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Catalysis by surfactant aggregates in aqueous solutions

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Abstract Catalysis of organic reactions by unfunctionalized surfactant aggregates (micelles, vesicles) in aqueous solution is largely determined by medium effects induced at the micellar binding sites and by entropy effects due to compartimentalization. The efficiency of these catalytic effects responds to changes in size and shape of the surfactant assemblies. These effects are discussed for a series of 1-alkyl-4-alkylpyridinium halide surfactants using the highly medium dependent decarboxylation of 6-nitrobenzisoxazole-3-carboxylate (6-NBIC) as a model reaction. The decarboxylation of 6-NBIC is also strongly catalyzed in the presence of hydrophobically modified poly(alkylmethyldiallylammonium bromides), provided that the flexibility of the polymer main chain allows the formation of hydrophobic microdomains. A test for possible substrate orientation effects on the efficiency of micellar catalysis was performed for the reaction of the sulfonates $R_1SO_2CH_2OSO_2R_2$ with OH^- ions in the presence of CTAB micelles. Large variations in the hydrophobicities of R_1 and R_2 led to only small changes in the second-order rate constant for reaction in the micellar pseudophase. These results are in accord with recent insights into the structure of micellar aggregates.

INTRODUCTION

The enormous recent interest in supramolecular chemistry, i.e. the chemistry of molecular organized assemblies, reflects the current emphasis on noncovalent intermolecular interactions and molecular recognition. In this field, chemical research has entered into new dimensions leading to the design and understanding of hierachies of physically associated molecules. Surfactant self-organization constitutes a major area of interest. Particularly micelles and vesicles have received great attention. The relation between surfactant structure and morphology of the aggregate as well as the analysis of the different molecular interactions determining the properties of the aggregate are now beginning to be understood (ref.1). In this lecture I will briefly dwell upon some salient features of catalytic effects exercised by micelles in aqueous solution. The discussion will focus on work carried out in the author's laboratory and, consequently, the reader should consult recent reviews for a more comprehensive treatise of micellar catalysis and inhibition (ref.2).

Catalysis by micelles involves at least three main steps: (i) binding of the substrate(s) to the micelle, (ii) the actual chemical transformation in the micelle (usually at the micellar surface) and (iii) release of product(s). If we restrict ourselves here to nonfunctionalized surfactant micelles, the actual micellar rate effect is caused by a composite of noncovalent interactions

between the micelle on one hand and the reactant(s) and activated complex on the other hand. Since the micellar solution can be viewed as a microheterogeneous system, the micelle-catalyzed reaction is always influenced by a (complicated) local medium effect, characteristic of the "surface micropolarity" of the micelle. For unimolecular reactions, this is the sole effect on the rate constant for the process. The kinetics of these reactions are usually analyzed in terms of Menger's "enzyme model" (ref.3). One then obtains the first-order rate constant for the reaction in the micellar pseudophase (k_m) and the (kinetic) binding constant (K_m) of the substrate. Substrate binding constants can be determined independently (*e.g.* by ultrafiltration using an artificial kidney, ref.4) and usually these constants are in satisfactory agreement with the kinetic binding constants. The micellar catalytic efficiency is conveniently expressed in k_m/k_w in which k_w is the first-order rate constant in water in the absence of surfactant.

For bimolecular reactions there is an additional favorable entropy effect associated with binding of the two reactants within the micellar reaction volume ("compartimentalization"). A popular vehicle for kinetic analysis is the pseudophase ion-exchange (PPIE) model (ref.5), most frequently employed for S_N2 reactions and related processes involving a neutral substrate and an ionic nucleophile. If the nucleophile (X) is different from the surfactant counterion (Y), the ion exchange parameter K^Y_X is an important parameter in the analysis. For bimolecular reactions the efficiency of micellar catalysis is less easy to quantify than for unimolecular reactions, since k_m/k_w depends on an appropriate choice of the micellar reaction volume (ref.2c).

Rate accelerations by micelles formed from nonfunctionalized surfactants (k_m/k_w) are usually not higher than a factor of ca. 1000 (ref.2). Really dramatic catalytic efficiencies, sometimes approaching those of enzymes, and high turnover capabilities, are obtained by using functionalized surfactant micelles ("enzyme mimics") (ref.6). The use of micellar catalysis for synthetic purposes is associated with practical separation problems, but promising results have been obtained (ref.7). Industrial applications are to be envisaged.

