Coenzyme Models. Part 36.† Hydroxide-mediated Disproportionation of a Lipophilic Acridinium Salt in a Micellar System

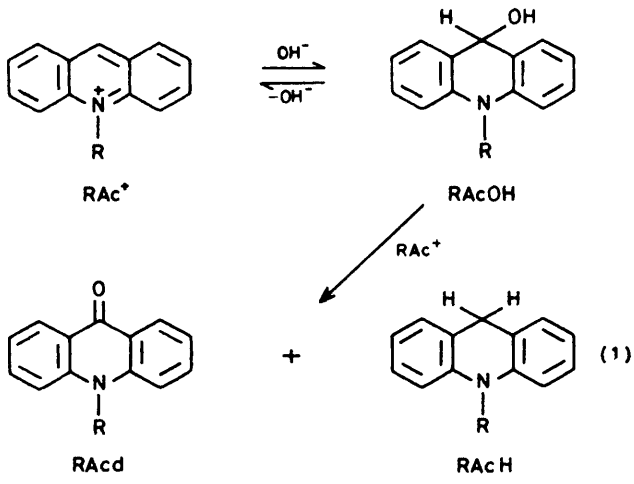
Seiji Shinkai,* Takaharu Tsuno, and Osamu Manabe
Department of Industrial Chemistry, Faculty of Engineering, Nagasaki University, Nagasaki 852, Japan

We have found that *N*-dodecylacridinium ion ($DodAc^+$) is rapidly disproportionated to *N*-dodecylacridone (DodAcd) and *N*-dodecylacridan (DodAcH) *via* hydroxy-adduct (DodAcOH) in the presence of cationic (CTAB) or non-ionic (Brij-35) micelles. Product analyses show that two moles of $DodAc^+$ produce one mole of DodAcd and one mole of DodAcH and the hydrogen is directly transferred from DodAcOH to $DodAc^+$. The reaction is similar to oxidation of alcohols by NAD^+ model compounds. Kinetic studies show that the reaction consists of two steps, the first an equilibrium for formation of the hydroxy-adduct and the second disproportionation to RAcd and RAcH. The first step is efficiently accelerated by CTAB and Brij-35 and the association constants (K) are enhanced by 10^5—10^6-fold. On the other hand, the second step is less susceptible to the micellar environment and is not base-catalysed. Thus the micellar effect on the first step is responsible for the overall rate enchancement. This is the first example of a micellar effect on the hydroxide ion-mediated disproportionation of heteroaromatic nuclei.

Acridinium salts have frequently been used as convenient NAD^+ model compounds.[1-8] In particular, they have served as useful hydrogen acceptors in the model reaction for NADH–NAD^+ transhydrogenation.[1-4,8] This is due to the electron-deficient nature of the acridinium ring system. However, the results obtained so far are somewhat ambiguous and must be discounted because of the formation of covalent adducts with nucleophiles as a competitive reaction path.[9-11] In contrast to a number of NADH model studies involving acridinium salts, little attention has ever been paid to the reactivity of the adducts formed between acridinium salts and nucleophiles. It thus seemed to us desirable to understand the reactivity of the covalent adducts to allow for the use of acridinium salts as NAD^+ model compounds.

We have been interested in the investigation of models for coenzyme–apoenzyme relationships.[12] It was found that some coenzyme-mediated reactions are efficiently catalysed, as for apoenzymes, by artificial molecular assemblies. In an extension of this work, we have synthesized a lipophilic acridinium salt, *N*-dodecylacridinium chloride ($DodAc^+$), and unexpectedly found that in cationic and non-ionic micelles in the neutral pH region a hydroxy-adduct is readily formed followed by oxidation by another $DodAc^+$ to yield *N*-dodecylacridan (DodAcH) and *N*-dodecylacridone (DodAcd) [equation (1)].

