

The Effect of Hydroxyl Groups on Solubilization of Pyridine Derivatives in Span 80–Water–*n*-Decane Reverse Micelles

I. V. Kopanichuk^{a, *}, S. D. Ochkalova^a, and A. A. Vanin^a

^aSt. Petersburg State University, St. Petersburg, 199034 Russia

*e-mail: kopan239@gmail.com

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Abstract—Computer simulation of pyridine, pyridine-2-ol, and pyridine-2,5-diol solubilization by Span 80–water reverse micelles in *n*-decane has been performed. All solubilized compounds are polar (their polarity increases in a series pyridine, pyridine-2,5-diol, and pyridine-2-ol) and have different numbers of donors/acceptors forming hydrogen bonds. The most probable positions of pyridine molecules relative to a reverse micelle change fundamentally with a rise in the number of hydroxyl groups in their structure. Pyridine, pyridine-2-ol, and pyridine-2,5-diol are located in the nonpolar medium, on the micelle surface between the head groups of surfactant molecules, and on the inside surface of the aqueous core, respectively. Thus, the number and arrangement of hydrophilic groups in the structure of a molecule, rather than its polarity, have the strongest effect on the ability to solubilization in the reverse micelles.

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INTRODUCTION

Oil-in-water and water-in-oil microemulsions are thermodynamically stable systems containing micelles in solvents with polarities opposite to those of micelle cores. These systems may be used as media for realization of chemical reactions between reagents having different polarities, because they substantially increase the contact areas of the regions occupied by hydrophilic or hydrophobic components. The increase in the contact area leads to a considerable change in the chemical reaction rate. Along with the change in the reaction rate, the implementation of a reaction in a microemulsion allows one to control the yield and mechanism of the reaction, as well as its regio- and stereoselectivity [1]. This makes the study of the micellar catalysis important from both practical and theoretical points of view. The principles of catalysis by normal micelles have been considered in detail in reviews [2, 3], while catalysis with the use of reverse micelles has been discussed in [4–10]. In water-in-oil microemulsions, control over the aggregate sizes and the ratios between the volumes of polar and nonpolar media is easier, thereby making the catalysis by reverse micelles more versatile.

For successful performance of catalysis, it is important to be aware of the system part (micelle or intermicellar solution) in which reagents are concentrated. The use of computer-simulation methods, including molecular dynamics (MD), allows one to determine explicitly the prevailing arrangement of reagent molecules relative to a micelle and the influ-

ence of the structural features of solubilized substance molecules on this arrangement. The aim of this work was to use MD for determining the structure of reverse micelles formed in a Span 80–water–*n*-decane three-component system and the most probable arrangement of molecules of pyridine and its hydroxy derivatives (pyridine-2-ol and pyridine-2,5-diol) solubilized in this system. The chosen compounds have different dipole moments and numbers of groups capable of hydrogen bonding. A comparative analysis of their positions in the stationary state allows one to determine the main factors affecting the solubilization of molecules in nonionic reverse micelles.

MODELS AND METHODS

In this work, a cubic cell with an edge length of 7.181 nm containing one reverse micelle surrounded by a nonpolar hydrocarbon medium and an analogous cell containing, in addition to the aforesaid, a molecule of one of three solubilized compounds (pyridine, pyridine-2-ol, or pyridine-2,5-diol) were simulated.

Molecules of a nonionic surfactant, Span 80; decane; and the solubilized compounds were described in terms of the united-atom model with the use of GRO-MOS96 force field (the 53A6 set of parameters) [11]. The molecular structures of the surfactant and solubilized compounds are presented in Fig. 1. A water molecule was described using the SPC model [12]. The effective charges on the force centers of Span 80 and solubilized compounds were calculated with the use of

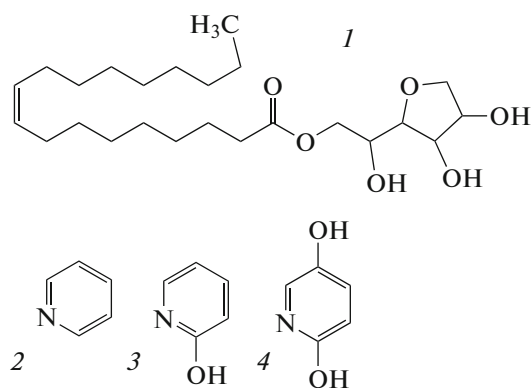


Fig. 1. Structural formulas of (1) Span 80, (2) pyridine, (3) pyridine-2-ol, and (4) pyridine-2,5-diol.

the Gaussian 09 software (the MP2/CHELPG method and the 6-311+G** basis) [13]. Molecular-dynamics simulation in the NVT ensemble was carried out with the use of the GROMACS v. 5.04 software [14]. The integration step in the used Verlet algorithm was equal to 2 fs. Electrostatic interactions were calculated by the PME method [15]. The cutoff radii for electrostatic forces and van der Waals forces were equal to 1.0 nm. All trajectories and configurations were analyzed using the VMD application [16] and our own software developed with the use of the JGROMACS library [17].

