*Bull. Chem. Soc. Jpn.*, **53**, 372—376 (1980) [Vol. 53, No. 2

# Studies of Spin Labeled Sodium Dodecyl Sulfate. I. Synthesis and Properties

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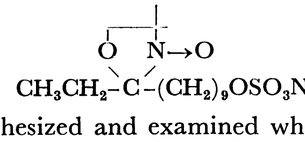
(Received July 20, 1979)

Nitroxide spin labeled surfactant, sodium salt of 2-ethyl-2-[9-(hydroxysulfonyloxy)nonyl]-4,4-dimethyloxazolidin-3-yloxyl, was synthesized and some properties of the compound were studied by means of ESR and conductivity measurements. From conductivity measurements it was found that the critical micelle concentration of the compound was 21.6 mmol kg$^{-1}$ at 25.0$\pm$0.1 °C and the micelle consisted of a small number of labeled surfactant ions. The ESR spectra of the labeled surfactant were measured as a function of concentration and temperature. These spectra showed a typical pattern interpreted in terms of spin exchange. Regarding spin exchange as chemical reaction, second order rate constant was determined from the analysis of line width and compared with the values obtained by diffusion controlled model.

Spin label method[1)] developed by Ohnishi and McConnell[2)] has become more important because the ESR spectrum reflects sensitively the rotational motion in the wide range, *i.e.*, $10^{-11}$—$10^{-3}$ s,[3)] the local environment, and the orientation of labeled compound. In particular, the application to biological system has offered many valuable information concerning the dynamic properties.[4)]

In general, it is well known that surfactant molecules form the ordered aggregates known as micelles. Since a dynamic study of micellar solution by means of ESR was first attempted by Waggoner *et al.*,[5)] many studies of micellar solution have been examined.[6—8)] However, most of the studies have been performed by spin probe method. In order to obtain more detailed information on micelle, it is desirable to use the sample of micellar solution which consists of the spin labeled surfactant molecules only. So, a nitroxide spin label compound,[9)] sodium salt of 2-ethyl-2-[9-(hydroxysulfonyloxy)nonyl]-4,4-dimethyloxazolidin-3-yloxyl (SL-SDS)



$CH_3CH_2\text{-}C\text{-}(CH_2)_9OSO_3Na$ (SL-SDS)

was synthesized and examined whether this compound is able to form micelle, characteristic of surface active molecule, or not.

In this paper, the results of a study of SL-SDS solution by means of ESR and conductivity measurements will be presented.

## Experimental

*Materials. Preparation of SL-SDS.*[9)] Dimethyl decanedioate was prepared by refluxing a mixture of 202 g (1 mol) of decanedioic acid, 800 ml of methanol, and 80 ml of concentrated sulfuric acid for 3 h. The reaction mixture was diluted with water of 3 times volume and the diester was extracted with 2000 ml benzene. After the removal of benzene under reduced pressure, the residue was transferred to a flask containing 85.6 g (0.5 mol) of anhydrous barium hydroxide in 1000 ml methanol. The flask was quickly closed with a soda-lime tube and the mixture was allowed to stand for 24 h with stirring at room temperature. The white barium salt collected by filtration was washed with two 200 ml portions of methanol and was shaken with a mixture of 1000 ml of 4 M HCl and 1000 ml of ether in a separatory funnel. The ether extract was washed with three 1000 ml portions of water. The ether was removed by evaporation and the residue was distilled under reduced pressure. The yield of methyl hydrogen decanedioate was 130 g (60%).

In a flask were placed 130 g (0.6 mol) of methyl hydrogen decanedioate and 143 g (1.2 mol) of thionyl chloride. The solution was gently warmed at 30—40 °C for 3 h and allowed to stand for 12 h at room temperature. The excess thionyl chloride was removed under reduced pressure and the residue was distilled, yielding 127 g (70%) of 9-(methoxycarbonyl)nonanoyl chloride.