For the *N*-methylacridinium salt ($MeAc^+$), a similar reaction took place only in alkaline solution. This novel reaction is in a sense a disproportionation similar to the Cannizzaro reaction, while it may also be regarded as an oxidation of an alcohol (*i.e.*, pseudo-base RAcOH) by an NAD^+ model (*i.e.*, RAc^+). Literature surveys show that there are a few analogues of the present reaction: for example, hydroxide ion-mediated disproportionation of 3-cyano-1-methylpyridinium perchlorate, 5-deazaflavins, 5-nitroisoquinolinium cation, *etc.*[13-15] To the best of our knowledge, however, no precedent exists for the micellar catalysis.



Results and Discussion

Product Analyses.—The reaction products from the acridinium salts in the micellar system were analysed by high-pressure liquid chromatography. The yields were determined by comparing the intensities with those of authentic samples. The results are summarised in Table 1. In anaerobic aqueous solutions containing CTAB (hexadecyltrimethylammonium bromide) or Brij-35, $DodAc^+$ gave DodAcH and DodAcd in a *ca.* 1 : 1 ratio. The reaction proceeded easily in the neutral pH region. When the reaction was carried out under aerobic conditions, the yield of DodAcH was slightly lowered while that of DodAcd was enhanced. Hence, DodAcH may be oxidised, although slowly, by molecular oxygen. The sum of DodAcH and DodAcd was in most cases better than 90% and was 77% even in the worst case. In contrast, the reaction did not take place at all in SDS (sodium dodecylsulphate) micelle. In $MeAc^+$, a similar reaction was detectable at pH 10 in the CTAB micelle, but the reaction was very slow. At pH 10.6, for instance, $MeAc^+$ in CTAB gave *N*-methylacridan (MeAcH) and *N*-methylacridone (MeAcd) in 31 and 40% yield, respectively, after 6 days. However, $MeAc^+$ was still detectable in the reaction solution.

To obtain further insight into the hydrogen-transfer mechanism from RAcOH to RAc^+, we carried out the reaction in an anaerobic D_2O solution (pH 7.0) containing 20mM-CTAB for 2 days. As a control experiment, $DodAc^+$ (5.0mM) was also treated in an anaerobic H_2O solution containing 20mM-CTAB. The DodAcH recovered from the H_2O solution gave a ratio of $M^+ + 1$ to M^+ ions in the mass spectrum of 29.1 ± 0.2, which is in accord with the theoretical

† Part 35, S. Shinkai, T. Tsuno, Y. Asatani, and O. Manabe, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1533.

Table 1. Product analyses for the reaction of acridinium salts in micellar systems [a]

Surfactant (mM)	pH	Yield (%) [b] of DodAcH	DodAcd
CTAB (5.0) [c]	6.1	49(44)	48(57)
CTAB (5.0) [c]	7.0	47(41)	49(55)
CTAB (5.0) [c]	8.1	38(39)	44(60)
CTAB (5.0) [d]	6.1	(46)	(57)
CTAB (5.0) [d]	7.0	(39)	(61)
CTAB (5.0) [d]	8.1	(32)	(63)
Brij-35 (3.0) [d]	6.1	48(48)	48(53)
Brij-35 (3.0) [d]	7.0	47(44)	52(57)
Brij-35 (3.0) [d]	8.1	42(37)	49(62)
SDS (10.0) [d]	6.1	0(0)	0(0)
SDS (10.0) [d]	7.0	0(0)	0(0)
SDS (10.0) [d]	8.1	0(0)	0(0)
CTAB (5.0) [d]	10.6	31 [e,f]	40 [e,f]
CTAB (5.0) [d]	12.0	48 [e]	51 [e]

[a] [DodAc$^+$] 1.00×10^{-3}M, room temperature, anaerobic (N_2). pH was adjusted with 0.06M-phosphate buffer. [b] The yield is an average of 2—3 runs. The values in parentheses indicate the aerobic yields. [c] Reaction time 3 days. [d] Reaction time 6 days. [e] Reaction products (MeAcH and MeAcd) from MeAc$^+$ (1.00×10^{-3}M). pH was adjusted with KOH. [f] MeAc$^+$ was still detected.

natural abundance value (27.94%).* The DodAcH recovered from the D_2O solution gave a ratio of 29.5 ± 0.2. The results show that no solvent deuterium is incorporated into the product DodAcH. Apparently, hydrogen is transferred directly from DodAcOH to DodAc$^+$, as in representative NADH model reduction.[1-6] Yoneda *et al.*[14] have reported direct hydrogen transfer for hydroxide ion-mediated disproportionation of 5-deazaflavin in 60% aqueous potassium hydroxide.

