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BINDING AND PHOTOIONIZATION OF N-SUBSTITUTED 2-CHLOROPHENOTHIAZINES IN SDS MICELLES

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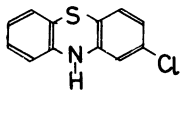
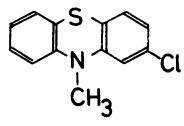
The analogs of chlorpromazine with different length of methylene unit, were synthesized and examined on their binding sites and on the photochemical reactions in the aqueous micelle of sodium dodecyl sulfate (SDS). In spite of the difference of the binding position in the micelle, all the compounds employed show the same photochemical behaviors of the transient species and give the same types of photoproducts.

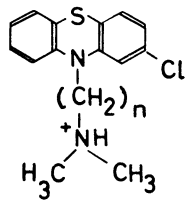
2-Chloro-10-(3-dimethylaminopropyl)-phenothiazine(IV), chlorpromazine, gives the sulfoxide from the reaction of the cation radical(R^+) with oxygen upon UV (>280 nm) irradiation.[1] The compounds(II - VI) which are different only in the length of the methylene chain from chlorpromazine(IV) were prepared and examined on the binding sites in SDS micelle with UV absorption and ^{1}H-FT-NMR spectrum.



I



II



III : n=2

IV : n=3

V : n=6

VI : n=10

Fig. 1. Structure of I, II and III - VI

Table 1. Positions of the second absorption bands and the chemical shifts of the N-substituted 2-chlorophenothiazines

Solvent	II	III	IV	V	VI
Ultraviolet absorptions(nm)					
n-Dodecane	257.0	Insol. (258.5)	Insol. (258.5)	Insol. (259.3)	Insol. (259.0)
p-Dioxane	257.5	258.0	257.5	258.7	259.0
Ethanol	256.0	256.5	257.5	257.7	258.0
Water	Insol.	252.0	254.5	256.3	256.0
10 mM SDS	256.5	255.0	257.3	259.0	259.5

(note) The values in parentheses are for free bases.

Chemical shifts of $-N^+H(C\underline{H}_3)_2$(ppm from TMS)					
n-Dodecane	3.28	Insol.	Insol.	Insol.	Insol.
Chloroform	3.35	2.83	2.66	2.73	2.76
Water	Insol.	2.85	2.80	2.82	2.87
10 mM SDS	3.28	2.89	2.80	2.80	2.87

(note) The value of II is the chemical shift of $N(C\underline{H}_3)$.

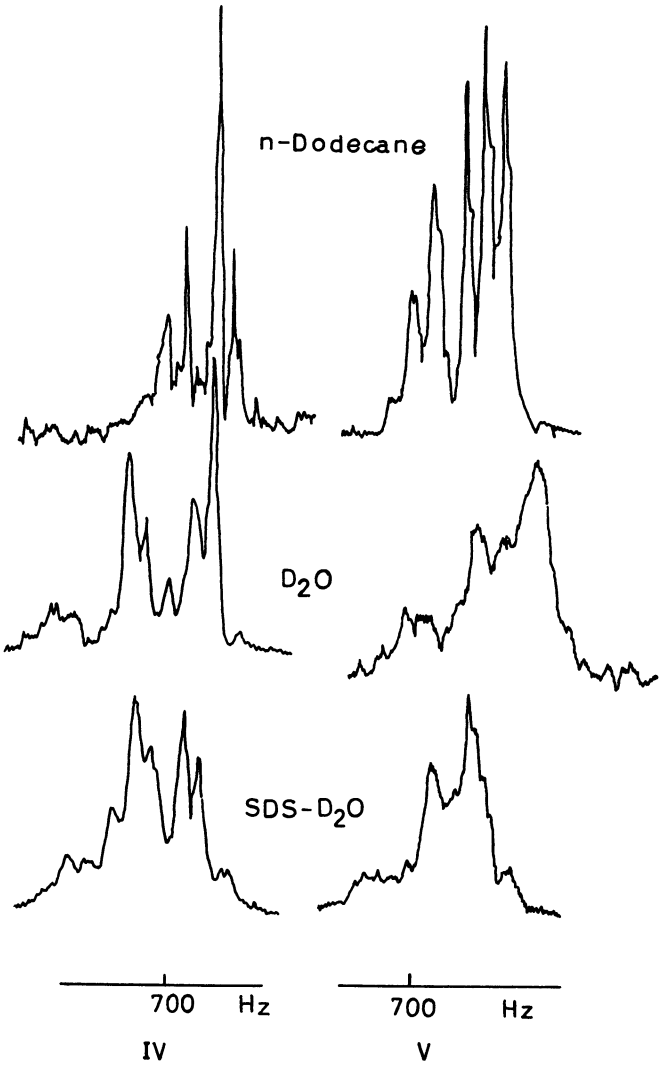


Fig. 2. NMR spectra of the aromatic protons of IV and V in n-dodecane, D_2O and SDS micellar solutions.

