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The Effect of Surfactants and β-Cyclodextrin on the Photooxidation of Stable Carbanions

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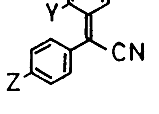
The micellar effect on the photochemistry of α-(4-hydroxyimino-2,5-cyclohexa-dienylidene)-α-phenylacetonitrile and its derivatives has been studied. 4-Nitrobenzophenone derivatives were obtained by the irradiation of ethanolic alkaline aqueous solutions of the oximes. 4-Nitrosobenzophenone derivatives formed as an intermediate were thermally oxidizced to give the corresponding nitro compounds. The reaction was found to be the photochemical oxidation by singlet oxygen. The addition of an anionic surfactant (sodium dodecyl sulfate) and a nonionic surfactant (Tween ♯80) to the reaction solution scarcely changed the pK_a values of oximes, whereas the addition of a cationic surfactant such as hexadodecyltrimethylammonium bromide (HTAB) caused a considerable decrease. This indicates that HTAB promotes the formation of a stable carbanion. The presence of HTAB enhanced the rate of photooxidation by a factor of 10^2. The catalytic effect becomes maximum at the pH value of the reaction solution near the pK_a measured in the presence of HTAB or β-CDX.

Various chemical reactions modeled to the specific enzymatic interactions have been carried out in recent years. The reactions in certain aqueous micellar systems and the kinetics of organic reactions have been dealt with as a model for the enzymatic interaction. In the photooxidation of chlorophyll-a the addition of a nonionic sufactant to the reaction solution increased the rate of photooxidation ($k_{obsd}/k_0=21$).[1] Luciferin has been found to be chemiluminescent in the presence of a micellar cationic surfactant, but not in an anionic ones.[2] Cationic surfactants enhance the stability of anions, and anionic ones stabilize cations by forming micelles with them.

Minch *et al.*[3] reported that (4-nitrophenyl)phenyl acetonitrile is converted into the stable carbanion form in an aqueous alkaline solution, the addition of HTAB to this solution greatly enhancing the formation of its carbanion. In order to study the micellar effects on the photochemical reactions of the ionic species, carbanions, we used the derivatives of α-(4-hydroxyimino-2,5-cyclohexadienylidene)-α-phenylacetonitrile (**1**) which dissociate to form stable carbanion in alkaline solution. The synthetic method of these oximes was reported by Davis and his co-workers.[4] They also reported that the hydrogen peroxide oxidation of these oximes in methanolic alkaline solution gives 4-nitrobenzophenones. This paper provides detailed information on the photooxidation of stable carbanions formed by the ionization of the oxime compounds, and the catalytic effects of various surfactants (hexadecyltrimethylammonium bromide (HTAB), sodium dodecyl sulfate (SDS), Tween ♯80, and β-cyclodextrin (β-CDX)). The kinetic has also been studied.



Compd	1	2	3	4	5	6	7	8	9	10
X	H	H	CH_3	CH_3	Cl	Cl	Cl	H	H	CH_3
Y	H	H	CH_3	CH_3	Cl	Cl	H	CH_3	Cl	H
Z	H	Cl	H	Cl	H	Cl	H	Cl	H	H

Chart.

Results and Discussion

Photoreaction of Oxime Derivatives. 4-Nitrobenzophenone derivatives and its dimers (4,4′-diaroylazoxybenzenes) were obtained as photoreaction products by irradiation of an ethanolic alkaline aqueous solution of oximes **1** and **2**. The structures of products were determined by comparison of mp, NMR and mass spectra with those of authentic samples. The photooxidation was carried out by irradiating an ethanolic alkaline aqueous solution of the oxime with a high pressure mercury lamp under aerobic conditions. The photooxidation was followed by means of UV spectroscopy (Fig. 1). The maximum absorbance of the oxime **1** at 405 nm decreased during the course of irradiation, a new maximum having an isosbestic point at 334 nm appearing at 288 nm. The maximum at 288 nm shifted to 264 nm which corresponds to that of 4-nitrobenzophenone. A new small absorbance corresponding to that of the dimer of oxime appeared at 345 nm together with one at 264 nm. The shift of

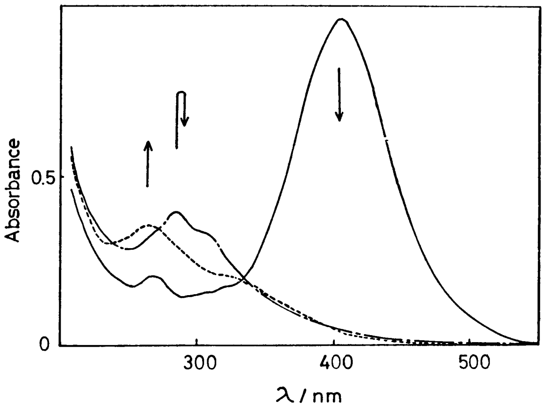


Fig. 1. Spectra of a 10% ethanolic aqueous buffer solution (pH 9.20) of oxime **1**. ——: Before irardiation, ———: after 80 min of irradiation, ---: after 240 min of irradiation.