The foregoing results indicate that two moles of acridinium salt gave one mole of acridan and of acridone and that cationic and non-ionic micelles are capable of strongly catalysing the reaction.

Derivation of Kinetic Equations.—The time-dependent spectral changes for disproportionation of acridinium salts (RAc$^+$) were apparently biphasic, *i.e.*, a rapid decrease in RAc$^+$ (359 nm) followed by a slow appearance of RAcd (405 nm) (Figure 1). The initial step corresponds to nucleophilic attack of OH$^-$ to form a pseudo-base RAcOH [equation (2)] and the second step is the oxidation of RAcOH by RAc$^+$ [equation (3)]. The rate of the initial nucleophilic reaction can be estimated by following the disappearance of RAc$^+$ at the

$$RAc^+ + OH^- \underset{k_r}{\overset{k_f}{\rightleftharpoons}} RAcOH \qquad (2)$$

$$RAcOH + RAc^+ \xrightarrow{k_2} RAcd + RAcH \qquad (3)$$

* The mass spectrum gave the relatively large $M^+ - 1$ peak [$(M^+ - 1)/M^+ = 0.112$]. This is due to the ready hydrogen elimination from DodAcH during the mass spectral measurement. Thus, the slightly large $(M^+ + 1)/M^+$ value (0.291) relative to the theoretical natural abundance value (0.2794) is attributed to hydrogen elimination. The DodAcH recovered from the D_2O solution gave $(M^+ - 1)/M^+$ 0.118, which is in fairly good agreement with that observed for DodAcH (0.112).

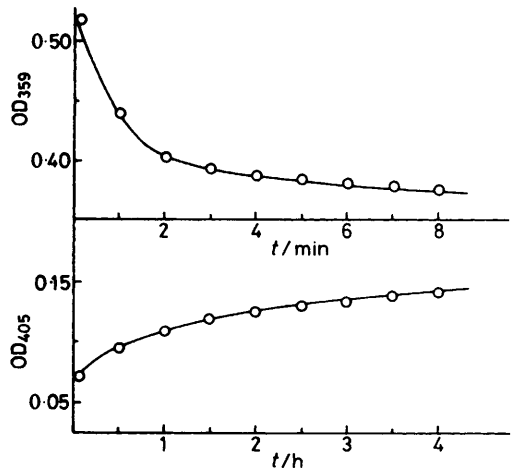


Figure 1. Plots of absorbances at 359 [equation (2)] and 405 nm [equation (3)] *versus* reaction time: 30 °C, N_2, pH 7.4, [DodAc$^+$] 5.30×10^{-5}M, [Brij-35] 1.0mM

isosbestic point of the second reaction (*ca.* 360 nm). One must consider the reaction to be reversible [13-17] like nucleophilic attack of CN$^-$ on nicotinamide salts.[18-22]

The k_f and k_r values can be determined from equation (4) from a plot of k_{obs} (pseudo-first-order rate constant) against [OH$^-$],

$$k_{obs} = k_f[OH^-] + k_f/K \qquad (4)$$
$$K = k_f/k_r$$

The rate of the second stage can be followed by the appearance of RAcd (405 nm) and is expressed by equation (5), where k_2 is the second-order rate constant for the oxidation of RAcOH by RAc$^+$. Equation (5) can be rewritten as (6).

