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Decomposition of Acetylsalicylic Acid and Its Derivatives in Solid State

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The decomposition of acetylsalicylic acid (I), acetyl-5-nitrosalicylic acid (II) and acetyl-5-chlorosalicylic acid (III) in solid state by water vapor were studied for an approach to elucidate the decomposition mechanisms of organic crystals by water vapor.

All three materials showed the sigmoid-type decomposition curves and the order of the intensity of acceleration at early stage was II>III>I. From the decomposition study of pre-decomposed I and II, it was revealed that the accumulation of formed salicylic acids and/or acetic were not the cause of acceleration.

Microscopic observation of advancement of reaction about II showed that the reaction starts partially on the crystals and then spread over all the crystals. It was concluded that the acceleration is attributed to the formation and growth of reaction nucleus as its wider sense.

The decomposition curves were anaylzed by the empirical equation ($dX/dt=(1-X)^m \times k^{l+1} \times t^l$), where X, t, and k are the decomposition fraction, decomposition time, and the apparent decomposition rate constant, respectively, and where m and l are parameters. The apparent activation energies of decomposition of three materials were 30 kcal/mol, and the k of II linearly increases as the relative humidity rises.

There are a number of kinetic studies on decomposition of pharmaceutical solid, but most of them are semiquantitative. They have failed in determining reaction mechanisms. The decomposition of acetylsalicylic acid (I) received considerable attention in this field, but as Leeson mentioned previously,[2] the reproducibility of the data is questionable. Recently, Gore suggested that the loss of salicylic acid from the reaction system by sublimation can incur appreciable errors in the direction of overestimation of the stability.[3] The decomposition time courses of I in solid state by previous researchers are possibly erroneous results. Consequently, one must obtain exact data employing methods unaffected by sublimation of formed salicylic acid, in order to determine the reaction rate.

Some pharmaceuticals are known to exhibit autocatalytic decomposition in solid state, and Leeson attributed the autocatalytic decomposition of I to pH change of the water films on the particles by accumulation of formed salicylic acid.[2] But, the decomposition time course of I represented by Leeson shows that the apparent maximum decomposition rate of I is attained when the decomposed fraction of I becomes 30% or more.[2] It is doubtfull, therefore, whether such a large quantity of formed salicylic acid is necessary in order to saturate the water layers on the particles, or not.

This paper reports on the decomposition of I and its two derivatives, acetyl-5-nitrosalicylic acid (II) and acetyl-5-chlorosalicylic acid (III) in solid state by water vapor, and on the mechanisms of the autocatalytic decomposition of these materials.

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[2] L.J. Leeson and A.M. Mattocks, *J. Am. Pharm. Assoc.*, 47, 329 (1958).

[3] A.Y. Gore, K.B. Naik, D.O. Kildsig, G.E. Peck, V.F. Smolen, and G.S. Banker, *J. Pharm. Sci.*, 57, 1850 (1968).

Experimental

1. **Materials**——I, obtained commercially and recrystallized from $CHCl_3$, was ground and sieved (80/150 mesh, mp 135°, salicylic acid contents were 0.08%).[4] II, synthesized by the method of Ciampa[5] and recrystallized from $CHCl_3$-EtOH mixtures (3: 1), was ground and sieved (80/150 mesh, mp 164°, 5-nitrosalicylic acid contents were 0.45%).[4] II, synthesized by the method of Ciampa and recrystallized from $CHCl_3$, was ground and sieved (80/150 mesh, mp 148°, 5-chlorosalicylic acid contents were 0.21%).[4] Inorganic salts for humidity control were of analytical grade and used without further treatment.

2. **General Procedure**——Sample powders were weighed out in 12 × 20 mm pyrex glass vials, and vials were set in the reaction vessels as shown in Fig. 1.[6] Reaction vessels were sealed with Valqua Tape Seal and silicon grease to prevent permeation of moisture from water bath. Sealed vessels were submerged beneath the water of 60°, 70°, 80°, and 90° constant temperature baths, and then, at various times, they were removed and analyzed for extent of decomposition.

3. **Analysis of Salicylic Acid Derivatives**——Formed salicylic acid derivatives in the vials were dissolved in ethanol. A suitable aliquot was transferred to a volumetric flask and sufficient ethanol was added to make the total ethanol content a certain volume. After the addition of 1% ferric chloride solution (0.1 N HCl) and the dilution of the solution up to a volume with water, the color intensity was measured at 532 mμ (salicylic acid (IV)), 493 mμ (5-nitrosalicylic acid (V)) and 535 mμ (5-chlorosalicylic acid (VI)). In order to avoid errors from rapid decomposition of II, formed V was determined by extrapolating the color intensity to the time when the acidic ferric chloride solution was added. Formed salicylic acid derivatives sublimed in saturated KCl and NaBr solution were determined spectrophotometrically at 303 mμ (IV), 309 mμ (V) and 316 mμ (VI) respectively. Sublimed IV in NH_4NO_3 solution was determined colorimetrically at 532 mμ, and that in KF solution was extracted with *n*-Butanol and measured spectrophotometrically at 297 mμ.

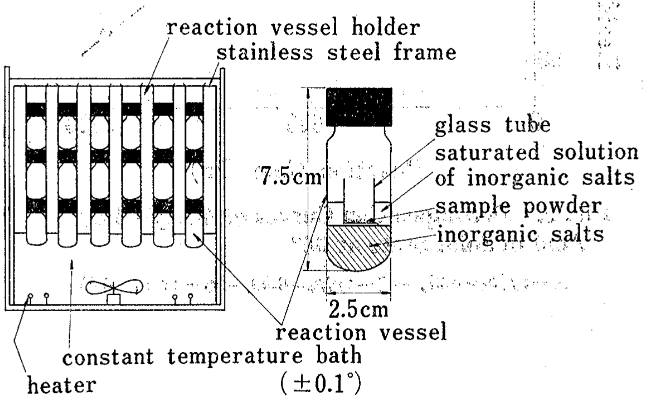

Fig. 1. Cross Section of Reaction Apparatus

4. **Microscopic Examination**——For microscopic examination, the reacted powders were withdrawn at appropriate times and dispersed on a slide glass by liquid paraffin. The dispersed powders were observed with the polarized microscope through crossed nicols.

Results

The residual ratios of I, II and III after storage at each temperature and humidity are shown in Fig. from 2 to 8. In Fig. 6, broken line shows the results about one lot of II which was prepared separately from another sample of II and the purity and the particle distribution of the two lot are identical.[7] The difference between the results is seemingly because of slight change in recrystallization condition. Fig. 9 shows the influence of particle size on the decomposition of II.