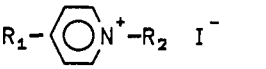
DECARBOXYLATION CATALYZED BY 1-ALKYL-4-ALKYLPYRIDINIUM HALIDE MICELLES. EFFECT OF THE SIZE AND SHAPE OF THE MICELLE

The morphology of a surfactant aggregate largely depends on the molecular architecture of the surfactant monomer (ref.1). An elegant analysis of packing constraints in the core of the essembly has been framed in terms of geometric considerations which can be (semi)quantitatively expressed in a packing parameter in which V is the volume of the hydrocarbon chain of the surfactant,

$$P = V/a_o.l_c$$

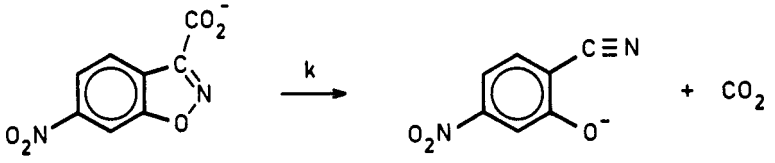
a_o is the optimal surface area per monomer, and l_c is the critical chain length (ref.1c). Depending on the magnitude of P, the surfactant preferably forms spherical micelles ($P<0.33$), threat-like (or rod-like) micelles ($0.33\ P<0.5$) or (closed) bilayers ($0.5<P<1.0$).

Recently, we have synthesized a large series of 1-alkyl-4-alkylpyridinium halides in a study of the relation between surfactant structure and aggregate morphology (ref.1d,1e,8). The availability of these surfactants offered the possibility to examine the catalytic effects of their aggregates as a function of changes in surfactant structure including changes in chain length



(R_1; 1 - 4), counterion (4,5), chain stiffness (6), chain branching (R_1 = C_{12}-alkyl; 4, 7 - 11) and length of the R_2 group (4, 12 - 15). For the micelles an

estimate of the micropolarity in the Stern region can be obtained from the position (λ_m^{CT}) and transition energy (E_T) of the intramolecular charge-transfer (CT) absorption band (ref.1d,1e,8). As a model reaction we have choosen the highly medium dependent, unimolecular decarboxylation of 6-nitrobenzisoxazole-3-carboxylate (6-NBIC) (ref.9).



This reaction is akin to many other decarboxylation reactions, including those occurring in biological systems (ref.10). The large medium effects are governed primarily by hydrogen-bonding interactions in the initial state and London-dispersion interactions of the charge-delocalized, highly polarizable activated complex. Of course, electrostatic interactions play an important role in electrolyte solutions and in catalytic effects of cationic surfactant aggregates. As anticipated, nonionic micelles have only a small effect on k_{obs} whereas anionic micelles repel the negatively charged substrate (ref.11). Table 1 summarizes our results. All surfactant aggregates speed the reaction quite effectively (k_w = 7.6 x $10^{-6}s^{-1}$). The k_{obs} values as a function of surfactant concentration were analyzed using Menger's kinetic model (ref.3). The values for K_m/n (n is the micellar aggregation number) obtained by this procedure are listed in Table 1. The first conclusion is, that for the micelles (1-10, 12-15) the catalytic effects are of the same order of magnitude (for 1, k_m/k_w = 42, for 15, k_m/k_w = 129). A substantially larger rate effect is found for the vesicles formed from 11 (k_m/k_w = 224). The variation in k_m/k_w by a factor of only 3 in the micellar series indicates that 6-NBIC undergoes decarboxylation at cationic binding sites that differ relatively little in (average) micropolarity. This is quite interesting since the alkyl chain packing varies considerably in the various aggregates (ref.12). In fact, the micropolarity in the Stern layer of the micelles lies in between that for methanol (k_{MeOH} = $2.5x10^{-4}s^{-1}$) and ethanol (k_{EtOH} = $10x10^{-4}s^{-1}$). This conclusion is in accord with that based on λ_m^{CT} and the transition energy, E_T (for 2-4,6,7,9,10,12,13 and 15, λ_m^{CT} = 286±1 nm, E_T = 100.3 kcal.mol^{-1}; for 8, λ_m^{CT} = 293 nm, E_T = 97.9 kcal.mol^{-1}; for 14, λ_m^{CT} = 290 nm, E_T = 98.9 kcal.mol^{-1} (ref.8). For EtOH, λ_m^{CT} = 288 nm, E_T = 99.6 kcal.mol^{-1}).