The basic simulation cell contained 1000 molecules of *n*-decane and one reverse micelle consisting of 40 molecules of Span 80 and 120 water molecules (water number $w_0 = 3$).

The formulated problem was solved by simulating the solubilization in the selected reverse micelle of three different heterocyclic compounds: pyridine, pyridine-2-ol, and pyridine-2,5-diol. In each case, all possible initial configurations of the heterocycle position relative to the preliminarily assembled micelle were considered: (a) in the core, (b) on the micelle surface between the head groups of the surfactant, and (c) outside of the micelle, i.e., in nonpolar medium. Moreover, for each compound, the self-assembly of a micelle containing a heterocyclic molecule initially placed in the cell was simulated (d). When using this method, identical configurations obtained in calculations (a)–(d) confirm the absence of an effect of the initial position of a solubilisate molecule on its final position in the reverse micelle. The algorithm of the construction of the simulation cell containing the initial configuration for the self-assembly of a reverse micelle has been described in detail in our previous work [18]. The time of the simulation of reverse micelle self-assembly was 50 ns. Then, a heterocycle was placed into the system in one of the (a)–(c) positions, and the calculation was begun, which lasted 35 ns to ensure that the system reaches a stationary

state. After this calculation was completed, another 10 ns long was performed with generating a configuration each 1 ps (10 thousand configurations) to obtain data for averaging the geometric parameters of the objects in the system.

The positions of the solubilized molecules were determined from the positions of the density peaks in the radial profiles with respect to the mass center of the micelle. The density profiles were calculated as functions of the distance from the mass center of the micelle and were averaged over all possible zenith and azimuth angles; thus, the radial density profiles did not take into account fluctuations of the micelle shape, but enabled us to determine the prevailing positions of the components from the distribution peaks. The plots of the density distributions for solubilized molecules were represented in different scales because of the specific feature of the radial profile calculation: the volumes of spherical layers increased as the squared distance from the mass center of a micelle; therefore, the local density due to one molecule was higher near the center and lower at the periphery of the system. We were interested only in the positions of the peaks, rather than the values of the densities of solubilized molecules.

RESULTS AND DISCUSSION

The structure of a reverse micelle formed in the Span 80–water–*n*-decane system is shown in Fig. 2 as the radial density profiles calculated for the components relative to the mass center of the micelle. In the micelle under consideration, surfactant molecules are oriented in a manner such that their head groups surround the water core, and the hydrocarbon tails are extended from the core into *n*-decane. In the center of the micelle, the local density of water is as high as 35 nm^{-3} , which corresponds to the density of bulk water. The micelle is sufficiently large to contain water molecules that are not involved in the formation of the hydration shells at the head groups of the surfactant molecules, and the polar head groups of Span 80 are entirely enveloped by the hydration shells. The micelle surface may be represented as a sphere $1.1 \pm 0.1 \text{ nm}$ in radius, which coincides with the position of the peak in the density of the surfactant head groups.

Solubilized molecules were chosen so as to be different in the polarity and the number of groups capable of acting as donors or acceptors of hydrogen bonds. All studied molecules were polar, with their polarity increasing in a series pyridine, pyridine-2,5-diol, and pyridine-2-ol according to their structure (see Fig. 1). In the used united-atom model, the absolute values of the dipole moments for pyridine, pyridine-2-ol, and pyridine-2,5-diol were 1.1, 5.4, and 2.1 D, respectively. The number of hydrogen bonds per molecule depended on the number of hydroxyl groups in its structure. For example, the average numbers of hydro-

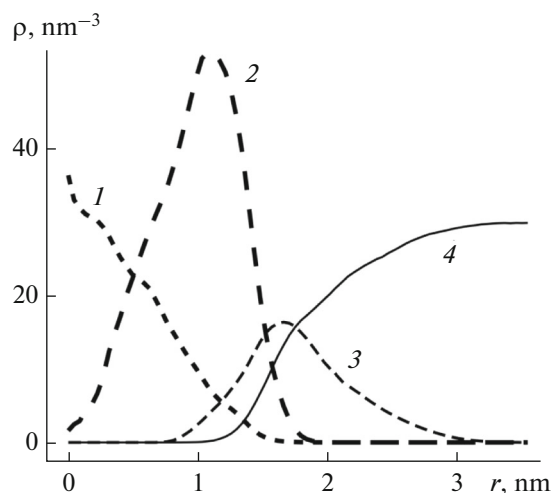


Fig. 2. Radial density profiles of the components in a Span 80 micelle: (1) water, (2) head group of a surfactant molecule, (3) its tail, and (4) decane.

