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^{1}H NMR Study of Mixed and Inverse Micelles: Solvent Effects on Chemical Shifts of Aromatic and Heterocyclic Protons in Some *N*-Methylnicotinyl and *N*-Methylisonicotinyl Esters

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Changes in solvent polarity and the concentration of added anionic surfactant on the chemical shifts and on the shape of signals of aromatic and heterocyclic protons in a series of *N*-methylnicotinyl and *N*-methylisonicotinyl esters were studied. It was concluded that mixed and inverse micelles were formed which differently affect the proton chemical shifts.

Aqueous and reverse micelles are believed to be crude simplified models for the chemistry of "the real world," i.e., processes occurring at biomembranes which perform important functions in living organisms. NMR spectroscopy is a convenient and simple technique which can yield information on the structure of micelles and on interactions between the micelle and the organic substrate. However, these studies have been hampered by the relatively low solubility of organic compounds in water and small concentrations of the surfactant present in systems under investigation (*1–3*). In spite of numerous publications which deal with this subject all details of the solubilization process and the orientation of the organic molecule in the micelle are still not known (*4*). In most cases, the NMR technique was used to study the influence of changes in the media on chemical shifts of aromatic compounds, phenols (*5–9*), and ω-phenylalkanoates (*10*) in particular. These compounds are to a certain degree soluble in water, and the aromatic protons are clearly discernible from the proton signals of the aliphatic chains of the surfactant. From other studies it was concluded that micelles contain a certain number of water molecules in their inner sphere which should influence the chemical shifts and the shape of NMR signals (*11*) in a manner similar to that of water in organic solvents (*12*). Quaternary *N*-methylnicotinyl and *N*-methylisonicotinyl esters **1** and **2** (Scheme 1) were found to be suitable organic substrates for such studies. These esters are quite soluble in water and behave similarly to cationic surfactants. This should enable their complexation with the ionic head of an anionic surfactant molecule such as sodium dodecyl sulfate (SDS). Both types of NMR signals, from the heterocyclic "head" and the aromatic "tail," in **1** and **2** could be studied, thus giving information on the orientation of the organic substrate relative to the outer and inner spheres of the micelle. The NMR data

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1 2

a: $R_1 = R_2 = H$

b: $R_1 = CH_3$, $R_2 = H$

c: $R_1 = CH_3$, $R_2 = CH_3$

d: $R_1 = Ph$, $R_2 = H$

e: $R_1 = CN$, $R_2 = H$

SCHEME 1

were taken in pure D_2O, in D_2O containing varying amounts of SDS, and in different organic solvents.

EXPERIMENTAL

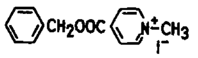
SDS was of commercial quality (Fluka) and used without further purification. Esters **1a–1e** and **2a–2e** were prepared by standard procedures from the corresponding alcohols and nicotinyl and isonicotinyl chloride, respectively, using pyridine as solvent. The quaternization was performed with methyl iodide in acetone. The products were purified by recrystallization from acetone–petroleum ether. The purity and identity of the final material were determined by ir and ^1H NMR spectroscopy and elemental analysis. Since all these esters are easily hydrolyzable in water (*13*), samples were prepared immediately before the spectra were taken. A Jeol 90 FXQ spectrometer was used and the chemical shifts determined at 22 ± 0.1°C relative to D_2O when water was the solvent or relative to TMS when organic solvents were used. Solutions (10^{-2} M) in D_2O were used in all cases except with **1b** where the concentration of the organic substrate was 10^{-1} M.

RESULTS AND DISCUSSION

The results are shown in Table 1 and Figs. 1 and 2. A different trend can be seen for changes in chemical shifts for protons connected to the heterocyclic head of the molecule, i.e., close to the positively charged nitrogen atom (Fig. 1), and for those bound to the aromatic ring (Fig. 2). Shifts for the first-mentioned set of protons increase with increasing concentration of the ester while the opposite is true for the aromatic protons. This can be explained by assuming that micellization occurring above the critical micelle concentration (CMC) increases the polarity of the medium. This causes increasing chemical shifts of the heterocyclic protons which are in contact with the aqueous medium. On the contrary the aromatic protons are becoming more protected from the influence of the polar

TABLE 1

^{1}H NMR Chemical Shifts of Ester **2a** in D_2O



Concentration of ester **2a** (mol dm^{-3})	H_a	H_b	CH_2	CH_3	H_o	H_m	H_p
10^{-2}	8.841	8.381	5.406	4.379	7.460	7.440	7.420
5×10^{-2}	8.895	8.406	5.378	4.418	7.424	7.403	7.364
10^{-1}	8.912	8.4105	5.357	4.430	7.395	7.366	7.310

solvent as the concentration is increasing, which results in decreasing shifts as shown in Fig. 2.

