Saccharide Effect on the Deswelling Process of the Thermosensitive Poly(*N*-isopropylacrylamide) Gel

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The kinetic parameters of deswelling and the change of a lower critical solution temperature (LCST) for poly(*N*-isopropylacrylamide) gel, poly(NIPAAm) gel, were investigated in the presence of glucose and other sugars as hydrophilic probes. The enthalpy of activation ($\Delta H^{\neq}$) and the entropy of activation ($\Delta S^{\neq}$) for deswelling were influenced by the concentration of additive sugars. Plots of $\Delta H^{\neq}$ against $T\Delta S^{\neq}$ fell on a straight line, of which the slope was approximately 0.91–0.94. This result shows a compensation effect of the free energy of activation ($\Delta G^{\neq}$) concerning the relationship between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ for deswelling of poly(NIPAAm) gel. The molecular interaction between sugar and water clusters involved with the polymer is responsible for the compensation effect between $\Delta H^{\neq}$ and $\Delta S^{\neq}$. The equatorial hydroxy groups of sugar molecules interact easily with water clusters around the hydrophobic isopropyl groups (the iceberg) to form hydrogen bonds, which give rise to change the situation of polymer hydration. A decrease of the LCST has close connections with the number of equatorial hydroxy groups of sugars as additives. The LCST decrease in sugar solutions was regarded as the situation change of polymer hydration in the iceberg.

Poly(*N*-isopropylacrylamide) gel, poly(NIPAAm) gel, is well-known as thermosensitive gel deswollen above a lower critical solution temperature (LCST).[1–3] We have studied kinetically the deswelling process of poly(NIPAAm) gels using conventional[4] and freeze-dry-treated gels.[5,6] The treatment of a freeze-dry (FD) and hydration made the poly(NIPAAm) gel to accelerate the deswelling rate 10^3 times faster than that of the untreated gel.[7] As the kinetic parameters, the apparent activation energy (E_a) and the entropy of activation at 313 K (ΔS_{313}) for the rate-determining step in the process of gel deswelling were obtained in aqueous solutions containing alkali metal halides as probes.[4,5] E_a and ΔS_{313} were dependent on the concentration (C) of alkali metal halide in the solutions. E_a increased with increasing ΔS_{313}, and every curve for E_a vs C had a maximum at the same concentration of alkali metal halides as that for ΔS_{313} vs C. It was deduced that additive cations and anions could change the situation of polymer hydration, and also change the rate-determining step for the deswelling. From the above results, we considered that there should be a uniform rule between E_a and ΔS_{313} during deswelling in the presence of additives.

A hydrophilic glucose molecule is considered to interact easily with water clusters. This is because the stereospecific structure of glucose conforms to the chair-form resembles that of ice (tridymite structure).[8] It is expected from the above reasoning that the resemblance to the tridymite structure for sugars is dependent on the numbers of equatorial hydroxy groups in a sugar molecule. On the other hand, hydrated water around the hydrophobic isopropyl groups is known as ice-like clusters (iceberg). The deswelling rate of the gel was considered to change in the sugar solution due to the situation change of the iceberg. Accordingly, we selected sugars as probes to study the relationship among the kinetic parameters for deswelling. It is also known that the situation change of polymer hydration in the gel is connected with the LCST change.[2,5] It is worthwhile to survey the relationship between the LCST change in various sugar solutions and the resemblance of sugars to the tridymite structure.

In this paper, the relationship between the enthalpy of activation ($\Delta H^{\neq}$) and the entropy of activation ($\Delta S^{\neq}$) for gel deswelling is discussed from the viewpoint of compensation effects for the free energy of activation ($\Delta G^{\neq}$). Also, the relationship between the LCST change and additive sugars is discussed in connection with the situation of the polymer hydration in the gel.

Experimental

Materials. NIPAAm was purchased from Wako Pure Chemical. All other chemicals were of guaranteed grade or the best commercially available.

Preparation of Freeze-Dry-Treated Gels. Cylindrical poly(NIPAAm) gels (2 mm in inner diameter of the mold) were prepared within silicone tubes. Polymerization of the gel crosslinked by *N*,*N*′-methylenediacrylamide (MDA) [MDA/NIPAAm = 4/96 (mol/mol)] was initiated by ammonium peroxodisulfate, and accelerated by *N*,*N*,*N*′,*N*′-tetramethylethylenediamine. Gel rods swollen at 295 K were frozen at 243 K, and then freeze-dried.[7] The FD-treated gel rods were re-swollen in various concentrations of glucose, xylose, fructose, maltose, and saccharose solutions.

