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Photocontrol of Micelle Triggered by Malachite Green Carrying a Long Alkyl Chain

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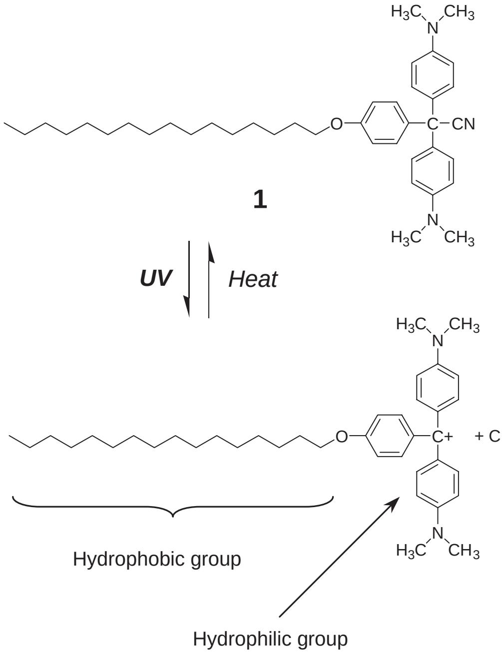
A Malachite Green derivative carrying a long alkyl chain has been designed to realize the photoinduced uptake of oily substances based on its photogenerated amphiphilicity. NMR spectroscopy was used to evaluate the solubility of benzene in cetyltrimethylammoium chloride solution with Malachite Green carrying a long alkyl chain. We found that UV irradiation drastically increased the solubility of benzene in the system of Malachite Green carrying a long alkyl chain. The results for the photoinduced solubilization are in good agreement with the photoionization ratio of Malachite Green carrying a long alkyl chain, which can play an important role in the control of molecular assemblies.

The widespread use of surfactant mixtures for the industrial purposes has stimulated the interest of researchers in the control of formation and rupture of surfactant assemblies such as micelles. In aqueous solution, micelles solubilize lipophilic substances in their interior, which consists of a hydrophobic group of the surfactant. Several studies aiming at the control of uptake and release of lipophilic substances were carried out by external stimuli using pH,[1] temperature,[2] and additives.[3] In particular, light is one of the most desirable methods of stimulus for clean and rapid control of micelle formation. Photochromic compounds such as azobenzene,[4–6] spirobenzopyran,[7] and stilbene[8] were introduced to amphiphilic molecules for the photochemical control of micelle formation. Though the photoinduced trans-cis isomerization of azobenzene and stilbene derivatives induces a structural change,[4–6,8] both of the isomers are still amphiphilic. The photocontrol in the system of spirobenzopyran derivatives,[7] which generates a zwitter ion, was only achieved by shifting the amphiphilicity between the two isomers. Nevertheless, there are few reports concerning the photogeneration of amphiphilicity from a simply lipophilic substance. We have designed Malachite Green leuconitrile carrying a long alkyl chain **1** (Scheme 1),[9] which controls micelle formation photochemically. Malachite Green leuconitrile, a triphenylmethane dye, undergoes photoionization by dissociating the cyanide ion with a high quantum efficiency,[10,11] thus affording a positive charge generation on the molecule by UV irradiation. Therefore, Malachite Green **1**, when ionized photochemically, exhibits hydrophilicity by its triphenylmethyl cation and hydrophobicity by its long alkyl chain (Scheme 1). On the other hand, under dark conditions, **1** behaves only as a lipophilic compound. Once it is irradiated by UV light, it turns out to be a cationic surfactant. Thus, a drastic effect on micelle formation is expected. We have succeeded in the photocontrol of critical micelle concentration (cmc) of cetyltrimethylammonium chloride (CTAC) by a small amount of **1**, i.e. 1.0×10^{-5} mol·dm^{-3} of **1** decreased the cmc from 0.6 to 0.1 mmol·dm^{-3} by UV irradiation.[9]



Scheme 1. Photogenerated amphiphilicity on **1**.