As Gore pointed out,[3] it is recognized from Fig. 10 that a considerable portion of formed IV sublimes and this trend is remarkable at the early stage of the decomposition. The lower the reaction temperature and humidity are, the greater the ratio of sublimed IV is. The underestimation of decomposition ratio of I in solid state will be serious, if the solids should be stored at lower temperature and sublimed IV should be neglected. On the other hand, V showed no sublimation and VI sublimed slightly.

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[4] Contents of the salicylic acid derivatives were determined by the analytical methods described below.

[5] G. Ciampa, *Ann. Chim.* (*Rome*), **54**, 975 (1964).

[6] The influence of sample weight on decomposition curves was not observed within 30—80 mg, and the accelerating effect of glass surface was not detected in these conditions.

[7] The particle distributions of II were determined with πMC Particle Measurement Computer System.

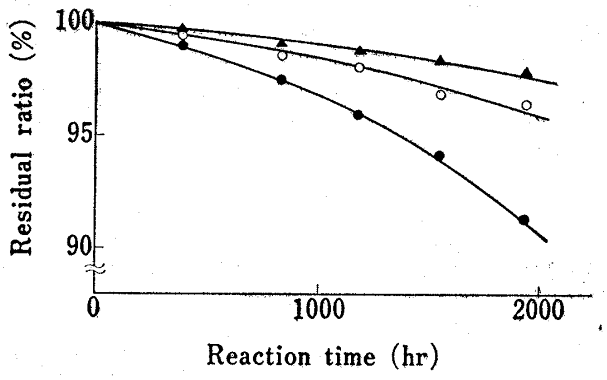

Fig. 2. Decomposition Curves of Acetylsalicylic Acid in Solid State at 60°

—▲—: $p/p_0=0.21$, —○—: $p/p_0=0.50$, —●—: $p/p_0=0.81$

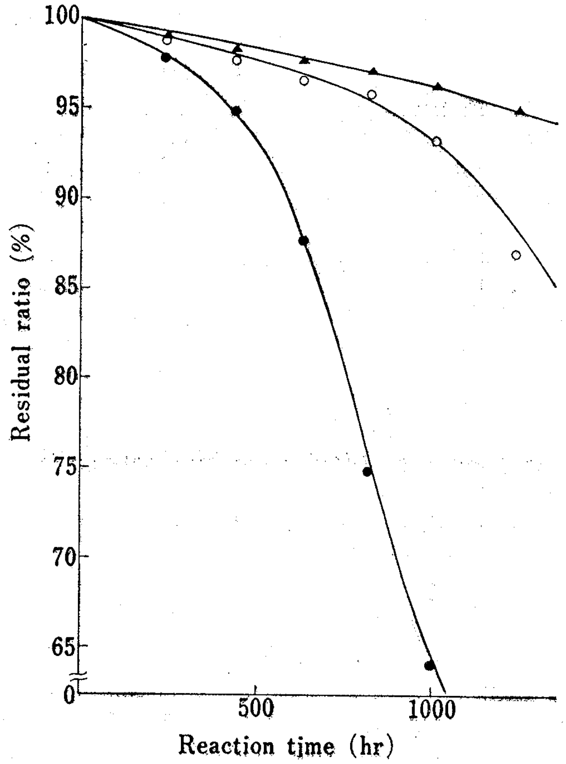

Fig. 3. Decomposition Curves of Acetylsalicylic Acid in Solid State at 70°

—▲—: $p/p_0=0.22$, —○—: $p/p_0=0.51$, —●—: $p/p_0=0.80$

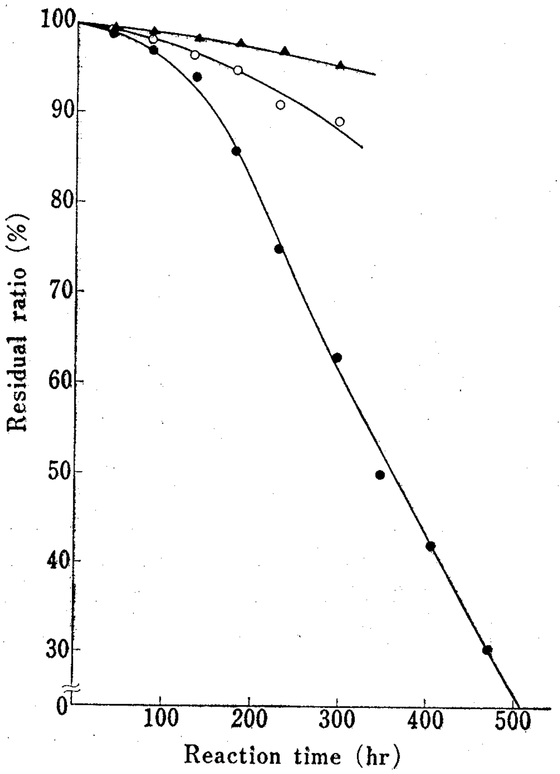

Fig. 4. Decomposition Curves of Acetylsalicylic Acid in Solid State at 80°

—▲—: $p/p_0=0.23$, —○—: $p/p_0=0.51$, —●—: $p/p_0=0.80$

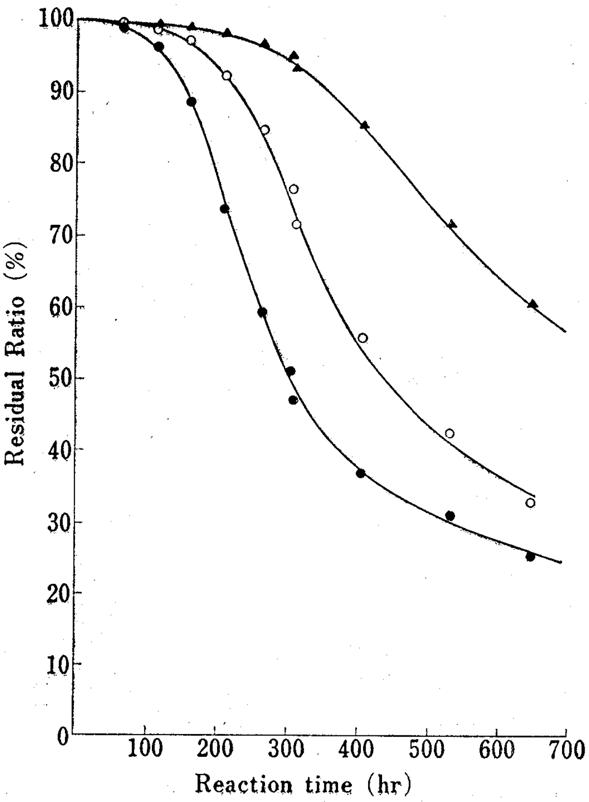

Fig. 5. Decomposition Curves of Acetyl-5-nitrosalicylic Acid in Solid State at 70° (lot B)