A solution of ethyl bromide 30.2 g (0.2 mol) in 100 ml of anhydrous ether was added to the 100 ml ether solution containing a 0.2 g atom of magnesium turnings and the mixture was refluxed for 30 min longer. To the mixture was portion-wise added 18.3 g (0.1 mol) of anhydrous cadmium chloride at 0 °C. The mixture was refluxed until a Gilman test[10)] for the Grignard reagent was negative. The ether was completely removed and 200 ml of anhydrous benzene was added. The mixture in benzene was refluxed for 1 h. A solution of acid chloride, 9-(methoxycarbonyl)nonanoyl chloride 47 g (0.2 mol), dissolved in 50 ml anhydrous benzene was slowly added to the solution of the organo-cadmium compound and refluxed with stirring for an additional hour. The reaction product was cooled in an ice bath and decomposed by dropping of 50 ml of ice water, followed by an addition of 20% sulfuric acid sufficient to produce two transparent layers. The benzene solution was washed successively with 100 ml of water, 100 ml of 5% sodium hydrogencarbonate, 100 ml of water, and 50 ml of saturated sodium chloride. Then, the benzene solution was dried on anhydrous sodium sulfate. After removal of benzene, the reaction product was distilled (bp 115—117 °C/399 Pa), yielding 32 g (70%) of methyl 10-oxododecanoate; IR 1710 (C=O) and 1735 cm$^{-1}$ (ester C=O); NMR ($CCl_4$) $\delta$=0.99 (3H, t, $J$=7.6 Hz, $CH_3$).

To 500 ml of toluene were dissolved 22.8 g (0.1 mol) of the methyl 10-oxododecanoate, 89 g (1.0 mol) of 2-amino-2-methyl-1-propanol, and 100 mg (0.5 mmol) of *p*-toluenesulfonic acid monohydrate. The mixture was refluxed for 3 days using a Dean-Stark trap for continuous water removal. The toluene solution was washed 6 times with 200 ml portions of saturated sodium hydrogencarbonate solution and 4 times with 200 ml portions of water and dried through a column of anhydrous sodium sulfate. The toluene was then removed with a rotary evaporator. The residue containing the oxazolidine derivative was directly used to the following reaction for oxidation. Identification of oxazolidine was as follows: NMR ($CCl_4$) $\delta=3.43$ (2H, s, $CH_2O$); IR 1080—1190 $cm^{-1}$ (triplet bands).[11]

A 15 g of the mixture containing the oxazolidine was dissolved in 300 ml of anhydrous ether and cooled at 0 °C in an ice bath. A cold solution of 100 ml ether containing 9 g (0.05 mol) of *m*-chloroperbenzoic acid was added drop-wise to the oxazolidine solution over a period of 2 h. The mixture was allowed to stand for 48 h with stirring at room temperature. The ether solution was then washed 4 times with 200 ml portions of saturated sodium hydrogencarbonate solution and water successively, and dried on anhydrous sodium sulfate. After removing ether under reduced pressure, a yellow oil was eluted with hexane–ether (7: 3) through a column of activated alumina. The yield of 2-ethyl-2-[8-(methoxycarbonyl)octyl]-4,4-dimethyloxazolidin-3-yloxyl based on methyl 10-oxododecanoate was 40%.

10 ml anhydrous ether solution containing 17.5 mg (0.46 mmol) of $LiAlH_4$ was cautiously added to 20 ml anhydrous ether solution of 144 mg (0.46 mmol) of 2-ethyl-2-[8-(methoxycarbonyl)octyl]-4,4-dimethyloxazolidin-3-yloxyl at −15—−20 °C and the mixed solution was allowed to stand for 30 min at 0 °C. Then, to the solution were carefully added 5 ml of cold water and 10 ml of 5% sulfuric acid at −15—−5 °C. After separation of the ether layer, the aqueous layer was extracted with two 30 ml portions of ether. The ether solutions were dried over anhydrous sodium sulfate. After removing the ether, a yellow oil was eluted with hexane–ether (1: 1) through a column of activated alumina. The nitroxide alcohol, 2-ethyl-2-(9-hydroxynonyl)-4,4-dimethyloxazolidin-3-yloxyl, was obtained in 70% yield after eluting the nitroxide ester. Found: C, 66.90; H, 11.30; N, 4.70%. Calcd for $C_{16}H_{32}O_3N$: C, 67.09; H, 11.26; N, 4.88%; mol wt 286.4.