Returning now to the data in Table 1, we conclude that k_m/k_w does not depend on the alkyl chain length (1 - 4; k_m = $3.4±0.3x10^{-4}s^{-1}$). However, K_m/n and also K_m, since n decreases going to shorter chain lengths, decreases strongly upon shortening of R_1. This effect has been observed previously, but a detailed understanding is lacking. Binding of 6-NBIC to the micelle will respond to electrostatic and hydrophobic interactions, but one may wonder whether undulation forces (ref.13) also affect K_m. The slightly higher k_m for 5 as compared with that for 4 can be explained in terms of the smaller degree of counterion binding for Br^-, leading to an increased micellar surface charge. Stronger electrostatic interactions are probably also reflected in the higher K_m/n for 5.

Perhaps unexpectedly, the micellar catalytic effect was hardly influenced by the introduction of a rigid acetylenic segment in the center of the 4-dodecyl substituent (6). However, compared to 4, the value of K_m/n is reduced sixfold. This may be rationalized by assuming that, because of the increased stiffness of the alkyl chain, less alkyl chain ends reside at the micellar surface (ref.12), thereby reducing the contribution of hydrophobic interactions to the binding of 6-NBIC.

The catalytic effects of the spherical micelles formed from the branched surfactants 7 - 10 are slightly larger than those for 4 but vary little within the series. The K_m/n values are also rather similar to that for 4, but K_m will be decreased because quite generally n is lower for micelles formed from branched surfactants.

TABLE 1. Decarboxylation of 6-NBIC catalyzed by micelles of 1-alkyl-4-alkylpyridinium halide surfactants at 30.00°C and pH 11.3

	Surfactant R_1	R_2	X^-	$k_m \times 10^4$ s^{-1}	K_m/n M^{-1}	k_m/k_w
1	$n\text{-}C_8H_{17}$	CH_3	I^-	3.2	60	42
2	$n\text{-}C_{10}H_{21}$	CH_3	I^-	3.3	730	43
3	$n\text{-}C_{11}H_{23}$	CH_3	I^-	3.7	1200	49
4	$n\text{-}C_{12}H_{25}$	CH_3	I^-	3.5	1200	46
5	$n\text{-}C_{12}H_{25}$	CH_3	Br^-	4.4	1800	58
6	$-(CH_2)_4C{\equiv}C\text{-}C_6H_{13}\text{-}n$	CH_3	I^-	4.1	200	54
7	$-CH(CH_3)(n\text{-}C_{10}H_{21})$	CH_3	I^-	3.9	1700	51
8	$-(CH_2)_8C(CH_3)_3$	CH_3	I^-	4.2[a]	1400[a]	55
				6.2[b]	8200[b]	82
9	$-(CH_2)_7CH(C_2H_5)_2$	CH_3	I^-	4.6	990	61
10	$-(CH_2)_5CH(n\text{-}C_3H_7)_2$	CH_3	I^-	4.0	930	52
11[c]	$-CH_2CH(n\text{-}C_5H_{11})_2$	CH_3	I^-	17	170	224
12	$n\text{-}C_{12}H_{25}$	C_2H_5	I^-	5.2	1500	68
13	$n\text{-}C_{12}H_{25}$	$n\text{-}C_3H_7$	I^-	6.2	1700	82
14	$n\text{-}C_{12}H_{25}$	$i\text{-}C_3H_7$	I^-	8.6	880	113
15	$n\text{-}C_{12}H_{25}$	$n\text{-}C_4H_9$	I^-	9.8	600	129

[a] Spherical micelles. [b] Rod-like micelles. [c] Vesicles.

Variation of the 1-alkyl substituent (4,12 - 15) results in k_m values which increase with the chain length. A similar dependence was found for micelles formed from cetyltrialkylammonium bromides (ref.14). Since λ_m^{CT} is virtually constant (except for 14, vide supra), the kinetic effect may stem from a decreased hydration of 6-NBIC if the length of R_1 is increased.