The influence of different concentrations of SDS on chemical shifts of protons bond to different parts of the substrate molecule (**1** and **2**) is presented in Table 2. A sudden drop in $\Delta\delta$ values was observed when the concentration of SDS was increased from 0 to 0.05 M. Above this concentration a gradual increase in $\Delta\delta$ values occurs relative to water (Fig. 3). This behavior can be explained by

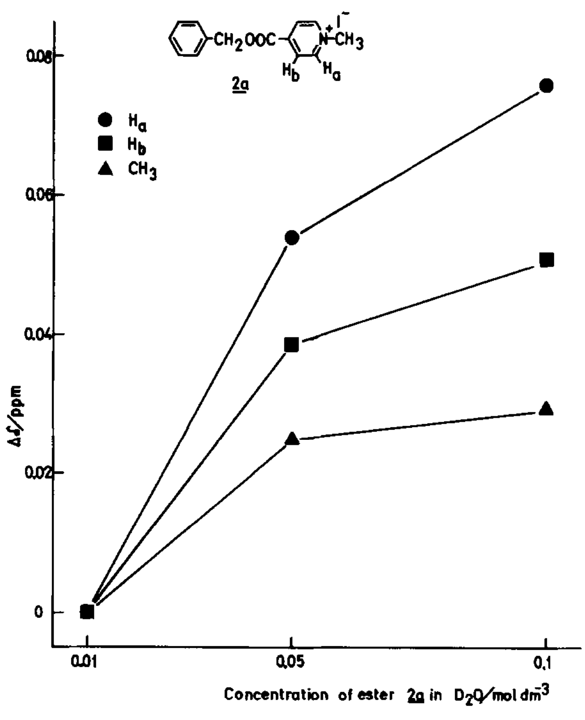


FIG. 1. Graph of chemical shift changes ($\Delta\delta$) for the "head" protons of ester **2a** as a function of its concentration.

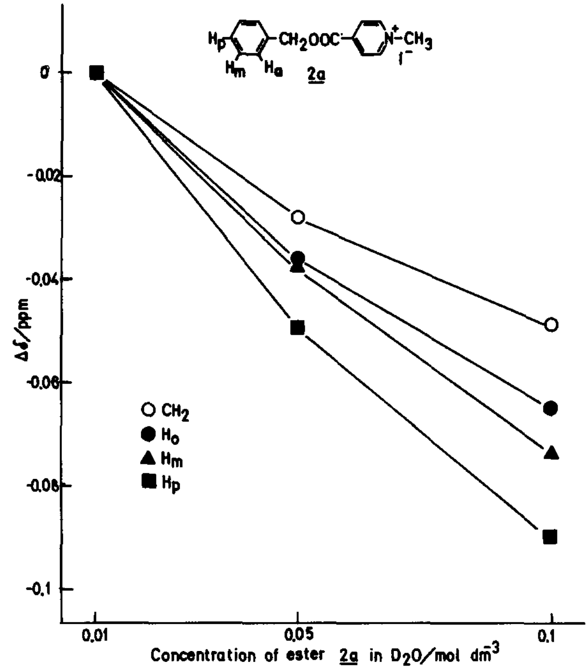


FIG. 2. Graph of chemical shift changes (Δδ) for the "tail" protons of ester **2a** as a function of its concentration.

assuming that when the substrate/SDS ratio is 1, a compact mixed micelle is formed—the largest shift occurring with the aromatic proton in the *para*-position (H_p, Figs. 3 and 4) which is most distant from the polar head. With a further increase in the SDS concentration a more loose micelle is formed allowing the penetration of water into the micelle and consequently a decrease in Δδ values of

