Summary

The infrared spectra of 25 kinds of benzenesulfinamide and *p*-toluenesulfinamide derivatives were measured. The S–N bands were observed between 928 cm^{-1} and 872 cm^{-1} as in benzenesulfonamide and methanesulfonamide derivatives. Moreover, the bands near 1090 cm^{-1} were found in all of the sulfinamide derivatives. The spectral change on deuteration were examined. In the compounds having –S–NH– and –S–NH$_2$ form, the bands near 900 cm^{-1} region shifted to the lower wave number (about 110~18 cm^{-1}). But no such shift has been observed in the bands near 1090 cm^{-1} and in the range 1075~1035 cm^{-1}.

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177. Hisashi Nogami, Tsuneji Nagai, and Akira Suzuki[*1]: Studies on Powdered Preparations. XIII.[*2] Reaction between Dried Aluminum Hydroxide Gel and Organic Acid.[*3]

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It was described in previous papers,[1~3] that the rate of reaction between dried aluminum hydroxide gel (DAHG) and such an inorganic acid as hydrochloric, nitric, and/or sulfuric acid was not in accordance with the Noyes-Whitney equation,[4] but was expressed by

$$-\frac{dH}{dt}=K_1WH^n \tag{1}$$

where H is the hydrogen ion concentration in bulk liquid at the time t, K_1 the apparent rate constant, W the amount of test sample, and n the apparent order of the reaction. In the cases of hydrochloric acid and nitric acid, n was nearly zero, while it was around 0.5 in the case of sulfuric acid. K_1 was dependent not only on the acid used, but also on the total amount of electrolyte and/or test sample, even if the same kind of samples were used. Based upon this point, a method was established for the quantitative evaluation of the antacidic reactivity of DAHG.

Generally organic acids are weak. Therefore, the rate of dissolution of DAHG into organic acid is considered to be not always in accordance with equation (1) and, paying an attention on the pH change in bulk liquid, the apparent order of the reaction with respect to the hydrogen ion may be influenced by the dissociation constant of acid.

[*1] Present adress: Pharmaceutical Research Laboratory, Tanabe Seiyaku Co., Ltd., Kashima-cho, Higashi-yodogawa-ku, Osaka.

[*2] Part Ⅻ. H. Nogami, Y. Nakai: Presented at the 82nd Annual Meeting of Pharmaceutical Society of Japan, Yokohama, April 1962; cf., This Bulletin, **11**, 1389 (1963).

[*3] Presented at the 83rd Annual Meeting of Pharmaceutical Society of Japan, Kanazawa, April 1963.

[*4] Hongo, Tokyo (野上 寿, 永井恒司, 鈴木 章).

1) Part Ⅶ. H. Nogami, T. Nagai: This Bulletin, **10**, 728 (1962).
2) Part Ⅷ. H. Nogami, T. Nagai: *Ibid.*, **10**, 741 (1962).
3) Part Ⅸ. H. Nogami, J. Hasegawa, T. Nagai, M. Miyamoto: *Ibid.*, **10**, 747 (1962).
4) A. A. Noyes, W. R. Whitney: J. Am. Chem. Soc., **19**, 930 (1897).

In this study, in addition to the pH change, the concentration of aluminum ion produced in bulk liquid was measured with the lapse of time to investigate the reaction between DAHG and organic acid. DAHG is expected to be insoluble in weak acid, and it may be attributed to the formation of polynuclear complex of aluminum hydroxide in the higher pH region than about 4.[5] In this study, therefore, four comparatively strong acids, *i.e.*, salicylic, trichloroacetic, monochloroacetic, and formic acid were examined.

Experimental

Materials——DAHG J.P. from the same lot, supplied by Chugai Pharmaceutical Co., Ltd., was used through the experiments. Salicylic acid and $AlCl_3 \cdot 6H_2O$ were used after recrystallization. The rest of the materials were of the purest reagent grade and used without further purification.