The above discussion is restricted to spherical micelles. However, those surfactants which possess relatively high P values ($0.33<P<0.5$, vide supra) have an increased tendency to form rod-like micelles as evidenced by a low critical rod concentration (crc). For example, 8 undergoes a transition to rod-like micelles at 30×10^{-3}M as evidenced by substantial broadening of the alkyl group NMR resonance (ref.1d,1e,8). Interestingly, the micellar effect on the decarboxylation of 8 increases abruptly around the crc. The catalytic efficiency of the rod-like micelles is 1.5 times that of the spherical micelles, indicating that the micropolarity at the binding sites of 6-NBIC is further reduced upon the transition to the rods. Surfactant 11 preferably forms vesicles, and these lamellar aggregates are still better catalysts than the rod-like micelles (Table 1). The k_{obs} value upon complete binding to the vesicles is similar to that found for decarboxylation of 6-NBIC in carbon tetrachloride. Since λ_m^{CT} is approximately equal for micelles and vesicles, the higher catalytic effect for the vesicles is probably the result of a different location of the probe leading to a smaller micropolarity and a concomitant higher shielding of 6-NBIC from water.

DECARBOXYLATION OF 6-NBIC CATALYZED BY POLYSOAPS

In aqueous solution, sufficiently hydrophobic alkyl chains, bound to the monomeric unit of polyelectrolytes, may associate intramolecularly to form hydrophobic microdomains (ref.15). As a result, these types of polyelectrolytes ("polysoaps") reside in a compact coil as supported by viscosity measurements and fluorescence probe studies. It is interesting to compare the catalytic

effects of conventional micelles with those induced by the "intramolecular micelles" in the polysoap solutions. To this end, we have synthesized a series of homo- (Pol C-n) and copolymers (Copol C n-m(x/y)) via cyclo(co)polymerization of alkylmethyldiallylammonium bromides (Fig.1). Side-chain aggregation leading to the formation of hydrophobic microdomains was shown by UV/VIS spectral data of hydrophobic dyes bound to the domains (ref.16) and by studies using pyrene as a fluorescence probe (ref.17). Efficient intramolecular micellization did only occur for those polysoaps which possess a polymer main chain of sufficient flexibility for the formation of a compact-coil conformation.

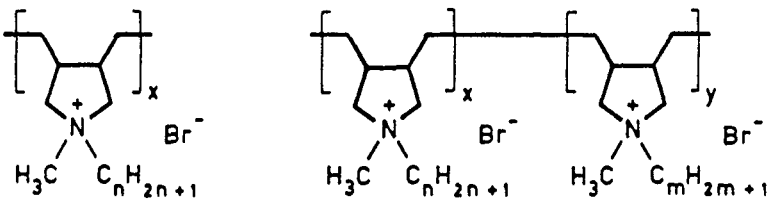


Fig.1. Cationic polysoaps

Kinetic data for decarboxylation of 6-NBIC in aqueous solution in the presence of the homo- and copolymers are listed in Table 2. The polysoaps Copol C 1-12 (87/13), Copol C 4-12 (97/3) and Copol C 5-12 (98/2) are extraordinarily effective catalysts. The kinetics and dependence of the rate constant on

TABLE 2. Decarboxylation of 6-NBIC catalyzed by polysoaps at 30.00°C and pH 11.3

(Co)polymer	$k_p x10^4$ s^{-1}	K_p M^{-1}	k_p/k_w
Copol C 1-12 (87/13)[a]	7700	52	1045
Copol C 4-12 (97/3)[a]	4300	59	585
Copol C 5-12 (98/2)[a]	2900	80	395
Copol C 1-8 (61/39)[b]	1300		176
Copol C 1-8 (68/32)[b]	400		54
Copol C 1-8 (77/23)[b]	100		14
Pol C-1[c]	28		3.8
Pol C-5[c]	76		10.3

[a] k_p and K_p according to the Menger-Portnoy model (ref.3). [b] At $40x10^{-3}$ unit M. [c] At $25x10^{-3}$ unit M.

