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Decomposition of Dithiocarbamates. VI.[1] The Decomposition of N-Monosubstituted Dithiocarbamic Acids in Acidic Solutions

Fumitaka Takami, Kanji Tokuyama, Shigeru Wakahara,
and Takashi Maeda

Shionogi Research Laboratory, Shionogi & Co., Ltd.[2]

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The kinetics of decomposition of four N-monosubstituted dithiocarbamic acids (I) to parent amines and carbon disulfide were investigated over a wide range of acid concentrations from pH to acidity function regions. The experimental first-order rate constants in acidity function region are proportional to the mole fraction of I as with the case of pH region, and decrease with increasing acid concentrations. The reaction pathway is established based on the rate-acidity profile.

$$\begin{tikzcd} \mathrm{IV} \arrow[r, shift left, "K_{\mathrm{I}}"] & \mathrm{I} \arrow[l, shift left] \arrow[r, shift left, "K_{\mathrm{II}}"] \arrow[d, "k"] & \mathrm{II} \arrow[l, shift left] \\ & \mathrm{RNH_2 + CS_2} & \end{tikzcd} \qquad \text{(eq. 5)}$$

The linear relationship between log k and pKa of parent amine (pK_{N}), (eq. 6), is interpreted in terms of the rate-determining N-C bond cleavage along with the synchronous proton transfer.

The decomposition of dithiocarbamic acid (DTC) in acid solutions involves a rapid equilibrium-controlled protonation to give its acid form (II-H), which, in a rate-limiting unimolecular heterolysis, decomposes to corresponding amine and carbon disulfide.[3,4] With the structure of II-H, two forms, I and V, were proposed.[5] Miller, *et al.* ruled out the possibility of V due to spectral evidence.[6] Chakrabarti and his coworkers supported I, based on findings of the solvent effects in aqueous methanol and aqueous dioxane systems.[7] The decrease of dielectric constants of the solvents enhanced the decomposition rates of DTC having smaller N-substituents such as methyldithiocarbamic acid (Ia) and retarded those having bulkier ones such as diisopropyldithiocarbamic acid. Thus they supposed VI in which the N-C bond was solvated. However, the solvation is a critical factor in the stability of the DTC.[7]

The steric crowding of the substituents is well known to cause the acceleration of the decomposition of DTC.[4-6] As with the steric effects, the determination of the electronic ones are important for the establishment of the reaction mechanism. However, the electronic effects have not been unequivocally determined. Later authors suggested an inclination that log k increased with the increase of pK_{II} by examining the decomposition of N,N-disubstituted

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[1] *a*) For Part V. See Ref. 9. A part of this paper was reported in preliminary forms: F. Takami, S. Wakahara, and T. Maeda, *Chem. Pharm. Bull.* (Tokyo), **20**, 619 (1972); *idem*, *Chem. Lett.*, **1972**, 159, 409; *b*) Pyrimidines. Part XIV, for Part XIII see Ref. 9.

[2] Location: *Fukushima-ku, Osaka, 553, Japan.*

[3] G.D. Thorn and R.A. Ludwig, "The Dithiocarbamates and Related Compounds," Elsevier, New York, 1962.

[4] D.J. Halls, *Mikrochim. Acta*, **1969**, 62.

[5] P. Zuman and R. Zahradnik, *Z. Physik. Chem.* (Frankfurt), **208**, 135 (1957); R. Zahradnik and P. Zuman, *Collection Czech. Chem. Commun.*, **24**, 1132 (1959).

[6] D.M. Miller and R.A. Latimer, *Can. J. Chem.*, **40**, 246 (1962).

[7] S.J. Joris, K.I. Aspila, and C.L. Chakrabarti, *J. Phys. Chem.*, **74**, 860 (1970); R.R. Vandebeek, S.J. Joris, K.I. Aspila, and C.L. Chakrabarti, *Can. J. Chem.*, **48**, 2204 (1970).

