those cases, the rearrangement of formaldehyde blocked by one oxirane molecule into the end of chain was observed:[5,6]

$$—CH_2CH_2—O—CH_2—O—\mathbf{CH_2}—\mathbf{O}—CH_2CH_2—OH \rightleftarrows —CH_2CH_2—O—CH_2—O—CH_2CH_2—OH$$
$$+ \mathbf{CH_2O} \rightleftarrows —CH_2CH_2—O—CH_2—O—CH_2CH_2—O—\mathbf{CH_2}—\mathbf{O}H$$

Here, we found that the first 2 mol of EO did not block the formaldehyde. This was probably related to the acidity of the X—H groups, where X is the nitrogen atom or C-5 carbon atom in BA. We found that the stronger the acidity of X—H was, the more

facile was the release of the formaldehyde.[7] The presence of two labile formaldehyde molecules in HMBA suggested that the parent BA molecule (from which the HMBA was synthesized) had two clearly acidic protons. On the basis of the determination of

formaldehyde, it was not possible to recognize which of the two groups, $\rangle$N—H or $\rangle$C$_5$—H, were responsible for the formaldehyde release. When PO was used in the reaction, the small steric hindrance from the methyl group in the hydroxyalkyl derivatives retarded the formaldehyde rearrangement to the end of the chain, which resulted in its partial blocking already in the reaction of HMBA with 1 mol of this oxirane.

Determination of the AN

The products of the reaction between HMBA and oxiranes (especially those obtained at a low molar excess of oxirane) had nonzero ANs. Even HMBA itself, which formally does not contain any acidic function, indicated a quite substantial AN (AN$_{found}$ = 129.6 mg of KOH/g). During the titration, the single formaldehyde molecule was split from HMBA with the formation of an acidic group (N—H or C$_5$—H):[1]

$$X—CH_2OH \rightleftarrows X—H + CH_2O$$
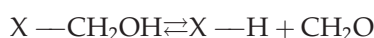
where X is N or C$_5$ in the HMBA molecule.

The obtained AN was about 69% of the value calculated for the previous irreversible reaction (AN$_{calcd}$ = 187.6 mg of KOH/g) based on titration with 0.1M aqueous KOH:

$$X—H + KOH \longrightarrow X^- K^+ + H_2O$$
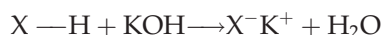
When we took into account that the change of AN in products during consecutive addition of oxirane was related to the disappearance of acidic groups (N—H or C$_5$—H) upon reaction with oxirane and the number of available moles of TEA (catalyst) in the system (0.31 mol), it was possible to estimate the AN of the initial reaction mixture. The calculation procedure can be exemplified as follows: the 1 : 1 HMBA : EO mixture was dissolved in DMSO to give a mass ratio 57.0% HMBA, 28.5% DMSO, 8.7% EO and 5.8% TEA. From this, the mass of the mixture containing 1 mol (287 g) of HMBA could be calculated. Thus, 100 g of the mixture contained 57 g of HMBA, and x grams of the mixture contained 287 g of HMBA. This gives x = 503.5 g. Thus, the AN should be

$$\frac{56100}{503.5} = 111{,}2 \text{ mg of KOH/g}$$

When we took into account that the determined AN is usually 69% of the theoretical value, the obtained AN was equal to 76.9 mg of KOH/g. The catalyst TEA
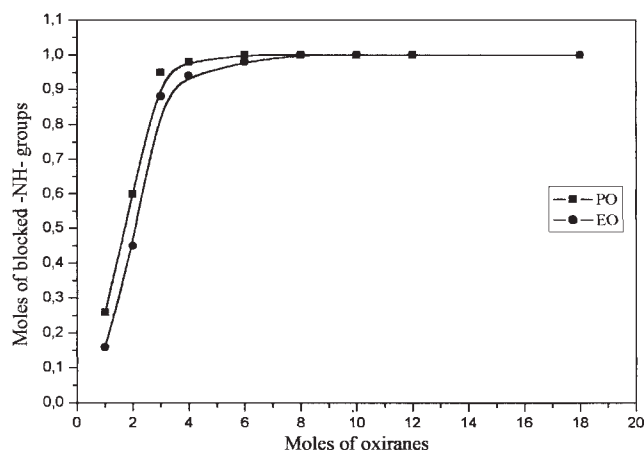
Figure 2 AN changes of the postreaction mixtures of HMBA with oxiranes.

diminished the value of AN because of the blocking of X—H groups according to the following reaction:

$$X—H \quad + \quad :N(C_2H_5)_3 \quad \longrightarrow \quad X^{\ominus} \overset{\oplus}{N}(C_2H_5)_3 \atop | \atop H$$

