Russian Journal of General Chemistry, Vol. 71, No. 3, 2001, pp. 383–388. Translated from Zhurnal Obshchei Khimii, Vol. 71, No. 3, 2001, pp. 419–425.

Micelle-Forming and Catalytic Properties of *n*-Alkyl(2-hydroxyethyl)dimethylammonium Bromides in the Phosphorylation of Tetrakis(dimethylaminomethyl)-calixresorcin[4]arene

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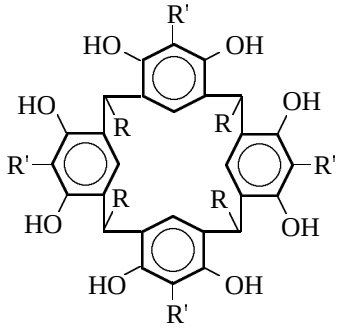
Received June 7, 2000

Abstract — Micelle formation by *n*-alkyl(2-hydroxyethyl)dimethylammonium bromides in chloroform was studied by dielcometric titration and kinetic method. Increase in the length of the hydrocarbon chain leads to reduced critical micelle concentration. The region of structural reorganization of micelles was determined. *n*-Alkyl(2-hydroxyethyl)dimethylammonium bromides catalyze phosphorylation of tetrakis(dimethylaminomethyl)calixresorcin[4]arene. The catalytic activity of micelles depends on the hydrophobic properties and concentration of the surface-active substance, as well as on structural features of its aggregates.

The presence in a low-polar nonaqueous medium of a cationic surface-active substance possessing a 2-hydroxyethyl group leads to a considerable (up to two orders of magnitude) increase in the apparent rate constants for nucleophilic substitution in phosphorus acid esters and also changes the relative contributions of possible reaction pathways [1, 2]. The effect of surface-active substances on the rate and mechanism of such processes is generally attributed to formation of reversed micelles and transfer of the reaction zone from the bulk of solution into micelle pseudophase. However, the micelle formation process, the possibilities for structural variation of aggregates formed by hydroxyethyl-containing surface-active substances, and the relation between the latter factor and catalytic activity of micelles were almost not studied [1, 2].

Helpful information on the nature of association processes in liquid medium can be obtained by dielcometric titration and mathematical modeling. Dielcometric titration [3] gives concentration dependences of the dielectric permittivity (ε) of multicomponent mixtures. This technique was successfully applied to determination of critical micelle concentration (CMC) in solutions of non-ionogenic surface-active substances [4, 5]. Unlike graphical analysis [3], mathematical processing of experimental concentration dependences of physical parameters allows reliable determination of such association parameters as aggregation number, association constant, and degree of accumulation even when no significant bend is present on the respective plot [6].

In the present work we used dielcometric titration, mathematical modeling, and spectrophotometric technique to examine micelle formation in chloroform solutions of *n*-alkyl(2-hydroxyethyl)dimethylammonium bromides **I**–**III** (alkyl is *n*-$C_{12}H_{25}$, $C_{15}H_{31}$, or $C_{18}H_{37}$) in the presence and in the absence of tetrakis-(dimethylaminomethyl)calixrezorcin[4]arenes **IV** and **V**. We also studied the effect of micelle formation on the reaction of calixarene **IV** with *p*-nitrophenyl bis-(chloromethyl)phosphinate.



R = *n*-C_nH_{2n+1}, *n* = 9 (**IV**), 11 (**V**); R' = $CH_2N(CH_3)_2$.

Micelle formation by compounds **I**–**III** can be described by Eq. (1).

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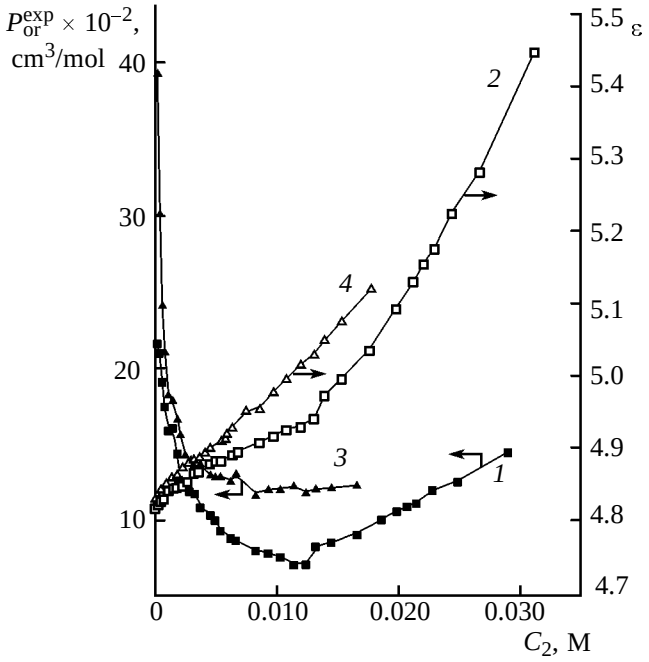