the maximum at 288 nm to 264 was observed both under irradiation and in the dark. The first band appearing at 288 nm agrees very closely with the characteristic absorbance (λ_{max} 283 nm) of nitrosobenzene. 4-Nitrosobenzophenone seems to be formed as an intermediate.

Source of the Oxidizing Agent. Photochemical oxidation with oxygen is known in bioorganic chemistry. Chlorophyll-a was photooxidized by a molecular oxygen.[1] The photooxidation of bilirubin proceeds with singlet oxygen, bilirubin acting as a sensitizer to form singlet oxygen. As a source of energy to form the highly reactive species, singlet oxygen, the triplet dye was recognized in many oxygenation reactions.[6] The mechanism of the present photooxidation is considered as that of the photooxidation of bilirubin.

TABLE 1. EFFECT OF β-CDX AND HTAB ON THE VISIBLE SPECTRA[a)]

Compd	λ_{max} nm	λ_{max}^{CDX} b) nm	λ_{max}^{HTAB} c) nm
1	371, 407	372, 417	378, 440
2	376, 418	377, 423	377, 435
3	368, 413	368, 416	369, 424
4	369, 419	370, 420	372, 433
5	369, 418	372, 428	372, 448
6	378, 441	378, 442	379, 455
7	375, 415	375, 417	377, 433
8	371, 414	373, 417	373, 436
9	374, 420	377, 423	377, 440
10	374, 417	376, 417	377, 433

a) A left line of λ_{max}; in neutral solution. A right line of λ_{max}; in alkaline solution. b) In 2.81×10^{-3} M β-CDX. c) In 10^{-2} M HTAB.

TABLE 2. EFFECT OF β-CDX AND HTAB ON THE ACID DISSOCIATION OF OXIMES

Compd	pK_a	$\Delta pK_{a\ CDX}$[a)]	$\Delta pK_{a\ HTAB}$[b)]
1	8.60	0.24	1.44
2	9.36	0.30	1.07
3	10.10	0.32	0.51
4	9.88	0.08	0.60
5	8.01	0.30	1.61
6	7.99	0.08	1.00
7	8.33		0.98
8	9.09		1.40
9	7.88		0.94
10	9.23		0.56

a) $pK_a - pK_{a\ CDX}$; in 5×10^{-3} M β-CDX. b) $pK_a - pK_{a\ HTAB}$; in 10^{-2} M HTAB.

TABLE 3. EFFECT OF SDS AND TWEEN ♯80 ON THE ACID DISSOCIATION OF OXIMES

Compd	$\Delta pK_{a\ SDS}$[a)]	$\Delta pK_{a\ Tween}$[b)]
1	−0.48	−0.12
2	0.53	0.32

a) $pK_a - pK_{a\ SDS}$; in 10^{-2} M SDS. b) $pK_a - pK_{a\ Tween}$; in 6.6×10^{-2} g/dl Tween ♯80.

The photooxidation proceeds extremely slowly in the absence of oxygen. In the presence of β-carotene (1.27×10^{-5} M), which is a singlet oxygen quencher,[7] the quantum yield of the reaction decreases by a factor of 5. However, it increases considerably in the presence of Rose Bengal (7.70×10^{-6} M), a photosensitizer to form singlet oxygen,[6a)] by a factor of 12. In the presence of a free radical inhibitor such as 2,6-di-*t*-butylphenol (up to 1×10^{-2} M),[6a,8)] the reaction is not suppressed. It is obvious that the reaction is photochemical oxidation by singlet oxygen.

The Effect of Surfactant on Visible Spectra. Remarkable micellar effects of HTAB are observed in the visible spectra of the oxime. The addition of HTAB to the neutral and alkaline solution containing the oxime causes a red shift of the λ_{max} values for the neutral and anion form of the oxime. A similar effect was also observed on addition of β-CDX. The λ_{max} values for the neutral and anion forms of the oxime in 25—10% ethanolic water, aqueous HTAB, and β-CDX are given in Table 1.