Apparatus and Procedure for the Measurement——The apparatus and procedure for the measurement of pH change and aluminum ion concentration were the same as described in detail in the previous paper,[1] except that the standard curve for the concentration of aluminum ion was obtained using the recrystallized $AlCl_3 \cdot 6H_2O$. A flask containing 200 ml. of 0.01*N* acid was kept in a constant temperature bath. A given amount of DAHG was added to the acid, while it being stirred constantly at a speed of 500 r.p.m. The pH was measured and the concentration of aluminum ion was determined using 1 ml. of the suspension taken from the liquid at appropriate intervals.

Results and Discussion

Three stages of reaction were observed with the progress of dissolution of DAHG into organic acid, *i.e.*, the initial stage, the main, and the fianal, as shown in Figs. 1 to 3 by broken, solid, and chain lines, respectively.

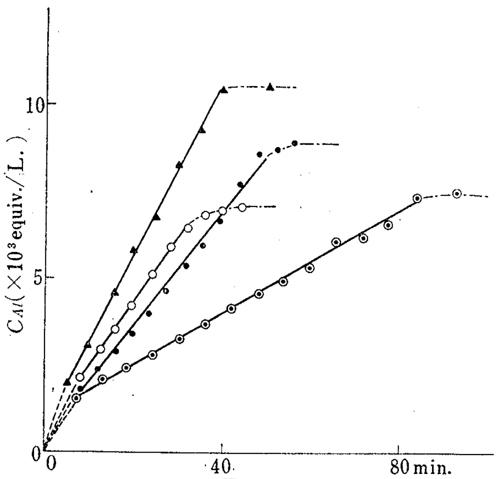

Fig. 1. Dissolution of DAHG in Various Acids at 30° under 0.500 g. of DAHG and 200 ml. of Acid

—▲— Salicylic acid
—○— Formic acid
—●— Trichloroacetic acid
—⊙— Monochloroacetic acid

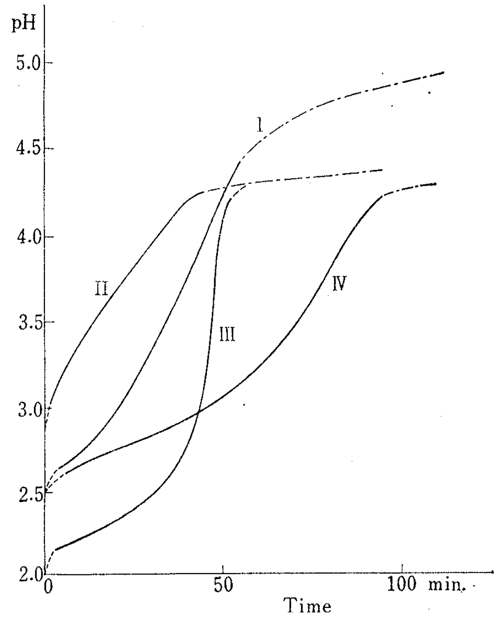

Fig. 2. pH Change in the Reaction between DAHG and Acids at 30° under 0.500 g. of DAHG and 200 ml. of 0.01*N* Acid

I : Salicylic acid
II : Formic acid
III : Trichloroacetic acid
IV : Monochloroacetic acid

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[5] C. Brosset : Acta Chem. Scand., **6**, 910 (1952).

Initial Stage of the Reaction

This stage is concerned with the rapid increase of pH immediately after DAHG was brought into contact with acid. This phenomenon was considered to be due primarily to the adsorption of acid[6] by DAHG and also to the rapid dissolution of aluminum ion which might exist on the surface of DAHG as was expected from the experiments on the dissolution of colloidal boehmite in hydrochloric acid.[7]