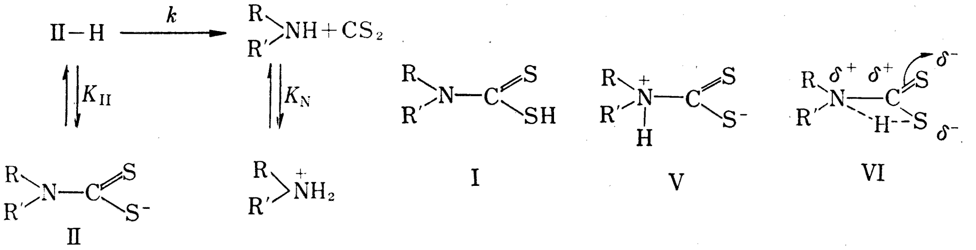
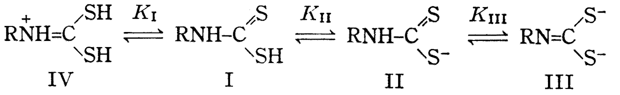


Chart 1

DTCs[8] but further studies seemed to be required by our inspection of their data. The N,N-disubstituted DTCs are inadequate for the detection of such electronic effect because of the existence of both of the steric and electronic factors.

The lack of certain results on the electronic effects prompted us to study the decomposition of N-monosubstituted dithiocarbamic acid (I) to eliminate the steric effects. Thus, the kinetics of the decomposition were studied using ethyl-(Ib), benzyl-(Ic), and [(4-amino-2-methyl-5-pyrimidinyl)]methyldithiocarbamic acids (Id) and Ia. In relation to the dissociation scheme of I presented in the preceeding paper of this series,[9] the role of the further protonated form of I (IV) was also studied in strongly acidic solutions.



$$\underset{\mathrm{IV}}{\mathrm{R\overset{+}{N}H{=}C}\begin{smallmatrix}\mathrm{SH}\\ \mathrm{SH}\end{smallmatrix}} \overset{K_{\mathrm{I}}}{\rightleftharpoons} \underset{\mathrm{I}}{\mathrm{RNH{-}C}\begin{smallmatrix}\mathrm{S}\\ \mathrm{SH}\end{smallmatrix}} \overset{K_{\mathrm{II}}}{\rightleftharpoons} \underset{\mathrm{II}}{\mathrm{RNH{-}C}\begin{smallmatrix}\mathrm{S}\\ \mathrm{S^-}\end{smallmatrix}} \overset{K_{\mathrm{III}}}{\rightleftharpoons} \underset{\mathrm{III}}{\mathrm{RN{=}C}\begin{smallmatrix}\mathrm{S^-}\\ \mathrm{S^-}\end{smallmatrix}} \qquad \text{(eq. 1)}$$

Experimental

Materials——The sodium salts of I, except Id, were synthesized by the methods appeared in literatures.[10] The compound Id was obtained as inner salt.[11] Buffers of a constant ionic strength were prepared by the method of Perrin.[12] All reagents were of reagent grade.

Rate Measurements——a) In Weakly Acidic Solutions: The decomposition reactions, which are first-order under the conditions used, were followed spectrophotometrically with a Hitachi two-wave length/double-beam spectrophotometer, model 356, with a thermostat cell compartment. Temperature control was within 0.1° with a Haake thermostat. The reactions were run at initial concentrations of about 5×10^{-5}M of I in well-deairated solutions of 0.001—1N HCl and buffer solutions.[12] At pH above 3.8, the reaction was run in an ampule. The measurements of pH were made with a Towa-Dempa pH-meter, model HM-8. Reactions were followed by recording a change in absorbance at the wave-length near at 270 nm with a chart recorder. First-order rate constants were calculated from plots of $\ln(A_t - A_\infty)$ *vs.* time (in minutes) by the least-squares method. Reactions were followed for at least 3 half-lives and usually for 10 half-lives. Energies of activation were calculated from the Arrhenius equation by the least-squares method, using the rate constants in 1N HCl at 15—35°.

b) In Strongly Acidic Solution: Decomposition rates of Ia, Ib, and Id were measured at initial concentrations of about 5×10^{-3}M in carefully deairated sulfuric acid solutions of known concentrations. The solution was maintained at 25±0.1°; at various intervals 1 ml aliquot was withdrawn and diluted to 100 ml with 1N NaOH quenching solution under cooling. Pseudo first-order rate plots by the use of the absorbance near at 280 nm were made in a manner similar to the above. Plots were generally linear over 2—3 half-lives.

