Nucleophilic Ion Pairs. Part II.[†] Micellar Catalysis of Proton Abstraction by Hydroxamate Anions

By **Seiji Shinkai** and **Toyoki Kunitake**,* Department of Organic Synthesis, Faculty of Engineering, Kyushu University, Fukuoka 812, Japan

Hydroxamate anions in a cationic (cetyltrimethylammonium bromide. CTAB) micelle were found to serve as excellent catalysts for proton abstraction from α-ketols. Proton removal from benzoin by *N*-methylmyristohydroxamate anion (MMHA) in the CTAB micelle was 3 500 times faster than the corresponding reaction in a non-micellar system. and 56 times faster than that by the much more basic hydroxide ion. A similar. dramatic rate enhancement was attainable by addition of small amounts of CTAB or methyltri-n-octylammonium chloride (TMAC) to MMHA solubilized in aqueous non-ionic micelles. On the other hand. the MMHA.NEt_4 ion pair in organic solvents was also effective for proton abstraction. MMHA.NEt_4 in highly dehydrated acetonitrile gave a rate 10^3 higher than that in aqueous media. Minute amounts of H_2O and NaI efficiently quenched the reaction in dry organic solvents. and it was inhibited in protic solvents. It was suggested from these experimental data that the rate enhancement of MMHA in the presence of a cationic micelle largely stems from formation of a hydrophobic ion pair which is loose and desolvated in the micellar phase.

RECENTLY, a variety of anionic nucleophiles such as alkoxide,[1,2] oximate,[3,4] thiolate,[5] imidazole,[6] and hydroxamate [7-9] anions have been found to be unusually active toward phenyl esters in cationic micelles [1-8] as well as in cationic polysoaps.[9] The nucleophilicity toward *p*-nitrophenyl acetate, for instance, is improved by two or three orders of magnitude compared with that predicted from the Brönsted relationship. These results suggest that

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[†] Part I, ref. 21.

[1] C. A. Bunton and L. G. Ionescu,. *J. Amer. Chem. Soc.*, 1973, **95**, 2912.

[2] K. Martinek, A. V. Levashov, and I. V. Berezin, *Tetrahedron Letters*, 1975, 1275.

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[4] W. Tagaki, I. Takahara, and D. Fukushima, paper presented at the 32nd annual meeting of the Chemical Society of Japan, Tokyo, 1975.

[5] W. Tagaki, T. Amada, Y. Yamashita, and Y. Yano, *J.C.S. Chem. Comm.*, 1972, 1131.

[6] K. Martinek, A. P. Osipov, A. K. Yatsimirski, V. A. Dadolt, and I. V. Berezin, *Tetrahedron Letters*, 1975, 1279.

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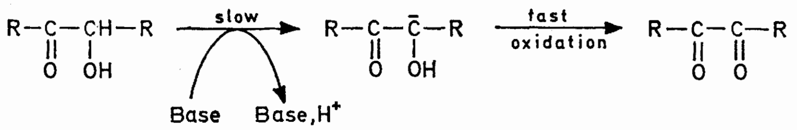
the anionic nucleophiles combined with cationic micelles would also serve as effective catalysts for a number of other, base-catalysed organic reactions.

Proton abstraction from carbon acids is a representative, base-catalysed reaction by which the carbanion precursor for reactions such as condensation, racemization, and enolization is formed. The rate-determining step of the oxidation of α-ketols to the corresponding diketones was also verified to be a carbanion formation process.[10,11] This claim was recently re-established in connection with oxidation of α-ketols by flavins (vitamin B_2 analogues),[12] the mechanism of which is biologically important.[13,14] Since the product diketones absorb strongly at longer wavelengths in the u.v. region, this is one of the most convenient reactions for investigating the efficiency of proton abstraction from carbon acids.



(1)

In the present study, we employed hydroxamate anions in micelles of a cationic surfactant, cetyltrimethylammonium bromide (CTAB), as catalysts for proton abstraction from the α-ketols, benzoin and furoin. This reaction was also studied in organic solvents by using a tetraethylammonium hydroxamate, in order to obviate complications that arise from the use of micellar systems. Molecular oxygen saturated in the reaction medium was used as an oxidizing agent which rapidly traps the carbanion intermediate formed. Hydroxamic acids employed are *N*-methylmyristohydroxamic acid (MMHA) and *N*-benzylbenzohydroxamic acid (BBHA).