TABLE 2

^{1}H NMR Chemical Shifts of Ester **2a** in SDS Solution in D_2O

Concentration of SDS in D_2O (mol dm^{-3})	H_a	H_b	H_o	H_m	H_p
0	8.892	8.404	7.424	7.403	7.364
0.001	8.907	8.421	7.449	7.425	7.343
0.005	8.955	8.464	7.489	7.465	7.386
0.01	8.936	8.451	7.465	7.440	7.218
0.05	8.897	8.285	7.240	7.138	7.070
0.1	8.915	8.292	7.242	7.148	7.078
0.5	9.022	8.433	7.389	7.332	7.277
1	9.063	8.473	7.425	7.376	7.326

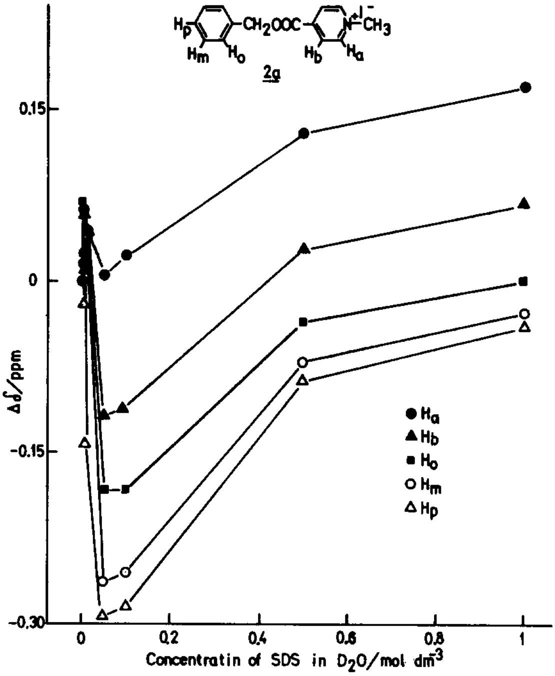


FIG. 3. Graph of chemical shift changes (Δδ) for the aromatic protons of ester **2a** as a function of SDS concentration.

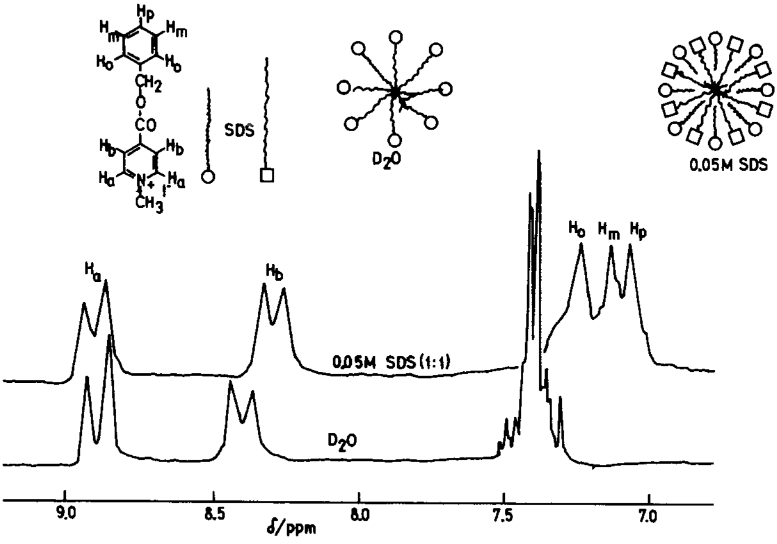


FIG. 4. ¹H NMR spectra of ester **2a** (0.05 M) in 0.05 M SDS and D_2O. In D_2O ester **2a** yields micelle and in a water solution of SDS it yields a mixed micelle.

TABLE 3

^{1}H NMR Chemical Shifts of Ester **2a**[a] in Micelles, D_2O, and Organic Solvents

Solvent	E_T	H_a	H_b	CH_2	CH_3
0.05 M SDS	—	8.879	8.285	5.267	4.423
D_2O	63.1	8.892	8.406	5.406	4.418
CD_3CN	46.0	8.939	8.445	5.445	4.420
CD_3OH	55.5	9.118	8.512	5.468	4.501
CD_3SOCD_3	45.0	9.210	8.542	5.476	4.676
CD_3COCD_3	42.2	9.470	8.694	5.510	4.760