Because 0.31 mol of TEA was present in the system, the value of AN was as follows:

$$AN = 76.9(1 - 0.31) = 53.06 \text{ mg of KOH/g}$$

The experimental AN of the initial mixture (AN$_{found}$ = 53.2 mg of KOH/g) corroborated well with the previous equation. After completion of the reaction, the AN decreased to 45.3 mg of KOH/g. Considering the changes of AN in the postreaction mixture in the function of moles of oxirane attached to HMBA, we showed that the product of the reaction between HMBA and PO did not contain the splittable protons after the attachment of 3 mol of this oxirane, whereas the product of the reaction of HMBA with EO behaved similarly after the attachment of 8 mol of EO (Fig. 2). The reason was the different reactivity of the oxiranes; EO was more reactive but less selective. Therefore, it reacted also with the hydroxymethyl groups of HMBA, and consistently, it had a lower contribution in the reaction with N—H groups.

Spectral analysis of the products

The ^{1}H-NMR spectra of products of the reaction between HMBA and oxiranes corroborated well with the outlined picture. The samples for NMR analysis were prepared by the removal of DMSO under a reduced pressure at 60°C. Partial removal of formaldehyde from the hydroxymethyl groups of the products at this conditions occurred; therefore,

the spectral analysis was rather qualitative. The spectral features were as follows:

- In the ^{1}H-NMR spectrum of the products obtained from the HMBA : EO 1 : 1 system, a resonance centered at 3.3–3.4 ppm appeared, which belonged to oxyethylene group protons. Its intensity grew in the products obtained from the systems with higher excesses of EO. Moreover, the imide proton resonance at 11.4 ppm was present in the first two products [obtained from the 1 : 1 and 1 : 2 systems; Fig. 3(a)] because of the thermal dissociation of formaldehyde from N-hydroxymethyl groups (during distillation), which were still not blocked by oxirane.
- In the course of the addition of the next equivalents of EO, the intensity of the resonance at 11.4 ppm decreased, and eventually, the resonance disappeared after the addition of 3 mol of EO [Fig. 3(b)]. This indicated that, initially, EO reacted with N-hydroxymethyl groups. The reaction could proceed by the rearrangement of formaldehyde (blocked by one molecule of oxirane) into the end of chain according to the following scheme:

$$\text{N}-\text{CH}_2\text{O}-\text{CH}_2-\text{CH}_2\text{OH} \longrightarrow \text{N}-\text{CH}_2-\text{CH}_2-\text{O}-\text{CH}_2\text{O}-\text{H}$$
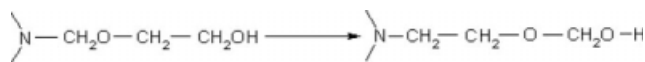
- Consistently, the intensity of the resonance of the $\text{N}-\text{CH}_2-\text{OH}$ methylene proton centered at 5.1 ppm also decreased; the resonance disappeared completely upon the reaction of 3 mol of EO with 1 mol of HMBA [Fig. 3(b)]. It clearly demonstrated that N-hydroxymethyl groups were initially blocked by oxirane.
- When a threefold excess of EO was used, the stepwise disappearance of the resonance at 3.7 ppm (attributed to hydroxymethyl groups attached to C_5) was observed [Fig. 3(c)]. This resonance finally disappeared upon the addition of 6 mol of EO.
- The resonances in the region 4.5–4.7 ppm (assigned to semiacetal groups) did not disappear, even upon the reaction with an excess of EO. However, in this region, the resonances from dioxymethylene protons were also present; these groups were formed upon mutual condensation of semiacetal groups,[1] and additionally, the resonances from terminal oxymethylene protons were observed, which originated from terminal formaldehyde.
- TEA formed with polyetherols the hydrogen-bonded adducts, and therefore, the catalyst could not be removed from the postreaction
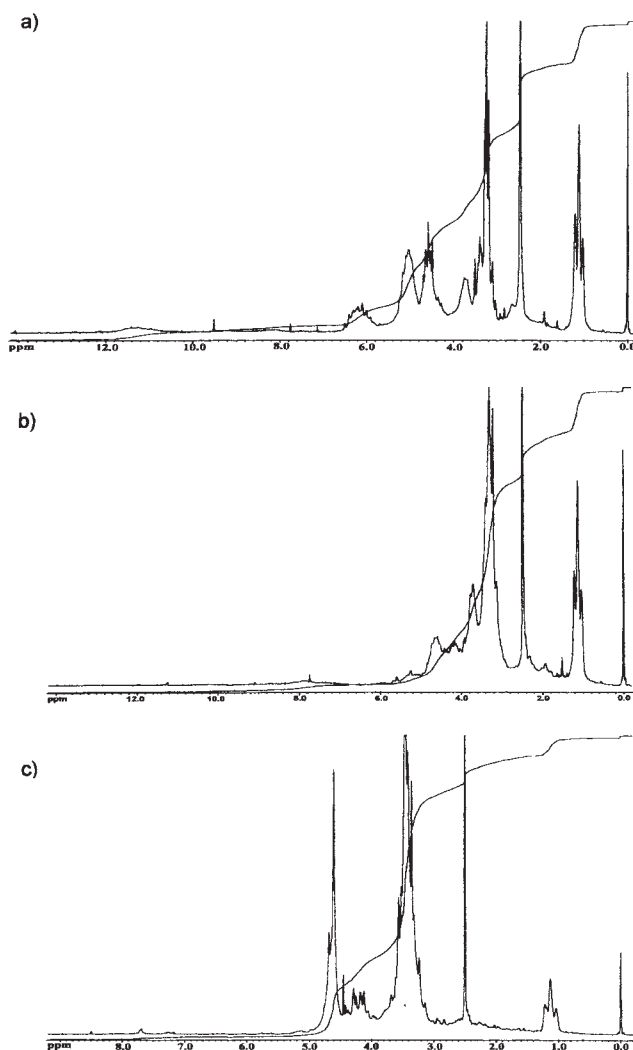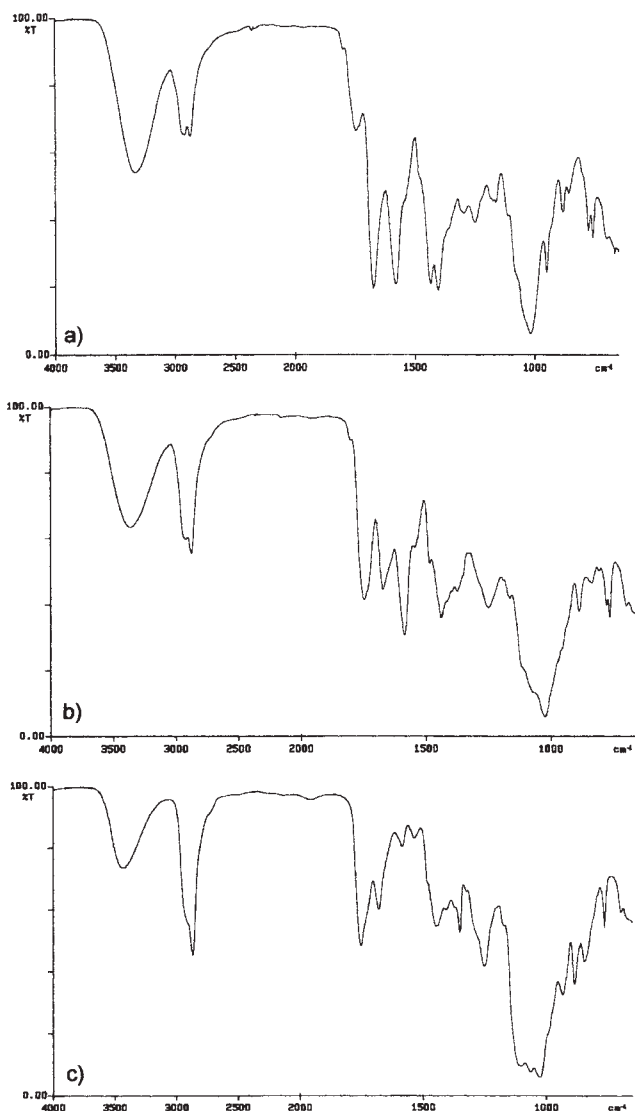

Figure 3 ^{1}H-NMR spectrum of the product of the reaction of 1 mol of HMBA with (a) 1, (b) 3, and (c) 8 mol of EO.

mixtures by vacuum distillation; the methyl group resonances of TEA were present at 1.1–1.2 ppm.
- The resonance at 4.6 ppm originated from two overlapping signals; the hydroxyl proton resonance from $-\text{CH}_2\text{CH}_2\text{O}H$ group and the methylene proton resonances from $-\text{CH}_2-\text{O}-\text{CH}_2-$ groups formed upon the condensation of hydroxymethyl groups. After the addition of D_2O to the sample, the former signal disappeared and left the low-intensity residual signal of the latter protons; the intensity of the residual signal indicated the low percentage of $-\text{CH}_2-\text{O}-\text{CH}_2-$.