$$d[RAcd]/dt = k_2[RAcOH][RAc^+] \qquad (5)$$

$$d[RAcd]/dt = k_2K[OH^-]\left(\frac{[RAc^+]_0 - 2[RAcd]}{1 + K[OH^-]}\right)^2 \qquad (6)$$

Integration of equation (6) gave (7) where equation (8) holds.

$$\frac{1}{[RAcd]} = \frac{2}{[RAc^+]_0} + \frac{1}{[RAc^+]_0^2 k_{app}} \cdot \frac{1}{t} \qquad (7)$$

$$k_{app} = k_2K[OH^-]/(1 + K[OH^-])^2 \qquad (8)$$

Thus one can determine k_{app} at constant pH from the plot of $[RAcd]^{-1}$ against t^{-1}. It is expected that k_{app} plotted against pH would result in a bell-shaped curve. The bell-shaped pH dependence can be expressed by equation (9), which suggests a linear relationship between $([OH^-]/k_{app})^{1/2}$ and [OH$^-$]. K And k_2 can be determined independently from the slope $[(K/k_2)^{1/2}]$ and the intercept $[(k_2K)^{-1/2}]$ of the linear relationship (9).

$$\left(\frac{[OH^-]}{k_{app}}\right)^{1/2} = \frac{1}{(k_2K)^{1/2}} + \left(\frac{K}{k_2}\right)^{1/2}[OH^-] \qquad (9)$$

pH *Dependence of the Reaction Rates.*—The disappearance of RAc$^+$ and the appearance of RAcd were followed as a function of the pH of the medium in anaerobic reaction media. The pseudo-first-order rate constants (k_{obs}) for the disappearance of RAc$^+$ are illustrated in Figure 2. In addition, the apparent second-order rate constants (k_{app}) for the

Table 2. Typical rate constants, k_{obs} and k_{app} [a]

	k_{obs}/s^{-1} for the disappearance of Ac^+				$k_{app}/l\ mol^{-1}\ s^{-1}$ for the appearance of Acd			
pH	CTAB + $DodAc^+$	Brij-35 + $DodAc^+$	SDS + $DodAc^+$	CTAB + $MeAc^+$	CTAB + $DodAc^+$	Brij-35+ $DodAc^+$	SDS + $DodAc^+$	CTAB + $MeAc^+$
7.0	4.62×10^{-2}	9.27×10^{-3}	No reaction	No reaction	1.65	2.62	No reaction	No reaction
7.8	4.15×10^{-1}	9.59×10^{-2}	No reaction	No reaction	0.707	2.52	No reaction	No reaction
8.1	very fast	1.95×10^{-1}	No reaction	No reaction	0.363	1.75	No reaction	No reaction
11.0	very fast	very fast	1.60×10^{-5}	1.65×10^{-4}	very slow	very slow	0.661	0.724
12.0	very fast	very fast	4.09×10^{-5}	7.80×10^{-4}	very slow	very slow	1.52	0.740

[a] 30 °C, N_2, $[DodAc^+] = [MeAc^+] = 5.30 \times 10^{-5}$M, [CTAB] 3.0mM, [Brij-35] 1.0 mM, [SDS] 10mM. Buffer: 0.06M-phosphate for pH 5.0—8.1, KOH for pH > 10.

Table 3. Equilibrium constants (K) and rate constants (k_f and k_2)

Reaction system	$K/l\ mol^{-1}$ [a]	$K/l\ mol^{-1}$ [b]	$k_f/l\ mol^{-1}\ s^{-1}$ [a]	$k_2/l\ mol^{-1}\ s^{-1}$ [b]
$DodAc^+$ in CTAB	10^7—10^8 [c]	2.8×10^7	4.1×10^5	18
$DodAc^+$ in Brij-35	10^6—10^8 [c]	4.9×10^6	1.4×10^5	14
$DodAc^+$ in SDS	1×10^2		1.8×10^{-3}	
$MeAc^+$ in CTAB	1×10^3		5.2×10^{-2}	*ca.* 5 [d]

[a] Determined from equation (4). [b] Determined from equation (9). [c] The intercepts (k_f/K) were so close to zero that the K values could not be determined accurately. [d] The low accuracy is because the k_2 value was estimated by the data taken at narrow pH region (10.6—12.0).