RESULTS

Hydroxide Catalysis.—The proton abstraction reaction was examined in the absence of hydroxamate anions, and the second-order rate constants for OH^- catalysis (k_{OH}) are summarized in Table 1. In general, the logarithmic rate constants increased linearly with increasing pH (pH 9—11) with slope of 1.0. Therefore, the reaction is predominantly hydroxide ion-catalysed (for kinetic details, see Experimental section). In the presence of CTAB micelles, rate augmentations of only 1.4 and 7.0 were observed at pH 11 for the oxidation of furoin and benzoin, respectively. These small rate increases may be explained by the increase in the local concentration of hydroxide ion at the micellar surface and/or by the stabilization of the carbanion intermediate by the cationic environment of the CTAB micelle. In fact, a non-ionic micelle of POOA (polyoxyethyleneoleyl alcohol) decelerated the oxidation by factors of 2—5. Apparently, the α-ketols solubilized in the non-ionic micelle are shielded from attack of hydroxide ion. The micellar effects (acceleration by CTAB and deceleration by POOA) are larger for benzoin than for furoin. This is explicable by the favourable partitioning of benzoin in micellar phases compared with furoin because of a smaller solubility of benzoin in aqueous media.

TABLE 1

Rate constants (k_{OH}) for hydroxide-catalysed proton abstraction reaction from furoin and benzoin [a]

α-Ketol	[Additive] [c]/ (mM)	k_{OH}/ l mol⁻¹ s⁻¹	k_{rel} [b]
Furoin		2.80	1.0
Furoin	CTAB (5.0)	4.00	1.4
Furoin	POOA (10.0)	1.77	0.6
Benzoin		0.081	1.0
Benzoin	CTAB (5.0)	0.569	7.0
Benzoin	POOA (10.0)	0.016	0.2

[a] 30 °C, pH 11.0, [furoin] = 5.04×10^{-5}M, [benzoin] = 6.05×10^{-5}M, 1% v/v water–acetonitrile. [b] Relative reaction rate. [c] C.m.c.: 9.2×10^{-4}M for CTAB at 25 °C and *ca.* 10^{-6}M for POOA at 25 °C.[17]

Hydroxamate Catalysis in Non-ionic and Anionic Micelles.—The second-order rate constants (k_{HA}) of proton abstraction catalysed by hydroxamate anions were determined at fixed hydroxamate concentrations by using equation (4) (see Experimental section). The hydroxamate concentration was kept constant in order to avoid possible changes in the micellar structure. The results are summarized in Tables 2 and 3. In contrast to the hydroxide catalysis, the reactivity of the hydroxamate ions was enhanced in the presence of the non-ionic POOA micelle. The catalytic reactivity of MMHA in the nonmicellar system cannot be determined due to its sparing solubility. If the k_{HA} value for MMHA in the absence of micelles is approximated by

TABLE 2

Rate constants (k_{HA}) for hydroxamate-catalysed proton abstraction reaction in the presence of POOA [a]

α-Ketol	Hydroxamate [d]	[POOA]/ M	k_{HA}/ l mol⁻¹ s⁻¹	k_{rel}
Furoin	BBHA	0.01	0.195	3.4
Furoin	MMHA	0.01	0.558	10
Furoin [b]	MMHA	0.01	4.38	78
Furoin [c]	MMHA	0.01	6.50	116
Furoin	BBHA	0	0.056	1.0
Benzoin	MMHA	0.01	0.039	30
Benzoin	BBHA	0	0.0013	1.0

[a] 30 °C, pH 11.0, [furoin] = 5.04×10^{-5}M, [benzoin] = 6.05×10^{-5}M, 1% (v/v) water–acetonitrile. [b] [TMAC] = 3.33×10^{-3}M. [c] [CTAB] = 1.00×10^{-3}M. [d] [BBHA] = 3.00×10^{-4}M, [MMHA] = 4.39×10^{-4}M.

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[11] P. D. Bartlett and C. H. Stauffer, *J. Amer. Chem. Soc.*, 1935, **57**, 2580.