[a] Concentration of ester **2a** was 0.05 M.

the aromatic protons. The opposite phenomenon is observed when the same substrate (**2a**) is dissolved in an organic solvent containing small amounts of water (~1%) (Table 3, Fig. 5). Here the aromatic protons are unaffected by the change in medium relative to water, but protons associated with the polar heterocyclic head show a downfield shift. This can be taken as an indication than an inverse micelle was formed; the protons on the aromatic tail remain unaffected while the polar head is in contact with water molecules causing its protons to shift (Fig. 5). These reasonings, which pertain to compound **2a**, can be extended to all the other compounds of this series (**2a–2e**). Nicotinyl esters **1a–1e** show also differences in the shape of signals for the heterocyclic protons when the molecule is bound to the

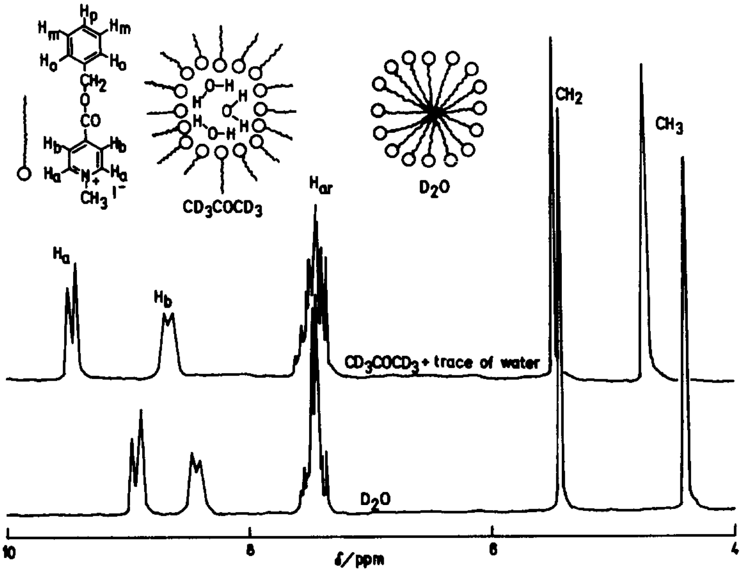


FIG. 5. ^{1}H NMR spectra of ester **2a** (0.05 M) in CD_3COCD_3 and D_2O. In D_2O ester **2a** yields micelle and in CD_3COCD_3 with traces of water it yields inverse micelle.

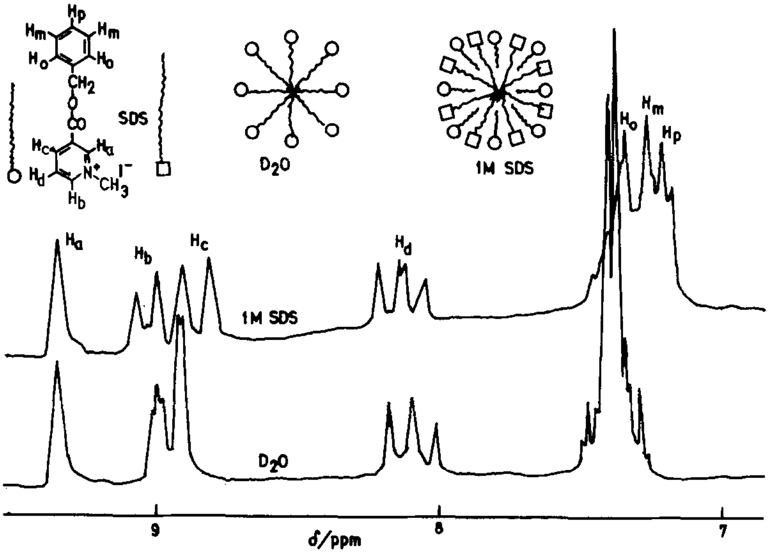


FIG. 6. ^{1}H NMR spectra of ester **1a** (0.05 M) in 0.1 M SDS and D_2O. In D_2O ester **1a** yields micelle and in a water solution of SDS it yields mixed micelle.

micelle. In water as well as in anhydrous organic solvents protons H_b and H_c are almost equivalent to the NMR spectrum causing the signal for proton H_d to appear as a triplet. The formation of a mixed micelle destroys the equivalence of protons H_b and H_c, H_c being more shielded inside the micelle shifts upfield, while H_b is