In a 10 ml flask equipped with a magnetic stirrer were placed 100 mg (0.35 mmol) of nitroxide alcohol, 1 ml of anhydrous dioxane and 0.02 ml of anhydrous pyridine. The solution was stirred and sulfur trioxide-pyridine,[12] 55.5 mg (0.35 mmol), was portion-wise added over a period of 5—10 min at 20—25 °C. Thereafter, the mixture was allowed to stand for 24 h with stirring at 30—40 °C, then cooled, neutralized with 10% sodium hydroxide and poured into 10 ml of cold methanol. After filtration, solvents were evaporated under reduced pressure. A paste-like residue was washed many times with 2 ml portions of ether, dissolved in the ethanol of 10 ml, and filtered. Removing the ethanol, SL-SDS was obtained as the yellow solid in 25% yield. Found: C, 48.88; H, 8.07; N, 3.50%. Calcd for $C_{16}H_{31}O_6NSNa$:C, 49.46; H, 8.04; N, 3.60%; mol wt 388.4.

Sodium dodecyl sulfate (SDS), sodium decyl sulfate (SDeS), and Würster's blue perchlorate were prepared by conventional methods.

3-Carbamoyl-2,2,5,5-tetramethyl-3-pyrrolin-1-yloxy (CTMPY) was purchased from Aldrich Chemical Co.

*Measurement of ESR and Conductivity.* The samples for ESR measurement were carefully deoxygenated by the repetitive freeze-thaw technique and then substituted by dry nitrogen gas. ESR spectra were recorded on JEOLCO model PE-1X spectrometer equipped with a variable temperature accessory. The temperature control was checked with a copper-constantan thermocouple and found to be stable within ±0.5 °C. The magnetic field sweep was calibrated by a Würster's blue perchlorate sample.[13] The measurements of electrolytic conductivity were carried out by means of Yokogawa-Hewlett-Packard (YHP) model 4255A conductivity outfit connecting 4440B decade capacitor (YHP) at 25.0±0.1 °C.

## Results and Discussion

The relations of conductivity against concentration for SL-SDS and SDS are shown in Fig. 1. The kink point in the conductivity curve indicated that the critical micelle concentration (CMC) of SL-SDS was 21.6 mmol $kg^{-1}$ at 25.0±0.1 °C. The CMC of SL-SDS lies between those of SDS (8.3 mmol $kg^{-1}$) and SDeS (33.2 mmol $kg^{-1}$). It is found at first sight that the slope of a straight line below the CMC of SL-SDS is almost the same as that of SDS, but above CMC the slope of the line for SL-SDS is greater than that for SDS. The difference in the slope of conductivity *vs.* concentration for these surfactants above CMC may be largely dependent on the strength of hydrophobic interaction among the surfactant ions. That is, the smaller slope for SDS will be attributed to the strong hydrophobic interaction which gives rise to the rigid micelle with larger aggregation number, while the greater slope for SL-SDS will represent the weak hydrophobic interaction which produces the soft micelle with smaller aggregation number. The weak hydrophobic interaction of SL-SDS may be ascribed to hydrophilic oxazolidine ring introduced into the hydrocarbon chain.