The results given in Table 1 are concerned only with the position of the second absorption band since the first absorption band of these compounds is weaker and broader than the second band. The peak positions of II, V and VI in SDS micelle are practically the same with those in n-dodecane, respectively. Values of III and IV in micelle, on the other hand, are rather similar to those in ethanol. Considerable ambiguities arise from the slight differences in the peak positions, however NMR measurements about the chemical shifts of the aromatic protons reveal their binding positions clearly. The chemical shift of the methyl protons of the side chain amine is practically the same with those in water (Table 1) for all the compounds employed, whereas those of the aromatic protons are dependent on the length of the methylene chains (Fig. 2). The spectral patterns for the aromatic protons of II, V and VI in SDS micelle are nearly equal to those in n-dodecane with some line broadening. On the other hand, III and IV show the NMR spectra similar to those in the aqueous solution. Figure 2 shows the cases for IV and V for example. It is established from these results that π-electron moiety of III and IV exists in the core near the surface while that of II, V and VI is localized deeply in the micellar interior. All the compounds employed are solubilized into the micelle with the dimethylammonium group exposed

to water phase.

The transient absorptions of R^+ are weakly observed in the flash photolysis of the aerated aqueous solutions of III - VI, while no transient species are detected for II and free amines of III - VI in n-dodecane and isopentane. Flash photolysis of II - VI in the aerated micellar solution of SDS gives a high yield of photoionization of about five times of those in the aqueous solution, being estimated from the initial absorptions of R^+. Furthermore, practically the same yield of the photoionization has been found among these compounds in the micelle. As we reported earlier,[2] the photoionization of IV is extremely retarded by oxygen in the bulk phase. So this efficient photoionization in the micelle may be ascribed to the fact that the deactivation reaction of the excited molecule with oxygen is prevailed by the rapid photoionization process specific in the micelle. One possibility is that the ejected electron is quickly excluded from the micellar interior through the Stern Layer into the aqueous phase.[3] The other model explaining the above micellar effect is that the appropriate site for the photoionization in the micelle is well defined in the micellar interior and the excited π-electron chromophores move toward this trapping site within very short time[4] not enough to be quenched by oxygen. The negligible photoionization of II in the nonpolar solvent suggests that the reaction site is micellar interior near the surface. It should be, in any event, emphasized that the ionization occur in the same probabilities in the SDS micelle independent to their binding position in the ground state.

Quite small differences are found among these cation radicals(R^+) in their spectral shapes and kinetic behaviors. This supports strongly the fact that the cation radicals obtained, even for VI with highly hydrophobic $-(CH_2)_{10}-$ methylene chain, exist at the same site in the micelle. It is noticeable that the lifetime of R^+ for every compounds in the micelle is larger about two orders of magnitude than in the aqueous solution. Other intermediates which were observed in the aqueous solution[1] could not be detected.

Micellar effect on the overall photochemical reaction was observed. The bleaching rate is considerably increased with the existence of SDS micelle and the sulfoxide formation as well as the dechlorination reaction prevails over other side reactions. These micellar effects on the rate and yield were unexceptionally found for all the compounds employed. The relative yields of

the photoproducts to those in water suggest that the reaction of the intermediate cation radical(R^+) with water[2] is highly suppressed.

These micellar effects on the photoproducts and the lifetimes are explained by the model that the structure of the micelle[5] prevents the reaction of the cation radical(R^+) with water. The addition of L-ascorbic acid in the bulk water phase[6] affects the lifetime of R^+, the bimolecular rate constant of 4×10^5 M^{-1} s^{-1}, slower than that in the aqueous solution(10^7 M^{-1} s^{-1}), being obtained. Considering these results, the binding site of the cation radical (R^+) is concluded to be the micellar interior just beneath the surface. The agreement among the rate constants($1.2 - 1.6 \times 10^2$ s^{-1}) for II - VI suggests that practically the same binding position of R^+ is maintained for the compounds employed. It may be safely concluded that the electrostatic attraction of the 2-chlorophenothiazinyl radical with the head group of SDS micelle plays an dominant role for the site of the solubilization of R^+, exceeding the hydrophobic attraction of the methylene units with the tail of the micelle.

References

1) T. Iwaoka and M. Kondo, Bull. Chem. Soc. Jpn., 47, 980 (1974).
2) T. Iwaoka and M. Kondo, Bull. Chem. Soc. Jpn., 50, 1 (1977).
3) S. A. Alkaitis, G. Beck and M. Grätzel, J. Am. Chem. Soc., 97, 5723 (1975).
4) M. Grätzel and J. K. Thomas, "Modern Fluorescence Spectroscopy" vol. 2, E. L. Wehry, Ed. Plenum Press, New York, N. Y. 1976 p 196.
5) L. R. Fisher and D. G. Oakenfull, Chem. Soc. Rev., 16. 25 (1977).
6) The fact of the existence of L-ascorbic acid in the aqueous phase is evidenced by NMR measurements.

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