—▲—: $p/p_0=0.21$, —○—: $p/p_0=0.51$, —●—: $p/p_0=0.81$

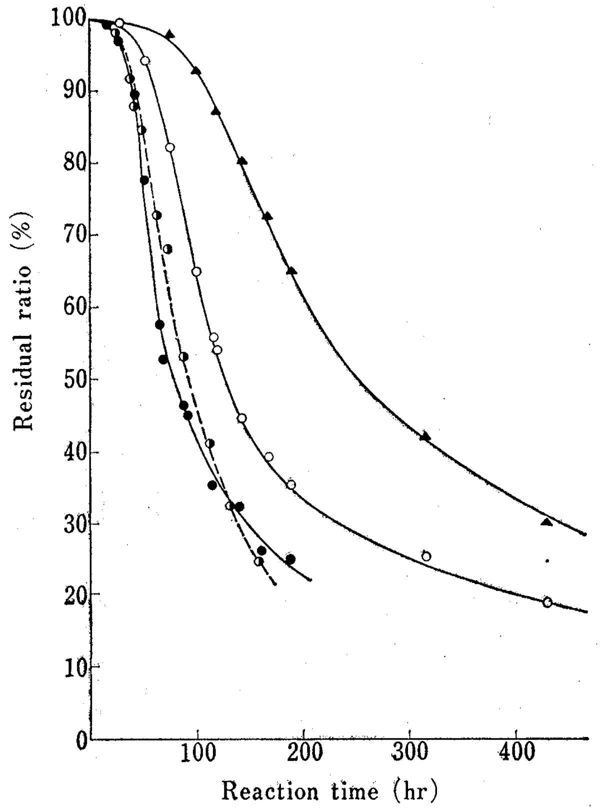

Fig. 6. Decomposition Curves of Acetyl-5-nitrosalicylic Acid in Solid State at 80°

—▲—: p/p_0=0.23,[a] —○—: p/p_0=0.51,[a]
—●—: p/p_0=0.80,[a] —◐—: p/p_0=0.80[b]
a) lot B, *b*) lot A

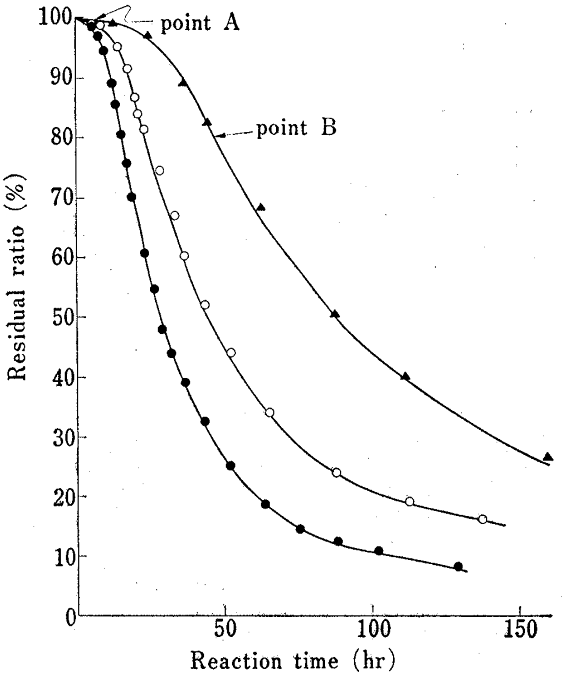

Fig. 7. Decomposition Curves of Acetyl-5-nitrosalicylic Acid in Solid State at 90° (lot A)

—▲—: p/p_0=0.23, —○—: p/p_0=0.51,
—●—: p/p_0=0.78

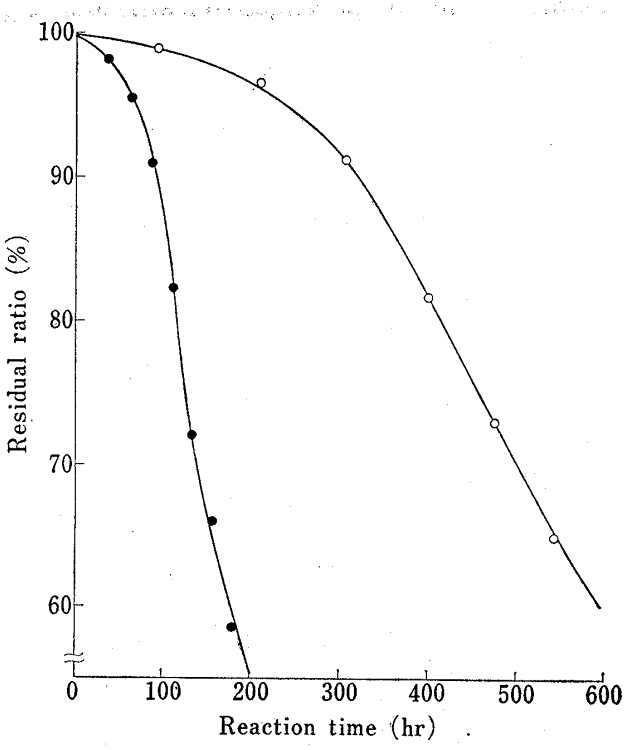

Fig. 8. Decomposition Curves of Acetyl-5-chlorsalicylic Acid in Solid State

—○—: 70°, p/p_0=0.81, —●—: 80°, p/p_0=0.80

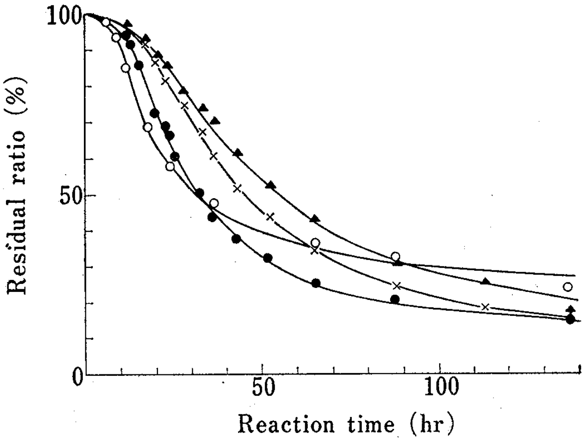

Fig. 9. Effect of Particle Size on the Decomposition of Acetyl-5-nitrosalicylic Acid (lot A) in Solid State at 90°, p/p_0=0.51

—▲—: 48/80 mesh, —×—: 80/150 mesh,
—●—: 150/250 mesh, —○—: fine powder[a]
a) This sample was obtained from the sample of 80/150 mesh by grinding with mortar for 30 min.

