Catalysis by Stearyltrimethylammonium Bromide of the Reaction between Long Chain Alkanethiols and *p*-Nitrophenyl Acetate

By WAICHIRO TAGAKI,* TORU AMADA, YUKIKO YAMASHITA, and YUMIHIKO YANO

(Department of Chemistry, Faculty of Technology, Gunma University, Kiryu, Gunma, Japan)

Summary The effect of stearyltrimethylammonium bromide (stab) upon the reaction between alkanethiols and *p*-nitrophenyl acetate has been examined in aqueous solution; below the critical micellar concentration (c.m.c.) of stab, the activities of thiols decrease with increasing carbon chain length, whereas, above the c.m.c., dodecanethiol is some 10^4 fold more reactive than in the absence of stab at pH 9.

The reactivity of thiols has been the subject of continued investigation because of the interest in functions of some sulphhydryl enzymes.[1] Thus, detailed studies have been reported for the reactions of *p*-nitrophenyl acetate (pnpa) with various thiols.[2] However, there has been no report on the micellar effect on the reactivity of thiols. Previously,[3] we showed that an imidazole group incorporated on a cationic micellar surface exhibits an unusually high reactivity in the hydrolysis of pnpa. We describe another example of such an enhanced reactivity of a long chain alkanethiol when mixed with a cationic surfactant.

The reactions of thiols of C_2—C_{12} with pnpa were examined in the presence and absence of stab. The rates of reaction of pnpa were determined by following the formation of *p*-nitrophenol[3] at pH 7—11 (under nitrogen to avoid oxidation of the thiol). The ratio, r, [stab]/[RSH], was varied (r = 0—20). In all the cases, the addition of stab showed a micellar effect on the rates to give the reported c.m.c. of stab (2·0 × 10^{-4} M). Above the c.m.c., a good pseudo first-order reaction was observed regardless of the ratio of [pnpa]/[RSH] (0·1—40). The values of k_{obs} thus obtained were linear with respect to the thiol concentration to give the apparent second-order rate constants, $k_2 = (k_{obs} - k_w)/[RSH]_T$. The k_2 values were pH dependent (the slope = 0·72 for the linear plots of log k_2 *vs* pH in the catalysis of dodecanethiol) indicating that the active species are thioanions.

TABLE. *Effects of Alkyl Chain Length*[a,b]

	k_2 (M^{-1} s^{-1})		
$C_nH_{2n+1}SH$	Thiol only (r=0) (×10^1)	Thiol+stab (r=5) (×10^{-1})	k_{rel} (×10^{-2})
n = 2	3·75	4·12	1·1
4	4·07	12·1	3·0
6	2·33	27·8	12
8	0·663	38·8	58
10	—	36·0	—
12	0·088	41·7	473

[a] Tris buffer (0·07 M) containing 6·5% ethanol; [pnpa] = 5 × 10^{-5} M; pH 9·0, 30°. [b] Thiol concentration range: r = 0; 5—20 × 10^{-4} M for n = 2—6 and 3—8 × 10^{-4} M for n = 8, 12; and r = 5, 4—40 × 10^{-5} M.

The reaction rate with dodecanethiol increased more than 10^4 fold (at pH 9) by the addition of a twice molar excess of stab over the thiol. Further addition of stab did not affect the rate very much. The effect of the thiol chain length on the rate is shown in the Table. In the absence of stab (or below the c.m.c), the rate decreases with increasing carbon chain length as observed for a nucleophilic reaction.[5] However, in the presence of stab (five molar excess), the rate increased with increasing chain length up to C_8, then levelled off. The ratios of the two sets of rate constants indicate that the rate increase is 10^2 and 10^4 fold for the thiols of C_2 and C_4, and C_8 and C_{12}, respectively. The values of log k_{rel} increase linearly with the chain length of thiol. This permits calculation of the standard free energy change associated with the rate increment per methylene group.[6] The calculated value, 1573 joule mol^{-1}, is in the range (1506—3756 joule mol^{-1}) suggested for hydrophobic interactions.[7] These results suggest that a major contributing factor for the enhanced reactivity of thiols is their binding on the cationic micelle by hydrophobic interaction. The binding and the positive charge on the micellar surface may cause the ionization of thiols to the more active thioanions. Furthermore, the possible thiol ester intermediate[2] may be decomposed rapidly by hydroxide ion which is also concentrated on the positive micellar surface.[3]

The ionization constants of thiols on the micellar surface are needed for more detailed analyses of the rates. Nevertheless, it is interesting to note that the activation of the essential thiol group of papain as compared to cysteine in the simple nucleophilic rections with cyanate and chloroacetate is in the same order of magnitude as observed in the present system.[8]

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