1562 © *1984 The Chemical Society of Japan* *Bull. Chem. Soc. Jpn.*, *57*, *1562—1566 (1984)* [Vol. 57, No. 6

# A Kinetic Study on Oxidation of a Pair of Associating Thiols Having Substituted Phenyl Groups with Oxygen

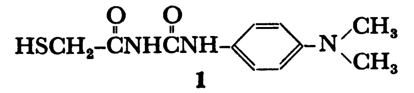
Tadashi ENDO,* Masao HASHIMOTO, Toyohiko ORII, and Masato M. ITO
*Department of Chemistry, College of Science and Engineering, Aoyama Gakuin University,*
*Chitosedai, Setagaya-ku, Tokyo 157*

(Received May 31, 1983)

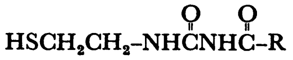
The rates of oxidation of 1 : 1 mixtures of associating thiols, each having the binding site ($-\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NH-$) and the recognition site [$p$-$(CH_3)_2NC_6H_4$ or R], with $O_2$ were measured in 80% (v/v) acetonitrile-20% water in the range of 20 to 50 °C. Oxidation of the thiol having the $p$-$(CH_3)_2NC_6H_4$ group proceeds about 100 times faster than that of the thiols with R. It has been found that oxidation of 1 : 1 mixtures of the thiols is first-order with respect to thiols and 0.7 th-order with respect to triethylamine by means of the method of initial rates. The $k_{1.7}$ values for $R=C_6H_5$, $p$-$CH_3C_6H_4$, and $p$-$C_2H_5C_6H_4$ were similar to one another; this makes a sharp contrast with our previous work that the selectivity (the logarithmeric ratio of the yield of the unsymmetrical disulfide to twice that of the symmetrical disulfide) changes greatly with the structures of R and temperature. It is concluded that the product ratio does not depend upon the $k_{1.7}$. The large negative activation entropies (−51 to −45 cal $K^{-1}$ $mol^{-1}$)† suggest that the oxidation would proceed through a highly ordered transition state.

The recognition of the methyl groups on nucleotide bases plays a significant role in living cells, whether prokaryotes or eukaryotes.[1] It is striking that highly complicated *in vivo* reactions are controlled by a rather simple modification, methylation, of the aromatic rings. Therefore, an approach to the problem of methylation from a chemical point of view would serve to elucidate the factors governing chemical reactions including those in biological systems.

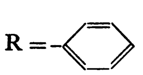
As a continuing study on molecular recognition,[1–6] we examined the effect of methylation of the benzene ring on chemical selectivity.[1] A pair of thiols (**1** and **2**) were used as model compounds. Thiols **1** and **2** each

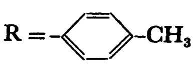


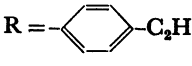
**1**



$$HSCH_2CH_2-NH\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}-R$$

**2a** 

**2b** 

**2c** 

**2d** $R=(CH_2)_2CH(CH_3)_2$

have the binding site ($-\overset{O}{\overset{\|}{C}}NH\overset{O}{\overset{\|}{C}}NH-$) participating in intermolecular hydrogen bonding and the recognition site ($p$-$Me_2NC_6H_4$ or R) participating in the specific discrimination. As a model reaction, we used oxidation of a 1 : 1 mixture of **1** and **2** with oxygen in the presence of a catalytic amount of triethylamine ($Et_3N$) (Eq. 1):

$$\underset{\mathbf{1}}{HS\text{-}X} + \underset{\mathbf{2}}{HS\text{-}Y} \xrightarrow{O_2} \underset{\mathbf{3}}{\begin{matrix}S\text{-}X\\|\\S\text{-}X\end{matrix}} + \underset{\mathbf{4}}{\begin{matrix}S\text{-}X\\|\\S\text{-}Y\end{matrix}} + \underset{\mathbf{5}}{\begin{matrix}S\text{-}Y\\|\\S\text{-}Y\end{matrix}} \qquad (1)$$

The temperature dependence of the selectivity in the above oxidation has previously been reported as a function of the structures of R in 80% (v/v) acetonitrile-20% water (Fig. 1);[1,2] the selectivity ($r$) is represented here by the logarithmeric ratio of the yield of the unsymmetrical disulfide (**4**) to twice that of the symmetrical disulfide (**3**) $\{r=\ln([\mathbf{4}]/(2\,[\mathbf{3}]))\}$. The selectivity for $R=p$-$MeC_6H_4$ displayed a minimum ($r=-0.86$) at 35 °C, whereas for $R=C_6H_5$ the selectivity passed through a maximum ($r=1.6$) at 35 °C; for $R=p$-$C_2H_5C_6H_4$ a plot of the selectivity against temperature showed a sigmoid-like curve.