polysoap concentration (saturation behavior) are similar to those for conventional micelle-catalyzed reactions. Application of Menger's enzyme model (ref.3) affords rate constants (k_p) under conditions of complete binding of 6-NBIC to the domains as well as the actual substrate binding constants K_p. The catalytic effectiveness, expressed in k_p/k_w, is much higher than that for the reactions listed in Table 1 and, in fact, for several other types of cationic micelles and hydrophobically modified polyelectrolytes (ref.18). For example, for the popular cationic surfactant cetyltrimethylammonium bromide (CTAB), k_m/k_w amounts to only 48 (ref.19). It is clear that 6-NBIC, bound to the hydrophobic microdomains, senses a very favorable microenvironment for decarboxylation. This may be primarily caused by strong electrostatic interactions at the binding sites which could also explain the high K_p values. Initially, it was not anticipated that for the copolymers Copol C n-m (x/y) elongation of n (Me → n-Bu → n-Pent) would lead to a decrease of their catalytic effects (Table 2). However, in accord with spectroscopic evidence (ref.16), it is likely that

microdomain formation is partly governed by the flexibility of the copolymer main chain. An increase of the length of the second alkyl substituent at nitrogen reduces this flexibility and hampers intramolecular association of the alkyl chains. However, compact coil formation will also depend on the molar percentage of the n-dodecyl chain in the three copolymers. Finally, an increase of the length of the second alkyl substituent at the nitrogen atom may induce unfavorable steric effects on the catalytic efficiency of the polysoap. In the Copol C 1-8 series, a decrease of the molar percentage of the n-octyl chain greatly reduces the catalytic effect on the decarboxylation, whereas the homopolymers Pol C-1 and C-5 are still less effective catalysts. In these cases the kinetic data were not processed in terms of the enzyme model. Current research focuses on a detailed analysis of the high catalytic effects of these and other types of polysoaps in aqueous solution.

SUBSTRATE BINDING TO MICELLES

Micellar catalysis critically depends on the interactions of the micelle with the substrate(s) and the activated complex. This is an extremely complicated problem because a number of different interactions are involved including those associated with the headgroup of the surfactant, different segments of the alkyl chain and the counterions. All these interactions are strongly modulated by hydration effects. The complexity of the problem is further increased by the possibility that different binding sites (corresponding with different substrate orientations) are involved and by the highly dynamic character of the micellar surface (connected with appealing concepts like undulation forces and steric protrusion forces). I can only touch on this problem here and refer to recent studies in which rates and regioselectivities of synthetically useful organic reactions in micellar media are modified by differences in the hydrophilic/hydrophobic character of the substrate (ref.7b). Previously we have made an attempt to affect substrate orientation in the micelle via systematic variation of the structure of the substrate (ref.20,21). This was done for the reaction of the sulfonylmethyl sulfonates **16a-g** with hydroxide ions in the presence of CTAB micelles at 50°C. The reaction mechanism involves nucleophilic attack of OH^- ion at the sulfonate sulfur atom with considerable bond making in the activated complex (ref.22). The S_N-2-type process is speeded by CTAB micelles (rate accelerations 7-14 times). The observed rate constants were analyzed in terms of the PPIE model (<u>vide supra</u>). The binding constants for the

$$\underset{\textbf{16a-g}}{R_1SO_2CH_2OSO_2R_2} + 2\ OH^- \xrightarrow{k} R_1SO_2^- + CH_2O + R_2SO_3^- + H_2O$$

sulfonate (K_m) were either obtained by ultrafiltration using Thomapore tubular membranes or were estimated using Rekker's hydrophobic fragmental constants (ref.23). The data in Table 3 show that the catalysis is due to compartimentalization of the neutral and anionic reactant in the micellar reaction volume. The actual rate constant for the nucleophilic substitution at the micellar binding sites (k_m) is <u>lower</u> than that for the same reaction in the bulk aqueous phase (k_w). The sulfonate binding constants K_m are quite sensitive to changes in the overall hydrophobicity of the sulfonate.