[12] S. Shinkai, T. Kunitake, and T. C. Bruice, *J. Amer. Chem. Soc.*, 1974, **96**, 7140.

[13] G. A. Hamilton, *Progr. Bio-org. Chem.*, 1971, **1**, 83.

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that of BBHA * in the nonmicellar system, the relative rate constant k_{rel} (= $k_{micellar}/k_{nonmicellar}$) of MMHA in the POOA micelle was 10 for furoin and 30 for benzoin. The BBHA–POOA system yielded a smaller rate increase.

TABLE 3

Rate constants (k_{HA}) for hydroxamate-catalysed proton abstraction reaction in the presence of CTAB micelle [a]

α-Ketol	Hydroxamate [b]	[CTAB]/ mM	k_{HA}/ l mol^{-1} s^{-1}	k_{rel}
Furoin	BBHA	0	0.056	1.0
Furoin	MMHA	5.0	23.1	413
Benzoin	BBHA	0	0.0013	1.0
Benzoin	BBHA	5.0	0.489	376
Benzoin	MMHA	5.0	4.53	3 500

[a] 30 °C, pH 11.0, [furoin] = 5.04 × 10^{-5}M, [benzoin] = 6.05 × 10^{-5}M, 1% (v/v) water–acetonitrile. [b] [BBHA] = 3.00 × 10^{-4}M, [MMHA] = 4.39 × 10^{-4}M.

An anionic micelle (sodium lauryl sulphate, 5.0 × 10^{-3}M) efficiently suppressed the reactivity of MMHA, and the catalytic term was virtually undetectable ($k_{HA} < 10^{-3}$ l mol^{-1} s^{-1}) for furoin.

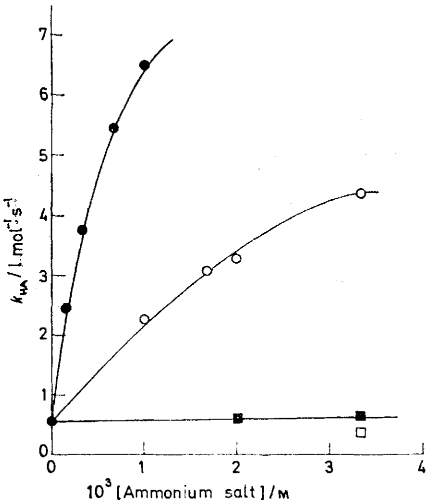
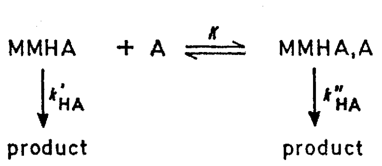


FIGURE 1 Effect of quaternary ammonium salts on the hydroxamate-catalysed oxidation of furoin in the presence of POOA micelle. 30 °C, pH 11.0 with KOH, [POOA] = 0.01M, [MMHA] = 4.39 × 10^{-4}M: ●, CTAB; ○, TMAC; ■, Bu^n_4NBr; □, Et_4NBr

The influence of several ammonium salts on the reactivity of the MMHA–POOA system was then examined. As shown in Figure 1, addition of tetraethylammonium bromide and tetrabutylammonium bromide hardly affected the oxidation rate of furoin. On the other hand, CTAB and methyltri-n-octylammonium chloride (TMAC) produced distinct rate enhancements. TMAC, a typical phase transfer catalyst, is much more hydrophobic than tetraethyl- and tetrabutylammonium bromide, but cannot form a micelle by itself. In fact, it exists as an oily suspension in aqueous media without non-ionic micelles. Therefore, most TMAC molecules must be trapped in and/or on the non-ionic micelles. It is also noteworthy that the concentration of added CTAB is definitely below its critical micelle concentration (c.m.c.) (see footnote to Table 1). Therefore, the effect of CTAB cannot be attributed to formation of cationic micelles.

