Bull. Chem. Soc. Jpn., ***76***, *601–605 (2003)*

Micelle-Enhancing Effect on a Flavin-Photosensitized Reaction of Benzyl Alcohols in Aqueous Solution

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(Received September 9, 2002)

The tetra-*O*-acetylriboflavin (Fl)-photosensitized dehydrogenation of benzyl alcohols **1** proceeded more efficiently in aqueous solutions in the presence of sodium dodecyl sulfate (H_2O/SDS) than acetonitrile solutions. The fluorescence quenching of Fl with **1** occurred efficiently in H_2O/SDS. The apparent rate constants (k_Q) for the fluorescence quenching were determined by Stern–Volmer plots. The plots of k_Q vs the free-energy changes for the electron transfer from **1** to the excited singlet of Fl showed the Rehm–Weller-type correlation. However, plots for H_2O/SDS were deviated from a curve calculated by the Rehm–Weller equation, although plots for MeCN were fitted to the calculated curve. The deviation in H_2O/SDS is attributable to the incorporation of Fl and **1** into the hydrophobic domain of the SDS micelle, where the condensation, less-polar medium, and exteior negative charge operate favorably for efficient electron transfer.

Flavins are well-known to be biologically important coenzymes, and have received much attention as electron-transfer photocatalysts.[1] The photochemistry of the flavin and their analogs in organic solvents is well documented,[2] allowing them to be used as photocatalysts for a variety of reactions involving the splitting of cyclobutane compounds[3] and deamination.[4] In aqueous solution, however, efficient flavin-photosensitization is still unsuccessful, although a biologically important reaction occurred in aqueous solution.

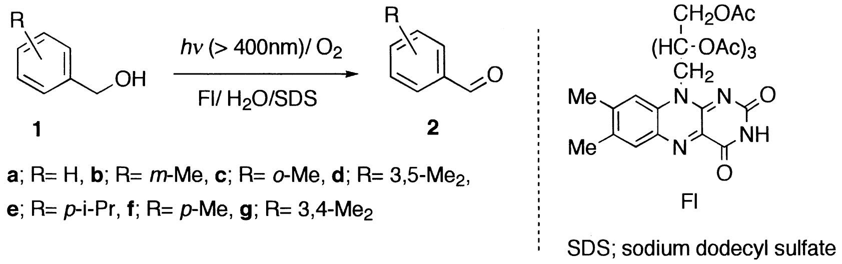
In our recent work on the flavin-photosensitized monomerization of *cis*, *syn*-cyclobutane dimers of 1,3-dimethylthymine and 1,3-dimethyluracil, which is a model reaction of enzyme-dependent photorepair for UV-damaged DNA,[5] we found that flavin-photosensitized monomerization occurred efficiently in aqueous solution by the addition of a surfactant. Thus, a micellar effect has operated effectively to activate flavin-photosensitization in aqueous solution.

Dehydrogenation is a major family of flavin-photosensitized reactions. In the dehydrogenation of benzyl alcohols photosensitized by flavin and their analogs, Fukuzumi et al. and other groups have well elucidated the additive effects of an acid[6,7] or the Mg ion[8] and the mechanistic aspects[8] in MeCN. Therefore, we report here on the micellar effect concerning the dehydrogenation of benzyl alcohol derivatives **1** photosensitized by tetra-*O*-acetylriboflavin (Fl) in aqueous solution (Scheme 1).

Results

Fl-Photosensitized Dehydrogenation of 1. The irradiation of an oxygen-saturated aqueous solution (2 cm^3) containing Fl (0.5 mmol dm^{-3}), **1** (10 mmol dm^{-3}), and sodium dodecyl sulfate (SDS; 30 mmol dm^{-3}) at 405 nm gave the benzaldehydes **2** as the sole product. We used substituted benzyl alcohols **1a–k** with widely varying oxidation potentials ($E_{1/2}^{ox}$ vs Ag/AgCl) from 1.14 to 1.78 V (Table 1). A typical example is the Fl-photosensitized dehydrogenation of *p*-methylbenzyl alcohol (**1f**) in aqueous solution in the presence of SDS (H_2O/SDS), which gave **2f** in 94% conversion after irradiation for 18 h. The turnover number in the formation of **2f**, based on the initial amount of Fl, exceeded 1900%. On the contrary, the Fl-photosensitized dehydrogenation in MeCN was very inefficient; the conversion was $< 5\%$ (Fig. 1), as has been reported.[8] In the cases of methoxy-substituted benzyl alcohols **1h–k**, the Fl-photosensitized reaction gave complex mixtures.[6]