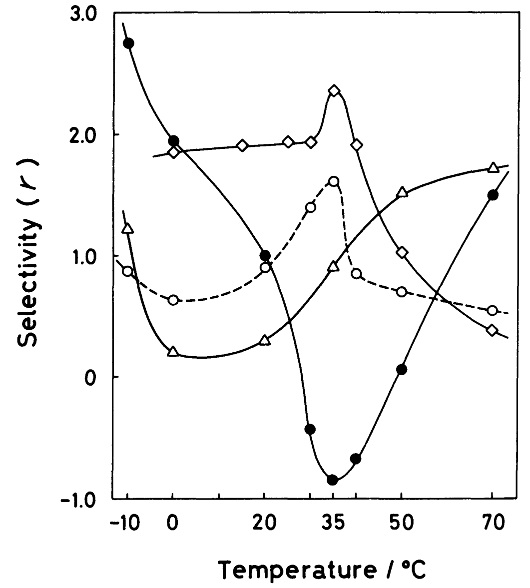


Fig. 1. Temperature dependence of the selectivity ($r$) in oxidation of 1 : 1 mixtures of **1** and **2** with $O_2$ in 80% (v/v) acetonitrile-20% water. ○, **1** and **2a**; ●, **1** and **2b**; △, **1** and **2c**; ◇, **1** and **2d**. We have previously represented the selectivity as the ratio of the yield of unsymmetrical disulfide **4** to that of symmetrical disulfide **3**.[1,2]

In order to elucidate the mechanism of the oxidation described above, we made a kinetic study on the oxidation under conditions similar to those where the selectivity was investigated. Measurements were performed on overall rates for 1 : 1 mixtures of thiols **1** and **2a—c** as well as on rates for the individual thiols,

---

† 1 cal=4.184 J.

by titration of remaining thiols with iodine. For comparison, the rates were also determined for **2d**—the thiol with an isopentyl group as the recognition site—and a 1:1 mixture of **1** and **2d**; for oxidation of the 1:1 mixture of **1** and **2d**, a plot of the selectivity against temperature showed a sharp peak of maximum selectivity ($r$=2.4) at 35 °C[2] under the same conditions as with oxidation of **1** and **2a**—**c** (Fig. 1).

## Results

*Kinetic Behavior of Catalytic Oxidation of Thiols.* Oxidation of each thiol (**1** or **2**) was carried out in oxygen-saturated 80% (v/v) acetonitrile–20% water in the presence of $Et_3N$ as a catalyst. Figure 2 summarizes the time course of thiol consumption where $[RSH]_0$ represents the initial concentration of thiols. Downward curvature was observed for **1** in a plot of log ($[RSH]/[RSH]_0$) against time in the presence of 0.1 equivalent of $Et_3N$. The use of 2.0 equivalents of $Et_3N$ led to the pseudo first-order reaction, as might be expected from the results by Wallace *et al.*[7] that oxidation of thiols follows pseudo first-order kinetics in the presence of 2.0 equivalents of a base.

For oxidation of 1:1 mixtures of **1** and **2**, total concentration of thiols was measured. Remarkable downward curvatures were observed (Fig. 2) in the presence of 0.1 equivalent of $Et_3N$, the same concentration of $Et_3N$ as in the oxidation whose selectivity is given in Fig. 1. However, on addition of 20 equivalents[8] of $Et_3N$, the oxidation has proved to follow pseudo first-order kinetics.