The rate increased with increasing concentration of these ammonium salts and showed saturation tendencies. This rate enhancement is conceivably caused by formation of ion pairs between MMHA anion and the hydrophobic quaternary ammonium ion (A), as discussed below. Then, the influence of the added cations can be quantitatively treated according to the procedure of Connors *et al.*[15,16]

Assuming that 1 : 1 ion pairs are formed, the hydroxamate anion will react as paired and unpaired species (Scheme,



SCHEME

where K is the association constant for the 1 : 1 ion pair, k'_{HA} is the second-order rate constant for unpaired MMHA, and k''_{HA} is that for the MMHA,A ion pair). Then, equation (2) is obtained for [MMHA] ⩽ [A] where k_{HA} is the

$$\frac{k'_{HA}}{k_{HA} - k'_{HA}} = \frac{1}{qK[A]} + \frac{1}{q} \qquad (2)$$

apparent second-order rate constant and $q = k''_{HA}/k'_{HA} - 1$. Plots of $k'_{HA}/(k_{HA} - k'_{HA})$ against 1/[A] are given in Figure 2. K and k''_{HA} could be determined from the slope and the intercept: K = 1 330 l mol^{-1} and k''_{HA} = 10.9 l mol^{-1} s^{-1}

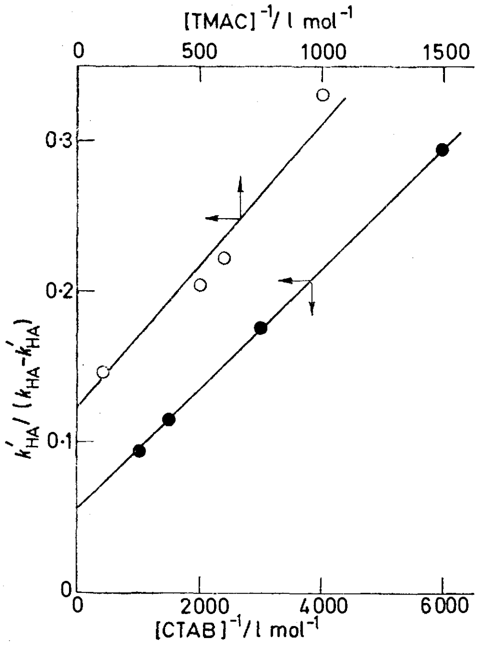


FIGURE 2 Plots of $k'_{HA}/(k'_{HA} - k_{HA})$ against 1/[A]: ●, CTAB, ○, TMAC

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* The pK_a value for BBHA (9.20 at 30 °C) is not much different from aliphatic hydroxamic acids (*e.g.*, isobutyrohydroxamic acid, pK_a 9.08). Therefore, the reactivity of MMHA in nonmicellar systems may be assumed to be similar to that of BBHA.

[15] J. A. Mollica, jun., and K. A. Connors, *J. Amer. Chem. Soc.*, 1967, **89**, 308.

[16] P. A. Kramer and K. A. Connors, *J. Amer. Chem. Soc.*, 1969, **91**, 2600.

for CTAB (r 0.99); $K = 550$ l mol^{-1} and $k''_{HA} = 5.52$ l mol^{-1} s^{-1} for TMAC (r 0.98). It is interesting that these k''_{HA} values are not very different from that of MMHA in the CTAB micelle (23.1 l mol^{-1} s^{-1}).

Hydroxamate Catalysis in Cationic Micelles.—In the nonmicellar system, BBHA is much less reactive than hydroxide ion, 1/50 in the case of furoin and 1/62 in the case of benzoin (Tables 1 and 2). This simply reflects the much greater basicity of hydroxide ion. In contrast, the catalytic activity of BBHA in the presence of CTAB micelles is considerably enhanced and exceeds that of hydroxide ion (see Table 3). A more pronounced influence of the CTAB micelle is found for catalysis by MMHA. In the proton abstraction from benzoin, the activity of the MMHA–CTAB mixed micelle is 3 500 times as large as that of BBHA in the nonmicellar medium, and 56 times as large as that of hydroxide ion. A similar trend is demonstrated by furoin as shown in Table 3.

Effects of Ionic Strength and Surfactant Concentration.—The k_{HA} value decreased with increasing ionic strength in micellar systems. An example is shown in Figure 3 for the MMHA–TMAC system in the non-ionic POOA micelle.