The quantum yields (Φ) for the formation of **2a–g** were determined at various concentrations of SDS. As an example, Fig. 2 shows the dependence of Φ on the concentration of SDS (0–40 mmol dm^{-3}) in the Fl-photosensitization of an oxygen-saturated aqueous solution (2 cm^3) containing Fl (0.5 mmol



Scheme 1.

Table 1. Fluorescence Quenching of Fl by Benzyl Alcohols **1** in MeCN and Aqueous SDS Solution

Quencher **1**	$E_{1/2}^{\mathrm{ox}}$ a)	ΔG b)	log k_Q c)	
	V	kJ mol^{-1}	MeCN	H_2O/SDS
$C_6H_5CH_2OH$ (**1a**)	1.78	+20.5	no$^{d)}$	8.60
m-$MeC_6H_4CH_2OH$ (**1b**)	1.73	+15.5	no$^{d)}$	9.66
o-$MeC_6H_4CH_2OH$ (**1c**)	1.72	+14.6	no$^{d)}$	9.75
3,5-$Me_2C_6H_3CH_2OH$ (**1d**)	1.72	+14.6	no$^{d)}$	10.21
p-*i*-$PrC_6H_4CH_2OH$ (**1e**)	1.70	+12.5	7.46	9.96
p-$MeC_6H_4CH_2OH$ (**1f**)	1.65	+7.9	8.00	10.15
3,4-$Me_2C_6H_3CH_2OH$ (**1g**)	1.65	+7.9	8.30	10.31
m-$MeOC_6H_4CH_2OH$ (**1h**)	1.62	−11.3	9.48	10.40
p-$MeOC_6H_4CH_2OH$ (**1i**)	1.43	−13.4	9.52	10.39
3,5-$(MeO)_2C_6H_3CH_2OH$ (**1j**)	1.34	−22.2	9.70	10.52
3,4-$(MeO)_2C_6H_3CH_2OH$ (**1k**)	1.14	−41.4	9.98	10.68

a) Oxidation potentials in V vs Ag/AgCl. b) Free energy changes (kJ mol^{-1}) from the electron transfer from **1** to ^{1}Fl* calculated according to Eq. 1 using −0.99 V (95.4 kJ mol^{-1}), 241 kJ mol^{-1}, and 5.4 kJ mol^{-1} as $E_{1/2}^{\mathrm{red}}$(Fl), $E^{0\text{-}0}$, and $e^2/\varepsilon a$ term, respectively. c) The rate constants (k_Q) in mol dm^{-3} for the fluorescence quenching determined by Stern–Volmer plots. Lifetimes (τ_F) of Fl are 7.2 ns and 5.0 ns for MeCN and an aqueous solution with SDS (30 mmol dm^{-3}), respectively. d) Not observed.