Fig. 1. Plots of (*1*, *3*) orientational polarization and (*2*, *4*) dielectric permittivity versus concentration of 2-hydroxyethyl(dimethyl)pentadecylammonium bromide (**II**) in chloroform at 20°C (*1*, *2*) in the absence and (*3*, *4*) in the presence of 5×10^{-4} mol/l of calixarene **V**.

$$N\,\mathrm{SAS} \overset{K_{as}}{\rightleftharpoons} \mathrm{SAS}_N, \qquad (1)$$

where, K_{as} is the equilibrium constant for association of surface-active substance (SAS):

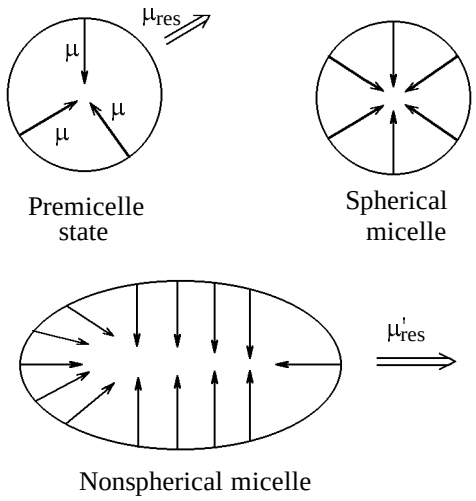
$$K_{as} = [\mathrm{SAS}_N]/[\mathrm{SAS}]^N,$$
$$K_{as} = \alpha c/[(1 - N\alpha)^N c^N].$$

Here, $[\mathrm{SAS}_N]$ is the concentration of associated SAS, α is the degree of accumulation of SAS_N associates, N is the aggregation number, and $c = [\mathrm{SAS}] + N[\mathrm{SAS}_N]$.

The processes of SAS association and micelle structurization were studied by analyzing concentration dependences of the dielectric permittivity ε and orientational polarization P_{or}. For dilute SAS solutions (in the concentration range from ~10^{-3} to ~10^{-2} M), R_{or}^{exp} values were calculated from the experimental values of ε and refractive indices (n) using Eq. (2) [7], where the subscripts "12" and "1" refer to the solution and solvent, respectively. The quantity P_{or}^{exp} is the effective orientational polarization of a surface-active substance, i.e., an integral parameter of a mixture consisting of SAS molecules and their associates calculated per mole of SAS.

$$P_{or}^{exp} = \frac{3\times10^3}{C}\left[\frac{\varepsilon_{12}-\varepsilon_1}{(\varepsilon_1+2)^2} - \frac{n_{12}^2 - n_1^2}{(n_1^2+2)^2}\right]. \qquad (2)$$

Figure 1 shows the dependences of ε and P_{or}^{exp} [calculated by Eq. (2)] on the concentration of compound **II** in chloroform in the absence and in the presence of calixarene **V**. In the concentration range from 0 to 0.002–0.004 M (plot *1*) P_{or}^{exp} decreases (part I). A bend is observed (CMC-1), and P_{or}^{exp} further decreases up to a concentration of **II** equal to 0.011–0.012 M (part II). Here, one more bend is observed (CMC-2), and P_{or}^{exp} increases (part III). Taking into account that the dipole moment of a solute is a function of its orientational polarization [8] and hence the apparent orientational polarization is directly related to the dipole moment of the mixture, calculated per mole of SAS, the observed pattern may be interpreted as follows. Part I corresponds to gradual decrease of the concentration of free polar SAS molecules with a dipole moment μ and accumulation of less polar associates (premicelle state) with a dipole moment μ_{res}.