Figure 4 shows the influence of the surfactant concentration on k_{HA}. The concentration–rate profile for the MMHA–CTAB system gave a maximum at 3 × 10^{-3}M-CTAB, which is close to its c.m.c.[17] In contrast, k_{HA} for MMHA–TMAC in POOA simply descended with increasing POOA concentration. It should be noted that the c.m.c. of the POOA micelle is much lower than the POOA concentration employed here.

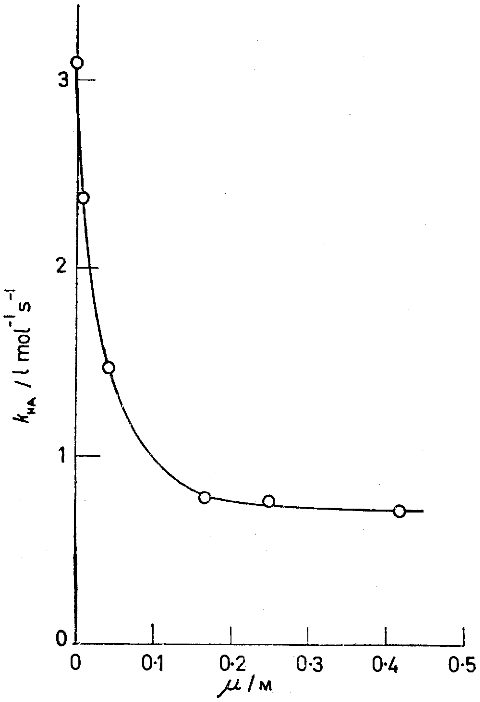

FIGURE 3 Effect of ionic strength on oxidation of furoin catalysed by the POOA–MMHA–TMAC system: 30 °C, pH 11.0 with KOH, [POOA] = 0.01M, [MMHA] = 4.39 × 10^{-4}M, [TMAC] = 1.67 × 10^{-3}M

Hydroxamate Catalysis in Organic Solvents.—The oxidation of furoin was conducted with a nucleophilic ion pair MMHA,NEt$_4$ as catalyst mainly in acetonitrile. This solvent was chosen because its Z value (71.3) is close to that estimated for the cationic micellar surface (85.8).[18-20] Typical rate constants are summarized in Table 4. When BBHA in the nonmicellar medium was taken as reference, the reactivity of MMHA,NEt$_4$ in carefully dried acetonitrile (3.9mM-H$_2$O) increased 760-fold. The reaction rate was very dependent on the water content, and k_{HA} decreased from 42.6 to 1.43 l mol^{-1} s^{-1} as the water content in acetonitrile increased from 3.9 to 940mM. Consistent with this fact, k_{HA} in protic solvents (ethanol and formamide) was

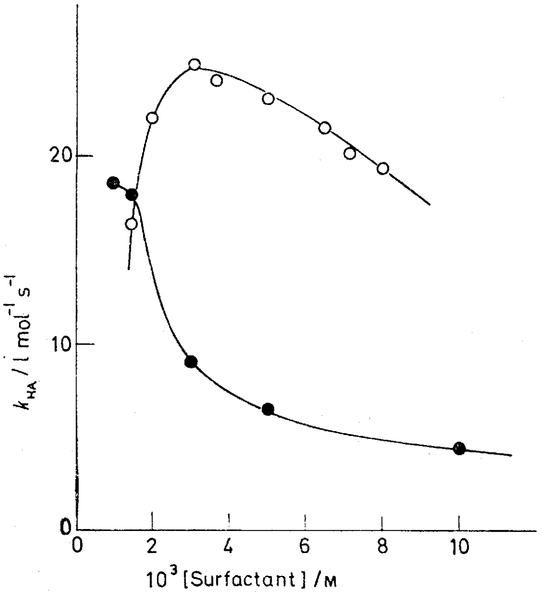

FIGURE 4 Second-order rate constants for proton abstraction from furoin as a function of CTAB and POOA. 30 °C, pH 11.0 with KOH: ○, for CTAB, [MMHA] = 4.39 × 10^{-4}M, [furoin] = 5.04 × 10^{-5}M; ●, for POOA–TMAC, [MMHA] = 4.39 × 10^{-4}M; [TMAC] = 3.33 × 10^{-4}M, [furoin] = 5.04 × 10^{-5}M