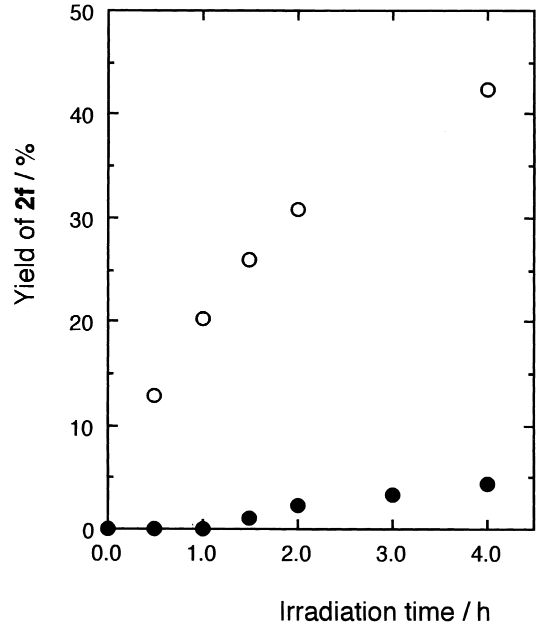


Fig. 1. Time-conversion plots for Fl-photosensitized dehydrogenation of **1f** in aqueous SDS solution (○) and in MeCN (●).

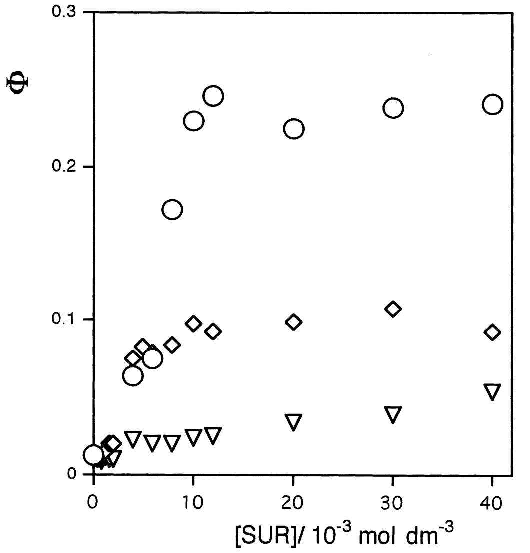


Fig. 2. Dependence of *Φ* on [SUR] for Fl-photosensitized dehydrogenation of **1f**: SUR: SDS (○), CTAC (◇), and PED (▽).

dm^{-3}) and **1f** (10 mmol dm^{-3}). In the absence of SDS, *Φ* was 0.07. By the addition of SDS in concentrations higher than the critical micelle concentration (CMC = 8 mmol dm^{-3}) to the solution, *Φ* increased to reach 0.24. A similar micelle-enhancing effect of SDS was observed in the Fl-photosensitized dehydrogenation of **1a**–**e**,**g** in aqueous solution. However, the other surfactants, such as hexadecyltrimethylammonium chloride (CTAC) and polyethylene glycol dodecyl ether (PED), showed no remarkable micelle-enhancing effect (Fig. 2).

For a kinetic analysis, *Φ* were measured at several concentrations of **1a**–**g**. Double-reciprocal plots of *Φ* vs the concentration of **1a**–**g** gave straight lines. The ratio (*I*/*S*) of the intercept (*I*) to the slope (*S*) in the plots are listed in Table 2.

Fluorescence Quenching. The fluorescence quenching of Fl (0.5 mmol dm^{-3}) by **1a**–**k** (0–30 mmol dm^{-3}) was performed in an aqueous solution in the presence of SDS (30 mmol dm^{-3}). Under excitation at 358 nm, the emissions of Fl were observed at 517 nm in H_2O/SDS, regardless of the presence of **1**. The ratio of the intensities (I_0/I) in the absence to that in the presence of the given concetration of **1** was plotted against the macroscopic concentrataion of **1**, giving straight lines for all cases. For the case that the kinetics in H_2O/SDS obeys the Stern-Volmer equation, the slope (K_{SV}) = $k_Q\tau_F$, the apparent rate constants (k_Q) for fluorescence quenching were determined using the slope of the plots and lifetimes (τ_F), which was 7.2 ns in H_2O/SDS. The observed k_Q are listed in Table 1.