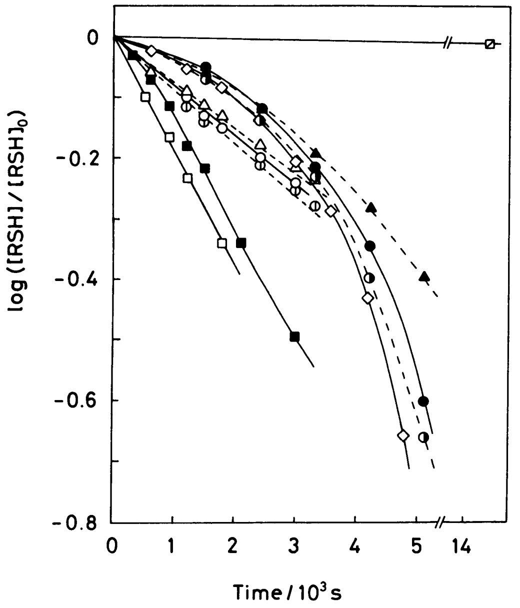


Fig. 2. Dependence of log ($[RSH]/[RSH]_0$) on time for oxidation of **1**, **2**, and their 1:1 mixtures at $[RSH]_0$=0.020 M in 80% (v/v) acetonitrile–20% water at 35.0 °C. The concentration of $Et_3N$ as a catalyst was 0.0020 M, unless otherwise mentioned. ■, **1**; □, **1** ($[Et_3N]$=0.040 M); ▨, **2b**; ◑, 1:1 mixture of **1** and **2a**; ●, 1:1 mixture of **1** and **2b**; ▲, 1:1 mixture of **1** and **2c**; ◇, 1:1 mixture of **1** and **2d**; ⦶, 1:1 mixture of **1** and **2a** ($[Et_3N]$=0.40 M); ○, 1:1 mixture of **1** and **2b** ($[Et_3N]$=0.40 M); △, 1:1 mixture of **1** and **2c** ($[Et_3N]$=0.40 M).

Table 1. Initial rates for oxidation of individual thiols (**1** and **2**) and overall initial rates for their 1:1 mixtures

| Compd | $[Et_3N]\times10^3$/M | $v_0\times10^{8\,a)}$/mol l$^{-1}$s$^{-1}$ |
|---|---|---|
| **1** | 2.0 | 440 |
| **2a** | 2.0 | 3.3 |
| **2b** | 2.0 | 3.1 |
| **2c** | 2.0 | 3.3 |
| **2d** | 2.0 | 2.9 |
| **1**+**2a** | 2.0 | 200 |
| **1**+**2b** | 2.0 | 180 |
| **1**+**2c** | 2.0 | 180 |
| **1**+**2d** | 2.0 | 210 |
| **1**+**2a** | 400 | 610 |
| **1**+**2b** | 400 | 480 |
| **1**+**2c** | 400 | 450 |

a) Average rates until 10% consumption of thiols ($[RSH]_0$=0.020 M) (1 M=1 mol dm$^{-3}$) at 35.0 °C in oxygen saturated 80% (v/v) acetonitrile–20% water.

Initial rates ($v_0$)—average rates until 10% consumption of thiols—for the oxidation are listed in Table 1. The thiol with the isopentyl group (**2d**) was similar to the thiols with the aromatic groups (**2a**—**c**) both in kinetic behavior (Fig. 2) and in the initial rates (Table 1).

*Rate Equation for Oxidation of 1:1 Mixtures of Thiols.* The observed downward curvatures for oxidation of 1:1 mixtures at $[Et_3N]=2.0\times10^{-3}$ M (1M=1 mol dm$^{-3}$) showed that rate equations were impossible to derive directly from the plots in Fig. 2. Thus we used the method of initial rates in order to determine the rate equation for the $Et_3N$-catalyzed oxidation. Since the concentration of oxygen is considered to be constant for low levels of conversion,[9] the rate equation becomes Eq. 2

$$v = k_n[RSH]^{n-m}[Et_3N]^m \tag{2}$$

where $n$ represents the overall reaction order and $k_n$ the $n$-th order overall rate constant for the oxidation. Putting Eq. 2 into logarithmeric form yields Eq. 3.

$$\log v = \log k_n + (n-m)\log[RSH] + m\log[Et_3N] \tag{3}$$

The $v_0$ values were measured at various $[RSH]_0$, with the molar ratio of **1**, **2b**, and $Et_3N$ being fixed (1:1:0.2). Since $[Et_3N]=0.1\,[RSH]_0$, Eq. 3 can be rewritten as Eq. 4.