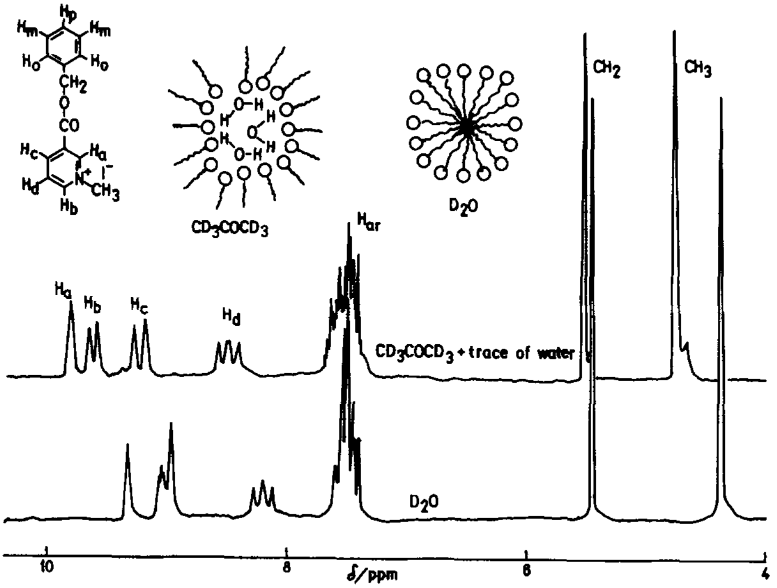


FIG. 7. ^{1}H NMR spectra of ester **1a** (0.05 M) in CD_3COCD_3 and D_2O. In D_2O ester **1a** yields micelle and in CD_3COCD_3 with traces of water it yields inverse micelle.

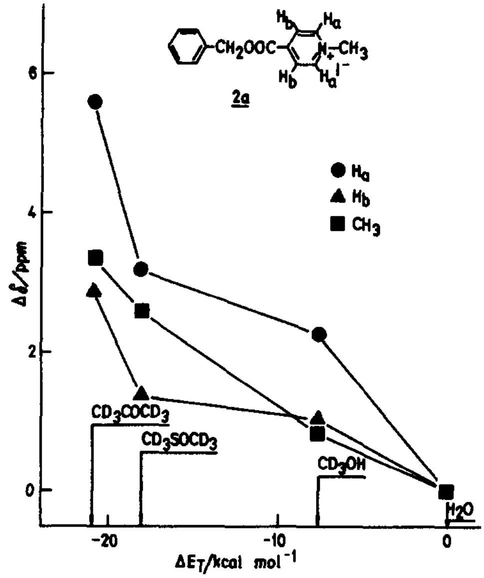


FIG. 8. Graph of chemical shift changes (Δδ) for the "head" protons of ester **2a** as a function of changes in solvent polarity (ΔE_T).

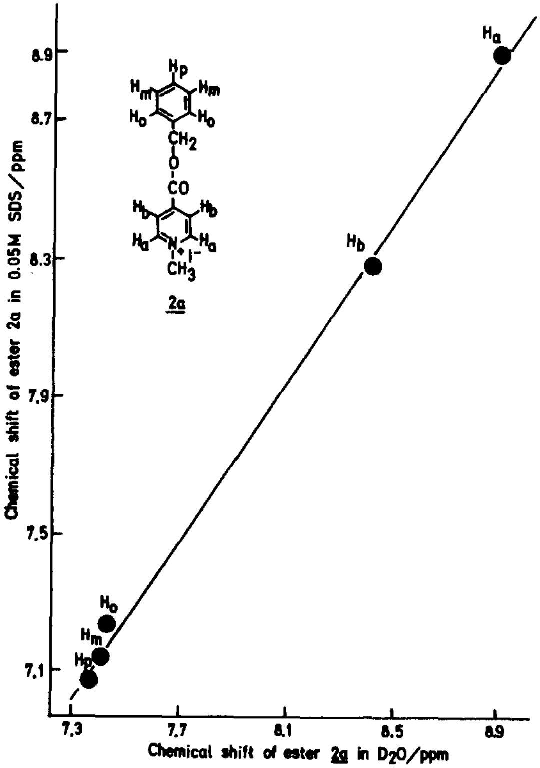


FIG. 9. Linear correlation of chemical shifts of ester **2a** in 0.05 M SDS with chemical shifts in D_2O.