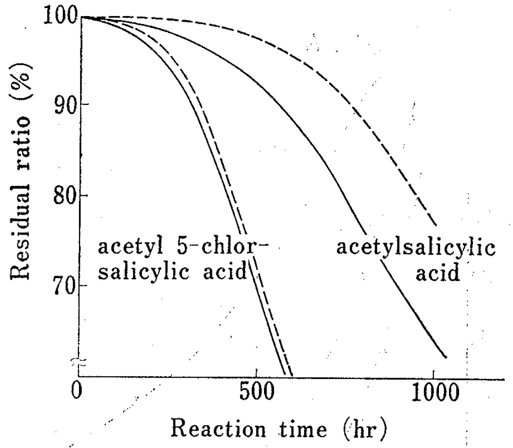

Fig. 10. Comparison of Decomposition Curves with and without estimating the Sublimed Salicylic Acids at 70°, $p/p_0=0.81$

----: decomposition curves from the analysis of salicylic acids in the sample tube
——: decomposition curves from the analysis of salicylic acid in the sample tube and the saturated solution of inorganic salts

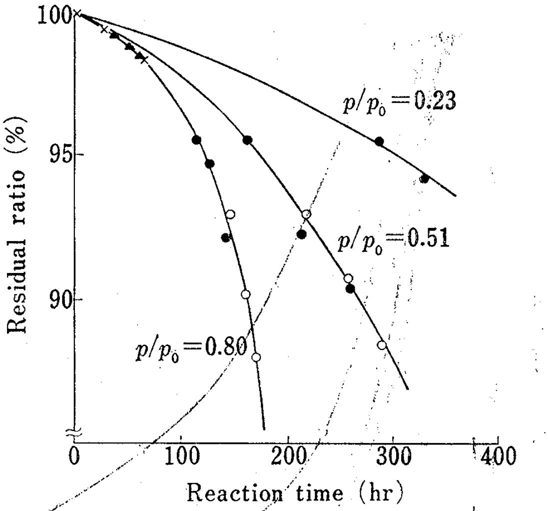

Fig. 11. Decomposition of Pre-treated Acetylsalicylic Acid in Solid State at 80°

	condition of pre-decomposition temp.	p/p_0	decomposed fraction (%)	condition of post-treatment	salicylic acid content (%)
●	80°	0.51	4.6	dried at 80° *in vacuo* (48 hr)	0.6
○	80°	0.51	7.8	dried at 80° *in vacuo* (48 hr)	1.3
▲	60°	0.81	0.8	dried at room temp. *in vacuo* (24 hr)	0.2
×				mechanical mixture	9.2

——: decomposition curves of pure acetylsalicylic acid (80/150 mesh)

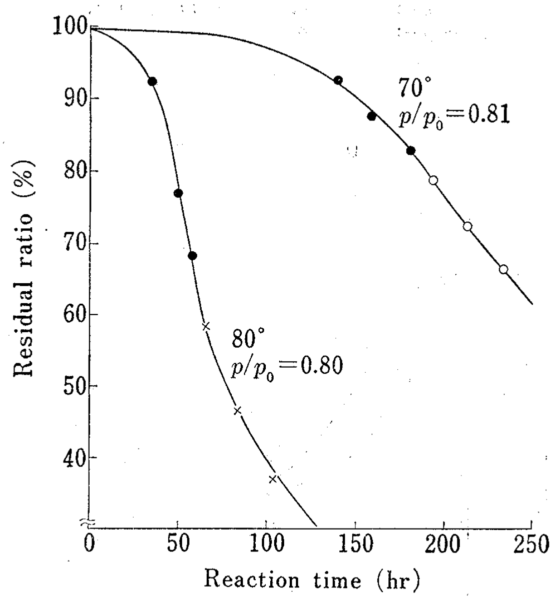

Fig. 12. Decomposition of Pre-treated Acetyl-5-nitrosalicylic Acid (lot B)

	condition of pre-decomposition	condition of post-treatment
○	70° $p/p_0=0.81$	evacuated for 12 hr at room temperature
●	70° $p/p_0=0.51$	
×	80° $p/p_0=0.80$	

——: decomposition curves of pure acetyl-5-nitrosalicylic acid (lot A, 80/150 mesh)

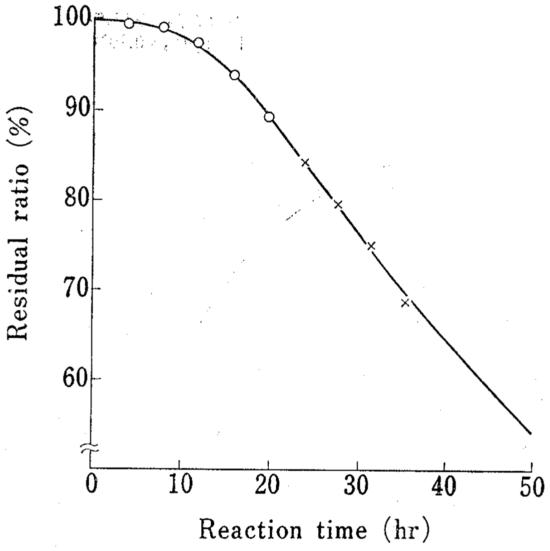

Fig. 13. Decomposition of Pre-treated Acetyl-5-nitrosalicylic Acid at 90° and $p/p_0=0.78$ (lot A, 48/80 mesh)

○: pure sample dried for 12 hr at 85° *in vacuo* ($X=0.0045$)
×: pre-decomposed at 90° and at $p/p_0=0.78$ ($X=0.16$), and evacuated for 24 hr at room temperature
——: decomposition curve of pure acetyl-5-nitro salicylic acid (lot A, 48/80 mesh)

In the attempt to check the effect of formed salicylic acid or acetic acid on the reaction rate, decomposition studies of pre-decomposed I and II powders, that were post-treated under various conditions after being decomposed to a certain extent, were conducted. The results are shown in Fig. from 11 to 13.[8]

Discussion

1. Acceleratory Period

Decomposition time courses of the three compounds in this study show acceleratory periods, and the acceleration of II is more remarkable than I. The decomposition rate of the former at the inflexion points is more than twenty times as fast as the early stages. For example, in Fig. 7, the slope of the decomposition time course at the point B is nearly thirty times of that at the point A. But the pH-rate profile of the hydrolysis of these compounds in aqueous solution shows that the increment of apparent first order rate constant of I in lower than pH 6 is greater than that of II.[9] These facts suggest that the pH change of adsorbed water layer on solid following the progress of decomposition cannot be the cause of acceleration in this study. Thus a new theoretical approach about this phenomenon is to be proposed. Furthermore, Fig. from 11 to 13 show that the decomposition rates of the samples which were pre-decomposed and evacuated in the conditions described in the footnotes of Fig. from 11 to 13 depend upon only predecomposed fraction but not upon salicylic acids contents or conditions of post-treatment. These results also disagree with the Leeson's theory that the accumulation of formed salicyclic acid is the driving force of acceleration.