In order to apply the photocontrol of micelle formation in various fields including those of cosmetics, perfumes, and foods, it is desirable to use conventional systems with commercially available surfactants. Therefore, this requires a photoresponsive compound which controls molecular assemblies formed by conventional surfactants. In addition to the industrial application, so-called "photoresponsive command compound" may afford more sophisticated systems because only a small amount of it is able to control the molecular assem-

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blies. The purpose of this work is to control solubilization of oily substances in CTAC micelle by photoresponsive command compound **1**.

Experimental

Synthesis. Bis[4-(*N*,*N*-dimethylamino)phenyl][4-(hexadecyloxy)phenyl]methanenitrile or Malachite Green Carrying a Long Alkyl Chain 1: Dimethyl sulfate (33.3 mmol) and 4-hexadecyloxybenzoic acid (7.3 mmol) were added to a mixture of dry acetone (300 cm^3) and K_2CO_3 (33.3 mmol). After the reaction mixture was refluxed for 8 h, the acetone was evaporated off under vacuum. The residue was extracted with water and benzene and the solvent evaporation of the organic phase afforded methyl 4-hexadecyloxybenzoate. 4-Bromo-*N*,*N*-dimethylaniline (18.0 mmol) was dissolved in anhydrous tetrahydrofuran (THF) (31 cm^3) and the solution was kept at −78 °C in a methanol bath with dry ice under an argon atmosphere. A hexane solution of butyllithium (20.3 mmol) was injected gradually into the THF solution while stirring. To the mixture was added dropwise a THF (38.5 cm^3) solution of methyl 4-hexadecyloxybenzoate (7.7 mmol). The reaction mixture was allowed to warm slowly to room temperature and then stirred for an additional hour. After the reaction, the THF was evaporated off under vacuum and water (100 cm^3) was added to the residue. The aqueous phase was then neutralized by 0.1 mol•dm^{-3} hydrochloric acid. Extraction with benzene, followed by vacuum evaporation of the solvent, afforded a dark-green oily product of bis[4-(*N*,*N*-dimethylamino)phenyl][4-(hexadecyloxy)phenyl]methanol, which was used for the subsequent cyanization without further purification. The crude product (approximately 7.75 mmol) was dissolved in dimethyl sulfoxide (20 cm^3) and heated at 60 °C in a hood. Hydrochloric acid (94 mmol) and then KCN (347 mmol) were added to the solution and the mixture was stirred for 10 min. For complete dissolution of the KCN, an appropriate amount (up to 100 cm^3) of water was added. The reaction mixture turned light yellow and then a crude product of Malachite Green **1** precipitated. Recrystallization of the filtered precipitate from hexane yielded a white solid of **1** (27%): mp 84 °C, ^{1}H NMR (270 MHz, $CDCl_3$) δ 0.87 (t, $J = 6.7$ Hz, 3H, CCH_3), 1.24–1.42 (m, 26H, $(CH_2)_{13}$), 1.76 (m, 2H, CCH_2C), 2.94 (s, 12H, NCH_3), 3.93 (t, $J = 6.6$ Hz, 2H, OCH_2), 6.63 (d, $J = 9.0$ Hz, 4H, *m*-H of NPh), 6.80 (d, $J = 8.7$ Hz, 2H, *m*-H of OPh), 7.02 (d, $J = 8.7$ Hz, 4H, *o*-H of NPh), 7.10 (d, $J = 8.7$ Hz, 2H, *o*-H of OPh). Anal. Calcd for $C_{40}H_{57}N_3O$: C, 80.62; H, 9.64; N, 7.05%. Found: C, 80.28; H, 9.67; N, 7.00%.

Other Materials. Cetyltrimethylammonium chloride (CTAC) was recrystallized from THF. Deuterium oxide had a purity of 99.9%. Water was deionized. Other materials were analytical grade and were used without further purification.