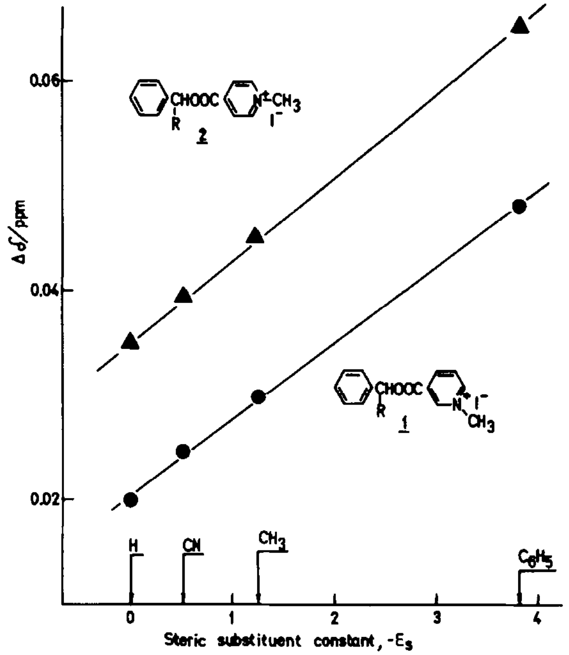
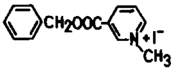


FIG. 10. Dependence of chemical shifts (Δδ) of esters series **1** and **2** on steric substituent constant ($-E_s$).

deshielded and shifts downfield. Because of this inequivalence the signal for proton H_d now appears as a doublet of doublets (Fig. 6). The same was observed for the formation of the inverse micelle (Fig. 7), while signals for all other protons behave as described for compound **2a** (see above). It was also found that Δδ values in different organic solvents containing traces of water decrease with increasing ΔE_T values (*14*), which is contrary to the behavior of compounds which

TABLE 4

^{1}H NMR Chemical Shifts of Ester **1a**[a] in Micelles, D_2O, and Organic Solvents



Solvent	H_a	H_b	H_c	H_d	CH_2	CH_3
0.05 M SDS	9.384	9.077	8.911	8.223	5.260	4.362
D_2O	9.351	8.944	8.928	8.103	5.454	4.403
CD_3CN	9.259	8.9635	8.937	8.148	5.466	4.407
CD_3OH	9.498	9.132	9.050	8.223	5.485	4.495
CD_3SOCD_3	9.557	9.194	9.009	8.252	5.500	4.533
CD_3COCD_3	9.713	9.533	9.156	8.435	5.519	4.773

[a] Concentration of ester **1a** was 0.05 M.

cannot form micelles (Fig. 8). Chemical shifts (δ values) of **2a** in 0.05 M SDS are linearly correlated with chemical shifts in D_2O (correlation coefficient 0.999, Fig. 9) with protons farther from the polar head being the least affected. Both series of compounds also show a good correlation of $\Delta\delta$ values with E_s values (*15*) (Fig. 10) with additionally supports the proposed rationalization of the observed phenomena.

Incidentally, our results offer an explanation of the strange behavior of some pyridinium salts under solvolytic conditions. Katritzky and Brycki (*16*) have found that the solvolysis rates of similar compounds in aqueous organic solvents are practically insensitive to changes in both the Grunwald–Winstein Y values and the E_T values. We believe that this is caused by the formation of inverse micelles containing water molecules in their inner sphere which render them insensitive to changes in the organic component of the medium.

CONCLUSION

Chemical shifts in the ^1H NMR spectra of aromatic compounds of structures similar to cationic micelles (**1a–1e** and **2a–2e**) in D_2O, aqueous SDS solutions, and in organic solvents indicate the formation of micelles, mixed micelles, and inverse micelles of probably spheric structure. It was found that most stable micelles are formed when the substrate–SDS ratio is 1. An explanation is proposed for the insensitivity of solvolysis rates of some pyridinium derivatives to changes in the ionizing power of the solvent. However, the question whether the formation of micelles is preceded by the formation of complexes such as dimers cannot at present be answered.

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