$$\log v_0 = \log k_n + n\log[RSH]_0 - m \tag{4}$$

Figure 3 plots the logarithm of $v_0$ against log $[RSH]_0$. Linear relationship was found to exist between them. The slope of a log $[RSH]_0$—log$v_0$ plot for a 1:1 mixture of **1** and **2b** gave the $n$ value of 1.7 for the oxidation.[10]

The initial rates were then measured at different $Et_3N$ concentrations with $[RSH]_0$ fixed. In this case the first two terms on the right-hand side of Eq. 3 can be regarded as constant. Since a linear relationship exists between log $v_0$ and log $[Et_3N]$ (Fig. 4), the slope of the straight line gives $m$ value in Eq. 3. The $m$ value turned out to be 0.7, indicating that the reaction is first-order with respect to thiols.[11] Thus the rate follows the equation:

$$v = k_{1.7}[RSH][Et_3N]^{0.7} \tag{5}$$

The 1.7th-order rate constants for oxidation of 1:1 mixtures ($k_{1.7}$) were obtained at 20.0, 35.0, and 50.0 °C using Eq.5. The results are listed in Table 2. In all cases, the linear relationship existed between ln $k_{1.7}$ and $1/T$, demonstrating that Eq. 5 holds true for the temperature range described above. Activation parameters for the oxidation are also given in Table 2.

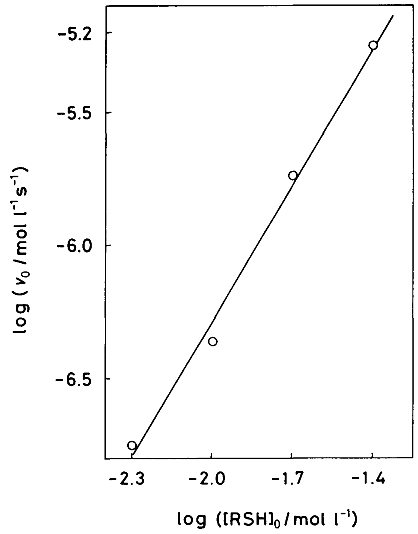


Fig. 3. Dependence of initial rates ($v_0$) on initial concentration of a 1:1 mixture of **1** and **2b** at [Et3N]=0.1 [RSH]0. The other conditions are as in Fig. 2.

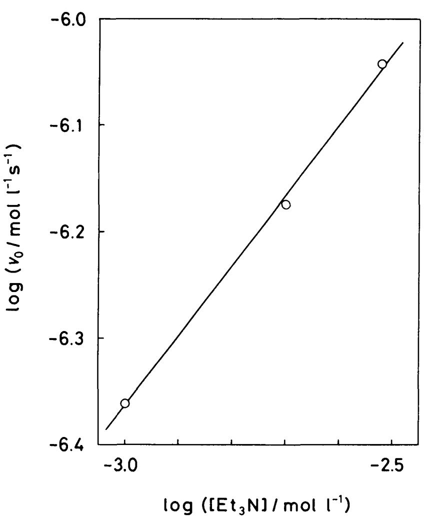


Fig. 4. Dependence of initial rates ($v_0$) on initial concentration of Et3N at [RSH]0=0.010 M. The other conditions are as in Fig. 2.

## Discussion

*Mechanism of the Oxidation.* Base-catalyzed oxidation of thiols is known to proceed through the following reaction paths (Eqs. 6—10).[12–15]

$$\mathrm{RSH + Et_3N \overset{K_6}{\rightleftharpoons} RS^- + Et_3NH^+} \quad k_{+6},\, k_{-6} \tag{6}$$

$$\mathrm{RS^- + O_2 \longrightarrow RS\cdot + O_2^{\overline{\cdot}}} \quad k_7 \tag{7}$$

$$\mathrm{RSH + O_2^{\overline{\cdot}} \longrightarrow RS\cdot + OOH^-} \tag{8}$$

$$\mathrm{OOH^- \longrightarrow OH^- + \frac{1}{2}O_2} \tag{9}$$

$$\mathrm{2\,RS\cdot \longrightarrow RS\text{-}SR} \tag{10}$$

The equilibrium shown in Eq. 11 would contribute to the recovery of Et3N.[13] These yield Eq. 12 as the overall stoichiometry of the oxidation.