The Effects of Surfactants on the pK_a *Value.* The pK_a values determined in 25—10% ethanolic aqueous solution with and without surfactants are given in Tables 2 and 3. The pK_a values of all oximes decrease when the micellar concentration of HTAB is used. This is also the case for β-CDX. On the other hand, the pK_a values of the oximes are random in the case of SDS and Tween ♯80. The decrease in the pK_a values results from the stabilization of the anion form of the substrates, arising from (a) an electrostatic interaction with cationic head groups of HTAB and the anion form, and (b) an electron delocalization by the hydrogen bond between an adjacent hydroxyl group of β-CDX and an oxygen atom of 4-nitroso group of the substrate which forms 1:1 inclusion complex with β-CDX.

Effects of Surfactants on Quantum Yields. The quantum yields of the catalytic action of the HTAB (Φ_2) in the photooxidation of oximes were analyzed by means of a modified form of Lineweaver-Burk equation.[14] Φ_0 and Φ_{obsd} are the quantum yields for the formation of oxidized products in the absence and presence of the HTAB. The quantum yield (Φ_2) increased by a factor of 370 in the presence of

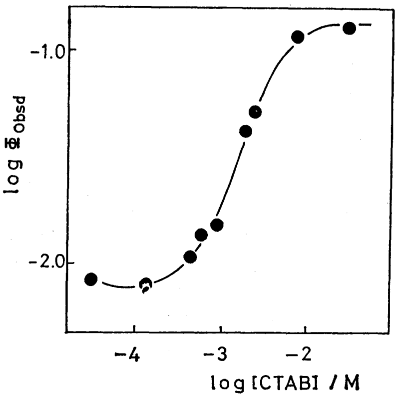


Fig. 2. Effect of HTAB on the quantum yield for the photooxidation of 5.18×10^{-5} M of oxime **1** in 10% ethanolic aqueous buffer (pH 7.31).

TABLE 4. THE QUANTUM YIELDS AND ASSOCIATION CONSTANTS FOR THE PHOTOOXIDATION OF **1** IN THE PRESENCE OF HTAB AND β-CDX

Surfactant	HTAB[a]	β-CDX[c]
$\Phi_0 \times 10^4$	1.66	77.7
$\Phi_{\text{obsd}}^{\text{max}} \times 10^3$	62.4[b]	9.67[d]
$\Phi_2 \times 10^2$	3.64	1.03
$\Phi_{\text{obsd}}^{\text{max}}/\Phi_0$	370	1.24
Φ_2/Φ_0	220	1.33
$K \times 10^{-2}/\text{M}^{-1}$	327	4.16

a) In 20% ethanolic buffer (pH 7.31, H_3BO_3-NaCl). b) [HTAB]$=3\times10^{-2}$ M. c) In 20% ethanolic water (0.01 M NaOH). d) [β-CDX]$=7\times10^{-3}$ M.

TABLE 5. THE RELATIVE RATE CONSTANTS AND ASSOCIATION CONSTANTS OF THE COMPOUNDS HAVING CHLORO-SUBSTITUENT[a]

Compd	X	Y	Z	k_0	k_{obsd}[b]	k_2	K	k_2/k_0
1	H	H	H	1.0	1.0	1.0	1.0	1.0
7	Cl	H	H	1.2	1.1	1.5	0.032	1.2
9	H	Cl	H	0.045	0.025	0.046	0.0079	1.0
2	H	H	Cl	0.65	0.76	0.76	0.47	1.2

a) In 25% ethanolic buffer (pH 9.20). b) In the presence of 10^{-2} M of HTAB.

HTAB (1×10^{-2} M). The critical micellar concentration (CMC) of HTAB in the photooxidation of **1** is estimated to be 6×10^{-4} M from the plot of $\log \Phi_{\text{obsd}}$ *vs.* $\log C_{\text{D}}$(surfactant concentration) as shown in Fig. 2. The quantum yield of this photooxidation becomes maximum at the surfactant concentration of 10^{-2} M. The value of Φ_{obsd} varies with the concentration of β-CDX, reaching maximum at a certain concentration. Such a phenomenon is characterized in the enzyme reaction which follows Michaelis-Menten kinetics. A general mechanism involving the micell-substrate complex similar to that used for an enzymatic catalysis[9] was applied. The effect of HTAB and β-CDX at a particular pH value was examined according to the Scheme (Experimental), using a technique worked out by Colter *et al.*[10] The results are given in Table 4. The quantum yield for the photooxidation of **1** in the micellar phase is large by a factor of 220 as compared with that in aqueous phase.