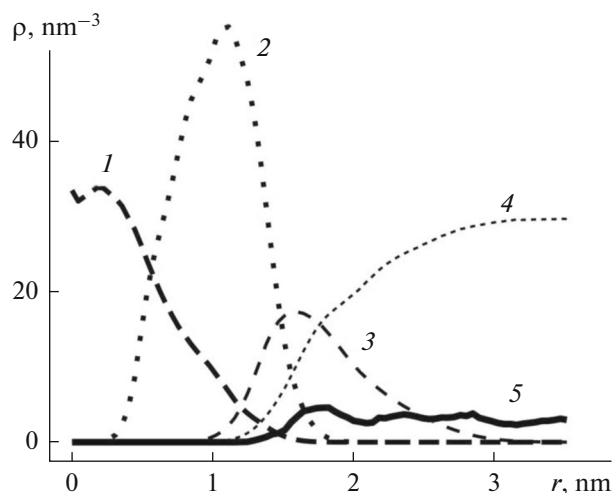


Fig. 3. Radial density profile of pyridine relative to Span 80 micelle: (1) water, (2) surfactant head group, (3) its tail, (4) decane, and (5) pyridine. Pyridine density is given in a scale of 200 : 1.

gen bonds formed by pyridine-2-ol as an acceptor and a donor were 1.7 and 1.0, respectively. Pyridine-2,5-diol formed, on average, 3.6 hydrogen bonds as a donor and 2.0 as an acceptor.

The most probable positions of solubilized molecules were determined from the positions of the peaks in the radial density profile relative to the mass center of a micelle. The solubilized molecules with the density peak located at a distance larger than 1.1 nm from the mass center of the micelle were considered to be located outside of the micelle, i.e., in the nonpolar medium. The solubilized molecules, the density peak of which was located at a distance from the mass center of the micelle equal to 1.1 ± 0.1 nm were believed to be located on the micelle surface, while the molecules with the position of density peak at a shorter distance from the mass center of the micelle were considered to be inside of the micelle.

Unsubstituted pyridine molecules have been found to be located exclusively in the nonpolar *n*-decane medium and not to penetrate into the reverse micelle. Their local density profile shows a small maximum in the vicinity of the position of surfactant tails, at an approximate distance of 1.8 ± 0.1 nm (see Fig. 3). This may be explained by the electrostatic interactions between a pyridine molecule and hydrocarbon tails of Span 80: in spite of the electrical neutrality of the molecules as a whole, the force centers bear effective charges. The density peak of pyridine-2-ol occurs exactly under the density peak of Span 80 head groups; i.e., pyridine-2-ol is located on the surface of the reverse micelle (see Fig. 4a). The distance between the density peak of pyridine-2,5-diol and the mass center of the micelle is less than 1.1 nm, i.e., pyridine-2,5-diol occurs in the aqueous core and forms a larger

number of hydrogen bonds with water molecules as compared with the other of solubilized molecules. Figures 3, 4a, and 4b testify that, in the series pyridine, pyridine-2-ol, and pyridine-2,5-diol, the stationary position of a solubilized molecule in a reverse micelle is shifted toward its center of mass according to the number of hydrogen bonds potentially formed by this molecule. Pyridine molecules containing no substituents do not penetrate into the micelle. Pyridine-2-ol contains one OH group and is located exactly on the surface; its density maximum coincides with the density maximum of the surfactant head groups. Pyridine-2,5-diol has two OH groups and is situated in the aqueous core of the micelle.

The calculation results lead us to suppose that the polarity of molecules is of a low significance for the solubilization process. Pyridine is a polar compound (1.1 D), but it is predominantly located in the nonpolar medium. Concerning the pyridine-2-ol/pyridine-2,5-diol pair, it is less polar pyridine-2,5-diol (2.1 D) that penetrates into the aqueous core of the micelle, whereas more polar pyridine-2-ol (5.4 D) remains on the micelle surface.

Figure 5 reflects the dynamic character of the solubilization of molecules in a reverse micelle. The positions of solubilized molecules in the stationary region of the trajectory do not depend on their positions in the initial configuration. An analogous behavior was observed previously in [19]. In an initial configuration, a pyridine-2,5-diol molecule was located outside of a reverse micelle at a distance of about 3 nm from the mass center of the micelle and 2 nm from its surface. The wandering of the molecule in the nonpolar medium being solubilized lasted a little longer than 1 ns, and the passage from the nonpolar medium into