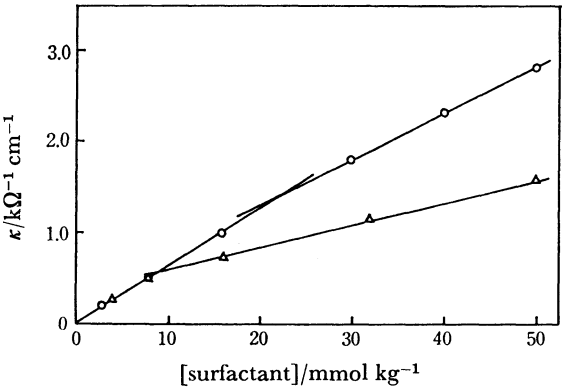


Fig. 1. Relation of specific conductivity *vs.* concentration for SL-SDS(○) and SDS(△) at 25.0±0.1 °C.

Kimizuka and Satake[14] presented the equation for estimating aggregation number from conductivity data as follows:

$$\left(\frac{\Lambda_0-\Lambda}{\Lambda_0-\Lambda_m}\right)^2 = \left\{(z_d-z_c)+(z_d+z_c)\frac{m}{m_m}\right\}\Big/(z_g+z_d), \quad (1)$$

where $\Lambda_0$ and $\Lambda_m$ are the equivalent conductivities at infinite dilution and CMC, respectively. Further, $z_g$ and $z_d$ denote the charges of gegen and detergent ions, respectively, $m$, the concentration in the gram formula weight per kilogram, $m_m$, critical micelle concentration, and $z_c$, the aggregation number of micelle. For SL-SDS, $\Lambda_0=69.4$, $\Lambda_m=63.6$, $|z_g|=|z_d|=1$ and $m_m=21.6$ mmol $kg^{-1}$ were obtained respectively. The aggregation number of SL-SDS micelle, $z_c\simeq6$, was evaluated by inserting these values in Eq. 1. This value is very small as compared with the aggregation number ($z_c\simeq60$) of SDS. The increase in CMC and the decrease in micellar aggregation number of SL-SDS compared with SDS indicate that the micelles are formed under the influence

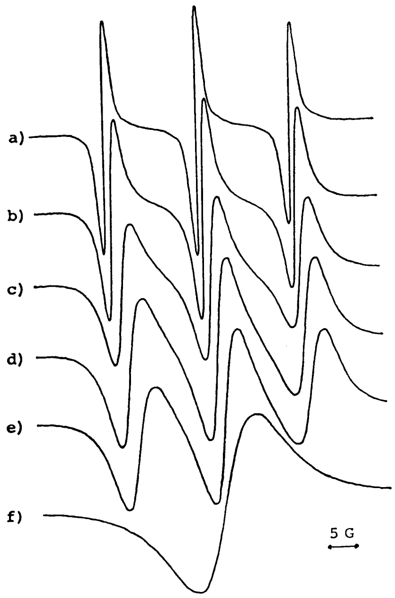


Fig. 2. ESR spectra of SL-SDS in a) 8, b) 16, c) 30, d) 40, e) 50, and f) 250 mmol kg$^{-1}$, respectively, at 25 °C.

of the weak hydrophobic interaction as well as the steric hindrance due to oxazolidine ring.

Figure 2 represents the ESR spectra of SL-SDS as a function of concentration at 25 °C. As the concentration of SL-SDS increases, each line width of nitroxide radical becomes broader and two side bands ($M=\pm 1$ lines, where $M$ is the nuclear spin quantum number) shift gradually to the center of the spectrum so that the individual lines coalesce into one broad line at about 250 mmol kg$^{-1}$. These phenomena can be well interpreted in terms of spin exchange which results from the collision among the radical molecules.[15]

Above CMC, the ESR spectrum of micellar solution with both large aggregation number and low CMC may indicate the superposition of the three sharp lines and single broad line caused by singly dispersed and micellar surfactants, respectively.[16] However, in the case of SL-SDS the superposed monomer-micelle signal was not observed. On the other hand, the ESR spectrum of SL-SDS solution containing 1 mol kg$^{-1}$ NaCl gave rise to the superposed signal as shown in Fig. 3. This implies that the aggregation number of the micelle increases by the added salt. Therefore, the fact that the superposed signal is not observed in SL-SDS solution may be ascribed to a small aggregation number of SL-SDS micelle in agreement with the result of the conductivity measurement. Taking account of the results mentioned above, the observed spectra in (c)—(f) of Fig. 2 are explained as the effect of spin exchange caused by the interaction between the singly dispersed surfactant ions and the surfactant ions of a soft micelle with a small aggregation number.