Recently, Carstensen predicted that, in most acetylated compound, the layers of formed acetic acid are mediators of the decomposition in solid state.[10] And Bawn derived a theoretical equation which expresses sigmoid-shaped decomposition curve, assuming that the decomposition products liquefy the reacting molecules and increase the decomposition rate.[11] But, since it is reasonable to think that acetic acid is more volatile than salicylic acid, acetic acid of pre-decomposed samples are probably removed by the evacuation in the conditions described in the footnote of Fig. 11. So, the acceleration observed in this experiment cannot be ascribed to the surface liquefaction of particles by acetic acid.

In general, thermal decompositions of inorganic salts show sigmoid shaped decomposition curves, and many mathematical theories are presented.[12] But the most of them, for example "Kawakita" equation, "Prout-Tompkins" equation and "Avrami" equation cannot fit the decomposition time courses of this experimental result about II, because of the high acceleration in early stage and the extreme decrease of the decomposition rate in later stage in the present data. Only the power expression can well fit the decomposed fraction in acceleratory period,

$$X = c \times t^{\beta} \qquad (1)$$

where X is the decomposed fraction, t is decomposition time, and c and β are constant.[13] Almost all results other than of I in p/p_0 (relative humidity)$=0.8$ can be represented by eq. 1 from $X=0$ to $X=0.2$ as shown in Fig. 14. The β values obtained from the slopes of log X against log t plots are presented in Table I. These values of the same sample do not vary

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[8] In Fig. from 11 to 13, solid lines represent the same decomposition curves with that in Fig. from 2 to 8, and the first points of every plot indicate the pre-decomposed fractions.

[9] A.R. Fersht and A.J. Kirby, *J. Am. Chem. Soc.*, **90**, 5826 (1968).

[10] J.T. Carstensen and M.N. Musa, *J. Pharm. Sci.*, **61**, 1112 (1972).

[11] W.E. Garner (ed.), "Chemistry of the Solid State," Butterworth Scientific Publication, London, 1955, p. 255.

[12] E.G. Prout and F.C. Tompkins, *Trans. Faraday. Soc.*, **43**, 148 (1947); K. Kawakita, *Rev. Phys. Chem. Japan.*, **14**, 79 (1940); M. Avrami, *J. Chem. Phys.*, **7**, 1103 (1939).

[13] W.E. Garner (ed.), "Chemistry of the Solid State," Butterworth Scientific Publication, London, 1955, p. 191.

with decomposition temperature or humidity except in case of I. This suggests that the mechanism of acceleration in other than I does not change by decomposition condition.

Hirota obtained an analytical solution of Lacy's model about gas-solid reaction by introducing some assumptions for simplification and skillfully applied it to oxidation of ascorbic acid in compressed tablet.[14] This theory predicts that the decomposition fraction should be proportional to $t^{3/2}$, but such an intense acceleration as in II ($X \propto t^3$) cannot be explained by his theory. Ishida and Wen postulated a model that is intermediate between the unreacted core model and the homogeneous models about gas-solid reaction, but also this model does not predict such intense acceleration.[15] Furthermore, the fact that the decomposition rates of pre-decomposed samples depend upon their pre-decomposed fractions but not upon

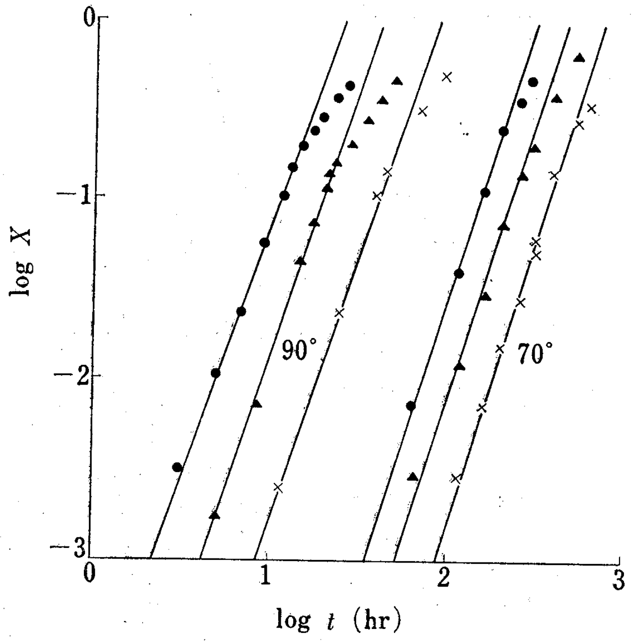

Fig. 14. Plots of log X against log t about Acetyl-5-nitrosalicylic Acid

	90°		70°	
	p/p_0	sample	p/p_0	sample
—●—:	0.78	lot A, 80/150 mesh	0.80	lot B, 80/150 mesh
—▲—:	0.51	lot A, 80/150 mesh	0.51	lot B, 80/150 mesh
—×—:	0.23	lot A, 80/150 mesh	0.22	lot B, 80/150 mesh

TABLE I. β-Values

Sample	Particle size	Temperature	Relative humidity (p/p_0)	β
II (lot A)	80/150	90°	0.78	3.0
II (lot A)	80/150	90°	0.51	3.1
II (lot A)	80/150	90°	0.23	3.1
II (lot A)	48/80	90°	0.51	3.0
II (lot A)	150/250	90°	0.51	3.2
II (lot A)	fine powder	90°	0.51	3.0
II (lot A)	80/150	80°	0.80	3.2
II (lot B)	80/150	80°	0.80	3.5
II (lot B)	80/150	80°	0.51	3.4
II (lot B)	80/150	80°	0.23	3.5
II (lot B)	80/150	70°	0.81	3.2
II (lot B)	80/150	70°	0.51	3.2
II (lot B)	80/150	70°	0.22	3.3
III	80/150	80°	0.80	2.2
III	80/150	70°	0.81	2.4
I	80/150	80°	0.80	a)
I	80/150	80°	0.51	1.4
I	80/150	80°	0.23	1.3
I	80/150	70°	0.81	a)
I	80/150	70°	0.51	1.2
I	80/150	70°	0.22	1.1
I	80/150	60°	0.81	1.2
I	80/150	60°	0.50	1.2
I	80/150	60°	0.21	1.1

a) In these conditions logarithmic plots of X against t did not become liner.