Kinetic Parameters. The deswelling rate of the gel was determined in the same way as described in our previous paper.[5] The temperature of the gel rod was jumped from 295 K to the desired temperature above the LCST. The length change of the gel rod was measured from pictures recorded by video-tape. The deswelling rate, $-\mathrm{d}(L/L_o)^3/\mathrm{d}t$, was determined from the slopes of straight lines given by plots of $(L/L_o)^3$ against time (t), where L_o and L are the lengths of the gel rod at 0, and *t* s, respectively. The initial deswelling rates, which are regarded as the deswelling rate constant (*k*),[5] were plotted according to the Arrhenius equation. The values of $\Delta H^{\neq}$, $\Delta S^{\neq}$, and $\Delta G^{\neq}$ were calculated from the slopes and intercepts of the plots for ln *k* vs 1/*T*.

LCST Measurement. The freeze-dried gel rods were reswollen in sugar solutions. The equilibrated length (*L*) of the gel rod was determined at every temperature elevated stepwise. The values of $(L/L_o)^3$ were plotted against the temperature. The LCST (T_L) was determined from the deswelling curve at the temperature where the slope is the steepest. According to our previous report,[5] depression of the LCST (ΔT) was defined as

$$\Delta T\,(K) = T_L - 307, \tag{1}$$

where 307 is the LCST of the poly(NIPAAm) gel in water. The LCST depressing constant (K_d)[5] was calculated as the slopes of straight lines, which were obtained from plots of ΔT against the sugar concentration.

Results and Discussion

Compensation Effect of $\Delta G^{\neq}$. It was reported in our previous papers[4–6] that the E_a vs *C* curves showed the same tendency as the ΔS_{313} vs *C* curves in every figure irrespective of the probes. In order to verify the compensation effects for $\Delta G^{\neq}$, the $T\Delta S^{\neq}$'s were plotted against the $\Delta H^{\neq}$'s for the deswelling process of conventional gels and the FD-treated gels in various alkali metal halide solutions[4,5] as shown in Fig. 1. The $T\Delta S^{\neq}$'s (T = 313 K, defined as ΔS_{313} in the previous papers) and $\Delta H^{\neq}$'s were cited from previous papers. The plots fell on straight lines. All slopes of the lines were approximately 1.0, and the values of $\Delta G^{\neq}$ calculated from each data at 313 K were +92–96 kJ mol^{-1} for the conventional gel and +81–84 kJ mol^{-1} for the FD-treated gel, respectively. These results indicate that the increase of $\Delta H^{\neq}$ is always accompanied by an increase of $\Delta S^{\neq}$ to keep $\Delta G^{\neq}$ nearly constant. A linear correlation between enthalpy and entropy changes has been observed for various solution processes in aqueous media.[9,10] However, there is no paper on the compensation effects concerning the volume-change process of the gel.

In the case of the conventional gel, we took the following view in our previous study.[4] The hydrophobic skin layer, formed at the gel surface after heating, obstructs to squeeze water out. Accordingly, the process of water release makes the rate-determining step for deswelling.[11] The skin barrier can probably be broken by inner pressure generated inside the gel due to deswelling. The deswelling pressure originally results from a collapse of the iceberg around the hydrophobic isopropyl groups. On the other hand, the FD-treated gel can exhaust water out with low deswelling pressure due to flexible partitioned polymer-network formed during the freezing process.[6,7] We considered that the polymer chains were gathered and condensed when the free water was frozen in the gel. A bundle of polymer chains for the FD-treated gel made frames and partitioned the gel, of which the frame could work as a water channel during deswelling.

According to our viewpoint, the difference in $\Delta G^{\neq}$ between the conventional and the FD-treated gel could be explained as follows: $\Delta G^{\neq}$ of the FD-treated gel was smaller than that of the conventional gel. This is because the FD-treated gel deswelled easier than the conventional gel. The conventional gel is considered to need a larger $\Delta G^{\neq}$ in order to obtain a higher deswelling pressure, resulting from a collapse of the iceberg.