TABLE 4

Effect of solvents and additives on rates of proton abstraction reaction from furoin catalysed by MMHA,NEt$_4$ [a]

Solvent	[H$_2$O]/ mM	[NaI]/ mM	k_{HA}/ l mol^{-1} s^{-1}	k_{rel}
Acetonitrile	3.9		42.6	761
	45		8.81	157
	940		1.43	26
	5 500		0.13	2.3
	5.0	0.56	17.8	318
	5.0	1.11	7.85	140
	5.0	5.55	1.85	33
Ethanol [b]	26.6		$<10^{-4}$	$<2 \times 10^{-3}$
Formamide [b]			$<10^{-4}$	$<2 \times 10^{-3}$
Water [c]			0.056	1.0

[a] 30 °C, [MMHA,NEt$_4$] = 4.84 × 10^{-4}M, [furoin] = 5.04 × 10^{-5}M. [b] 3.3% (v/v) water–acetonitrile. [c] BBHA used.

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[17] E. J. Fendler and J. H. Fendler, *Adv. Phys. Org. Chem.*, 1970, **8**, 271.

[18] E. M. Kosower, *J. Amer. Chem. Soc.*, 1958, **80**, 3253, 3261, 3267.

[19] E. H. Cordes and C. Gitler, *Progr. Bio-org. Chem.*, 1972, **2**, 1.

[20] A. Ray and P. Mukerjee, *J. Phys. Chem.*, 1966, **70**, 2138, 2144, 2150.

$< 10^{-4}$ l mol^{-1} s^{-1}. It is remarkable that there is rate differences of $> 10^6$ between aprotic (dry acetonitrile) and protic solvents in spite of their comparable polarities; Z values for ethanol and formamide are 79.6 and 83.3, respectively.[18] The addition of small amounts of NaI also caused large rate decreases in acetonitrile.

DISCUSSION

As mentioned in the Introduction, several kinds of anionic nucleophiles including hydroxamate show much enhanced reactivities in cationic micelles, and these results have been attributed to various aspects of the micellar effect. The data given in Table 3 clearly establish that a similar extent of rate acceleration (3 500 times for benzoin) is achieved by the cationic micelle in proton abstraction. Therefore, the cationic micelle produces large increases in basicity (*i.e.*, affinity for proton) as well as in nucleophilicity. The accelerated proton abstraction may be attributed to the increased stabilization of the carbanionic intermediate formed or to the increased reactivity of the hydroxamate anion. If the former factor predominates, the rate of proton abstraction by hydroxide ion should be accelerated to a similar extent in the presence of the cationic micelle. However, k_{OH} for furoin was increased by a factor of only 1.4 in the presence of the CTAB micelle. Therefore, the observed micellar effect may be mainly ascribed to the increased reactivity of the hydroxamate ion. It is noteworthy that the MMHA–CTAB mixed micelle is 56 times more effective than hydroxide ion, in spite of its much lower pK_a (*ca.* 10).[9]

In Part I,[21] we proposed that the enormous rate enhancements observed for the reaction of anionic nucleophiles with phenyl esters in cationic micelles are due to formation of hydrophobic ion pairs between anionic nucleophiles and cationic surfactant molecules. This proposition was supported by the high reactivity of a zwitterionic nucleophile in non-ionic micelles and by the increased reactivity of a long chain hydroxamate in the presence of hydrophobic ammonium ions.

This concept can be applied to the present results as well. The reactivity increase of the hydroxamate anions in proton abstraction was at most 10-fold in the presence of the non-ionic micelle of POOA; however, it was further enhanced by addition of hydrophobic ammonium ions. The reactivity of the MMHA ion pairs could be estimated by the method of Connors [15,16] which postulates an equilibrium between the paired and unpaired hydroxamate ions. The correlation coefficient observed (r 0.98—0.99) implies that the enhancement mechanism is satisfactorily approximated by the Scheme. The increases in the POOA concentration and ionic strength caused the rate decrease (Figures 3 and 4). Conceivably, the dissociation of the MMHA—TMAC ion pair occurs due to dilution by added POOA and due to the decreased electrostatic attraction between the ions caused by added salts.