The concentration of associates attains its maximal value at CMC-1. Part II of the plot reflects accumulation of weakly polar reversed spherical micelles whose concentration is maximal at CMC-2. Further raising the concentration of **II** (part III) is likely to result in asymmetrization of spherical micelles and accumulation of more polar [4] nonspherical micelles with a dipole moment μ'_{res}; subsequent enlargement of nonspherical micelles leads to some increase of P_{or}^{exp} and hence of the apparent dipole moment of the mixture. Thus the macroscopic parameter ε may be regarded to some extent as that chatacterizing not only polarity of the medium but also its ordering [4]. From this viewpoint, the shape of curve *2* in Fig. 1 can be interpreted as continuous inspissation of

a mixture of **II** with chloroform. This process includes (in succession) association of SAS molecules to give initially premicelle state and spherical micelles containing chloroform molecules, contraction of the inner micelle volume due to increase of the aggregation number and displacement of solvent molecules from the polar nucleus of spherical micelles, enlargement of spherical micelles, their asymmetrization to form nonspherical micelles, and enlargement of the latter. These qualitative conclusions are well consistent with the results of studying solutions of cetylpyridinium iodides in carbon tetrachloride by dielcometric titration, Rayleigh scattering, and IR and ^{1}H NMR (using spin probe) spectroscopy [4, 5]. Plots *3* and *4* in Fig. 1, which describe structurization of mixtures of **II** with chloroform and calixarene **V**, may be interpreted as follows. When the point corresponding to CMC-1 is attained (which almost coincides with CMC-1 for solutions of **II** in chloroform), further inspissation of the medium is not accompanied by increase of the apparent dipole moment.

Quantitative processing of the concentration dependences of P_{or}^{exp} was accomplished by the iteration procedure using CPESSP software [9]. The procedure consists of the following. On the basis of the mass action law different versions of association process are considered [in our case, according to Eq. (1)], each being characterized by its own physical parameters *Q*. Theoretical concentrations dependences of these parameters are calculated and are then compared with those obtained experimentally. The correlation quality is estimated using the functional *F* [Eq. (3)], which should have a minimal value.

$$F = \sum_{m}^{z}[(Q_m^{exp} - Q_m^{theor})W_m]^2. \quad (3)$$

Here, *m* changes from 1 to *z* (the number of experimental points), and W_m is the mean-square deviation. The minimal value of *F* is determined by the iteration procedure for each theoretically possible association model.

As experimental physical parameter *Q* we chose orientational polarization P_{or}. The theoretical value of P_{or} was calculated by the formula

$$P_{or}^{theor} = \alpha P_{or}^{as} + (1 - N\alpha)P_{or}^{m}.$$

Here, P_{or}^{as} and P_{or}^{m} are the orientational polarizations of the associated and monomeric forms of SAS, respectively. Mathematical treatment of the experimental concentration dependence of P_{or} (Fig. 1, plot *1*) using Eq. (3) gave values of *N* and K_{as} for

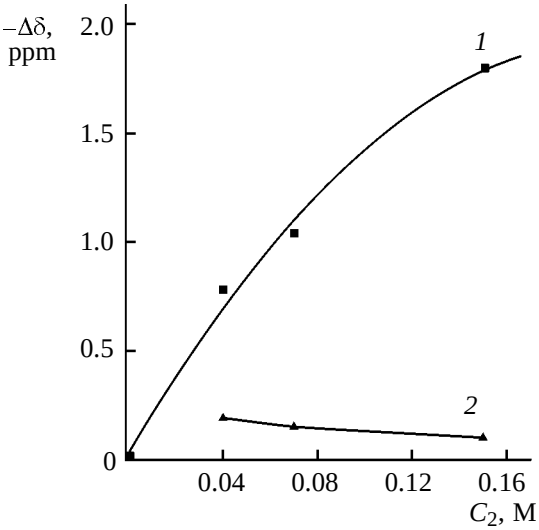


Fig. 2. Variation of the chemical shifts of (*1*) OH protons of calixarene **IV** and (*2*) NCH_3 protons of compound **II**; $CDCl_3$, $c_{\mathbf{IV}}$ = 0.02 M.

compound **II** in chloroform in the absence of calixarene **V**. The best correlation between the experimental and theoretical dependences was found for $N = 8$ and $\log K_{as} = 20.8 \pm 0.3$, $P_{or} = 12.8$ ($F_{min} = 2.0$ at $m = 29$). Further increase in *N* does not lead to reduction of F_{min}.