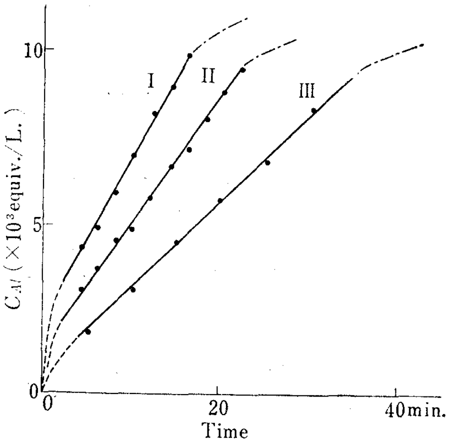

Fig. 3. Dissolution of DAHG in 200 ml. of 0.01*N* Salicylic Acid at 30°

I : 1.00 g. of DAHG
II : 0.75 g. of DAHG
III : 0.50 g. of DAHG

Main Stage of the Reaction

At this stage, as shown in Figs. 1 and 3, the rate of the dissolution of DAHG in acid seemed to be of the zero order with respect to aluminum ion concentration. Obtaining each slope of solid line in Fig. 3, the rate of the reaction was found to be proportional to the amount of test sample of DAHG, *W*, as shown in Fig. 4.

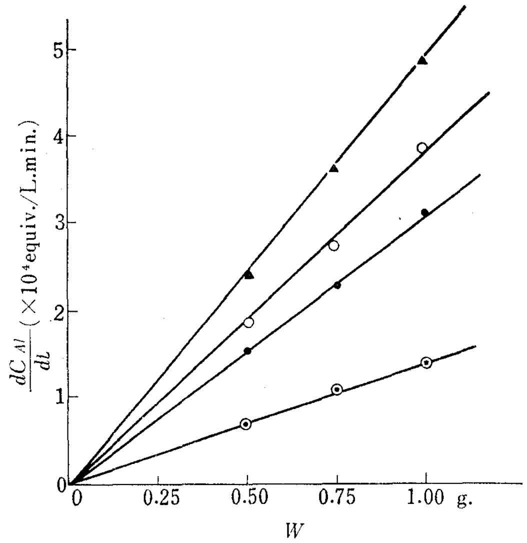

Fig. 4. Effect of the Amount of Test Sample on the Rate of Dissolution of DAHG in 200 ml. of 0.01*N* Acid at 30°

—▲— Salicylic acid
—○— Formic acid
—●— Trichloroacetic acid
—⊙— Monochloroacetic acid

Accordingly, the rate of dissolution of DAHG in organic acid could be expressed by

$$\frac{dC_{Al}}{dt}=K_2W \qquad (2)$$

where C_{Al} is the concentration of aluminum ion produced in bulk liquid, and K_2 the apparent rate constant.

On the other hand, the apparent order of the reaction with respect to the hydrogen ion varied with the acid used, as is clear from the different curvatures in Fig. 2. According to the finite differences diagram of the pH change,[1] the values of the apparent order of reaction were estimated to be nearly 0, 0.6, 0.8, and 1.5 in the cases of trichloroacetic acid, monochloroacetic acid, salicylic acid, and formic acid, respectively. In the case of trichloroacetic acid, the value obtained was similar to that of the case of hydrochloric acid or nitric acid described in the previous paper. An increasing tendency of these values was the same to a decreasing tendency of the dissociation constant.[8] The apparent order of the reaction with hydrogen ion is influenced by various factors because of the diverse physico-chemical properties of DAHG as was described in the previous paper, but the effect of dissociation constant was considered to be predominant in this study from the above results.

The rate constant, K_2 varied with the acid used as shown in Table I and its decrease is as follows :

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[6] A. W. Thomas, R. D. Vartanian : J. Am. Chem. Soc., **57**, 4 (1935).

[7] J. Bugosh : J. Phys. Chem., **65**, 1789 (1961).

[8] G. Kortüm, W. Vogel, K. Andrussow : "Dissociation Constants of Organic Acids in Aqueous Solution," IUPAC Section of Analytical Commission on Electrochemical Data, (1961), Butterworths, London.