The reactivity of the MMHA ion pairs thus estimated amounted to 5—10 l mol^{-1} s^{-1}; 20—40% of the reactivity of MMHA in the CTAB micelle. Thus, the rate enhancement in the cationic micelle can largely be explained by formation of the hydrophobic ion pair, and the high charge density or peculiar microenvironments of the cationic micelle play only a secondary role.

This conclusion was further corroborated by experiments in organic solvents. The crucial importance of desolvation in the nucleophilic displacement has been well established by Parker.[22] An anionic nucleophile is readily deactivated in protic solvents, since it must lose the surrounding protic molecules before it can form a covalent bond. Thus, chloride ion reacts with methyl iodide (1—2) $\times 10^6$ times faster in dimethylformamide and acetonitrile than in methanol.[23,24] In this study, we also found the rate difference of $> 10^6$ between dry acetonitrile and protic solvents. Furthermore, the rate was suppressed by extremely small amounts of water. In fact, the rate constants in Table 4 would be meaningless without accurate indications of the water content. The enhanced reactivity observed in aqueous CTAB micelle toward furoin (23.1 l mol^{-1} s^{-1}, Table 3) was readily achieved by the use of MMHA,NEt_4 ion pair in dry acetonitrile (42.6 l mol^{-1} s^{-1}; Table 4). These results strongly suggest that the large rate enhancements observed for hydroxamate ions in cationic micelles is associated with desolvation of the anion in the relatively hydrophobic, cationic micellar phase.

In conclusion, the present study shows that hydroxamate anions can abstract protons from carbon acids much more efficiently than expected from their pK_a values, if they are placed in appropriate microenvironments. The proposed concept may be applicable more generally to the catalysis of oxyanions in organic and enzymatic reactions.

EXPERIMENTAL

Materials.—Preparations of MMHA and BBHA were reported previously.[9,25] MMHA,NEt_4 was prepared by mixing equimolar amounts of MMHA and tetraethylammonium hydroxide. Recrystallization from benzene–light petroleum gave crystals, m.p. 43—45 °C. The product was dried in a vacuum desiccator at 0.1 mmHg over P_2O_5, $\delta(CDCl_3)$ 0.8—1.3 (25 H, $CH_3[CH_2]_{11}$), 1.40 (12 H, 4 $\times$ CMe), 2.4 (2 H, CH_2CO), 3.20 (3 H, NMe), and 3.40 (8 H $[CH_2]_4$). Sodium lauryl sulphate (NaLS) and polyoxyethyleneoleyl alcohol (Tokyo Kasei) were used without further purification. Cetyltrimethylammonium bromide (CTAB) was recrystallized from ethanol. Furoin and bonzoin were used after recrystallization from water and methanol.

Kinetics.—Kinetic measurements in aqueous solutions were carried out at 30 °C in 1% (v/v) aqueous acetonitrile by using modified Thunberg cuvettes. Buffer solutions of pH

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[21] T. Kunitake, S. Shinkai, and Y. Okahata, *Bull. Chem. Soc. Japan*, 1976, **49**, 540.

[22] A. J. Parker, *Quart. Rev.*, 1962, **16**, 163.

[23] A. J. Parker, *J. Chem. Soc.*, 1961, 1328, 4398.

[24] R. Alexander, E. C. F. Ko, A. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, 1968, **90**, 5049.

[25] T. Kunitake, Y. Okahata, and T. Tahara, *Bio-org. Chem.*, in the press.

11 were prepared from potassium hydroxide and O_2-saturated water. Since the pK_a values of hydroxamic acids are usually 8.8—10,[26] MMHA and BBHA are fully ionized at this pH. A typical example of a hydroxamate-catalysed proton abstraction reaction is as follows. An O_2-saturated (*ca.* 10^{-3}M) [27] solution (3.0 ml; pH 11) containing surfactant and hydroxamate ion was placed in a Thunberg cuvette, and an acetonitrile solution (30 μl) of α-ketol was added to the sidearm of the cell. After being stoppered, the cell was equilibrated at 30 °C, and the content of the side-arm was rapidly mixed with the surfactant solution. The reactions were followed on a Hitachi 124 spectrophotometer at 280 nm for benzoin and 310 nm for furoin which are the wavelengths for the largest absorbance changes between α-ketols and diketones. The pH of the reaction mixture did not vary as confirmed from pH measurements (Toa digital pH meter, model HM-15 A) before and after the reaction.