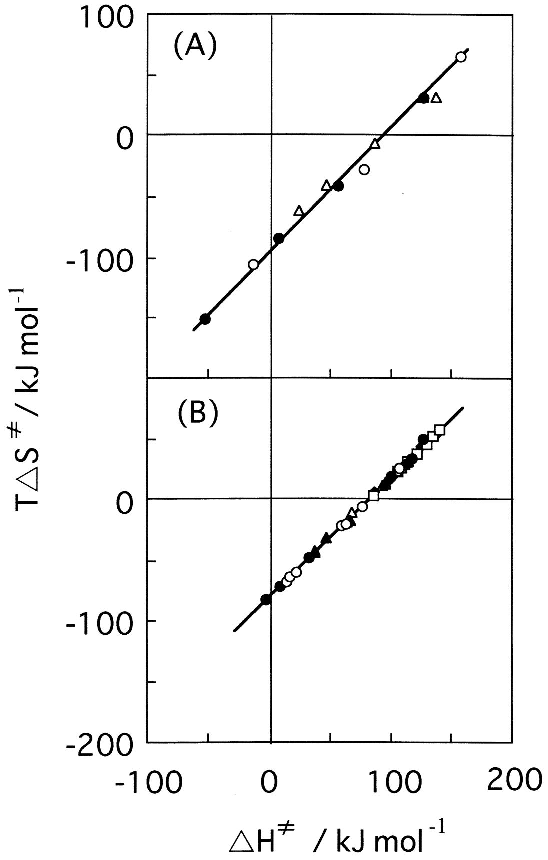

Fig. 1. Relationship between $T\Delta S^{\neq}$ and $\Delta H^{\neq}$ for deswelling of (A) the conventional and (B) the FD-treated gels. (A) The gels deswelled in water (△), NaCl (○), and KCl solution (●). (B) The gels deswelled in NaCl (○), KCl (●), LiCl (▲), NaF (△), NaBr (□), and NaI (◆) solutions. The data of $T\Delta S^{\neq}$ and $\Delta H^{\neq}$ were re-calculated from data with respect to the conventional[4] and the FD-treated gels.[5] The lines are expressed as (A) $T\Delta S^{\neq} = 0.98\Delta H^{\neq} - 93$, and (B) $T\Delta S^{\neq} = 0.98\Delta H^{\neq} - 81$, respectively.

Kinetic Parameters for Gel Deswelling in Sugar Solutions. Monosaccharides or disaccharides were selected as a hydrophilic probe in order to verify the relationship between the compensation effect of $\Delta G^{\neq}$ and the situation of polymer hydration. The deswelling rates of the gels were determined in glucose, fructose, saccharose, or maltose solution. The deswelling profiles in maltose solutions are shown as the representative results in Fig. 2. As described in our previous report,[5] the deswelling rates for the FD-treated gels could be regarded as a zero-order reaction with respect to $(L/L_o)^3$. Therefore, the deswelling rate constant (*k*) was obtained from the slope of the straight line drawn on the plots of $(L/L_o)^3$ vs time as shown in Fig. 2. Figure 3 shows that Arrhenius plots of ln *k* vs 1/*T* gave straight lines, from which the kinetic parameters, $T\Delta S^{\neq}$ and $\Delta H^{\neq}$, were obtained by a thermodynamic calculation. The plots of $T\Delta S^{\neq}$ vs $\Delta H^{\neq}$ give straight lines in Fig. 4, in the same manner as in the case of alkali metal salts (Fig. 1). The slopes of the lines (Fig. 4) were approximately 0.9 for both

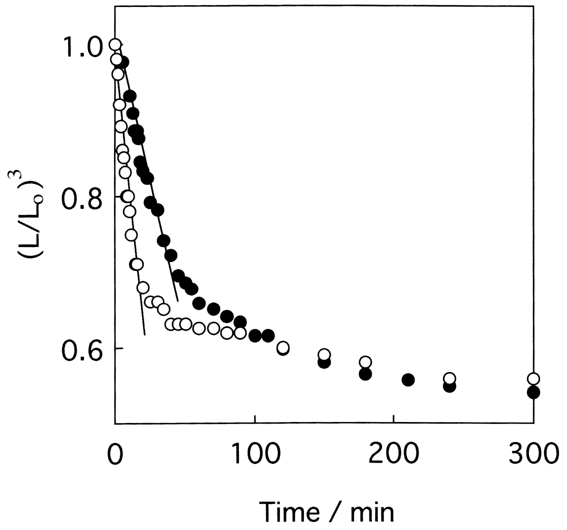

Fig. 2. Deswelling profiles of FD-treated poly(NIPAAm) gel. The gel rods equilibrated at 295 K were heated to 309 K (●), and 316 K (○) in 0.02 M maltose solutions.

