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THE EFFECTS OF THE NEIGHBORING METHOXYCARBONYL GROUP AND SULFUR ATOM(S) IN THE CARBON-SULFUR BOND CLEAVAGE AND THE ESTER EXCHANGE IN FLUORENE SYSTEMS

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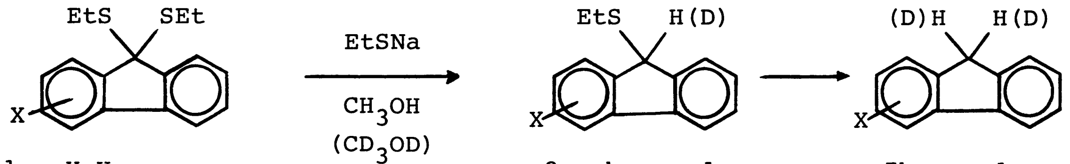
9,9-Bis(ethylthio)fluorene (1a) reacted with sodium ethanethiolate in methanol to give 9-ethylthiofluorene and diethyl disulfide suggesting that a C-S bond cleavage occurs by attack of a nucleophile at sulfur if a leaving group is sufficiently stable. The pseudo-first-order rate constans for the reaction of 1a and methoxycarbonyl-substituted 9-ethylthiofluorenes have suggested that the methoxycarbonyl group at 1-position exerts through space interaction with sulfur atom(s). The rate constants for ester exchange in 1-methoxycarbonylfluorene and its derivatives have been discussed on the ground of neighboring sulfur participation.

Intramolecular interactions between a carbonyl group and a sulfur atom have been studied. Leonard et al. reported evidence for charge transfer from the sulfur to the carbonyl group in 1-thiacyclooctan-5-one.[1)] Similar interactions have been studied by UV,[2)] IR,[3)] and NMR[3,4)] methods. Cleavage of the C-S bond in sulfides by nucleophiles is rather unusual,[5)] although a few exceptions are known.[6,7)] Ōki et al. reported the reductive cleavage of a C-S bond of α-carbonyl sulfides with soft bases suggesting the extra effects of the neighboring carbonyl group.[8)]

During the course of the study for the effects of a neighboring carbonyl group in the C-S bond cleavage by ethanethiolate ion,[8)] we have encountered the C-S bond cleavage in 9,9-bis(ethylthio)fluorene (1a). In this paper, we wish to report C-S bond cleavage of some thioethers by ethanethiolate ion, the effects of the neighboring carboxyl group for the reaction, and alternatively those of neighboring sulfur atom(s) in ester exchange in fluorene systems.

Although 9,9-bis(ethylthio)fluorene (1a) did not react with sodium methoxide in methanol at 65 °C, addition of ethanethiol to the solution caused the reaction of 1a to give 9-ethylthiofluorene (2a) and diethyl disulfide quantitatively. Eq. 1 shows the reaction. The pseudo-first-order rate constants for the reaction were measured.[9)] The dithioketal or thioether (0.050 mmol) was dissolved in 0.50 ml of methanol-d_4 containing sodium methoxide (0.10 mmol) and excess ethanethiol (0.2-0.3 mmol). The solution was enclosed in a 5 mm ϕ NMR tube and the reaction was monitored at 65 or 100 °C. Table 1 shows the results with 1,1-bis(ethylthio)-2,3-



(1)

1a; X=H
b; X=COOMe-1
c; X=COOMe-2
d; X=COOMe-3

2a, b, c, d.
($X=COOCD_3$)

7b, c, d.
($X=COOCD_3$)

diphenylindene (3), 1-ethylthio-2,3-diphenylindene (4), 4-methoxycarbonylbenzophenone diethyl dithioketal (5), and benzophenone diethyl dithioketal together with that of 1a. The results suggest that the stability of the anion formed by a C-S bond cleavage is an important driving force for the reaction: the reaction proceeds by the attack of ethanethiolate ion at the sulfur atom of the substrate giving diethyl disulfide and a carbanion. Namely, it is an S_N 2 type reaction at sulfide sulfur atom.[8)] The necessary condition for the reaction to occur is that the substrate has a sufficiently good leaving group.[10)]

The pseudo-first-order rate constants for 1-, 2-, and 3-methoxycarbonyl-9,9-bis(ethylthio)fluorenes (1b, 1c, and 1d, respectively) and -9-ethylthiofluorenes (2b, 2c, and 2d, respectively) were obtained under the conditions. Table 2 shows the results. The methoxycarbonyl substitution in 1a at 1-, 2-, and 3-positions increases the relative rates to 21, 26, and 39, respectively. The rate enhancement caused by the group in 1c, 1d, 2c, and 2d is attributed to inductive and mesomeric effects.

The steric hindrance and the decreased electronic effects of the methoxycarbonyl group should lower the rate constant for 1b.[11)] Indeed, the relative rate constant of 1b is 0.53 if that of 1d is 1.0. However, some rate enhancing effects of the group at 1-position may be pointed out. Although the steric inhibition of resonance is somewhat released in 2b, the rate constant for 2b is still expected to be smaller than that for 2d on the steric ground.[11)] Actually, however, the rate of 2b is 5.3-fold larger than that for 2d, suggesting a rate-enhancing mechanism. The direct or through-space interaction between the carboxyl carbon and the electron rich center in the transition state[12)] may be most reasonable for the explanation of the results (Fig. 1).