The values of P_{or}^{exp} for the system containing calixarene **V** (Fig. 1, plot *3*) differ from P_{or} which were calculated assuming the absence of interaction between compounds **II** and **V** (on the additivity principle). CPESSP treatment [9] of the concentration dependence (plot *3* in Fig. 1) showed that proper description of the experimental data requires not only association of **II** [Eq. (1)] but also interactions of **V** with both monomeric and micelle states of **II** to be taken into account. The two latter processes can follow schemes (4) and (5):

$$\mathrm{SAS} + \mathrm{AMC} \overset{K'_{as}}{\rightleftarrows} \mathrm{SAS{\cdot}AMC},$$

$$\log K'_{as} = 4.8 \pm 0.5, \; P_{or} = 22; \quad (4)$$

$$\mathrm{SAS}_N + \mathrm{AMC} \overset{K''_{as}}{\rightleftarrows} \mathrm{SAS{\cdot}AMC}.$$

$$\log K''_{as} = 26.7 \pm 0.3, \; P_{or} = 12. \quad (5)$$

The occurrence of such interactions is supported by the data of ^{1}H NMR spectroscopy (Fig. 2), according to which the NCH_3 signal of **II** in micelle solution in $CDCl_3$ shifts slightly upfield in the presence of calixarene **IV**. A stronger shift is observed for the OH proton signal of **V**. The shift of the NCH_3 signal

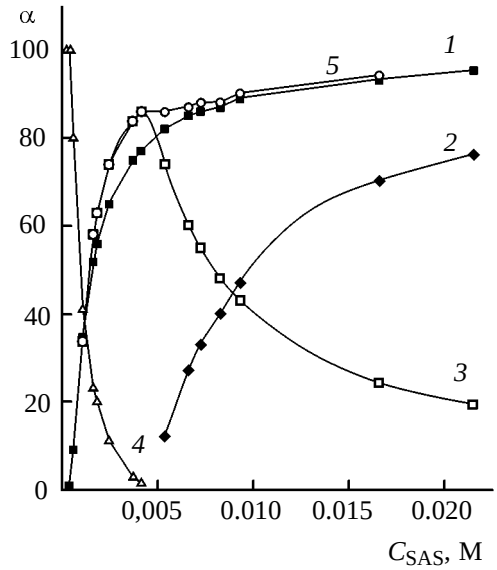


Fig. 3. Accumulation of (*1*, *2*) SAS_N, (*3*) $SAS_N \cdot AMC$, (*4*) $SAS \cdot AMC$, and (*5*) $SAS_N + SAS_N \cdot AMC$ associates in chloroform at 20°C with rise in SAS concentration (*1*) in the absence and (*2*–*5*) in the presence of 5×10^{-4} mol/l of calixarene **V**.

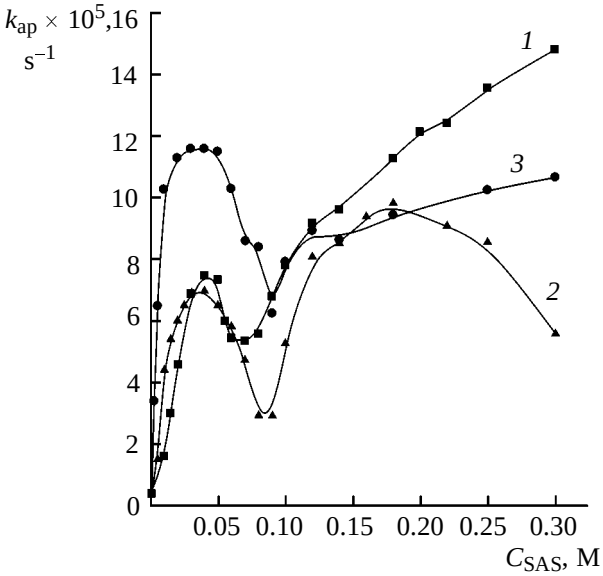


Fig. 4. Plots of the apparent rate constants of the reaction of *p*-nitrophenyl bis(chloromethyl)phosphinate with calixarene **IV** in chloroform at 50°C versus concentration of *n*-alkyl(2-hydroxyethyl)dimethylammonium bromides (*1*) **I**, (*2*) **II**, and (*3*) **III**; $c_{\mathbf{IV}}$ = 0.0002 M.