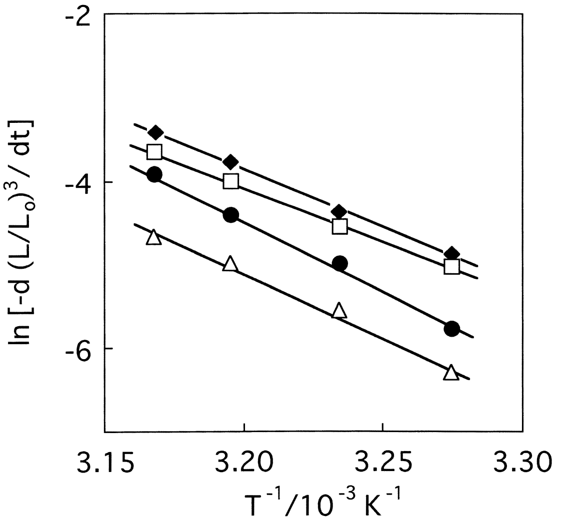

Fig. 3. The Arrhenius plots on the FD-treated gels in 0.01 M (△), 0.02 M (●), 0.1 M (◆), and 0.2 M maltose solutions (□).

mono- and disaccharides, and the $\Delta G^{\neq}$'s for the deswelling process calculated were +81–99 kJ mol^{-1}.

Since the sugar concentration acts as a functional factor in the kinetic parameters ($\Delta H^{\neq}$ and $\Delta S^{\neq}$), it is deduced that sugar molecules interact with the water clusters; this interaction may influence the dehydration rate of the hydrated polymers. $\Delta H^{\neq}$ and $\Delta S^{\neq}$ in water were obtained to be +22 kJ mol^{-1} and −190 J K^{-1} mol^{-1}, respectively. On the other hand, both maxima of $\Delta H^{\neq}$ (+140 kJ mol^{-1}) and $\Delta S^{\neq}$ (+140 J K^{-1} mol^{-1}) appeared at around 0.02 M for a maltose solution.

Kawasaki et al. measured the activities of water molecules in sugar solutions and discussed the relationship between the chemical potential of the water molecules in sugar solutions and the saccharide-induced volume phase transition of poly(NIPAAm) gel.[12] According to the paper, they concluded that the saccharide-induced volume phase transition of poly(NIPAAm) gels took place mostly as a result of the dehydration of the networks caused by the saccharide. It is plausible that the decrease of the chemical potential of water owing to adding sugars destabilizes the hydration of polymer chains and is responsible for the decrease of structured water with respect to hydrophobic hydration.