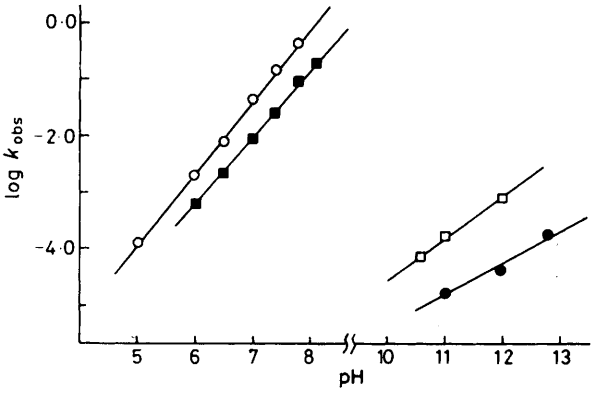


Figure 2. log k_{obs} *versus* pH. ○, CTAB + $DodAc^+$; ■, Brij-35 + $DodAc^+$; □, CTAB + $MeAc^+$; ●, SDS + $DodAc^+$

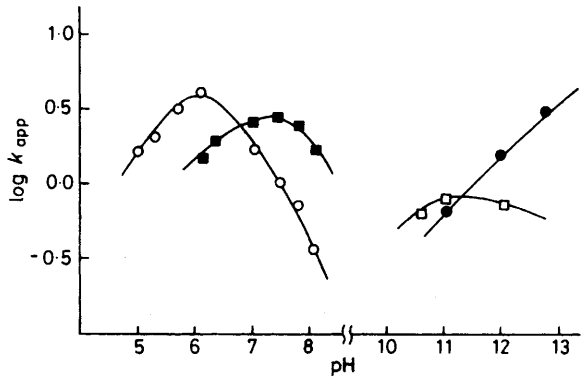


Figure 3. log k_{app} *versus* pH. ○, CTAB + $DodAc^+$; ■, Brij-35 + $DodAc^+$; □, CTAB + $MeAc^+$; ●, SDS + $DodAc^+$

appearance of RAcd were determined by equation (7). The typical rate constants are recorded in Table 2. It can be seen from Figure 2 that slopes of the plots between log k_{obs} and pH are linear and close to unity (1.3 for $DodAc^+$ in CTAB, 1.2 for $DodAc^+$ in Brij-35, 0.60 for $DodAc^+$ in SDS, and 0.84 for $MeAc^+$ in CTAB). Using equation (4), we determined k_f and K for adduct formation between OH^- and the acridinium salts. In all cases plots of k_{obs} *versus* $[OH^-]$ yielded a good linear relationship with $r > 0.98$. The rate constants are recorded in Table 3. The accuracy of some K values was somewhat inferior because the intercepts (*i.e.*, k_f/K) were quite close to zero. Plots of k_{app} *versus* pH are illustrated in Figure 3. As expected, the pH–rate profiles were bell-shaped and the rate maxima appeared at pH 6.1, 7.3, and 11.5 for $DodAc^+$ in CTAB, $DodAc^+$ in Brij-35, and $MeAc^+$ in CTAB, respectively. On the other hand, a rate maximum was not observed for $DodAc^+$ in SDS at up to pH 12.8. Using equation (9), we estimated K and k_2 and the results are summarised in Table 3.