Also, fluorescence quenchings was performed in MeCN

Table 2. Data for Kinetic and Fluorescence Experiments of **1a**–**g** in Aqueous SDS Solution

1	Φ^{∞} a)	I/S b)	K_{SV} c)
		$\mathrm{mol^{-1}\ dm^3}$	$\mathrm{mol^{-1}\ dm^3}$
1a	0.24	17	2
1b	0.50	94	23
1c	0.43	116	28
1d	0.32	111	81
1e	0.28	52	46
1f	0.54	79	70
1g	0.40	155	102

a) Limiting quantum yield obtained by the inverse of intercept of the double reciprocal plots of Φ vs [**1**]. b) Intercept-to-slope ratio of the double reciprocal plots of Φ vs [**1**]. c) Stern–Volmer constants for the fluorescence quenching of Fl with **1**.

solutions. The emission of Fl was observed at 505 nm under excitation at 358 nm. Undoubtedly, the rate constants (k_Q) for fluorescence quenching in MeCN were determined by the usual Stern–Volmer plots, using τ_F, which was 5.0 ns in MeCN (Table 1).

Discussion

Consideration Based on Rehm–Weller Equation. As shown in Table 1, the free-energy changes (ΔG) for an electron transfer from **1** to the excited singlet state of Fl ($^1\mathrm{Fl}^*$) were estimated by the Rehm–Weller equation (Eq. 1)[9] using the reduction potential of Fl ($E_{1/2}{}^{\mathrm{red}} = -0.99$ V), $E_{1/2}{}^{\mathrm{ox}}$ of **1** (see Table 1), and the excitation energy of Fl ($E^{0\text{-}0}$ = 241 kJ mol^{-1}),[10] respectively. The $e^2/\varepsilon a$ term denotes the Coulombic term, where e is the electronic charge, ε is the dielectric constant of the medium, and a is the effective radius of the solvent cavity. The $e^2/\varepsilon a$ term is usually 5.4 kJ mol^{-1} for MeCN ($\varepsilon = 37.5$).[8]

As shown in Fig. 3, the plots of log k_Q vs ΔG in MeCN and H_2O/SDS gave a Rehm–Weller-type correlation, showing the occurrence of electron-transfer quenching. Theoretically, the k_Q values can be predicted by a calculation according to the Rehm–Weller equation (Eq. 2) where the activation energy (ΔG^*) can be derived according to Eq. 3 at 296 K using an intrinsic barrier ($\Delta G^*(0)$). Rehm–Weller plots of the observed log k_Q in MeCN were fitted with that of the calculated log k_Q using 12.5 kJ mol^{-1} as $\Delta G^*(0)$, as shown in Fig. 3. On the other hand, the Rehm–Weller plots of the observed log k_Q in H_2O/SDS are horizontally and vertically deviated from the calculated curves (Fig. 3).

$$\Delta G = 96.4\,(E_{1/2}{}^{\mathrm{OX}} - E_{1/2}{}^{\mathrm{red}}) - e^2/\varepsilon a - E^{0\text{-}0} \tag{1}$$

$$k_Q = \frac{2 \times 10^{10}}{1 + 0.25\exp(\Delta G^*/RT) + \exp(\Delta G/RT)} \tag{2}$$

$$\Delta G^* = \frac{\Delta G}{2} + \sqrt{\left(\frac{\Delta G}{2}\right)^2 + \left(\frac{\Delta G^*(0)}{2}\right)^2} \tag{3}$$

$$\ln\frac{I_0}{I} = \frac{n[\mathbf{1}]}{[\mathrm{SDS}] - [\mathrm{SDS}]_0} \tag{4}$$