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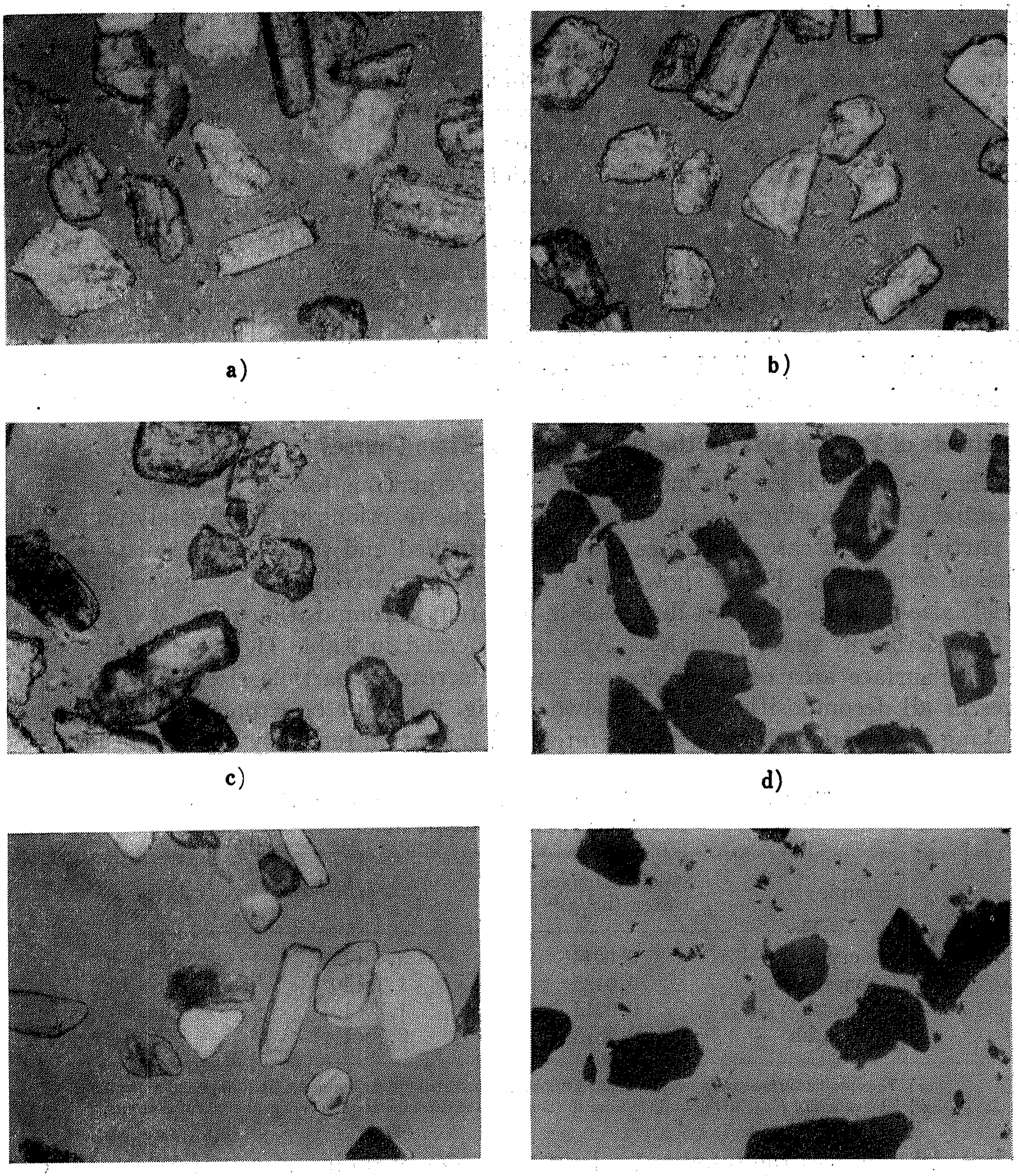
14) S. Hirota, *Chem. Pharm. Bull.* (Tokyo), **16**, 1982 (1968).
15) M. Ishida and C.Y. Wen, *Am. Inst. Chem. Eng. J.*, **14**, 311 (1969).



a) b) c) d) e) f)

Fig. 15. Microscopic Observation of Decomposed Crystals of Acetyl-5-nitrosalicylic Acid

|—| 200 μ

a) un-reacted crystal ($X=0.0045$)
b) dried at 90° for 181 hr ($X=0.0045$)[a]
c) decomposed at 90°, $p/p_0=0.78$ for 7.0 hr ($X=0.029$)
d) decomposed at 90°, $p/p_0=0.78$ for 18.0 hr ($X=0.27$)
e) decomposed at 90°, $p/p_0=0.78$ for 18.0 hr and dissolved off the surface with $CHCl_3$
f) decomposed at 70°, $p/p_0=0.81$ for 381.0 hr ($X=0.60$)

[a] This sample shows no observable change from pure crystals. So, it is apparent that the disintergration of crystals by heat does not occur.

the condition of pre-decomposition or after-treatment, deny the possible application of these reaction models to this results. Because, if the diffusion of water through the reaction zone is also the rate limiting step, the induction period must be observed in the decomposition curves of pre-decomposed samples, but this is not the fact. From these considerations, we suspect the occurrence and the growth of the nucleation in its widest sense as regions, where molecules are liable to react with water vapor, cause the acceleratory period.[16] The growth of nucleus means that the formation of product molecules induce strain in the crystal which produce cracks and form fresh surfaces on which decomposition can occur. In order to make sure of existence of reaction nucleus, we observed the extent of advance of reaction about II by a polarized microscope. Fig. 15 shows the results of microscopic observation about crystals of II whose decomposed fractions are from 2.9 to 60.0%. The dark parts on the photographs are probably representing the reacted surface of crystals, that is, the clusters of the microcrystals of formed 5-nitrosalicylic acid. These results show that the reaction occurred partially on the crystals and the individual crystals are different in the degree of decomposition. Fig. 15-d is the photograph at $X=0.27$, that is the stage of the maximum velocity. The unreacted surfaces are still observed on the photograph. Fig. 15-e suggests the difference in degree of decomposition in the individual particle. Seemingly these observations indicate that the acceleration is attributed to the formation of reaction nucleuses as its wider sense.