Preparation of Sample Solutions. Sample solutions were prepared using 0.1 mol•dm^{-3} acetate buffer (pH 4.8), unless otherwise noted. Photoirradiation was continued for 15 min. UV light source (<330 nm) was a xenon lamp (500 W) equipped with a photoguide tube and a Toshiba UV-D33S filter. For dynamic light scattering measurements, sample solutions were filtered first by a 0.45-μm Millipore filter and then by a 0.1-μm Millipore filter. Sample solutions for NMR measurements were prepared in D_2O, instead of deionized water, containing 1,4-dioxane (1 vol %) as the internal reference. To each of 1-cm^3 sample solution, benzene was added in excess (approximately 0.1 cm^3) and the excess of benzene was removed after the solubilization. The excess benzene never caused reversed micelle or emulsion in the prepared solutions. By a similar procedure, other series of sample solutions including known amounts of benzene were prepared; to each of 10-cm^3 sample vials equipped with silicone-rubber cap was added 1 cm^3 of sample solution. Benzene was added in a different amount to each of the vials, which was then sealed. The solution was withdrawn by a syringe from the vial just before its measurement. When excess benzene that did not dissolve in the aqueous solution was detected, the sample was withdrawn so as not to include the benzene.

Dynamic Light Scattering. Dynamic light scattering measurements were made using an Ohtsuka DLS-700 instrument equipped with a helium-neon laser (632.8 nm, scattering angle of 45°) at 25 °C.

^{1}H NMR. The experiment temperature was 25 °C. NMR measurements were carried out on a JEOL JNM-270 instrument operating at 270.05 MHz.

Photoionization Ratio. The ionization ratio was calculated, which is defined by A_{MGL}/A_{MGO}, where A_{MGL} and A_{MGO} are the absorbance at 610 nm of 1.0×10^{-5} mol•dm^{-3} **1** after UV irradiation and 1.0×10^{-5} mol•dm^{-3} Malachite Green oxalate in CTAC solution, respectively.

Results and Discussion

Photoisomerization of Malachite Green in CTAC Solution. Figure 1 shows a typical absorption-spectral change of the sample solution before and after UV irradiation. An absorption peak around 270 nm, which was decreased by UV irradiation, can be assigned to the electrically neutral leuconitrile form of **1**. Its ionized form was confirmed by the appearance of a peak at 610 nm after UV irradiation, indicating the photoinduced ionization of **1**. The sample solutions were 0.1 mol•dm^{-3} acetate buffer solutions (pH 4.8) containing 1.0×10^{-5} mol•dm^{-3} of **1** and 4.0 mmol•dm^{-3} of CTAC. Even without photoirradiation, the ionization of **1** was strongly promoted in solutions more acidic than pH 4.0. When the pH of the sample solution was above 5.0, the photoionized **1** was immediately hydroxylated and the positive charge on the Malachite Green moiety disappeared. Therefore, an appropriate buffer solution was necessary for all samples in this work. The photoionized **1** was stable in the buffer solution and the ab-

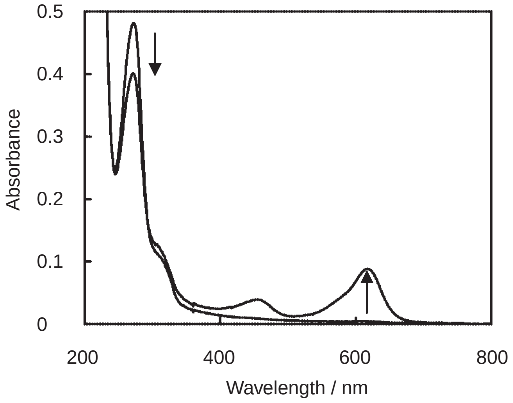

Fig. 1. Absorption-spectral changes of 0.1 mol•dm^{-3} acetate buffer solution containing 4.0 mmol•dm^{-3} of CTAC and 1.0×10^{-5} mol•dm^{-3} of **1** under dark conditions and after UV irradiation for 15 min. The arrows denote changes by photoirradiation.