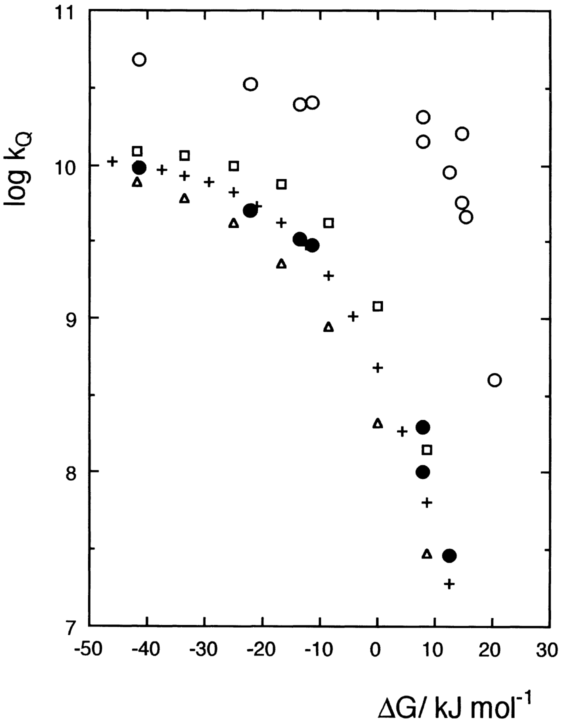


Fig. 3. Rehm–Weller plots of log k_Q for MeCN (●) and aqueous SDS solution (○) along with the Rehm–Weller plots of log k_Q calculated by Eq. 2 using 10.0 (□), 12.5 (+), 14.6 kJ mol^{-1} (△) as $\Delta G^*(0)$.

$$\frac{1}{\Phi} = \frac{1}{\alpha\beta}\left(1 + \frac{1}{k_Q\tau_F[\mathbf{1}]}\right) \tag{5}$$

$$I/S = k_Q\tau_F = K_{\mathrm{SV}} \tag{6}$$

Micelle-Enhancing Effect. Since Fl was less soluble in water and entirely solubilized upon the addition of SDS, Fl was incorporated into the SDS micelle. The incorporation of Fl into a micelle was confirmed by the circular dichroism (CD) spectra of Fl. The CD spectrum of Fl changed upon the addition of SDS into an aqueous solution of Fl (Fig. 4). Especially, a remarkable spectral change was observed upon the addition of SDS at concentrations higher than CMC, revealing the incorporation of Fl into a micelle. In the presence of 30 mmol dm^{-3} of SDS, the concentration of the micelle was of the same order as that of Fl (0.5 mmol dm^{-3}), because the mean aggregation number of the SDS micelle (n) of SDS was reported to be 60.[11] Therefore, we assume that one molecule of Fl is incorporated into one micelle.

Turro et al. analyzed the micelle effects by fluorescence quenching.[11] They used quenchers which partition themselves exclusively in a miceller phase. The fluorescence of the fluorophore in micelles was completely quenched by the quencher present in the same micelle. They proposed the Eq. 4 where [SDS] and $[\mathrm{SDS}]_0$ donote the macroscopic concentration of SDS and the free monomer concentration of SDS, which equals to CMC (8 mmol dm^{-3}), respectively.

According to Eq. 4, we made the plots of $\ln(I_0/I)$ vs. the concentration of **1k**, which was the most powerful quencher

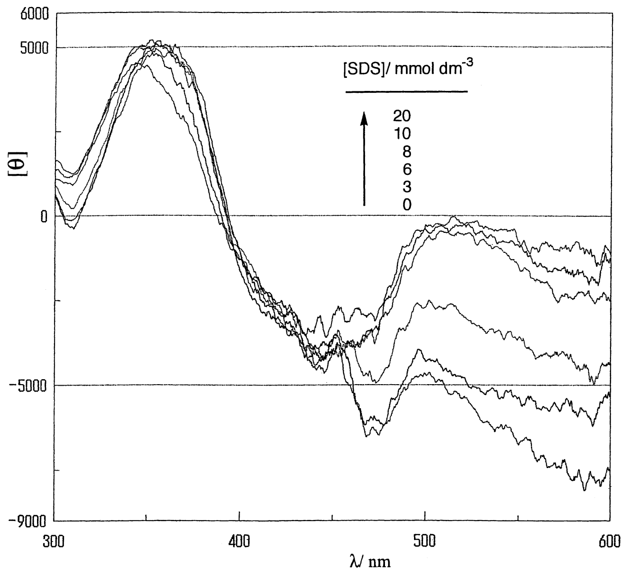


Fig. 4. CD spectral change of Fl in aqueous solution by the addition of SDS.

among **1**, as shown in Fig. 5. From the slope of the plots, n was calculated to be 4.3, which is largely different from the reported value ($n = 60$). Because quencher **1** was, to some extent, soluble in aqueous solution, **1k** might partition itself between an aqueous bulk solution and the hydrophobic domain of the SDS micelle. This is a reason why the observed n was not in agreement with the reported value.