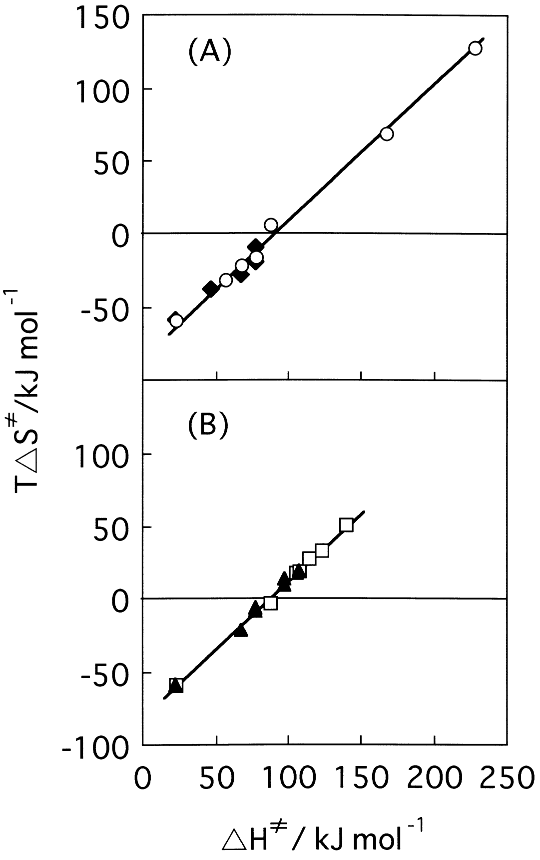

Fig. 4. Relationship between $T\Delta S^{\neq}$ and $\Delta H^{\neq}$ for deswelling of the FD-treated gels. (A) The gels deswelled in 0–0.3 M glucose (○), and fructose solutions (◆). (B) The gels deswelled in 0–0.3 M maltose (□), and saccharose solutions (▲). The lines are expressed as (A) $T\Delta S^{\neq} = 0.91\Delta H^{\neq} - 81$, and (B) $T\Delta S^{\neq} = 0.94\Delta H^{\neq} - 82$, respectively.

The $\Delta H^{\neq}$ and $\Delta S^{\neq}$ have maxima at around 0.02 M for the maltose solution, and decrease with increasing maltose concentration. Therefore, $\Delta H^{\neq}$ decreased with decreasing the chemical potential of water molecules in the presence of maltose ($C > 0.02$ M). A smaller $\Delta H^{\neq}$ means that less energy is necessary to break the water clusters around the hydrophobic moiety of the polymer. Since the smaller $\Delta S^{\neq}$ during the dehydration process results from dissociation of the smaller clusters of water, a $\Delta H^{\neq}$ decrease is always accompanied by a $\Delta S^{\neq}$ decrease.

It is known that the conformation of water clusters is similar to that of tridymite SiO_2, of which the distance between adjacent oxygen atoms is about 0.29 nm. On the contrary, the distance (0.286 nm) between adjacent oxygen atoms of β-D-glucopyranose is approximately equal to the distance of tridymite.[8] Equatorial hydroxy groups of β-D-glucopyranose could form hydrogen bonds easily with water molecules to construct

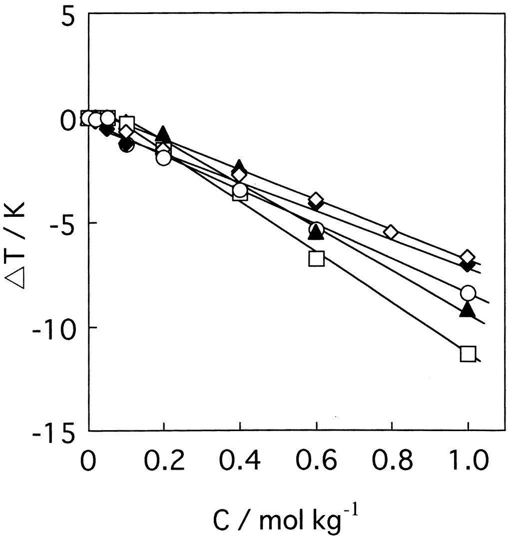

Fig. 5. Relationship between ΔT and concentration of sugars: fructose (◆), xylose (◇), glucose (○), saccharose (▲), and maltose (□). ΔT was given by Eq. 1.

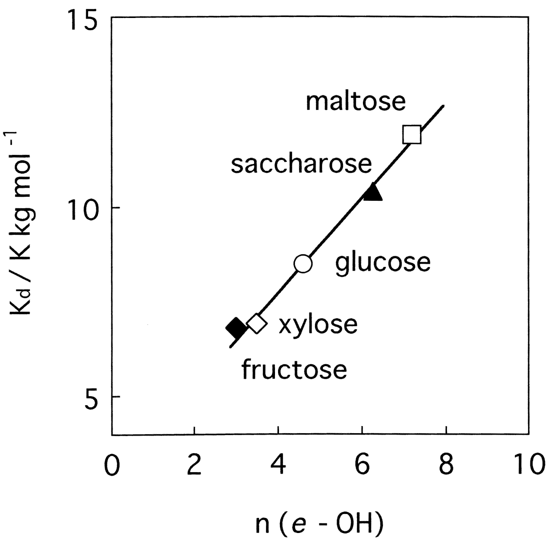

Fig. 6. Relationship between the number of equatorial OH groups in sugars [n(*e*-OH)] and the LCST depressing constant (K_d). The values of n(*e*-OH) were cited from the previous report.[14]

the tridymite structure. Therefore, it is plausible that the additive sugar molecules form hydrogen bonds with water clusters around the hydrophobic isopropyl groups in the gel.