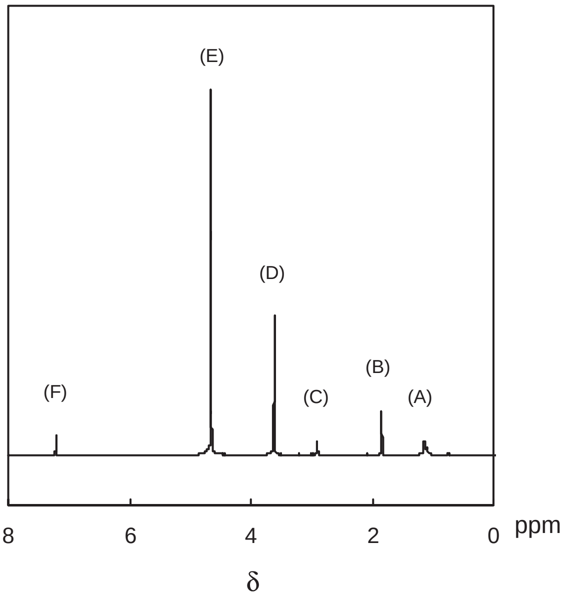

Fig. 2. ^{1}H NMR spectrum of D_2O solution of CTAC (20 mmol•dm^{-3}) saturated with benzene. –$(CH_2)_{14}$– (A), acetate (B), NCH_3 (C), 1,4-dioxane (D), HDO (E), and benzene (F).

sorbance at 610 nm, corresponding to ionized **1**, was maintained at room temperature for 1 week after the irradiation.

Dynamic light scattering measurements, carried out in 0.1 mol•dm^{-3} acetate buffer solutions containing 40 mmol•dm^{-3} CTAC and 1.0×10^{-5} mol•dm^{-3} **1**, afforded the diameters of 8.1 nm under dark conditions and 8.5 nm after UV irradiation with an error of about 4%. Though the addition of an electrolyte to the surfactant solutions causes an increase in the size of micellar aggregates,[12,13] the obtained value for the micelle diameter is appropriate for spherical micelles of CTAC. Therefore, the effect of the buffer solution on the micelle size and shape is negligible in this work.

Photoinduced Uptake of Benzene in Micelle Solution. A typical ^{1}H NMR spectrum of a CTAC D_2O solution saturated with benzene is shown in Fig. 2. The leftmost peak can be assigned to benzene protons. Some of the benzene molecules are in surfactant micelles and others in the bulk aqueous phase. And then the chemical shift of the benzene proton is generally different in these two environments. At the concentration of CTAC higher than its cmc, we assume that the rate of benzene exchange between the aqueous and micellar phase is faster than NMR time scale,[14,15] so the observed chemical shift (δ_{obs}) is the weighted average of the chemical shifts in the aqueous phase (δ_{aq}) and in the micellar phase (δ_{mic}).

$$\delta_{obs} = \left(\frac{C_{mic}}{C_{tot}}\right)\delta_{mic} + \left(\frac{C_{aq}}{C_{tot}}\right)\delta_{aq}, \tag{1}$$

$$C_{tot} = C_{mic} + C_{aq}. \tag{2}$$

Here, C_{mic}, C_{aq}, and C_{tot} are the concentrations of benzene in micellar phase, aqueous phase, and total concentration in the solution.

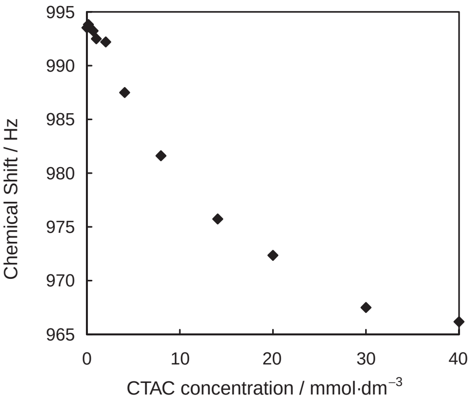

Fig. 3. Chemical shift of benzene protons as a function of CTAC concentration in D_2O solution of CTAC saturated with benzene.