2. Effects of Particle Size on the Decomposition Time Courses

There have been various models and kinetic equations for gas-solid reaction.[17] About unreacted core shrinking model, it is shown that the reaction rate is inversely proportional to the particle size in case of surface reaction controlled and to the square of particle size in diffusion controlled. Fig. 9 shows that the shapes of decomposition curves differ with the particle size changes and that decreases in apparent decomposition rates of the latter stages are remarkable in small particles. And as indicated in Table II, apparent decomposition rates per surface area of 1 cm² decrease with decreasing particle size. Furthermore, later stages of all decomposition curves shown in Fig. 9 cannot be expressed by any unreacted shrinking core models, because of the intense deceleration tendency of these results. So, we attempted to express the intense deceleration tendency taking in consideration the effect of particle distribution, by using the equation derived by Suito, *et al.* and assuming that overall reaction rate is controlled by surface reaction rate and the particles are spherical.[18] But this attempt ended in failure and the intense deceleration of decomposition curves can not be interpreted by the effect of particle distributions. These results seem to reject any application of simple reaction model to the latter stages assuming that the decomposition occurs on the whole surfaces of the particles after the inflexion point.

TABLE II. Effect of Particle Size on the Decomposition Rate of Acetyl-5-nitrosalicylic Acid

Sample	Specific surface area (m²/g)[a]	$K_{\max}$ (1/hr)[b]	K (g/cm² hr)
Large crystal	0.0014	3.4×10^{-3}	1.71×10^{-4}
48/80 mesh	0.0125	1.1×10^{-2}	8.8×10^{-5}
80/150 mesh	0.0216	1.7×10^{-2}	7.9×10^{-5}
150/250 mesh	0.0873	2.7×10^{-2}	3.2×10^{-5}

[a] The specific surface areas were calculated from particle distribution obtained from Millipore π-mc system.
[b] The values of $K_{\max}$ were obtained from the slopes of the decomposition curves at the inflexion points.

On the other hand, Garrett found that the smaller the particle size of aspirin anhydride is, the slower the decomposition rate of it becomes.[19] He explained about the result that large crystals solvate or contain trapped solvents which liquefy the solid to fasten the decom-

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[16] W.E. Garner (ed.), "Chemistry of the Solid State," Butterworth Scientific Publications, London, 1955, p. 256.
[17] T. Kagiya, "Kagaku-hanno no Sokudoronteki Kenkyuho," Kagakudojin, Kyoto, 1970.
[18] E. Suito, N. Hirai, and K. Taki *Nippon Kagaku Zasshi*, **72**, 713, 715 (1951).
[19] E.R. Garrett, E.L. Schumann, and M.F. Grostic, *J. Am. Pharm. Assoc.*, **48**, 684 (1959).

position. But, since dried samples of II, which was prepared from pure sample by being evacuated overnight at 85°, show same decomposition curves as that of the sample without such treatment (shown in Fig. 13), recrystallization solvent probably does not influence the decomposition in the present study.

As shown by microscopic observation, the reaction nuclei do not distribute uniformly at each particle. The decomposed fraction of each particle seems to be different at the point of maximum velocity, and high reactive and low reactive particles may exist together in the small particles. In Fig. 15-f, all of the large crystals seem to be covered with formed 5-nitrosalicylic acid, but some of fine crystals show still light surface, that is to say, the unreacted surface. These effects are probably the main factor to slow down the decomposition at latter stage of the small particles.

3. Empirical Formula

As the decomposition mechanism were very complex, it seems impossible to develop rate equations theoretically. We attempted to express the decomposition curves by empirical formula in order to investigate the influence of decomposition condition on the decomposition rate. Among many formulas which express sigmoidal curve, eq. (2) expresses well present data,

$$\frac{dX}{dt} = (1-X)^m \times k^{l+1} \times t^l \qquad (2)$$ 20)

where X, t and k are the decomposition fraction, decomposition time, and the apparent decomposition rate constant, respectively, and where m and l are parameters which change as the material or the history of the powders are different. Integrated form of eq. (2) is,

$$\left\{\left(\frac{1}{1-X}\right)^{m-1}-1\right\} = (m-1) \times p_l \times t^{l+1} \qquad (3)$$

where $p_l = \frac{1}{l+1} k^{l+1}$.

If the temporarily determined value of m is correct, the logarithmic plot of each side of equation (3) gives a straight line. The value of $l+1$ and k are obtained from the slope and

TABLE III. Obtained Parameters of Equation (3)

Sample	Particle size	Temperature	Relative humidity	m	$l+1$	k
II (lot A)	80/150 mesh	90°	0.78	4.0	3.3	6.80×10^{-2}
	80/150 mesh	90°	0.51	4.0	3.3	4.17×10^{-2}
	80/150 mesh	90°	0.23	4.1	3.3	2.11×10^{-2}
	48/80	90°	0.51	4.0	3.1	3.62×10^{-2}
	150/250	90°	0.51	4.5	3.3	4.60×10^{-2}
	fine powder	90°	0.51	5.9	3.3	7.09×10^{-2}
	80/150 mesh	80°	0.80	3.2	3.3	1.77×10^{-2}
II (lot B)	80/150 mesh	80°	0.80	5.8	4.6	2.50×10^{-2}
	80/150 mesh	80°	0.51	7.2	4.6	1.70×10^{-2}
	80/150 mesh	80°	0.23	6.0	4.6	8.30×10^{-3}
	80/150 mesh	70°	0.81	6.0	4.7	6.50×10^{-3}
	80/150 mesh	70°	0.51	4.8	4.7	3.95×10^{-3}
	30/150 mesh	70°	0.21	6.1	4.7	2.54×10^{-3}
III	80/150 mesh	80°	0.80	1.8	2.7	7.13×10^{-3}
	80/150 mesh	70°	0.81	1.8	2.9	2.13×10^{-3}
I	80/150 mesh	80°	0.80	2.0	2.6	4.03×10^{-3}
	80/150 mesh	70°	0.81	2.1	2.6	1.14×10^{-3}

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20) K. Komatu, *Nippon Kagaku Zasshi*, **78**, 1452 (1957).

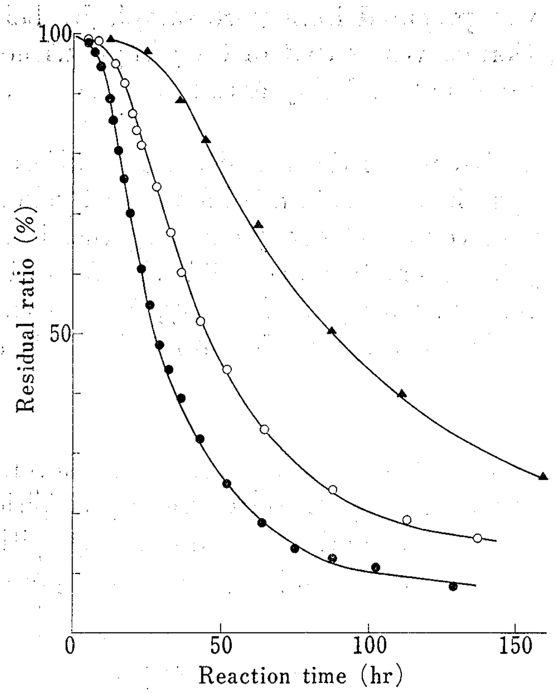

Fig. 16. Comparison of Experimental Data with Calculated Curves from Equation (3) (Acetyl-5-nitrosalicylic Acid, lot A, 80/150 mesh)