$$\mathrm{Et_3N + H_2O \overset{K_{11}}{\rightleftharpoons} Et_3NH^+ + OH^-} \tag{11}$$

$$\mathrm{2\,RSH + \frac{1}{2}O_2 \longrightarrow RS\text{-}SR + H_2O} \tag{12}$$

The rate-determining step of base-catalyzed oxidation of thiols is shown to be either the formation of thiolate anions (Eq. 6) or its oxidation to the corresponding thiyl radicals (Eq. 7).[12,13] This view appears to hold true for the oxidation presented here, considering that the oxidation is first-order with respect to thiols.[16] Uncertainty still remains about what causes the downward curvatures in kinetic profiles (Fig. 2).

An intriguing aspect of the kinetic results is the large negative activation entropies (Table 2). The activation entropies of −51 to −45 cal K$^{-1}$ mol$^{-1}$ for the present oxidation are more negative than those of about −20 to −10 cal K$^{-1}$ mol$^{-1}$ for ordinary bimolecular reactions[17]. Bimolecular reactions with highly ordered transition states generally have $\Delta S^{\ddagger}$ values of similar magnitude: −49 to −22 cal K$^{-1}$ mol$^{-1}$ for Diels-Alder reactions,[18] −43 to −22 cal K$^{-1}$ mol$^{-1}$ for 1,3-dipolar cycloadditions,[19] and −42 to −19 cal K$^{-1}$ mol$^{-1}$ for Menschutkin reactions between tertiary amines and alkyl iodides.[20] These observations suggest that the

Table 2. Temperature dependence of 1.7th order rate constants for oxidation of 1:1 mixtures of thiols (**1** and **2**) and activation parameters

| Compd | $T$ | $v_0 \times 10^7$ a) | $k_{1.7} \times 10^3$ | $\Delta E^{\ddagger}$ | $\Delta H^{\ddagger}$ | $\Delta S^{\ddagger}$ |
|---|---|---|---|---|---|---|
| | K | mol l$^{-1}$ s$^{-1}$ | l$^{0.7}$ mol$^{-0.7}$ s$^{-1}$ | kcal mol$^{-1}$ | kcal mol$^{-1}$ | cal K$^{-1}$ mol$^{-1}$ |
| **1**+**2a** | 293 | 7.9 | 3.1 | 11.2±1.9 | 10.5±1.9 | −45±6 |
| **1**+**2a** | 308 | 20 | 7.7 | | | |
| **1**+**2a** | 323 | 36 | 13.9 | | | |
| **1**+**2b** | 293 | 8.8 | 3.4 | 9.5±0.5 | 8.8±0.5 | −51±2 |
| **1**+**2b** | 308 | 18 | 7.0 | | | |
| **1**+**2b** | 323 | 31 | 12.2 | | | |
| **1**+**2c** | 293 | 6.7 | 2.6 | 10.7±3.0 | 10.1±4.0 | −47±13 |
| **1**+**2c** | 308 | 18 | 7.0 | | | |
| **1**+**2c** | 323 | 28 | 10.8 | | | |

a) The values at [Et3N]=2.0×10$^{-3}$ mol l$^{-1}$ in oxygen saturated 80% (v/v) MeCN-20% H2O.

oxidation presented in this paper would have a highly ordered transition state.

*Factors Governing the Selectivity.* Oxidation of thiol **1** proceeds more than 100 times faster than that of **2** (Table 1). The initial rates for oxidation of 1:1 mixtures of **1** and **2** decreased to about half ($v_0$=(1.8—2.1)$\times10^{-6}$ mol $l^{-1}$ $s^{-1}$) of that for oxidation of **1** ($v_0$=4.4$\times10^{-6}$ mol $l^{-1}$ $s^{-1}$), $[\mathbf{1}]_0$ for oxidation of 1:1 mixtures being half that for oxidation of **1** (Table 1). These results indicate that the thiolate anion which is formed predominantly from the 1:1 mixtures is that derived from **1**. Thus, the selective formation of symmetrical disulfide **3** might be expected at an early stage, though the oxidation gives the high selectivity ($r$) in most cases (Fig. 1). However, this is not the case, because the product ratio in this type of oxidation is kinetically controlled so that the selectivity does not vary with the reaction time.[2] This fact suggests the presence of fast exchange reaction between an anion and a thiol (Eq. 13) or between a radical and a thiol (Eq. 14).