Effects of Sugars on the LCST. ΔT was calculated by means of Eq. 1 with T_L obtained from deswelling profiles in various concentrations of sugar. Figure 5 shows plots of ΔT vs the sugar concentration. The plots converge at 307 K below 0.1 mol kg^{-1} sugars. The LCST remained constant in a region of lower than 0.1 mol kg^{-1} sugars, but the kinetic parameters, such as $\Delta H^{\neq}$ and $\Delta S^{\neq}$, were influenced by the sugar concentration. The plots fell on straight lines, where the sugar concentrations were above 0.1 mol kg^{-1}. The LCST, $\Delta H^{\neq}$, and $\Delta S^{\neq}$ decreased with increasing sugar concentration above 0.1 mol kg^{-1}.

It was considered that the additive sugar molecules could interact with the iceberg to form strong hydrogen bonds at the swelling-state of the gel. However, excess sugar can possibly work as a destroyer for the iceberg by forming hydrogen bonds. Sugar molecules act as an adhesive between water clusters at a lower concentration of sugar than 0.1 mol kg^{-1}, and as an iceberg destroyer at concentrations higher than 0.1 mol kg^{-1}.

The LCST depressing constant (K_d), determined as the slope of the line drawn in Fig. 5, was studied in connection with n(*e*-OH) as a constant for the individual sugar. n(*e*-OH) is defined as the mean number of OH groups for a sugar molecule in aqueous solutions with consideration of the various conformation of sugars;[8,13–15] i.e., the n(*e*-OH) of each sugar expresses the extent of similarity to the structure of the tridymite cluster. As shown in Fig. 6, a linear relationship appeared between K_d and n(*e*-OH). We cited all data of n(*e*-OH) in Fig. 6 from a paper by Uedaira et al.[14] Since maltose is a disaccharide derived from two molecules of glucose, it is reasonable that the n(*e*-OH) of maltose is roughly two-times larger than that of glucose. The K_d's of fructose, glucose, and maltose obtained were 6.8, 8.5, and 11.9, respectively.

The LCST of poly(NIPAAm) gel was supposed to reflect a distinctive temperature for the collapse of the iceberg.[16,17] It has been reported that the LCST of poly(NIPAAm) gel underwent changes in the presence of low molecular additives, such as salts and alcohols, of which hydration gave rise to a situation change of the polymer hydration in the gel.[2,18–20] At higher concentration of sugars than 0.1 mol kg^{-1}, the structure-breaking of the iceberg was caused by the hydrogen bonds due to the OH groups of the excess sugar molecules. Because n(*e*-OH) of maltose is the highest among five sugars, maltose may break the iceberg effectively at the minimum concentration of sugar. On the other hand, a five-membered ring of fructose may not interact with the tridymite cluster of the iceberg as easy as a six-membered ring of glucose, and give the lowest K_d.

Conclusion

A compensation effect between $\Delta H^{\neq}$ and $\Delta S^{\neq}$ was observed for the deswelling of poly(NIPPAm) gel in aqueous solutions of various salts or sugars. The $\Delta G^{\neq}$'s were nearly constant for the conventional gel (+92–96 kJ mol^{-1}) and the FD-treated gel (+81–84 kJ mol^{-1}) in various alkali metal halide solutions. This result indicates that the gel deswelling process is not spontaneous because $\Delta G^{\neq} > 0$, and the FD-treated gel could deswell easier than the conventional gel.

The results in sugar solutions are similar to those in alkali metal halide solutions for the compensation effect of $\Delta G^{\neq}$. The situation change of polymer hydration in the gel was deduced as the change of the LCST in sugar solutions, since the equatorial OH groups of the sugar molecule can form hydrogen bonds with the iceberg. Larger $\Delta H^{\neq}$ and $\Delta S^{\neq}$ are necessary in order to break the strong hydrogen bonds in the collapse process of the iceberg. The compensation effect of $\Delta G^{\neq}$ is considered to originate from the collapse of the iceberg.

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