●: $p/p_0=0.78$, 90°
○: $p/p_0=0.51$, 90°
▲: $p/p_0=0.23$, 90°
——: calculated curves from equation (3)

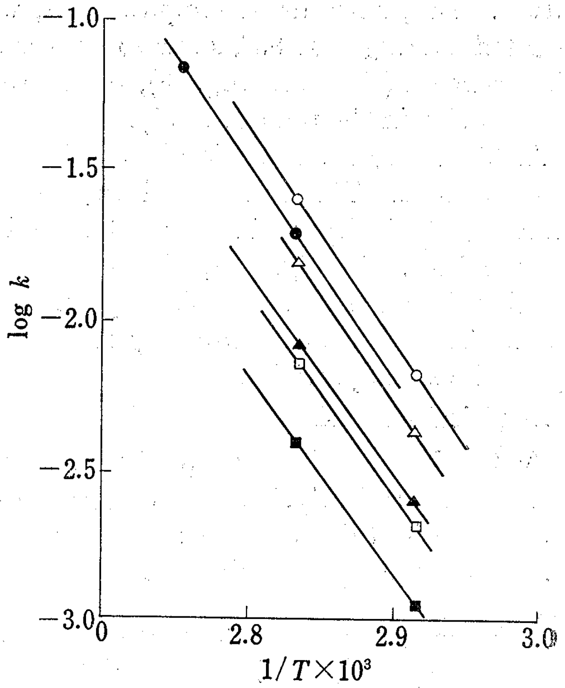

Fig. 17. Arrhenius Plot of Apparent Decomposition Rate Constants

	sample	lot	mesh	p/p_0
—○—:	acetyl-5-nitrosalicylic acid	A	80/150	0.80—0.81
—●—:	acetyl-5-nitrosalicylic acid	B	80/150	0.78—0.80
—△—:	acetyl-5-nitrosalicylic acid	A	80/150	0.51
—▲—:	acetyl-5-nitrosalicylic acid	A	80/150	0.21—0.23
—□—:	acetyl-5 chlorsalicylic acid		80/150	0.80—0.81
—■—:	acetylsalicylic acid		80/150	0.80—0.81

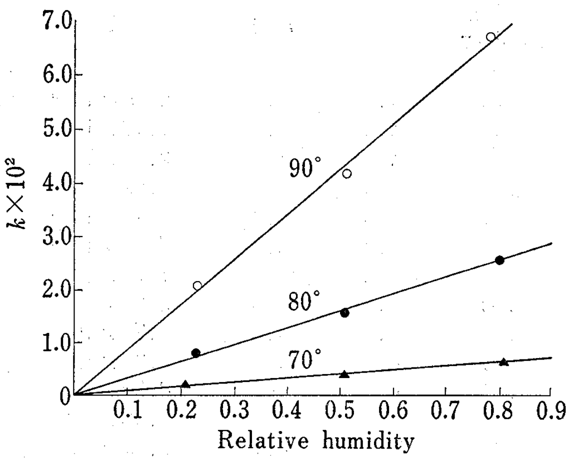

Fig. 18. Relationships between Apparent Decomposition Rate Constants and Relative Humidity about Acetyl-5-nitro-salicylic Acid

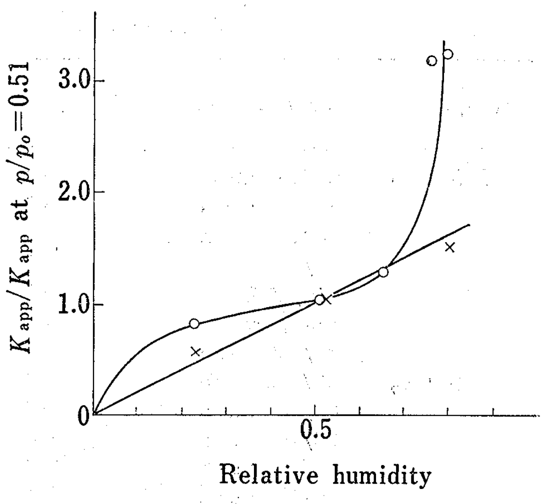

Fig. 19. Relationships between Apparent Decomposition Rate and Relative Humidity about Acetylsalicylic Acid (80°)

—○—: at $X=0.100$[a] —×—: at $X=0.010$[b]

[a] The values of K_{app} were obtained from the tangent of the decomposition curves at $x=0.010$.

[b] The values of K_{app} were obtained from the decomposition curves of pre-decomposed sample.

the intercept on the ordinate, respectively. These parameters are calculated with mini-max method by initial values obtained graphically and by the help of the Hitachi HITAC 5020 digital computer. Mini-max method determines the parameters which minimize the difference mostly between the experimental value and the calculated one about the point of showing the largest difference among the one series of the experimental results. The obtained parameters are shown in Table III, and the excellent agreement of computed results and experimental data can be seen in Fig. 16. From these results about II, it can be concluded that the reaction mechnism of II do not change with the changes of decomposition temperature and relative humidity. About I, the discrepancy between calculated results and experimental data was observed especially at early stage of decomposition. Probably, this comes from the effect of gas-phase reaction between vaporized I and water vapor. Fig. 17 is the Arrhenius plots of k about three compounds.[21] Apparent activation energies of these three compounds are 30 kcal/mol. As shown in Fig. 18, the decomposition rate constants of II linearly increase as the relative humidity rises. This fact suggests that the decomposition does not occur in the condensed water around the particles, but by the gas-solid reaction. If the reaction occurs in the condensed water, the overall reaction rate should be proportional to the amount adsorbed water, and the relation between the decomposition rate constants and relative humidity may become sigmoid shaped curve.

In case of I, since so many experimental data cannot be obtained as to be analyzed by eq. (3), the apparent decomposition rate at $X=0.01$ and $X=0.10$ versus relative humidity are plotted in Fig. 19. The result at $X=0.01$ is linear, but it at $X=0.10$ shows a sigmoidal curve. This suggests some change in decomposition mechanisms with the progress of the decomposition.

On the past studies of solid state decomposition of organic crystals by water vapor, the lack of reproducibility of the data prevented the exploration of reaction mechanism. As shown in this study, especially about II, the improvement of the reproducibility seems still possible. Further accumulation of accurate data about many other reactions of organic crystals with water vapor will reveal the mechanisms of this kind of reactions.

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[21] The values of k used in these plots were calculated from equation (3) by fixing the parameter m and l.