Electron transfer from **1** to ^{1}Fl* mainly occurred at the hydrophobic domain of the SDS micelle, where the polarity of the medium is lower than the bulk water, and the reactants would be free from strong solvation with water molecules. If the $e^2/\varepsilon a$ term varies depending on the medium polarity (ε), the ΔG value would be changed by the medium polarity according to Eq. 1. For a lower medium polarity, a larger $e^2/\varepsilon a$ and a more negative ΔG would be brought about. Therefore, it is deduced that the horizontal deviation in the Rehm–Weller plots in H_2O/SDS is due to the less-polar medium.

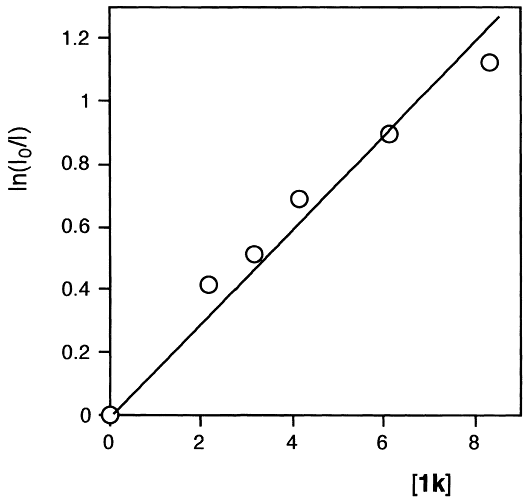


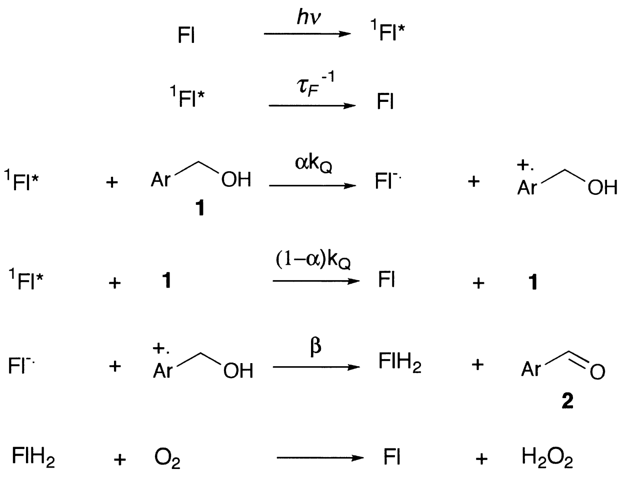
Fig. 5. Plots of $\ln(I_0/I)$ vs [**1k**].

The k_Q values apparently depended on the **1** used. In the cases of **1g–k**, where ΔGs for electron transfer were largely exoergic, k_Q exceeded the diffusional limit of the usual solvents ($k_Q = 1.60 \times 10^{10}$ mol dm^{-3}, $\log k_Q = 10.20$). Very fast electron transfer between **1g–k** and FL, located in a position very near to each other in the micelle occurred, resulting a vertical deviation from the curve calculated for dynamic quenching. Because the decrease in the electron-donating ability of **1**, i.e. $E_{1/2}{}^{ox}$ of **1**, was higher, the electron-transfer process between **1** and FL was slower, even in the micelle.

The Fl-photosensitization can be enhanced by an anionic surfactant, SDS, but not at all by either cationic (CTAC) or nonionic (PED) surfactants. As has been reported concerning the Fl-photosensitized monomerization of *cis*, *syn*-cyclobutane dimers of 1,3-dimethylthymine and 1,3-dimethyluracil,[5] the exterior anionic sulfate groups surrouding the SDS micelle are susceptible to hydrogen bonding with water molecules to form relatively rigid solvation shells, leading to a stabilization of the miceller particles having a dense hydrophobic domain. This operates favorably for effcient electron transfer. In the cases of CTAC and PED, hydrogen-bonding is too weak to form stable micelles with a dense hydrophobic domain.