The signal in micellar phase (δ_{mic}) is at the higher magnetic field than that in aqueous phase (δ_{aq}). Nakagawa et al. explained that it is caused by the large ring-current of benzene molecule[14] in the micelle interior where benzene molecules are stacked. The observed chemical shifts were referenced with respect to the protons of 1,4-dioxane, which was used as the internal standard,[16] and were plotted as a function of CTAC concentration in Fig. 3. The δ_{obs} was almost unchanged when the concentration of CTAC was less than its cmc (0.6 mmol•dm^{-3}). This is because, in the system without micelle formation, the δ_{obs} depends simply on the solubility of benzene in the aqueous phase. Above the cmc, the δ_{obs} was decreased with increasing in CTAC concentration (Fig. 3), i.e. the benzene peak was shifted to a higher magnetic field. Since the higher concentration of CTAC results in the higher ratio of C_{mic}/C_{tot}, the results in Fig. 3 agree with Eq. 1.

The CTAC solution containing **1** affords almost the same values for δ_{obs} without **1** under dark conditions. The full symbols in Fig. 4 (a, b, and c) were obtained under dark conditions in the systems of different concentrations of **1** and the δ_{obs} depends on the concentration of CTAC, not on the concentration of **1**. The result indicates that the amount of **1** is too small to affect the ratio of C_{mic}/C_{tot}. On the other hand, compound **1** plays an important role under UV-irradiated conditions. The photoirradiation caused a significant peak shift to the higher magnetic field (empty symbols in Fig. 4). Though the photoinduced shift is small in the solution containing 1.0×10^{-6} mol•dm^{-3} of **1** (Fig. 4a), a distinct shift is observed in the solutions containing 5.0×10^{-6} and 1.0×10^{-5} mol•dm^{-3} of **1** (Figs. 4b and c). Moreover, the higher concentration of **1** affords the more remarkable shift by UV irradiation. This result indicates that UV irradiation promotes the solubilization of benzene in micellar phase.

Since it is important to estimate the photoinduced solubilization of benzene quantitatively, we discuss the relationship between observed chemical shift and the solubility of benzene in the sample solution. If we also assume that the benzene concentration in aqueous phase (C_{aq}) is constant when C_{tot} is much higher than the solubility of benzene in aqueous phase, Eq. 3 is obtained from Eqs. 1 and 2:

$$\delta_{obs} = \left(\frac{C_{tot} - C_{aq,sat}}{C_{tot}}\right)\delta_{mic} + \left(\frac{C_{aq,sat}}{C_{tot}}\right)\delta_{aq}. \tag{3}$$

Here, $C_{aq,sat}$ is the saturated concentration of benzene (benzene solubility) in aqueous phase. And Eq. 3 is then rewritten