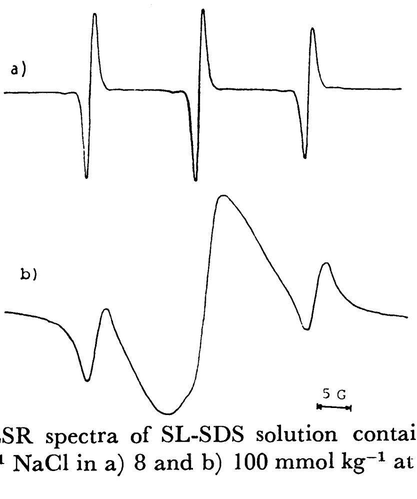


Fig. 3. ESR spectra of SL-SDS solution containing 1 mol kg$^{-1}$ NaCl in a) 8 and b) 100 mmol kg$^{-1}$ at 25 °C.

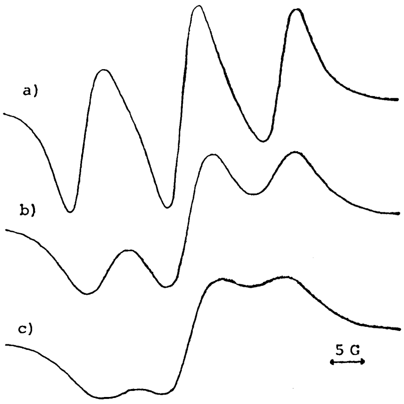


Fig. 4. ESR spectra of 50 mmol kg$^{-1}$ SL-SDS solution at a) 25 °C, b) 55 °C, and c) 70 °C.

The ESR spectra recorded at various temperature are shown in Fig. 4. The broadening of the line width and the shift reflect mainly the effect of spin exchange due to the rise in temperature.

Generally, the analysis of line width offers the important information on the dynamic state of the molecule. In SL-SDS solution, the variation of line width as a function of temperature and concentration may be mainly dependent on spin rotation,[17] dipolar interaction, spin exchange, and monomer-micelle exchange effect.

Foremost spin rotational relaxation is caused by the interaction between the rotational magnetic moment of a paramagnetic molecule and its spin magnetic moment. In order to examine the contribution to the line width of spin rotational relaxation, the line width was plotted against a function $T/\eta$, where $\eta$ is the viscosity of the medium and $T$ is the absolute temperature. For this system, the solution of $5\times 10^{-5}$ mol kg$^{-1}$ was used so that the other relaxation effects except spin rotation could be ignored. As shown in Fig. 5, the relation between line width ($M=+1$ line) and $T/\eta$ exhibits a small contribution to line width of spin rotational relaxation. In Fig. 5, in order to inquire the effect of small spherical molecule, the line width of CTMPY is also plotted against $T/\eta$. Clearly, the relaxation due to spin rotation of the latter was more dominant as compared with the former. However, it can be said that the effect of spin rotation of SL-SDS, is slightly dependent upon radical concentration.

Secondly, when radical concentration increases, it

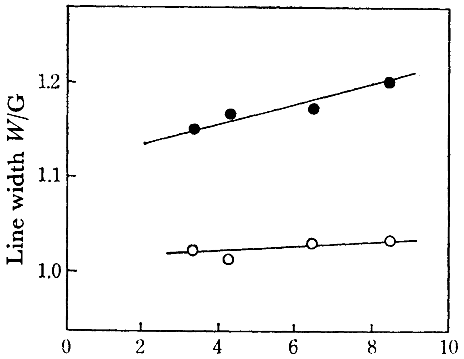


Fig. 5. Width of the $M=+1$ line vs. $T/\eta$ for SL-SDS(○) and CTMPY(●) at each $5\times10^{-5}$ mol kg$^{-1}$ solution.