$$\mathrm{XS^-} + \underset{\mathbf{2}}{\mathrm{YSH}} \rightleftharpoons \underset{\mathbf{1}}{\mathrm{XSH}} + \mathrm{YS^-} \qquad (13)$$

$$\mathrm{XS\cdot} + \underset{\mathbf{2}}{\mathrm{YSH}} \rightleftharpoons \underset{\mathbf{1}}{\mathrm{XSH}} + \mathrm{YS\cdot} \qquad (14)$$

The initial rates for oxidation of 1:1 mixtures of **1** and **2a—c** are expressed by a single rate equation (Eq. 5). Further, the rate constants for the oxidation do not change appreciably with the structures of R (Table 2); this makes a sharp contrast with our previous work[1] that the selectivity alters markedly with the structures of R (Fig. 1). Accordingly, the product ratio would not be controlled in the rate-determining step.[21]

We have reported that thiols **1** and **2** associate strongly in benzene *via* two NH···O intermolecular hydrogen bonds between the inner $-\mathrm{NH}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}-$ units in the $-\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{NH}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{NH}-$ group to form tetramers (**9—13**, reaction intermediates) as well as dimers (**6—8**) (Fig. 5).[1,22,23] The S–S bonds would be formed between the two proximate HS groups in tetramers **9—13**.[22] Each of the tetramers gives the corresponding disulfide(s) selectively when treated with oxygen.[4] The relative concentration of the tetramers would vary with the structures of R and temperature,[4] thereby leading to the selectivity alterations (Fig. 1). These selectivity data appear to reflect weak interactions[5] specific for the shape of the recognition sites of **1** and **2**.

## Conclusion

Triethylamine-catalyzed oxidation of 1:1 mixtures of **1** and **2a—c** in 80% (v/v) acetonitrile-20% water follows the rate equation $v=k_{1.7}$ $[\mathrm{RSH}][\mathrm{Et_3N}]^{0.7}$, although a detailed mechanism of the oxidation still remains to be elucidated. The $k_{1.7}$ values for the 1:1 mixtures are similar to one another, in sharp contrast to our previous work that the selectivity varies markedly with the structures of R and temperature. This indicates that the product ratio does not depend upon the $k_{1.7}$. The present results including the large negative activation entropies are consistent with our view that the formation of disulfides **3—5** occurs *via* tetrameric intermediates **9—13**.

## Experimental

*Materials.* All the thiols **1** and **2** were prepared as described previously.[1,24] Acetonitrile was dried and purified by distillation from calcium hydride and phosphorus pentaoxide, and stored over molecular sieves. The reaction solvent was prepared by mixing 62.58 g of dry acetonitrile with 19.96 g of water [4:1 (v/v) at 20 °C], and allowed to stand overnight under an oxygen atmosphere. Triethylamine was distilled over potassium hydroxide through a fractionating column. The iodine solution (0.001 M) containing potassium iodide (0.005 M) was titrated with 1.00$\times10^{-3}$ M aqueous sodium arsenite standard solution before use.

*Determination of Rates of the Oxidation.* Samples of thiols were accurately weighed into a two-necked flask and dissolved in 10.00 ml of the reaction solvent. The solution was placed in a well-stirred water bath thermostated to