The pseudo-first-order rate constants for ester exchange shown in Eq. 2 were also measured. A methyl ester (0.10 mmol) was dissolved in 0.50 ml of methanol-d_4 containing 0.200 mmol of p-toluenesulfonic acid. The solution was heated in a 5 mm ϕ NMR tube at 60.0 °C and monitored by ^1H NMR until 50-70 % completion of the reaction.

$$\text{Ar-COOCH}_3 + \text{CD}_3\text{OD} \xrightarrow{H^+} \text{Ar-COOCD}_3 + \text{CH}_3\text{OD} \qquad (2)$$

The rate constants are shown in Table 3. Those for methyl benzoate and 1-methoxycarbonyl-9-propylfluorene (6) are 3.6 and 0.27, respectively, if that for 1-methoxycarbonylfluorene (7b) is 1.0, which is 2.28 x 10^{-5} s^{-1}. The ortho effects have been discussed[13)] and it is reported that alkyl substitution at ortho position(s) in methyl benzoate lowers the rate constants in acid and base catalyzed hydrolysis. The rate constants for methyl benzoate, 6, and 7b show similar trend to those caused by alkyl substitution at ortho position in methyl benzoate.

Table 1. Pseudo-first-order rate constants for C-S bond cleavage.

Compound	$k_1'(s^{-1})$	T(°C)	Compound	$k_1'(s^{-1})$	T(°C)
1a	8.2×10^{-5}	65	4	4.7×10^{-5}	100
3	$\geq 10^{-2}$	65	5	7×10^{-6}	100
			$PhC(SEt)_2Ph$	Too slow to measure	100

Table 2. Pseudo-first-order rate constants for C-S bond cleavage.

Compound	$k_1'(s^{-1})$	$k_{rel.}$	T(°C)	Compound	$k_1'(s^{-1})$	$k_{rel.}$	T(°C)
1a	8.2×10^{-5}	1.0	65	2a	Too slow to measure		100
1b	1.7×10^{-3}	21	65	2b	3.1×10^{-4}	1.0	100
1c	2.1×10^{-3}	26	65	2c	2.3×10^{-5}	0.075	100
1d	3.2×10^{-3}	39	65	2d	5.8×10^{-5}	0.19	100

Table 3. Pseudo-first-order rate constants for ester exchange.

Compound	$k_1'(s^{-1})$	$k_{rel.}$	T(°C)	Compound	$k_1'(s^{-1})$	$k_{rel.}$	T(°C)
$PhCOOCH_3$	8.11×10^{-5}	3.6	60.0	2b	6.59×10^{-6}	0.29	60.0
7b	2.28×10^{-5}	1.0	60.0	1b[14)]	2.8×10^{-5}	1.2	60.0
6	6.24×10^{-6}	0.27	60.0				

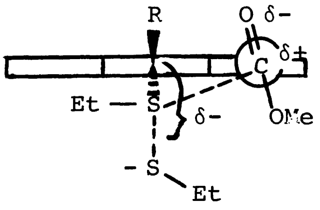


Fig. 1. Transition state for the C-S bond cleavage.

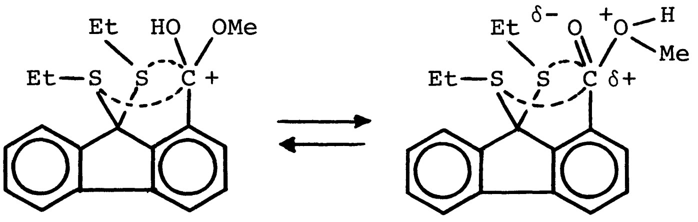


Fig. 2. Stabilizing effect of sulfur atoms for the protonated ester.

The rate constant for 2b is $6.59 \times 10^{-6}\ s^{-1}$ which is almost equal to that of 6. The results might be interpreted that, if the steric effects of n-propyl and ethylthio groups were not so different, the effect of the sulfur atom of 2b would be only steric. However, the rate constant for 1b[14)] is $2.8 \times 10^{-5}\ s^{-1}$ which is larger than those for 2b and 6, and even slightly larger than that for 7b. The steric effect of 9,9-bis(ethylthio) group is expected to be larger than that of a 9-propyl or 9-ethylthio group. There should be a mechanism to activate 1b.

The effects of the 9,9-bis(ethylthio) group are analogous to the stabilizing effects of neighboring sulfur atoms for dimethyl-1-fluorenylmethyl cation[12)] or that for transition states in the acetolysis of benzyl chlorides[15)] reported by Hojo et al. (Fig. 2). Although the through-space effects of the neighboring carboxyl group or sulfur atom(s) are rather small in the cases discussed above, probably due to the long distance between the two, weak contributions from them can not be neglected.

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9) If the reaction is S_N2 type, the rate should be written as:
$-d[R\text{-}SR']/dt = (k[EtS^-] + k'[EtSH]) \times [R\text{-}SR']$, where $k \gg k'$ and $[EtS^-] \approx [EtSH]$.
Then $-d[R\text{-}SR']/dt \fallingdotseq k_{obs} \times [R\text{-}SR']$, since $[EtS^-]$ is almost constant.
10) These results and others7,8) suggest that the C-S bond of R-SR' is expected to react under the conditions if the pk_a of R-H is smaller than ca. 20. For acidities see, a) E. Buncel, "Carbanions: Mechanistic and Isotopic Aspects," Elservier Scientific, Amsterdam (1975), Chap. 1; b) E. Block, "Reactions of Organosulfur Compounds," Academic Press, New York (1978), p. 46.
11) It was reported that a p-nitro group increased the rate constant for the base catalyzed hydrolysis of ethyl benzoate by 116-fold, but o-nitro group by only 8.7-fold. See ref. 13b), p. 16.
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14) In this case, the formation of diethyl sulfide was observed. It amounted to 17 % at 50 % completion of the reaction. The details will be described elsewhere.
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16) The effects of the carbonyl group of α-carbonyl sulfides8) may be explained similarly, a stabilizing effect due to its inductive effect and a through-space effect which is similar to that discussed above.

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