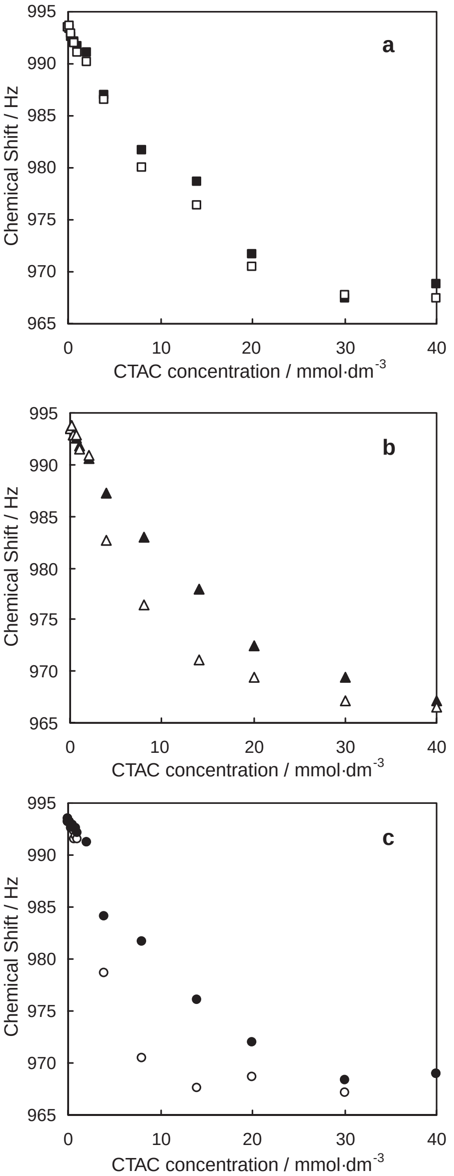

Fig. 4. Chemical shift of benzene protons under dark conditions (full symbols) and after UV irradiation (empty symbols). Concentration of **1**: 1.0×10^{-6} mol•dm^{-3} (a); 5.0×10^{-6} mol•dm^{-3} (b); 1.0×10^{-5} mol•dm^{-3} (c).

as Eq. 4:

$$\delta_{\mathrm{obs}} = \left(\frac{C_{\mathrm{aq,sat}}}{C_{\mathrm{tot}}}\right)(\delta_{\mathrm{aq}} - \delta_{\mathrm{mic}}) + \delta_{\mathrm{mic}}. \tag{4}$$

Thus, a plot of δ_{obs} vs $1/C_{\mathrm{tot}}$ should give a straight line. Finally, we obtain the relationship between the chemical shift of the solution at saturation (δ_{sat}) and the solubility of benzene in the solution (C_{sat}), which is expressed by Eq. 5:

$$\delta_{\mathrm{sat}} = \left(\frac{C_{\mathrm{nq,sat}}}{C_{\mathrm{sat}}}\right)(\delta_{\mathrm{aq}} - \delta_{\mathrm{mic}}) + \delta_{\mathrm{mic}}. \tag{5}$$

Typical plots of δ_{obs} vs $1/C_{\mathrm{tot}}$ are shown in Fig. 5. When the concentration of benzene applied to the sample is above C_{sat} ($C_{\mathrm{tot}} > C_{\mathrm{sat}}$), the excess benzene is separated from micelle solution. Accordingly, the chemical shift is constant up to $1/C_{\mathrm{sat}}$, and thereafter it increases with $1/C_{\mathrm{tot}}$. The data points in Fig. 5 were subjected to least-squares fitting to obtain two straight lines with an intersection, which in turn affords the values of C_{sat} and δ_{sat}. The solubility of benzene, C_{sat}, was increased with the concentration of CTAC (Fig. 5). Since the δ_{obs} values did not show any clear dependence on $1/C_{\mathrm{tot}}$ in the solution containing less than 4 mmol•dm^{-3} of CTAC, we did not find any intersection point and could not therefore obtain any value of C_{sat} and δ_{sat} at any magnetic field lower than 987 Hz.

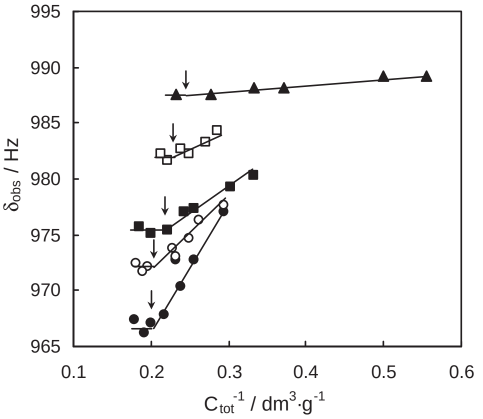

Fig. 5. Chemical shift of benzene protons as a function of $1/C_{\mathrm{tot}}$. Concentration of CTAC: 4 mmol•dm^{-3} (▲); 8 mmol•dm^{-3} (□); 14 mmol•dm^{-3} (■); 20 mmol•dm^{-3} (○); 40 mmol•dm^{-3} (●). The arrows indicate intersection points.