Examination of Table 3 reveals that (i) the K values for $DodAc^+$ in CTAB and Brij-35 are greater by 10^5—10^6 fold than that for $DodAc^+$ in SDS, (ii) compared with the k_f value of $MeAc^+$ in CTAB, the reaction between OH^- and $DodAc^+$ in CTAB and Brij-35 is speeded up by *ca.* 10^7-fold, while the reaction in SDS is inhibited to a small extent, and (iii) in contrast to the marked difference in K and k_f, the k_2 values are less affected by the reaction media. It has been established that the rate and equilibrium constants (k_f and K, respectively) for the addition of cyanide ion to nicotinamide salts with long alkyl chains are profoundly increased in dilute aqueous solution of cationic surfactants or cationic polymer micelles.[19,22] The remarkable enhancement is ascribed mainly to two representative micellar effects, (i) concentration of CN^- in the micellar phase to which nicotinamide salts are bound and (ii) as the reduction system produces a neutral adduct from a cation and an anion, the rate and equilibrium are favoured in non-polar micellar media. Effect (ii) is in line with the fact that the formation of adduct is favoured in solvents with low dielectric constants.[23] On the other hand, the contribution of effect (i) can be estimated separately by using the hydrophilic cationic polymer immobilising the nicotinamide salt as a pendant group.[21] In the present system, the fact that both CTAB and Brij-35 are able to enhance k_f and K implies that the non-polar environment of the micelles has the primary responsibility for the enhanced parameters. Probably, the slightly larger parameters of CTAB relative to

Brij-35 is attributed to effect (i). The inhibitory effect observed for SDS micelle can also be rationalised in terms of effect (i), *i.e.*, hydroxide ion is excluded from the anionic micelle surface because of the electrostatic repulsion between like charges.

In contrast to a number of investigations on NADH model reductions of carbonyl substrates, there are only a few examples of NAD^+ model oxidations of alcohol substrates.[24-28] Furthermore, the reaction mechanism is not yet established clearly.[26,27] In addition to conventional nicotinamide salts, several isoelectronic equivalents such as 5-deazaflavin, 5-deaza-10-oxaflavin, pyridodipyrimidine, and 3-hydroxy-*N*-methylacridinium ion have been used as NAD^+ model compounds.[29-33] Some of these NAD^+ model compounds require base catalysis and thus alcohols are oxidised to carbonyl compounds *via* $R^1R^2CHO^-M^+$ (M^+ = alkali-metal cation)[24,26,27,29,32,33] or $R^1R^2CHO^-MgBr^+$,[28] but oxidation in the absence of base is also reported for highly electron-deficient NAD^+ model compounds.[30,31] In the present system, the pH dependence is bell-shaped (Figure 3). The rate of the second reaction step is expressed by $v = k_2[RAcOH][RAc^+]$. The concentration of RAcOH must be low in the low pH region, whereas that of RAc^+ becomes low in the high pH region, resulting in a rate maximum at intermediate pH where [RAcOH] is comparable with $[RAc^+]$. Importantly, equation (3) which leads to the bell-shaped pH–rate profile of equation (8) does not involve the base-catalysed term. If the oxidation step is base-catalysed, one may expect that the k_2 value is enhanced in the CTAB micelle which is capable of concentrating hydroxide ions on the micelle surface. However, the k_2 value in CTAB is not much different from that in Brij-35 and only 3.6 times greater than that of $MeAc^+$ in CTAB. These results indicate that the oxidation of RAcOH by RAc^+ is not base-catalysed and is less susceptible to the reaction environment.

Conclusions.—The hydroxide ion-mediated disproportionation of acridinium salts to acridone and acridan is efficiently catalysed by cationic and non-ionic micelles while it is inhibited by anionic micelles. The kinetic examination established that the reaction consists of two steps, the first an equilibrium for formation of a hydroxy-adduct and the second disproportionation corresponding to oxidation of the pseudo-base RAcOH by the NAD^+ model RAc^+. The first step is very susceptible to the micellar environment and the effect is responsible for the overall rate enhancement, whereas the second step is less affected by the micelle. This is the first example to refer to the micellar effect on the hydroxide ion-mediated disproportionation of heteroaromatic nuclei.