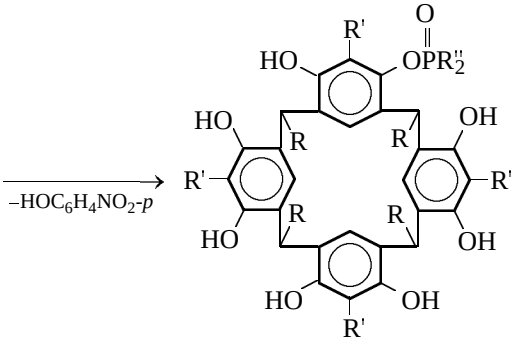
almost does not shift as the concentration of **II** rises, whereas the shift of the OH signal increases. Presumably, these data indicate increase in the relative amount of associated molecules of **II** which react with solubilized calixarene molecules.

Thus calixarene is bound by the surface-active substance in both monomeric and associated forms. Figure 3 shows the concentration dependences of the degree of accumulation of different associates in chloroform in the absence and in the presence of calixarene **V**. Curve *5* reflects the total change in the accumulation of associates in the system $CHCl_3$–surface-active substance–calixarene **V**. Greater values of α on plot *5* relative to plot *1* (accumulation of SAS_N in the system $CHCl_3$–SAS in the absence of calixarene) in the concentration range from 0.001 to 0.012 M indicate that clixarene favors aggregation of compound **II**.

Micelle formation process affects not only complexing power and spectral parameters of 2-hydroxyethylammonium derivatives but also its catalytic activity. Using the spectrophotometric technique we studied the kinetics of the reaction of calixarene **IV** with *p*-nitrophenyl bis(chloromethyl)phosphinate in chloroform in the presence of quaternary ammonium salts **I**–**III**. The process was monitored following variation of the optical density at λ 322.6–328.9 nm which corresponds to absorption of 4-nitrophenol.

Under conditions ensuring pseudounimolecular process, i.e., at a *p*-nitrophenyl bis(chloromethyl)-phosphinate (δ_P 39.5 ppm) concentration much lower than nucleophile concentration, the reaction results in formation of product **VI** (δ_P 38.4 ppm).

IV + $(ClCH_2)_2P(O)OC_6H_4NO_2$-*p*



VI

R = *n*-C_9H_{19}, R' = CH_2NMe_2, R" = CH_2Cl.

Figure 4 gives the plots of the apparent rate constants k_n) for formation of phosphorylated calixarene **VI** in chloroform at 50°C versus concentration of tetraalkylammonium bromides **I**–**III**. Under conditions of micelle formation the rate of the reaction increases by more than an order of magnitude. The concentration dependences pass through a maximum at $c_{SAS} \approx 0.05$ M and then through a minimum. In

Parameters of the reaction of *p*-nitrophenyl bis(chloromethyl)phosphinate with calixarene **IV**[a] in chloroform at 50°C in the presence of micelles formed by *n*-alkyl(2-hydroxyethyl)dimethylammonium bromides **I**–**III**

Ammonium bromide	K_S, l/mol	K_{Nu}, l/mol	$k_{2,m}$, l mol^{-1} min^{-1}	CMC, M	(k_{ap}/k_0)[b]	F_m	F_c	$F_m \times F_c$
I	253	10	0.88	0.014	18	0.71	24	17
II	471	4.8	1.6	0.009	17	1.3	13	17
III	578	3.5	3.3	0.0021	28	2.7	10	27

[a] $c_{\mathbf{IV}} = 0.0002$ M. [b] k_{ap} is the maximal apparent pseudofirst-order rate constant in micelle solutions of SAS, and k_0 is the pseudofirst-order rate constant in the absence of SAS.