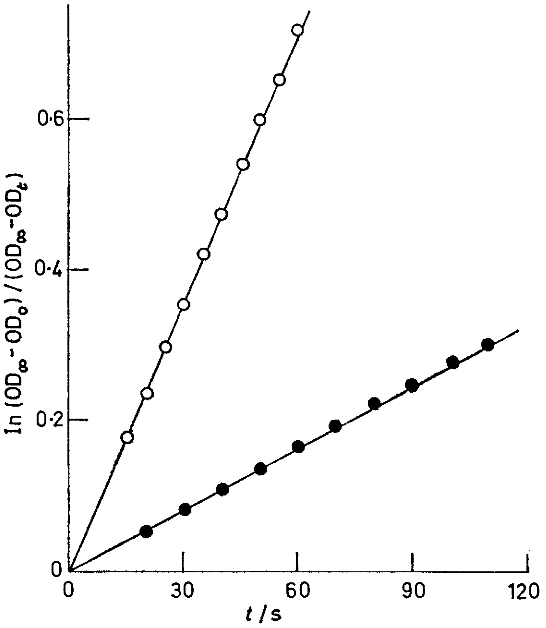

FIGURE 5 Typical plots of ln $(OD_\infty - OD_0)/(OD_\infty - OD_t)$ at 310 nm against time for the proton abstraction reaction from furoin at 30 °C: ○, [CTAB] = 5.0×10^{-3}M, [MMHA] = 4.39×10^{-4}M, [furoin] = 5.04×10^{-5}M; ●, [POOA] = 1.0×10^{-2}M, [TMAC] = 3.33×10^{-3}M, [MMHA] = 4.39×10^{-4}M, [furoin] = 5.04×10^{-5}M

The rate-determining step of the oxidation of α-ketols to the corresponding diketones is base-catalysed hydrogen abstraction.[10-12] Thus the oxidation rate is independent of the nature and concentration of the oxidizing agent (for the kinetic equations, see ref. 12). This proposition was also confirmed in the presence of the CTAB micelle, based on the following facts: (1) the oxidation rates of benzoin satisfied first-order kinetics and were independent of the extent of O_2 (oxidizing agent) saturation; (2) the oxidation rates of benzoin by lumiflavin (oxidizing agent) under anaerobic conditions were also independent of the concentration of lumiflavin (zero-order up to 80% reaction). Representative pseudo-first-order plots of the appearance of oxidized diketone with time are shown in Figure 5. Pseudo-first-order rate constants (k_{obs}) for the condition [base] $\gg$ [α-ketol], were calculated from the slopes. Since the k_{obs} values obtained for hydroxide catalysis are first order in OH^- (see Results section), the second-order rate constants (k_{OH}) are given by equation (3). The second-order rate constants for hydroxamate catalysis (k_{HA}) were estimated at the fixed hydroxamate concentration (4.93×10^{-4}M) according to equation (4) where k_{sp} denotes pseudo-first-order rate constants in the absence of the hydroxamate ion. From duplicate or repeated runs, k_{OH} and k_{HA} values were reproducible to within 5% or less in the presence and absence of micelles.

$$\text{for OH}^- \text{ catalysis, } k_{OH} = k_{obs}/[OH^-] \qquad (3)$$

$$\text{for hydroxamate catalysis, } k_{HA} = (k_{obs}\text{-}k_{sp})/[\text{hydroxamate}] \qquad (4)$$

The reactions in organic solvents were similarly performed by using Thunberg cuvettes. Stock solutions of MMHA, NEt_4 for kinetic measurements were prepared in acetonitrile on the day of use. The reaction mixture was obtained as follows. An O_2-saturated solution (2.9 ml) of α-ketol was placed in a Thunberg cell, and an acetonitrile solution (0.1 ml) of MMHA,NEt_4 was deposited in the side-arm. Dry O_2 was bubbled into the former solution for 5 min, and, after stoppering, the reaction was initiated by mixing. The water content in organic solvents was determined after the reaction with a Hiranuma aquacounter AQ-1.

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