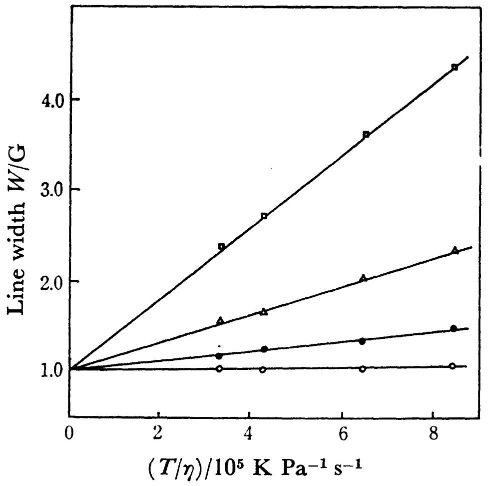


Fig. 6. Width of the $M=+1$ line vs. $T/\eta$ for SL-SDS in 0.05 (○), 4 (●), 8 (△), and 18 mmol kg$^{-1}$ (□), respectively.

will be necessary to consider the contribution to the line width by electron spin dipolar interaction and spin exchange.[18,19] Electron-electron intermolecular dipolar interaction should be proportional to $\eta/T$, while spin exchange interaction should be proportional to $T/\eta$. The observed line width in the concentration range from 0.05 to 20 mmol kg$^{-1}$ showed the dependence on $T/\eta$ and the intercept in each concentration coincides with each another, as shown in Fig. 6. This indicates that the relaxation by spin exchange is predominant in this concentration range. As a result, it may be concluded that the dipolar interaction would not exist in the above concentration range. Furthermore, the fourth effect, *i.e.*, monomer-micelle exchange is taken into consideration for the analysis of line width indicated below.

In Fig. 7, widths of $M=+1$ line vs. concentration of SL-SDS for each temperature are given, in which the line width is given by subtracting the line width ($W(0)$) due to spin rotation at $5\times10^{-5}$ mol kg$^{-1}$ SL-SDS from the observed line width ($W$). The line width ($W-W(0)$) remains almost constant below about 2 mmol kg$^{-1}$ but increases linearly with concentration in the range of 2—20 mmol kg$^{-1}$ due to spin exchange effect. Spin exchange effect is also dependent on temperature and the width increases with the rise in temperature. Above about 20 mmol kg$^{-1}$, which corresponds to CMC of SL-SDS obtained from the conductivity measurement, the plot of line width vs. concentration deviates from a straight line. The effect of monomer-micelle exchange on the line width is not clear because of the signal distortion above 20 mmol kg$^{-1}$ and the small aggregation number of the micelle.

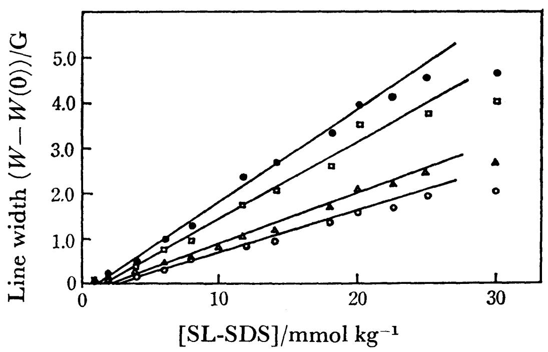


Fig. 7. Width of the $M=+1$ line vs. concentration of SL-SDS at 25 °C (○), 35 °C (△), 55 °C (□), and 70 °C (●).