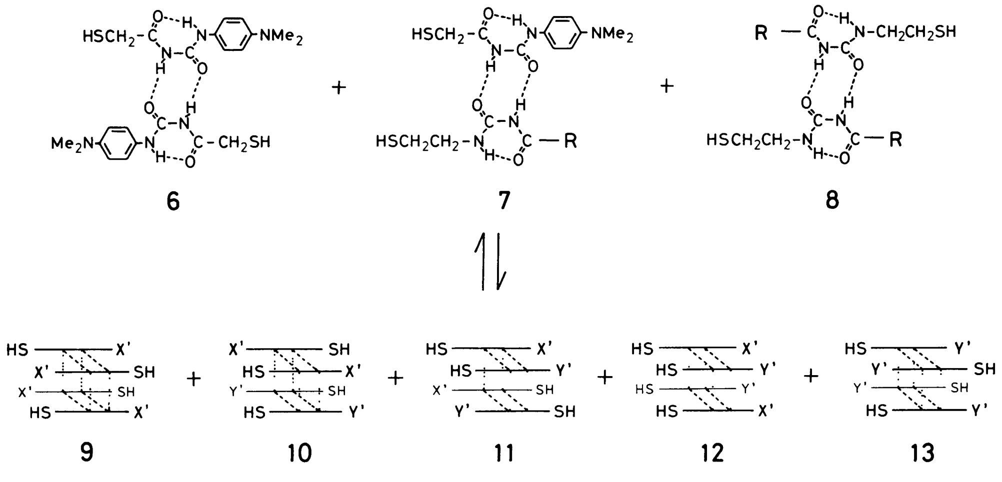


Fig. 5. Association patterns of three dimers **6—8** and association schemes of tetramers **9—13** formed by dimerization of the dimers. The hydrogen bonds (----) in the dimers and the noncovalent weak interactions (·····) responsible for the stabilization of the tetramers are shown. The symbols X′ and Y′ represent $p$-$\mathrm{Me_2NC_6H_4}$ and R, respectively.

±0.1 °C for 5 h with stirring under an oxygen atmosphere. Oxidation of thiols was negligible in the absence of $Et_3N$. At time zero, an appropriate amount of $Et_3N$ was added into the solution with a microsyringe, and time measurement was begun. At appropriate time intervals, a 0.50 ml portion of the reaction mixture was pipetted out and quenched in 5 ml of a 1 : 9 mixture of 3 M hydrochloric acid with acetonitrile. The amount of remaining thiols in the quenched solution was then determined by titration with the 0.001 M iodine solution.

Rate constants were determined by the method of initial rates.[17] Plots of concentration of thiols against time were constructed, and initial rates for 10% conversion were calculated. Initial rates presented in Tables 1 and 2 are average values of at least three, generally five, or more determinations. The reaction order and rate constants were evaluated from the initial rates measured at different initial concentrations of thiols and $Et_3N$ (Figs. 3 and 4), through least square optimization.

*Calculations of Activation Parameters.* Activation energies were determined from the slopes of Arrhenius plots (ln $k$ *vs.* $1/T$). Activation enthalpies and entropies were obtained from the plots of ln $(k/T)$ against $1/T$ based on Eyring equation.[17]

We thank Mr. Kazuo Guro and Mr. Hideki Ueda for valuable assistance. We are also grateful to the referees for helpful suggestions.

## References

1) T. Endo, A. Okubo, Y. Kaneko, M. Uehara, H. Tasai, A. Sato, K. Nikki, N. Nakagawa, and S. Kamei, *Bull. Chem. Soc. Jpn.*, **55**, 2224 (1982) and the references cited therein.

2) T. Endo, A. Kuwahara, H. Tasai, T. Murata, M. Hashimoto, and T. Ishigami, *Nature*, **268**, 74 (1977).

3) T. Endo, Y. Takeda, H. Kamada, S. Kayama, and H. Tasai, *Chem. Lett.*, **1980**, 417.

4) T. Endo, Y. Takeda, T. Orii, T. Murata, M. Sakai, N. Nakagawa, and K. Nikki, *Chem. Lett.*, **1980**, 1291.

5) T. Endo, K. Miyazawa, M. Endo, A. Uchida, Y. Ohashi, and Y. Sasada, *Chem. Lett.*, **1982**, 1989.

6) T. Endo, H. Tasai, K. Miyazawa, M. Endo, K. Kato, A. Uchida, Y. Ohashi, and Y. Sasada, *J. Chem. Soc., Chem. Commun.*, **1983**, 636.

7) T. J. Wallace, A. Schriesheim, and W. Bartok, *J. Org. Chem.*, **26**, 1311 (1963).

8) In the presence of 2.0 equivalents of $Et_3N$, downward curvature was still observed.