Isolation of N,N′-Dimethyl- (VIII) and N,N′-Diethylthiuram Disulfides (IX) from the Sulfuric Acid Solutions——A solution of Ia (34 mg) in 10% sulfuric acid solution (1 liter) was left at room tempetraure for 1 hr and then was extracted with chloroform (60 ml×3). The chloroform was washed with water (20 ml×3), dried over $MgSO_4$ and then evaporated under reduced pressure. The recrystallization of the residue

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[8] K.I. Aspila, V.S. Sastri, and C.L. Chakrabarti, *Talanta*, **16**, 1099 (1969).

[9] F. Takami, K. Tokuyama, S. Wakahara, and T. Maeda, *Chem. Pharm. Bull.* (Tokyo), **21**, 329 (1973).

[10] H.L. Klöpping and G.J. Van Der Kerk, *Rec. Trav. Chim.*, **70**, 917 (1951); D.J. Halls, A. Townshend, and P. Zuman, *Anal. Chim. Acta*, **40**, 459 (1968).

[11] A. Takamizawa, Y. Sato, S. Nakajima, and T. Ishiba, *Shionogi Kenkyusho Nempo*, **12**, 48 (1962).

[12] D.D. Perrin, *Aust. J. Chem.*, **16**, 572 (1963).

from petroleum ether containing a slight amount of chloroform (cooled with dry ice-acetone) gave colorless needles of VIII (7 mg), mp 97—99° (decomp.)[13] (lit.[14] 102°). N,N'-Diethylthiuram disulfide (IX; 4 mg), mp 76—77° (decomp.)[13] (lit.[14] 75°), was isolated in a procedure similar to the above from the reaction mixture of Ia (34 mg) in 10% sulfuric acid solution (1 liter).

Stability of Ia in 0.1N NaOH Solution——A solution of Ia (5×10^{-5}M) in 0.1N NaOH solution was left at 25°. The intensities of the two UV bands of Ia[9] showed no change for at least 24 hr.

Result and Discussion

Decomposition in weakly Acidic Solution

The rates of the decomposition were observed spectrophotometrically. From the pseudo first-order rate constants observed at pH-range (See Fig. 1 for Ia), the parameters k and K_{II} which fit with eq. 2 were determined by eq. 3, which is obtained by the rearrangement of eq. 2. A plot of $1/k_{\mathrm{obs}}$ *vs.* $1/[\mathrm{H}^+]$ then gives K_{II}/k as a slope and $1/k$ as an intercept. Thus obtained parameters are listed in Table.

$$k_{\mathrm{obs}} = k[\mathrm{H}^+]/([\mathrm{H}^+]+K_{\mathrm{II}}) \qquad \text{(eq. 2)}$$

$$1/k_{\mathrm{obs}} = K_{\mathrm{II}}/k[\mathrm{H}^+] + 1/k \qquad \text{(eq. 3)}$$

Decomposition in strongly Acidic Solutions

The observed values of the pseudo first-order rate constants of I decreased with the increase of acid concentrations. A plot of $\log k_{\mathrm{obs}}$ *vs.* Hammett's acidity function (H_0) fits with a dissociation curve as shown in Fig. 1 for Ia. A rate-acidity profile of this type may be accounted for by the following rate expression (eq. 4):

$$k_{\mathrm{obs}} = kK/(h_0+K) \qquad \text{(eq. 4)}$$

where k, K and h_0 are the limiting rate constant, dissociation constant and Hammett's non-logarithmic acidity function,[15] respectively. The values of k and K are calculated similarly with the case of eq. 2. The constants k and K obtained agree well with the rate constants determined from the reaction in weakly acidic solutions and the dissociation constants (K_{I}),[9] respectively, as shown in Table. The above results indicate that the decomposition reaction in strongly acidic solutions proceeds *via* I in the equilibrium, $\mathrm{I} \rightleftharpoons \mathrm{IV}$, followed by the rate-determining decomposition of I, but not *via* IV.