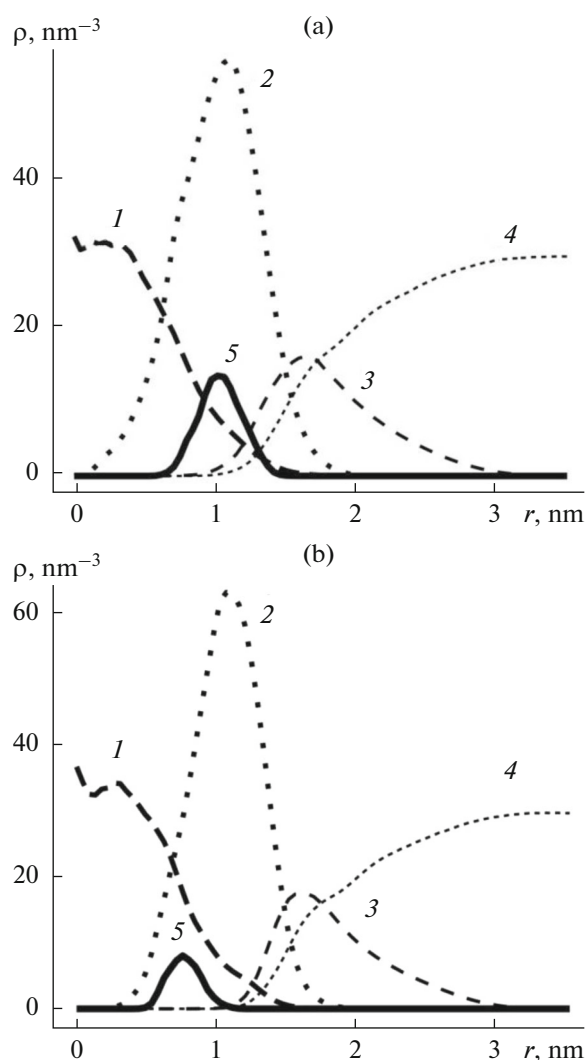


Fig. 4. Comparison between the positions of (a) pyridine-2-ol and (b) pyridine-2,5-diol in Span 80 micelles according to radial density profiles: (1) water, (2) head group of surfactant molecule, (3) its tail, (4) decane, and (5) solubilized compound. Densities of solubilized compounds are given in scales of (a) 10 : 1 and (b) 2 : 1.

the micelle occurred almost instantaneously. Inside of the micelle, the position of the molecule relative to the mass center of the micelle remained almost unchanged. On the contrary, a molecule of unsubstituted pyridine in the initial configuration was located inside of the reverse micelles and almost immediately began to diffuse toward the nonpolar medium, with the time of the movement to the micelle surface being significantly longer than the time of escaping from the surface into the nonpolar medium. In the case of pyridine, the passage to the nonpolar medium occurred jumpwise as it did in the case of pyridine-2,5-diol. In the nonpolar medium, pyridine molecule moved abruptly as a result of repulsion from the micelle after an accidental approach to its surface.

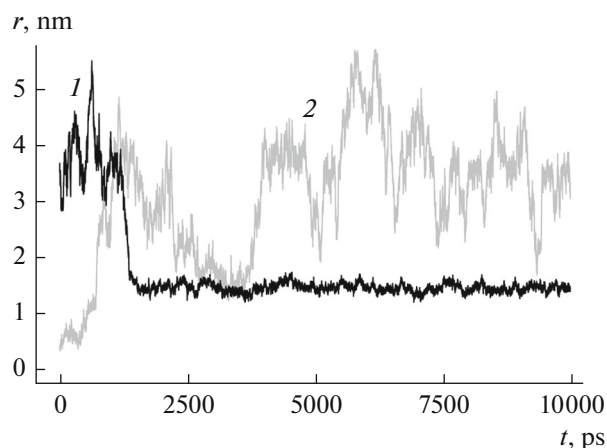


Fig. 5. Time dependences of the distances from the mass center of a reverse micelle for (1) pyridine-2,5-diol and (2) pyridine molecules.

CONCLUSIONS

Spherical reverse micelles are formed in a Span 80–water–*n*-decane system at a number ratio between nonionic surfactant and water molecules of 1 : 3. In a stationary system, the position of a molecule solubilized in the reverse micelle is independent of its initial position relative to the aggregate or the presence of preliminarily assembled aggregate in the system, but rather depends on the nature of the molecule. Among the studied substances, only compounds containing hydroxyl groups are capable of solubilization. For example, pyridine molecule free of polar functional groups is located in decane and does not penetrate into the reverse micelles. Pyridine-2-ol molecule occurs exactly on the surface of reverse micelles. Pyridine-2,5-diol molecule is located in the micelle core, but remains at the internal surface without further immersion. As the presence and number of OH groups rather than the polarity of the molecules affect their positions, it may be assumed that their ability to solubilization in reverse micelles of nonionic surfactants is governed by hydrogen bonding with water molecules composing the micelle core. This assumption has been confirmed by the calculations of the average numbers of hydrogen bonds formed by different molecules. Indeed, pyridine-2,5-diol forms hydrogen bonds in reverse micelles 2.1 times more often than pyridine-2-ol does.

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