Reaction Mechanism. Scheme 2 shows the mechanistic pathway of the photodehydrogenation of **1** involving electron transfer from **1** to the excited singlet state of Fl (^{1}Fl*). The steady-state analysis of Scheme 2 gives Eq. 5. According to Eq. 5, the ratio (I/S) for a double reciprocal plot of Φ vs [**1**] equals to $k_Q\tau_F$ (Eq. 6). In the Fl-photosensitized dehydrogenation of **1a–g**, the double reciprocal plots of Φ vs [**1**] were made. In the cases of **1d–g**, the I/S values are in satisfactory agreement with the K_{SV} values for fluorescence quenching (Table 2). These results show that the photosensitization of **1d–g** occurred through ^{1}Fl*. On the other hand, in the cases of **1a–c**, the k_Q values of the fluorescence quenching of Fl were slower than 6×10^9 mol^{-1} dm^3 s^{-1} and the I/S values did not agree with the K_{SV} values. This is a case where participation of the triplet state of Fl should be considered.

The limiting quantum yields (Φ^∞) which were obtained from the inverse of the intercept of the double reciprocal plots of Φ vs [**1**] equal to $\alpha\beta$ in Eq. 5. As shown in Table 2, the α values were relatively high, since $\beta < 1$. The exterior negative



Scheme 2.

charges surrounding the micellear pariticles might efficiently work as an electrostatic force to separate $\mathrm{Fl}^{-\bullet}$ and $\mathbf{1}^{+\bullet}$ to prevent any recombination of the radical ions.

Consequently the micelle-enhancing effect can be attributed to the incorporation of both **1** and Fl into the SDS micelle, where the condensation, less-polar medium, and the exteior negative charge operate favorably for efficient electron transfer.

Experimental

Fluorescence quenching was performed on a Hitachi F-4500 fluorometer for an acetonitrile and an aqueous SDS (30 mmol dm^{-3}) solution (3 cm^3) containing Fl (0.5 mmol dm^{-3}) and a given concentration of the quencher under deaerated conditions. The fluorescence lifetimes were determined on a Horiba NAES 550 instrument. CD spectra were obtained on a JEOL DIP1000. The redox potentials were measured for a MeCN solution containing $\mathrm{Et_4NBF_4}$ (0.1 mol dm^{-3}) as a supporting electrolyte on a BAS cyclic voltammetry at 23 °C at a scan rate of 0.3 V/s for **1** and 30 mV/s[12] for Fl using a glassy carbon (the working electrode), a Pt plate (the counter electrode), and Ag/AgCl (the reference electrode).

Benzyl alcohols were purchased from Aldrich and Wako Chemicals and were used without any further purification. Fl was prepared by a reaction of riboflavin with acetic anhydride in dry pyridine, and recrystallized from ethanol/chloroform mixtures.[13]

Photoreaction. Aliquot portions of an aqueous solution (2 cm^3) containing **1** (10–50 mmol dm^{-3}, usually 10 mmol dm^{-3}) and Fl (0.5 mmol dm^{-3}) in the presence of sodium dodecyl sulfate (SDS; 0–50 mmol dm^{-3}, usually 30 mmol dm^{-3}) were introduced into Pyrex tubes and bubbled by $\mathrm{O_2}$ gas under cooling with ice for 15 min. Irradiation was carried out for 0.5 h by a merry-go-round turntable by a high-pressure Hg lamp through a filter solution of an aqueous $\mathrm{CuSO_4}$ solution ($>$ 400 nm). GLC analyses of **1** and **2** were performed on a Hitachi G5000A using a capillary column (SGE, BPX 0.5mm × 20 m). An aqueous solution of potasium trioxalatoiron(III) was used as an actinometer for determining of the quantum yields (Φ).[14]

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