Consequently, the decomposition pathway in entire acidity region is summarized in eq. 5.

$$\begin{tikzcd}
\mathrm{IV} \arrow[r, shift left, "K_{\mathrm{I}}"] & \mathrm{I} \arrow[l, shift left] \arrow[r, shift left, "K_{\mathrm{II}}"] \arrow[d, "k"] & \mathrm{II} \arrow[l, shift left] \\
 & \mathrm{RNH_2} + \mathrm{CS_2} &
\end{tikzcd} \qquad \text{(eq. 5)}$$

Rate-Determining Step

Brønsted type plots of $\log k$ and $\mathrm{p}K'_{\mathrm{II}}$ *vs.* the pKa of parent amine ($\mathrm{p}K_{\mathrm{N}}$) clearily indicate the N-substituent effects as shown in Fig. 2. The equations 6 and 7 were obtained. The equation 7 well agreed with that previously proposed.[9] These relations manifest that an electron-donating group on the nitrogen atom increases the stability of I and decreases the acidity of I.

$$\log k = -0.3_7\mathrm{p}K_{\mathrm{N}} + 2.3_0 \qquad \text{(eq. 6)}$$

$$\mathrm{p}K_{\mathrm{II}}' = 0.5_3\mathrm{p}K_{\mathrm{N}} - 2.6_0 \qquad \text{(eq. 7)}$$

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13) Melting points were measured on a hot stage apparatus and uncorrected.

14) J.V. Braun, *Chem. Ber.*, **35**, 817 (1902).

15) M.A. Paul and F.A. Long, *Chem. Rev.*, **57**, 1 (1957).

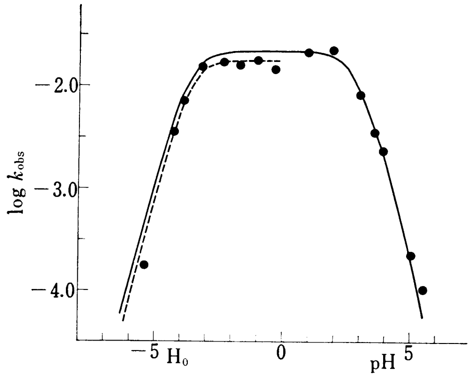

Fig. 1. Rate Profiles for the Decomposition of Ia at 25°:
— theoretical curve obtained in weak acids;
--- theoretical curve obtained in strong acids.

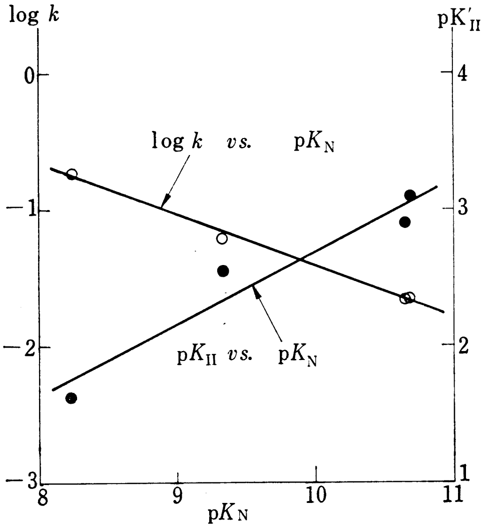

Fig. 2. Brønsted Plots of log k and $\mathrm{p}K'_{\mathrm{II}}$ vs. $\mathrm{p}K_{\mathrm{N}}$

Table I. Rate Constants (k), Dissociation Constants ($\mathrm{p}K'\mathrm{a}$) and Derived Data for the Decomposition of I in Acidic Media at 25°