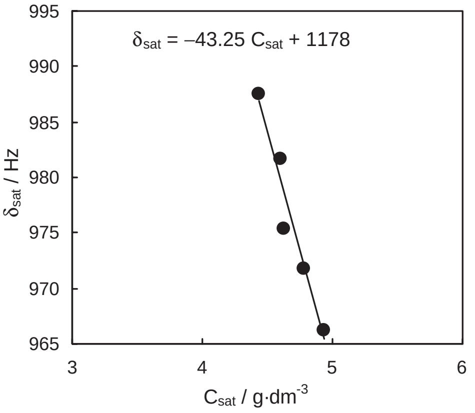

Fig. 6. Dependence of δ_{sat} on C_{sat}. The data points correspond to the intersections in Fig. 5.

By using the data at the intersection points in Fig. 5, we could plot the δ_{sat} values against C_{sat} in Fig. 6. A linear relation is obtained between C_{sat} and δ_{sat}, in the range from 966 to 987 Hz (Fig. 6). Accordingly, we can approximate the dependence of δ_{sat} on C_{sat} by a simple expression: $\delta_{\mathrm{sat}} = -43.25C_{\mathrm{sat}} + 1178$. Owing to this linear approximation, the values of chemical shifts in Fig. 4 afford their corresponding C_{sat}, because the chemical shifts for Fig. 4 are those of the solutions at saturation (δ_{sat}) after removal of the excess undissolved benzene from the sample solutions. Figure 7 shows the UV-induced change in the solubility of benzene for the systems containing concentrations of CTAC and **1**. Under dark conditions, the sol-

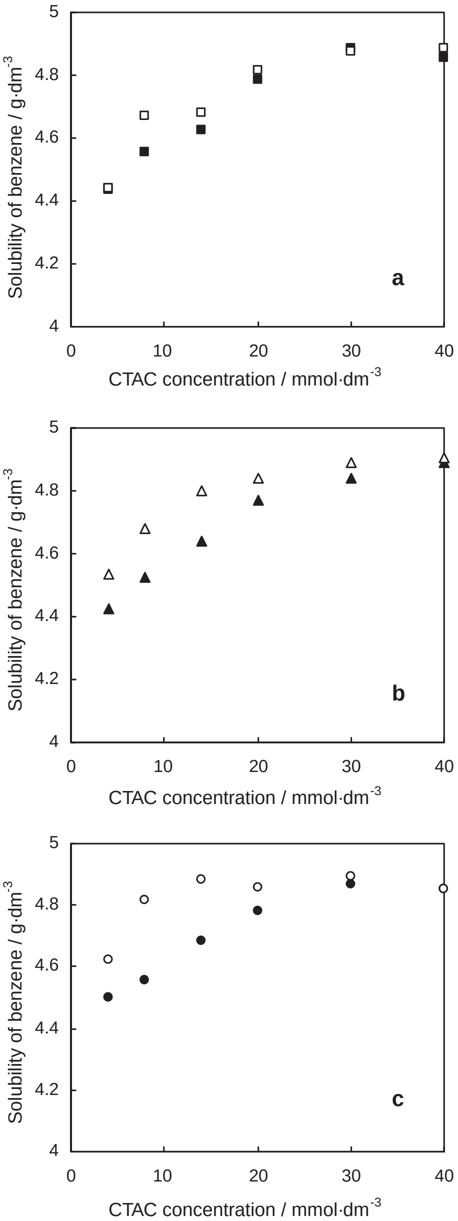

Fig. 7. Solubility of benzene in CTAC solution under dark conditions (full symbols) and after UV irradiation (empty symbols). Concentration of **1**: 1.0×10^{-6} mol•dm^{-3} (a); 5.0×10^{-6} mol•dm^{-3} (b); 1.0×10^{-5} mol•dm^{-3} (c).