Similar observations were noted for the products obtained from the HMBA : PO system. In the ^{1}H-NMR of the products, the resonances related to the presence of abnormal product were found.

Figure 4 IR spectrum of the product of the reaction of 1 mol of HMBA with (a) 4, (b) 6, and (c) 18 mol of EO.
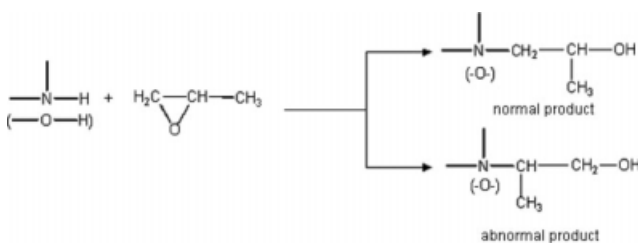

The methylene group protons of the normal product gave resonances at about 1.0 ppm, whereas those from the abnormal product were observed at 1.3 ppm.[8] The abnormal structure appeared in the products obtained from the system with greater than or equal to 6 mol of PO per mole of HMBA. Their percentage was the highest for the 1 : 6 HMBA : PO systems (18.7 mol %); later, it gradually decreased and finally equaled about 10 mol % in the product obtained from the 1 : 18 system.

The resonance from free formaldehyde at 8.5 ppm was observed in some spectra. The intensity of this resonance grew upon the addition of D_2O to the samples. This suggests the possibility of the dissociation of formaldehyde from N— or O-hydroxymethyl groups. Thus, it cannot be excluded that the formation of O-hydroxymethyl groups occurred upon the shift of formaldehyde into the end of the polyetherol chain due to a dissociation mechanism.

The course of the reaction was also confirmed by the IR observations of the products (Fig. 4). Upon consecutive addition of oxiranes to HMBA, the increase in the intensity of the band centered at about 1000 cm^{-1} was observed, which was related to the formation of C—O—C ether groups [cf. Fig. 4(a,b)]. Also, the intensity of the valence —CH$_2$— band (2830 cm^{-1}) increased at the expense of the intensity of the —OH valence band. The band centered at 1587 cm^{-1}, attributed to the deformation —NH— band, also grew. Its presence was consistent with the conditions of DMSO distillation; in the course of this operation, the elimination of UBF from —O—CH$_2$OH groups and then from —NH—CH$_2$OH groups occurred. Its intensity in the products of further addition of oxirane decreased; nevertheless, the band was present even in the spectrum of the product obtained from the HMBA : EO 1 : 10 system. This indicated that oxirane bound more facily to the hydroxyethyl groups of the semiproduct than to the —NCH$_2$OH groups. The band was no longer observed in the product obtained from the HMBA : EO 1 : 18 system [Fig. 4(c)]. The presence of the skeleton BA ring band at 935 cm^{-1} and the carbonyl group band at 1740–1750 cm^{-1} in the spectra of all of the products indicated clearly the preservation of the ketone tautomeric form of BA in the synthesized polyetherols.

CONCLUSIONS

1. On the basis of the analytical and spectral data, the approximate structure of the product obtained upon the addition of oxirane to HMBA was formulated. Thus, for the product obtained from HMBA : oxirane = 1 : ≤6, the major form was

(II)
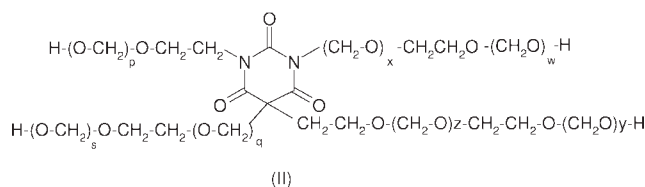
where $x + y + z + q + p + s + w = 5.3$ and w, x, y, z, q, p, and $s < 1$.

The formula (II) shows two independent methods of oxirane addition to N and C_5 atoms and hydroxymethyl groups, whereas the dominating structure present in the product obtained from HMBA:oxirane ≥ 6 was demonstrated by formula I, where R contains oxyethylene or oxypropylene groups alternating with oxymethylene groups.

2. The analysis of the reaction between HMBA and oxiranes indicated that the first moles of EO reacted with N-hydroxymethyl groups and blocked them in an unstable manner, whereas PO blocked the hydroxymethyl groups partially. Further addition of oxirane partially blocked the O-hydroxymethyl ($O\!-\!CH_2OH$) and C-hydroxymethyl ($C_5\!-\!CH_2OH.$) groups of the semiproducts formed in the course of the studied reaction.

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