Compound	pKa of Parent Amine($\mathrm{p}K_{\mathrm{N}}$)	$k \times 10^2 \mathrm{min}^{-1}$ Weak acid	Strong acid	E kcal·mole^{-1}	log A	$\Delta S^{\ddagger}_{298.20°K}$ e.u.	pKa′ $\mathrm{p}K'_{\mathrm{II}}$	$\mathrm{p}K'_{\mathrm{I}}$
Ia	10.67[a]	2.22[c]	1.77	20.0	13.1	−8.7	2.89[d]	−3.75
		2.50[d]		15±2[d]	14.2[e]		2.89[f]	−3.9[g]
		1.11[e]		21.7[e]				
Ib	10.70[a]	2.12	2.45	20.6	13.5	−6.9	3.09	−3.8
		2.4[d]		19±1[d]	14.1[e]		2.91[f]	−4.1[g]
		1.70[e]		21.6[e]			3.04[d]	
Ic	9.35[a]	6.12	h)	20.7	13.9	−5.1	2.56	h)
		7.59[e]		19.3[e]	13.1[e]		2.26[f]	
Id	8.24[b]	1.80×10	1.57×10	20.6	14.4	−2.8	1.63	−5.7
							1.73[f]	−5.2[g]

a) D.D. Perrin, "Dissociation Constants of Organic Bases in Aqueous Solution," Butherworths, London, 1965. *b*) S. Mizukami and E. Hirai, *Chem. Pharm. Bull.* (Tokyo), **14**, 1321 (1966). *c*) Ref. 18. *d*) Ref. 6. *e*) Ref. 5. *f*) Calculated by the equation: $\mathrm{p}K'_{\mathrm{II}} = 0.48\ \mathrm{p}K_{\mathrm{N}} - 2.23$ in Ref. 9. *g*) Determined spectrophotometrically in Ref. 9. *h*) Could not be measured because of the sparing solubility.

It is an important problem that rate-limiting step is whether the proton transfer, I→V or the N-C bond fission.[5,6] Equation 6 clearily excluded the former idea. If the proton transfer I→V were rate determining, the rate could increase in the presence of more electron-donating substituent. The formation of I must be initiated by the attack of the lone-pair electrons of the nitrogen atom of amine to the carbon atom of carbon disulfide acting as a Lewis acid to form an N-C bond. The principle of microscopic reversibility indicates that the proton of I is transfered from the sulfur to the nitrogen atoms concertedly with the N-C bond cleavage. The proton transfer will be assisted by the increase of basicity of the nitrogen atom on the lossing of N-C bond into the critical distance in the transition state. The proton transfer before the N-C bond cleavage will hardly occur, since the net charge (Q) of nitrogen atom was calculated to be positive due to resonance.[16] Consequently, we propose VII as

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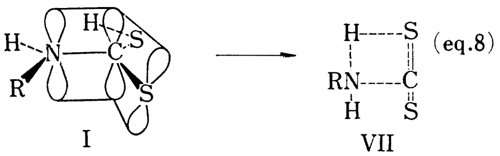
[16] M.J. Janssen, *Rec. Trav. Chim.*, **79**, 1006 (1960); Y. Ozias and L. Reynard, *Theoret.Chim. Acta* (Berl.), **20**, 51 (1971).



I VII

a transition state structure. The values of the activation entropies $\Delta S^{\ddagger}$ to be near zero satisfy the unimolecular rate-limiting step I to VII.[17]

It is well known that I is stabilized with resonance to have double bonded character of the N-C bond.[3,4] The resonance naturally demands that the lone-pair electrons of nitrogen atom and the π-electrons of thiocarbonyl group lie on the same plane as shown in eq. 8. Therefore, it is unlikely that I exists as intramolecularly hydrogen-bonded form as VI,[7] in which the lone pair and SH are required to situate on the same plane.

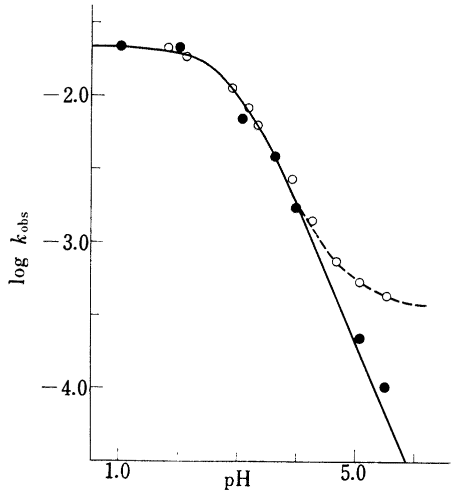


Fig. 3. Comparison of Rate Profiles for the Decomposition of Ia at 25°: ● present work; ○ work by Chakrabarti *et al.*[18]