ubilization curve is almost the same in each solution containing a different concentration of **1**. UV irradiation increases the solubility of benzene in each of the systems. The effect of photoirradiation on solubilization is not significant in Fig. 7a (1.0×10^{-6} mol•dm^{-3} of **1**), but the most drastic photoinduced enhancement of solubility is found in Fig. 7c (1.0×10^{-5} mol•dm^{-3} of **1**). The results lead to the conclusion that photoionized **1** contributes to increasing the solubility of benzene in micelle solutions. The most remarkable change by photoirradiation in Fig. 7 was attained with 8 mmol•dm^{-3} of CTAC containing 1.0×10^{-5} mol•dm^{-3} of **1**, the benzene solubility changing from 4.55 g•dm^{-3} under dark conditions to 4.81 g•dm^{-3} by photoirradiation. It should be noted that a small amount of **1** (1.0×10^{-5} mol•dm^{-3}) induces a significant increase (0.26 g•dm^{-3}) in the solubility of benzene. As a consequence, it suggests that **1** behaves as a command compound for the photoinduced uptake of oily substance in micelles.

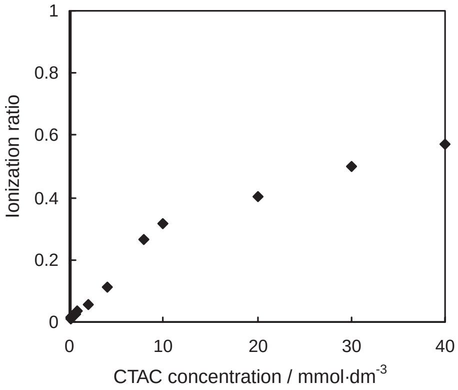

Fig. 8. Dependence of photoionization ratio of **1** on CTAC concentration.

Photoionization Ratio of Malachite Green. As shown in Figs. 4 and 7, the photoinduced uptake was enhanced in the solution with more than 4 mmol•dm^{-3} of CTAC. We consider that the solubilizing ability under UV-irradiated condition is concerned with the amount of ionized **1**. Since the molar absorptivity of Malachite Green cation (triphenylmethyl cation) in visible light region is almost the same as that of ionized **1**, the photoionization ratio of **1** can be calculated by the absorbance of Malachite Green oxalate (See: experimental section). The photoionization ratio of **1** in the solution is plotted against CTAC concentration in Fig. 8. The ratio does not show any significant increase up to 4 mmol•dm^{-3}, above which it increases abruptly. These results coincide with Fig. 4c, indicating that the photoionization of **1** contributes to increasing the photoinduced uptake of benzene into micelle solution. The main reason for the increasing photoionization ratio with the CTAC concentration is that the electrically neutral **1** is difficult to dissolve in water under dark conditions and that an appropriate concentration of micelle is required to dissolve it. UV irradiation promotes the ionization of **1** in the CTAC micelle, resulting in the abrupt increasing in the photoionization ratio. Besides, a gradual increase of ionization ratio was observed above 20 mmol•dm^{-3} of CTAC and this is in good agreement with the data for Fig. 7c, i.e. the benzene solubility is not highly enhanced by UV irradiation above 20 mmol•dm^{-3}. Therefore, the photoionized **1** participates in the CTAC micelle formation and causes the efficient photochemical uptake of benzene.

We conclude that the drastic photoinduced uptake of benzene is realized by a small amount of lipophilic Malachite Green **1**, which exhibits a distinct amphiphilicity photogenerated from the simply lipophilic substance. Since compound **1** works as a command compound to control the molecular assemblies, we expect to use this remarkable feature for the systems formed by amphiphilic compounds such as reversed micelle, liposome, LB membrane, and microcapsule. Furthermore, we also expect to apply this photoresponsive surfactant for controlling cation extraction and designing drug delivery systems.

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