In order to understand the behavior of the surfactant ions at molecular level, it is desirable and valuable to know the rate constant of spin exchange. Here, provided that spin exchange is regarded as a second order chemical reaction, a second order rate constant can be obtained from the line width.[19] Therefore, according to the method of Eastman *et al.*,[19] the rate constant was estimated and was compared with that obtained from the treatment of the diffusion controlled model.[20]

According to their theory, the second order rate constant $k_2$ is given as follows:

$$k_2 = \frac{3\sqrt{3}}{4}|\gamma_e|h, \tag{2}$$

where $\gamma_e$ is a magnetogyric ratio of a free electron, and $h$ is the slope of a linear plot of the line width vs. concentration at a constant temperature in Fig. 7. The values of $k_2$ at various temperatures were obtained from Eq. 2 and are given in Table 1.

TABLE 1. VALUES OF SECOND ORDER RATE CONSTANT FOR SPIN EXCHANGE

| $\frac{T}{\text{K}}$ | $\frac{k_2\times10^{-9}}{\text{kg mol}^{-1}\text{ s}^{-1}}$ | $\frac{k_2'\times10^{-9}}{\text{kg mol}^{-1}\text{ s}^{-1}}$ |
|---|---|---|
| 289 | 2.2 | 3.6 |
| 308 | 2.7 | 4.7 |
| 328 | 4.0 | 7.1 |
| 343 | 5.0 | 9.3 |

On the other hand, when the probability of spin exchange between two spins during an encounter is close to unity, the reaction limited by the rate of encounters is described as diffusion controlled.[20] Under these conditions, the second order rate constant $k_2'$ is determined by the collision frequency among the radicals. On using the Stokes-Einstein relation for the Brownian diffusion of SL-SDS molecules in the solution, the following equation for collision frequency $\nu$ can be obtained,

$$\nu = \frac{4kT}{3\eta}n^2, \tag{3}$$

where $n$ is equal to the radical concentration, $\eta$, solvent viscosity, and $k$, Boltzmann constant. In this case the second order rate constant $k_2'$ is given by

$$k_2' = \frac{N_A}{1000\rho}\frac{4kT}{3\eta}, \tag{4}$$

where $N_A$ is the Avogadro number and $\rho$, density of the solution. The calculated values using Eq. 4 are also represented in Table 1.

In Table 1, the values of $k_2$ and $k_2'$ at various temperatures are summarized. The dependence of these values on temperature is accounted as the increase of collision between spin molecules. These orders of $k_2$ and $k_2'$, $10^9$ kg mol$^{-1}$ s$^{-1}$, are well consistent with the spin exchange rates for several free radicals in solution.[19,21] This consistency indicates that spin exchange between SL-SDS molecules in this study also can be regarded as diffusion controlled process. However, though $k_2$ and $k_2'$ are of the same order, the values of the latter are approximately twice as large as those of the former. The fact that $k_2$ is not exactly in accord with $k_2'$ may be ascribed to the approximation in which SL-SDS molecule is assumed as small spherical one. In the case of long chain molecule such as SL-SDS, it is a problem whether Stokes-Einstein relation can be simply applied to the system or not. It is probable that diffusion constant of SL-SDS is slightly smaller than that of the simple spherical molecule. On the other hand, regarding SL-SDS molecule as a spherical one in using Stokes-Einstein relation, diffusion constant of SL-SDS becomes more or less larger than true diffusion constant. Therefore, the difference of $k_2$ and $k_2'$ may be ascribed to the incorrect estimation of diffusion constant. Considering the crudeness of the relation described above, the agreement would be satisfactorily good. In the end, it is concluded that the spin exchange for SL-SDS molecules is the same bimolecular reaction as that for small organic free radicals interpreted by diffusion controlled model.[21]

The authors wish to thank Dr. Junji Inanaga of Kyushu University for his helpful suggestions for SL-SDS preparation. We are also grateful to Dr. Sunao Tokii of Saga University for permitting us to use an ESR apparatus.

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