Oxidation Reaction

Complete deairation and relatively higher initial concentrations of I (5×10^{-3}M) were both required for the correct kinetic measurements in sulfuric acid. The oxidation reactions to yield N,N'-disubstituted thiuram disulfides were observed in sulfuric acid and interfered the measurements of rates. In 10% sulfuric acid, Ia and Ib were rapidly oxidized in the presence of oxygen to the compound having the peaks at 239—240 nm and at about 275 nm(sh) which were diminished very slowly. The oxidation products were successfully isolated and identified to be N,N'-dimethyl- (VIII) and N,N'-diethylthiuram disulfides (IX) for the case of Ia and Ib, respectively. The same type of spectral change was reported for Ia in hydrochloric acid, but the product remained unidentified.[6]

The similar interference was observed for the decomposition of I in weakly acidic solutions without sufficient deairation at high pH range. Chakrabarti, *et al.*[18] reported that log k of Ia observed at pH above 3.8 deviated from the theoretical curve determined in pH range below 3.8 (see Fig. 3). The deviation was attributed to the existence of the reaction into methylisothiocyanate (X), as expressed by eq. 9. The value of k' was obtained at 25° to be 3.26×10^{-4} min^{-1} using eq. 10, derived from eq. 9.

$$CH_3NH_2 + CS_2 \xleftarrow{k} \text{Ia} \overset{K_{II}}{\rightleftharpoons} \text{IIa} \xrightarrow{k'} \underset{\text{X}}{CH_3NCS} \qquad \text{(eq. 9)}$$

$$k_{obs} = k[H^+]/([H^+]+K_{II}) + k'\cdot K_{II}/([H^+]+K_{II}) \qquad \text{(eq. 10)}$$

The reaction was assumed to proceed *via* IIa at below pH 7, and *via* IIIa at above pH 7 as shown in eqs. 11 and 12.

$$\text{IIa} \overset{K_{III}}{\rightleftharpoons} \text{IIIa} \xrightarrow{k''} \text{X} + S^{2-} \qquad \text{(eq. 11)}$$

$$k_{obs} = k''\cdot K_{III}/(K_{III}+[H^+]) \qquad \text{(eq. 12)}$$

If the assumption were correct, the following equation should be hold, $k'=3.26\times10^{-4}\leq k''\cdot K_{III}/(K_{III}+[H^+])$ at above pH 7. Then k'' was estimated to be 3.26×10^{2} min^{-1}, assuming

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17) L.I. Schaleger and F.A. Long, "Advance in Physicl Organic Chemistry", Vol. 1, ed. by V. Gold, Acad. Press, London, 1963, p. 1.

18) S.J. Joris, K.I. Aspila, and C.L. Chakrabarti, *Anal. Chem.*, 42, 647 (1970).

the value of K_{III} to be 10^{-13}M.[4,19] If the correct value of $K_{III}(2.5\times10^{-18}\text{M})$[9] is used, greater k'' value ($1.30\times10^{7}\ \text{min}^{-1}$) can be obtained. The k'' value thus estimated predicts the half-life period of Ia at 25° in 0.1 N NaOH to be 2.1×10^{-3} min. However, no change of Ia was observed in such a solution during 24 hr. Furthermore, our reinvestigation at pH 5.0 and 5.5 under strictly non-oxidative conditions resulted in no deviation from the theoretical curve as shown in Fig. 3. Thus, the reaction of Ia to X supposed does not exist in detectable amounts in acidic solutions of the pH-range.

As described above, we first succeeded in the establishment of the decomposition mechanism of I in acidic solutions. The decomposition affords exclusively amine and carbon disulfide; the mechanism of which is expressed by eqs. 5 and 8.

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19) M. Wrónski, *Zeszyty Nauk. Uniw. Lódz., Nauki Mat.-Przyrod. Ser. II*, No. 6, 121 (1959) [*C.A.*, **55**, 4113 (1961)].