Table I. Apparent Rate Constant, K_2, of the Reaction between DAHG and Acid. (0.50 g. of DAHG and 200 ml. of acid)

Acid	K_2 ($\times 10^3$ equiv./L.g.min.)		
	30°	38°	48°
Salicylic acid	0.49	1.50	4.98
Formic acid	0.38	1.10	3.08
Trichloroacetic acid	0.31	0.86	2.74
Monochloroacetic acid	0.14	0.44	1.32

salicylic acid>formic acid>trichloroacetic acid>monochloroacetic acid. This decreasing tendency cannot be explained on the basis of acid strength, diffusibility of acid, or general acid-base catalysis. It was suggested, in previous papers,[1,2] that not only the kind of anion, but also the interaction of both properties of the anion and of the sample of DAHG was an important factor having influence on the rate of reaction between DAHG and inorganic acid. Clay and Thomas[9] observed that when "hydrous alumina," a substance similar to aluminum hydroxide gel in physicochemical properties, was dissolved in a certain acid, *e.g.*, hydrofluoric acid, phosphoric acid, or phosphorous acid, the rate of reaction was influenced by the anion of the acid, and concluded that the effect of anion on the rate of dissolution of hydrous alumina was a specific property of that anion and was not applicable to any generalization, giving an explanation based on the coordination structure of the hydrous oxide and the formation of a complex at the solid-liquid interface. Considering from these facts, further investigations should be made in order to know the reason why the rate constant differs with the acid used.

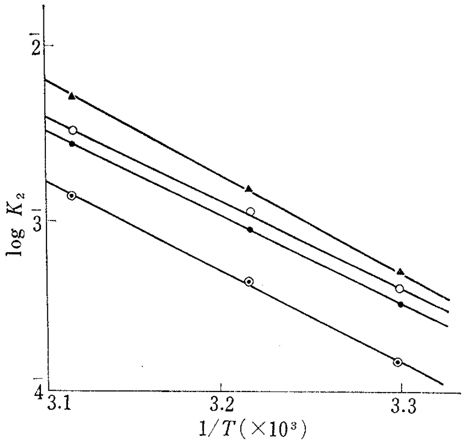

Fig. 5. Temperature Dependence of Apparent Rate Constant under 0.50 g. of DAHG and 200 ml. of 0.01*N* Acid

—▲— Salicylic acid
—○— Formic acid
—●— Trichloroacetic acid
—⊙— Monochloroacetic acid

Temperature dependence of the rate constant, K_2, is shown in Fig. 5 where T is the temperature in °*K*, and the estimated values of apparent activation energy are listed in Table II. These values ware almost 23,000~25,000 calories and were in neighbor of the values obtained in previous paper.[1~3] It follows as a result that the reaction between DAHG and organic acid is also chemically controlled.

Final Stage of the Reaction

This stage corresponds to the reaction in

Table II. Activation Energy, E_A, of the Reaction between DAHG and Acid

Acid	E_A(kcal/mol.)	Acid	E_A(kcal/mol.)
Salicylic acid	24.7	Trichloroacetic acid	23.5
Formic acid	22.6	Monochloroacetic acid	23.2

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[9] J.P. Clay, A.W. Thomas: J. Am. Chem. Soc., **60**, 2384 (1938).

the higher pH region than about 4. At this stage, the increase of aluminum ion was ceased apparently as shown in Fig. 1, because the equilibrium in polynuclear complex system between aluminum and the hydroxyl group (or ion) might be established.

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Summary

Reaction between DAHG and organic acid, *i.e.*, salicylic acid, trichloroacetic acid, monochloroacetic acid, or formic acid, was examined and the following results were obtained.

1. Three stages of the reaction, *i.e.*, the initial, the main, and the final stages, were observed with the progress of dissolution of DAHG in acid.
2. The initial stage is concerned with the rapid increase of pH, which was considered to be due primarily to the adsorption of acid by DAHG and also to the dissolution of aluminum ion on the surface of DAHG.
3. The rate of dissolution of DAHG at the main stage was in accordance with equation (2).
4. The order of the reaction with respect to the hydrogen ion was influenced by the dissociation constant.
5. The effect of anion on the apparent rate constant, K_2, was considered to be a specific property of that anion and not applicable to any generalization.
6. The estimated activation energy was 23,000~25,000 calories, indicating that the reaction between DAHG and organic acid might be chemically controlled.
7. At the final stage, corresponding to the reaction in the higher pH region than about 4, the increase of aluminum ion was ceased apparently.

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