9) No appreciable changes took place in kinetic profiles for the oxidation with $O_2$ whose pressure was slightly larger than 1 atm.

10) For a 1 : 1 mixture of **1** and **2d**, the overall order of the oxidation became 2.2 in the thiol concentration range similar to that for **1** and **2a**—**c**.

11) The fact that the oxidation is first-order with respect to thiols agrees with the results by Wallace *et al.* for base-catalyzed oxidation of simple aliphatic and aromatic thiols.[7]

12) G. Capozzi and G. Modena, "Oxidation of Thiols," in "The Chemistry of the Thiol Group," ed by S. Patai, Wiley, London (1974), Part 2, Chap. 17.

13) A. A. Oswald and T. J. Wallace, "Anionic Oxidation of Thiols and Co-oxidation of Thiols with Olefins," in "Organic Sulfur Compounds," ed by N. Kharash, Pergamon Press, New York (1965), Vol. 2, Chap. 8.

14) The initial rate for oxidation of a 1 : 1 mixture of **1** and **2b** decreased by 33% on addition of hydroquinone (0.020 M). This suggests the participation of free radicals in the oxidation [W. A. Pryor, "Free Radicals," McGraw-Hill, New York (1966), Chap. 21].

15) Though $O_2^{\cdot -}$ oxidizes thiols very readily [S. Oae, T. Takata, and Y. H. Kim, *Bull. Chem. Soc. Jpn.*, **54**, 2712 (1981)], it is uncertain whether or not the step in Eq. 8 contributes to the rate for the present oxidation, since $O_2^{\cdot -}$ is known to be labile in aqueous media [J. Rabani and S. O. Nielsen, *J. Phys. Chem.*, **73**, 3736 (1969)].

16) If the formation of thiolate anions (Eq. 6) is rate-determining, the rate may be expressed as

$$v = 2\,k_{+6}[\mathrm{RSH}][\mathrm{Et_3N}]$$

Thus the oxidation will be first-order with respect to both thiols and $Et_3N$. In contrast, if the oxidation of $RS^-$ (Eq. 7) is rate-determining, the rate may follow the expression

$$v = k'_7 K_6[\mathrm{RSH}]\left(\frac{[\mathrm{Et_3N}]}{K_{11}+K_6[\mathrm{RSH}]}\right)^{0.5} \quad (k'_7=2\,k_7[\mathrm{O_2}])$$

Provided that $K_{11} \gg K_6\,[\mathrm{RSH}]$, the oxidation will be first-order with respect to thiols and 0.5th-order with respect to $Et_3N$. Neither of the above equations completely agrees with the experimental results at an initial stage (0.7th-order with respect to $Et_3N$), suggesting the complex nature of the oxidation.

17) J. F. Bunnett, "From Kinetic Data to Reaction Mechanism," in "Investigation of Rates and Mechanisms of Reactions," 3rd ed, ed by E. S. Lewis, Wiley, London (1974), Part I.

18) J. Sauer and R. Sustmann, *Angew. Chem., Int. Ed. Engl.*, **19**, 779 (1980) and the references cited therein.

19) R. Huisgen, *Angew. Chem., Int. Ed. Engl.*, **2**, 633 (1963) and the references cited therein; R. Huisgen, G. Szeimies, and L. Möbius, *Chem. Ber.*, **100**, 2494 (1967) and the references cited therein.

20) A. P. Harris and K. E. Weale, *J. Chem. Soc.*, **1961**, 146.

21) Some examples have been reported in which chemical selectivity is controlled prior to the rate-determining step: see, for example, H. Ozaki, A. Tai, and Y. Izumi, *Chem. Lett.*, **1974**, 935.

22) T. Endo, Y. Takeda, T. Orii, Y. Kaneko, and M. Kondo, *Chem. Lett.*, **1979**, 1455.

23) Thiolate anions would be formed from dimers (**6**—**8**) and tetramers (**9**—**13**) as well as monomers (Fig. 5). It is uncertain whether or not the dissociation constants for the thiols alter when the thiols associate. The rate equation shown in Ref. 16 is based on the assumption that $[RS^-]$ is practically unaffected by the association.

24) T. Endo, K. Oda, and T. Mukaiyama, *Chem. Lett.*, **1974**, 443.