Returning now to the problem of substrate orientation, it was anticipated that the reaction site (the sulfonate sulfur atom) for those sulfonate *with a hydrophobic R_2 substituent* would be pulled into the micellar core, away from the micellar surface. Since the second reactant, the strongly hydrated OH^- anion, necessarily remains in the aqueous Stern layer, a decrease in the efficiency of micellar catalysis would result. If R_2 is only weakly hydrophobic (<u>i.e.</u> sulfonate **16d**), the sulfonate sulfur atom is expected to reside in the aqueous

Stern region and readily available for nucleophilic attack by OH^-. The data in Table 3 clearly show that these expectations are not borne out in practice. Since the ratio k_m/k_w still contains a factor determined by the different propensities of the sulfonate to respond to changes in micropolarity of the reaction medium, we have made an attempt to filter this factor out. To this end

TABLE 3. CTAB-catalyzed reaction of the sulfonates **16a-g** with hydroxide ions at 50°C.[a]

Sulfonate		$k_w x10^3$	$k_m x10^3$	K_m	$k_{dw} x10^{3b}$	k_{dw}/k_w[c]	k_m/k_{dw}[d]
R_1	R_2	$M^{-1}s^{-1}$	$M^{-1}s^{-1}$	mM^{-1}	$M^{-1}s^{-1}$		
16a p-$CH_3C_6H_4$	p-$CH_3C_6H_4$	25	3.5	3.3	5.4	0.18	0.8
16b p-$CH_3C_6H_4$	p-$CH_3(CH_2)_3C_6H_4$	21[e]	3.7	12	4.3	0.17	1.0
16c p-$CH_3C_6H_4$	p-$CH_3(CH_2)_7C_6H_4$	19	3.8	70	4.0	0.18	1.1
16d p-$CH_3C_6H_4$	CH_3	8.2	2.2	0.16	6.3	0.67	0.4
16e p-$CH_3C_6H_4$	$CH_3(CH_2)_3$	3.0	1.1	0.60	1.5	0.41	0.85
16f p-$CH_3C_6H_4$	$CH_3(CH_2)_7$	3.1	1.2	3.5	1.3	0.35	1.1
16g $CH_3(CH_2)_7$	p-$CH_3C_6H_4$	39	7.0	3.5	10	0.22	0.8

[a] Kinetic data analyzed according to the PPIE model. [b] Second-order rate constant in 1,4-dioxane-water (n_{H2O} = 0.83) in the presence of 0.3 M NaOH. [c] Calculated using k_w values determined in the presence of 0.3 M NaOH. [d] Calculated from $k_m k_w^{-1}(k_{dw}k_w^{-1})^{-1}$.

we have measured second-order rate constants for the reaction in 1,4-dioxane-water (k_{dw}) at a solvent composition (mole fraction of water, n_{H2O} = 0.83) for which the dielectric constant is similar to that at the surface of CTAB micelles (ϵ = 30, ref.24). Now k_m/k_{dw} should provide an approximate measure for orientational effects in the micellar catalyzed process. However, the k_m/k_{dw} values in Table 3 reveal no evidence for the supposed orientation effect or difference in depth of substrate penetration into the micelle. Even for sulfonates in which R_1 and R_2 differ greatly in hydrophobicity, the k_m/k_{dw} values are hardly different. Since the K_m values exhibit large variations with hydrophobicity of the sulfonates, the data appear to suggest that the apolar reactants bind *onto* the micelle rather than *into* the micelle. This conclusion is in line with recent models for the structure of micelles which imply the presence of hydrophobic binding sites at the micellar surface (ref.25). Additional support for the above explanation is found in the recent observation (ref.26) that the catalytic effect of CTAB micelles on the reaction of sulfonates **18** with OH^- ions is strongly reduced by binding of (low molecular weight) poly(propylene oxide) (PPO; 0.5 $g.dl^{-1}$) to the surface of the micelles. Kinetic analysis in terms of the PPIE approach suggests that part of the micellar-bound sulfonate is shielded by PPO for nucleophilic attack by OH^- ions.

EPILOGUE

Micelles and other types of surfactant aggregates are quite effective catalysts for many organic reactions. The catalytic effects are qualitatively understood, with compartimentalization and medium effects being major features of the catalysis. However, we are still far off from a quantitative understanding of micellar kinetic effects, largely because a complex composite of noncovalent interactions is involved in the binding of the reactant(s) and the activated complex. Problems include a quantitative analysis of the binding of apolar molecules to the fluid and highly dynamic micellar surface, and complexities due to local distortion of the aggregate induced by substrate binding, hydration effects (including those on the properties of counterions), the involvement of different substrate binding sites and effects due to aggregate polydispersity and the precise definition of the micellar reaction volume.

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