Experimental

Materials.—N-*Dodecylacridone* (DodAcd) was prepared from acridone and dodecyl bromide in the presence of sodium hydride. Oil-dispersed sodium hydride (7.4 g, 0.15 mol) was added in several portions to *NN*-dimethylformamide (DMF) solution (300 ml) containing acridone (6.0 g, 0.031 mol). After keeping the mixture at 60 °C for 4 h, the solution was cooled to room temperature and dodecyl bromide (38.3 g, 0.154 mol) was added dropwise. The precipitate (NaBr) was filtered off, the filtrate being concentrated to dryness *in vacuo*. The *residue* was recrystallised from hexane four times, m.p. 90—91 °C, yield 76% (Found: C, 82.5; H, 9.25; N, 3.6. $C_{25}H_{33}NO$ requires C, 82.6; H, 9.15; N, 3.85%).

N-*Dodecylacridan* (DodAcH) was obtained by the reduction of DodAcd. DodAcd (1.00 g, 2.75 mmol) was dissolved in hot absolute ethanol (30 ml), and sodium (1.26 g, 55.0 mmol) was carefully added to the hot solution. After 8 h, the solution was concentrated to dryness, the residual solid being washed with water. The *solid* was recrystallised from ethanol–ether, m.p. 55.5—57.0 °C, yield 62% (Found: C, 85.9; H, 10.0; N, 4.0. $C_{25}H_{35}N$ requires C, 85.9; H, 10.1; N, 4.0%), δ ($CDCl_3$) 0.94 (3 H, CH_3), 1.23 (20 H, $[CH_2]_{10}$), 3.73 (2 H, NCH_2), 3.83 (2 H, 9-CH_2), and 6.6—7.2 (8 H, ArH). In the i.r. spectrum (KBr disk), the $\nu_{C=O}$ (1 630 cm^{-1}) band of DodAcd disappeared.

N-*Dodecylacridinium chloride* ($DodAc^+$) was prepared by the oxidation of DodAcH. DodAcH (1.50 g, 4.29 mmol) was treated with $FeCl_3$ (2.80 g, 17.2 mmol) in ethanol (80 ml) for 5 h at room temperature. After evaporating the solvent, the residue was extracted with chloroform. The chloroform solution was concentrated to dryness, the *residue* being recrystallised from chloroform–hexane, m.p. 163—164 °C, yield 83% (Found: C, 75.6; H, 9.05; N, 3.5. $C_{25}H_{34}ClN\cdot 0.7H_2O$ requires C, 75.7; H, 9.0; N, 3.5%), δ ($[^2H_6]Me_2SO$) 0.84 (3 H, CH_3), 1.24 (20 H, $[CH_2]_{10}$), 5.40 (2 H, NCH_2), 7.8—8.8 (8 H, aromatic protons), and 10.08 (1 H, 9-H).

Kinetic Measurements and Product Analyses.—The rate measurements were carried out spectrophotometrically at 30 °C by using a thermostatted cell-holder. The anaerobic reaction mixture was prepared by using a Thunberg cuvette.

To a buffered surfactant solution (30 ml) was added a methanol solution (200 μl) of RAc^+. The concentration of RAc^+ in the reaction mixture was 1.00×10^{-3}M. After the appropriate reaction time (30 °C) the solution (5 ml) was withdrawn and extracted with chloroform. The concentration of RAcd and RAcH in the chloroform solution was estimated by using h.p.l.c.