the cases of compounds **I** and **III** the rate constants increase with further rise in c_{SAS}, while one more maximum is observed for bromide **II**. The catalysis by reversed micelles of a surface-active substance is commonly explained by concentrating of the reactants in the micelle phase and by the effect of micelle microenvironment on the process [10]. Raising the concentration of SAS in solution is accompanied by increase in the number of associates, which could lead to dilution of the solubilized reactants and hence reduction of the rate constant. The subsequent increase of k_{ap} is likely to result from structural reorganization of micelles. The concentration dependences shown in Fig. 4 can be described in terms of the pseudophase model developed by Berezin and co-workers [11, 12]:

$$k_{ap} = \frac{k_{2,0} + (k_{2,m}/V)K_S K_{Nu} C_{SAS}}{(1 + K_S C_{SAS})(1 + K_{Nu} C_{SAS})} .$$

Here, $k_{2,0}$ and $k_{2,m}$ (l mol^{-1} s^{-1}) are the second-order rate constants for the reactions in chloroform and in the micelle pseudophase, respectively; K_S and K_{Nu} are equilibrium constants for binding of the substrate and nucleophile with micelles; V is the molar volume of SAS; and c_{SAS} is its concentration minus CMC. The results of mathematical processing are given in table.

It is seen that increase in the length of the *n*-alkyl radical leads to increase of the bimolecular rate constant in the micelle phase and of the substrate–micelle binding constant. Simultaneously, the binding constant for calixarene (nucleophile) and critical micelle concentration decrease. In terms of the Berezin model, the maximal acceleration is given by the following equation [12]:

$$(k_{ap}/k_0)_{max} = \frac{k_{2,m}}{k_{2,0}} \frac{K_S K_{Nu}}{V[(K_S)^{1/2} + (K_{Nu})^{1/2}]^2} .$$

Here, the first factor in the right part reflects the effect of variation of microenvironment of solubilized reactants (F_m), and the second, the effect of increase of the reactant concentration in the micelle phase (F_c). The data in table show that the calculated values of $F_m F_k$ are well consistent with the experimental acceleration $(k_{ap}/k_0)_{max}$.

Increase in the hydrophobicity of surface-active substances leads to decrease in F_c and increase in F_m. However, in all cases the contribution of F_c to the catalytic activity is determining. The opposite change of the two factors is responsible for almost similar maximal catalytic activities of micelles formed by compounds **I** and **II** in the range of their concentration from CMC-1 to CMC-2 and for the higher maximal catalytic activity found for compound **III**. When the concentration of SAS exceeds CMC-2, i.e., after structural reorganization of micelles, the situation changes. At large SAS concentrations the highest catalytic activity was found for compound **I**, while bromide **II** is the least active (Fig. 4).

Thus, there is a relation between the structure of micelles and their catalytic activity in nucleophilic substitution in phosphinic acid ester. Therefore, proper analysis of the kinetic data requires that regions of structural transitions be taken into account, and parameters of catalytic reactions should be calculated at a SAS concentration corresponding to micelles with the same structure.

EXPERIMENTAL

The ^{31}P NMR spectra were recorded on a Bruker MSL-400 instrument (162 MHz). The ^{1}H NMR spectra were obtained on a Bruker-400 Fourier spectrometer relative to tetramethylsilane as internal reference. The proton chemical shifts were as follows, δ, ppm ($CDCl_3$): 3.36 s (6H, NCH_3, 0.1 mol/l of **II**) and 8.8 s (8H, OH, 0.02 mol/l of calixarene **IV**).

p-Nitrophenyl bis(chlormethyl)phosphinate and tetrakis(dimethylaminomethyl)calixarenes **IV** and **V** were synthesized by the procedures reported in [13, 14]. Compounds **I**–**III** were obtained by reaction

of 2-dimethylaminoethanol with the corresponding alkyl bromides [15]. Chloroform was purified by standard technique [16].

The kinetic measurements were performed by spectrophotometry under pseudounimolecular conditions using a Specord UV-Vis spectrophotometer. The apparent rate constants were calculated by the first-order equation using a PC AT-486.

Dielcometric titration was carried out as described in [3]. The dielectric permittivities of a set of solutions were determined on a setup consisting of an E12-I instrument operating in a hopping mode and a measuring device (a capacitor maintained at a constant temperature) [17]. The refractive indices were measured on an IRF-23 refractometer.

ACKNOWLEDGMENTS

This study was financially supported by the Russian Foundation for Basic Research (project no. 00-03-32 119a).

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