pH-*Dependence.* Stabilization of carbanion was examined in the photooxidation of oxime **1**, and was confirmed by measuring the quantum yields Φ_0 and Φ_{obsd} in the pH 3 to 12 region in the presence of HTAB, β-CDX, SDS, and Tween ♯80, respectively. As shown in Fig. 3, the presence of HTAB increases the quantum yield over the whole pH region. In the pH region above the pK_a value of oxime, the quantum yield increases irrespective of the presence or absence of the surfactant (Fig. 3). This indicates that the formation of the carbanion agrees with the increase in quantum yield. In the case of β-CDX, a similar phenomenon was observed. The extent of the catalytic effect of HTAB and β-CDX depends on the pH values of the reaction solution (Fig. 4). The catalytic effect become maximum in the pH value around the pK_a's of the oxime determined in the presence of surfactant. On the other hand, the relation of the pH value and the quantum yield is not clear when SDS and Tween ♯80 were used. From the results, the mechanism is considered as follows. The stabilization of the carbanion in the hydrophobic cavity of β-CDX does not increase the quantum yield as in HTAB. This is because the steric hindrance of β-CDX inhibits the attack of singlet oxygen on the carbanion. HTAB does not inhibit the approach of singlet oxygen for the loosely bound carbanion. Consequently the stabilization of the carbanion in the presence of HTAB is reflected on the increase in the quantum yield.

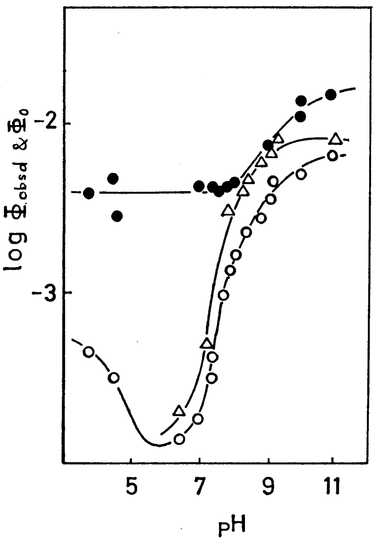


Fig. 3. pH-Dependence on the photooxidation of oxime **1** in a 10% ethanolic aqueous buffer (○), in the presence of 7.10×10^{-4} M HTAB (●), and 4.85×10^{-3} M β-CDX (△).

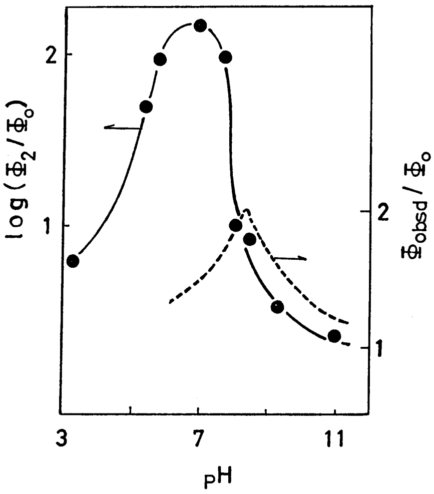


Fig. 4. pH-Dependence on the photooxidation of oxime **1** in the presence of HTAB (-●-) and β-CDX (——).

Effect of Chloro-Substituent on the Rate Constant and the Association Constant. There is some difference in the reactivity of three oximes having a chloro-substituent. The rate constants of the photooxidation of the oxime were determined in the presence or absence of HTAB. The rate constant k_2 for the formation of the product in the micellar phase and the association constants were calculated by means of Eq. 2. The relative values against those of **1** are given in Table 5. The steric hindrance is responsible for the least reactivity of the 2-chloro-substituted oxime. The catalytic effect of a cationic surfactant is recognized to be nearly equal to that observed for all the oximes, independent of the position of the chloro-substituent.

Experimental

All melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. The ultraviolet spectra were taken on Hitachi EPS-3T and Shimadzu UV-200 spectrometers, mass spectra on a Hitachi RMU-6E mass spectrometer. The pH was measured with a TOA Electronics, Ltd., model HM-5A pH meter. Buffer solutions were chosen[11] according to the required pH region. CH_3COOH (pH 3), M/15 KH_2PO_4–Na_2HPO_4 (pH 4—6), M/20 H_3BO_3–$Na_2B_4O_7$ (pH 6—8), M/20 H_3BO_3–KCl–NaOH (pH 8—10), and M/20 Na_2HPO_4–NaOH (pH 10—12). Column chromatography separation was carried out with Merck silica gel Art. 7734.

Materials. Commercial HTAB and SDS were recrystallized twice from methanol-ether and ethanol, respectively.[12,13] Other materials were used without further purification. All the compounds of oximes **1**—**10** were prepared from substituted nitrobenzene and substituted phenylacetonitriles by the procedure of Davis *et al.*[4a,b] The products were recrystallized twice from benzene.