References

1 D. J. Creighton, J. Hajdu, G. Mooser, and D. S. Sigman, *J. Am. Chem. Soc.*, 1973, **95**, 6855.
2 J. Hadju and D. S. Sigman, *J. Am. Chem. Soc.*, 1975, **97**, 3524.
3 A. Ohno, T. Shio, H. Yamamoto, and S. Oka, *J. Am. Chem. Soc.*, 1981, **103**, 2045.
4 S. Shinkai, T. Ide, H. Hamada, O. Manabe, and T. Kunitake, *J. Chem. Soc., Chem. Commun.*, 1977, 848.
5 A. K. Colter, G. Saito, F. J. Sharom, and A. P. Hong, *J. Am. Chem. Soc.*, 1976, **98**, 7833.
6 A. K. Colter, G. Saito, and F. J. Sharom, *Can. J. Chem.*, 1977, **55**, 2741.
7 R. E. Ballard, J. Jones, and E. Sutherland, *Tetrahedron Lett.*, 1982, **23**, 3677.
8 S. Shinkai, T. Ide, and O. Manabe, *Bull. Chem. Soc. Jpn.*, 1978, **51**, 3655.
9 P. van Eikeren, D. L. Grier, and J. Eliason, *J. Am. Chem. Soc.*, 1979, **101**, 7406.
10 A. van Laar, H. J. van Ramesdonk, and J. W. Verhoevan, *Recl. Trav. Chim. Pays-Bas.*, 1983, **102**, 401.
11 M. F. Powell and T. C. Bruice, *J. Am. Chem. Soc.*, 1982, **104**, 5834.
12 S. Shinkai, *Prog. Polym. Sci.*, 1982, **8**, 1.
13 F. M. Moracci, S. Tortorella, B. D. Rienzo, and F. Liberatore, *Tetrahedron*, 1979, **35**, 2591.
14 F. Yoneda, Y. Sakuma, and A. Koshiro, *J. Chem. Soc., Perkin Trans. 1*, 1980, 293.
15 J. W. Bunting and S. H. Kabir, *J. Org. Chem.*, 1978, **43**, 3662 and references cited therein.
16 J. W. Bunting and W. G. Meathrel, *Can. J. Chem.*, 1973, **51**, 1965.
17 J. W. Bunting and D. J. Norris, *J. Am. Chem. Soc.*, 1977, **99**, 1189.
18 R. N. Lindquist and E. H. Cordes, *J. Am. Chem. Soc.*, 1968, **90**, 1269.
19 J. Baumrucker, M. Calzadilla, M. Centeno, G. Lehrman, M. Urdaneta, P. Lindquit, D. Dunham, M. Price, B. Sears, and E. H. Cordes, *J. Am. Chem. Soc.*, 1972, **94**, 9164.

20 T. Okubo and N. Ise, *J. Am. Chem. Soc.*, 1973, **95**, 4031.
21 S. Shinkai, K. Tamaki, and T. Kunitake, *Makromol. Chem.*, 1977, **178**, 133.
22 S. Shinkai and T. Kunitake, *Biopolymers*, 1976, **15**, 1129.
23 M. R. Lamborg, R. M. Burton, and N. O. Kaplan, *J. Am. Chem. Soc.*, 1957, **79**, 6173.
24 A. Shirra and C. J. Suckling, *J. Chem. Soc., Perkin Trans. 2*, 1977, 759.
25 K. Wallenfels and W. Hanstein, *Angew. Chem., Int. Ed. Engl.*, 1965, **4**, 869.
26 Y. Ohnishi and M. Kitami, *Tetrahedron Lett.*, 1978, 4035.
27 A. Ohno, S. Ushida, and S. Oka, *Tetrahedron Lett.*, 1982, **23**, 2784.
28 S. Shinkai, H. Era, T. Tsuno, and O. Manabe, paper presented at the 47th Annual Meeting of the Chemical Society of Japan, 1983, Kyoto.
29 F. Yoneda, Y. Sakuma, and P. Hemmerich, *J. Chem. Soc., Chem. Commun.*, 1977, 825.
30 F. Yoneda, R. Hirayama, and M. Yamashita, *Chem. Lett.*, 1980, 1157.
31 F. Yoneda, H. Yamato, and M. Ono, *J. Am. Chem. Soc.*, 1981, **103**, 5943.
32 S. Shinkai, H. Hamada, H. Kuroda, and O. Manabe, *J. Org. Chem.*, 1981, **46**, 2333.
33 S. Shinkai, H. Kuroda, and O. Manabe, *Tetrahedron Lett.*, 1982, **23**, 1357.

Received 4th July 1983; *Paper* 3/1147