*Irradiation of **1** and **2**.* A solution of 1 g of **1** in 2 liter of ethanol–aqueous alkaline (NaOH) solution was irradiated with an Ushio UM-452 450W high pressure mercury lamp for 10 h. After irradiation, the solvent was removed with rotary evaporators, the oily residue being chromatographed on silica gel to give two products. These were identified as nitrobenzophenone, mp 126 °C (lit,[4] 120 °C) and MS, *m/e* 227 (M^{+}); and 4,4′-dibenzoylazoxybenzene, mp 198—199 °C (lit,[4] 202—203 °C) and MS, *m/e* 406 (M^{+}). Irradiation of **2** in a similar manner gave 4-chloro-4′-nitrobenzophenone, mp 99 °C (lit,[4] 100—101 °C) and MS, *m/e* 261 (M^{+}), and 263 ($M^{+}+2$); and 4,4′-bis(*p*-chlorobenzoyl) azoxybenzene, mp 292—296 °C (lit, [4] 291—293 °C) and MS, *m/e* 475 (M^{+}) and 477 ($M^{+}+2$).

pK_a Values. The pK_a values of all the compounds were calculated by means of the equation,[3]

$$\mathrm{p}K_a = \mathrm{pH_{obsd}} + \log\frac{A_{\max}-A_{\mathrm{obsd}}}{A_{\mathrm{obsd}}}. \qquad (1)$$

The $\mathrm{pH_{obsd}}$ is the pH value at the inflection point estimated from the plot of absorbance *vs.* pH value of the solution. $A_{\max}$ and A_{obsd} are the absorption values for fully dissociated and partially dissociated (at $\mathrm{pH_{obsd}}$) solutions of the oximes. The pK_a values of oximes in 5×10^{-3} M β-CDX, in 10^{-2}M HTAB, in 10^{-2} M SDS and in 6.6×10^{-2} g/dl Tween #80 were determined in a similar manner. All the compounds were dissolved in a small amount of ethanol before dilution with water, the final solution containing 25—10% ethanol.

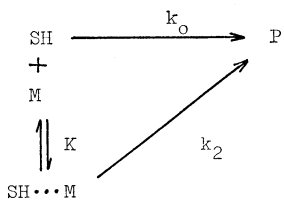
Kinetic Method. In numerous kinetic runs, the sample kept in the dark showed no measurable change in absorption at $\lambda_{\max}$ of carbanion during the course of run ($\leq$5 h). A solution of 2.51×10^{-5} M of **1** in 10% ethanolic aqueous buffer reached equilibrium within for a few minutes. The solution kept for 2 days in the air still retained 97% of its absorbance at $\lambda_{\max}$ of carbanion, showing no change in th mode of absorption.

All the photoreactions were followed under pseudo-first-order kinetics conditions by monitoring the consumption of reactant at the $\lambda_{\max}$ of the carbanion.

After argon gas had been bubbled in the reactant solution for 1 h to remove dissolved oxygen, it was irradiated and the rate was measured. The k_{obsd} obtained was less than in the presence of dissolved oxygen by a factor of 50. The result indicates that dissolved oxygen participates in the photooxidation.

Various concentrations of β-carotene, Rose Bengal, and 2,6-di-*t*-butylphenol were dissolved in the reactant solutions. The rate of the photooxidation of these solutions was compared with that of the original solution.

The effect of HTAB at a particular pH region was examined according to the Scheme. SH, unionized and ionized, is the total substrate present. Variation of surfactant concentration gave the rate constants for the product formation in the micellar phase, k_2, and the association constants for the substrate-micelle complex, K, by calculation by means of Eq. 2. The value of CMC obtained previously and the aggregation number (N 61 at HTAB) were used:



Scheme.

$$\frac{1}{k_{\mathrm{obsd}}-k_0} = \frac{1}{k_2-k_0} + \frac{1}{k_2-k_0}\cdot\frac{\mathrm{N}}{K(C_{\mathrm{D}}-\mathrm{CMC})}. \qquad (2)$$

C_{D} is the total concentration of the surfactant, k_0 the rate constant in the bulk solvent, and k_{obsd} the observed rate constant in the presence of HTAB. The estimated rate constant values were converted into the quantum yield.[14]

The effect of β-CDX was also examined according to the Scheme. The value of K, association constant of β-CDX-substrate complex, and k_2, the rate constant for the product formation in the bound species, were obtained by

$$\frac{1}{k_{\mathrm{obsd}}-k_0} = \frac{1}{k_2-k_0} + \frac{1}{k(k_2-k_0)[\mathrm{CDX}]}. \qquad (3)$$

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