to give 0.22 g of VII as colorless needles, mp 227—228°. IR (nujol) cm^{-1}: 3130, 1660. NMR ($CDCl_3$) τ: 3.1—2.2 (4H, m, aromatic protons), 2.58 (5H, s, C_6H_5), 2.36 (1H, s, C_3-H), 1.45 (1H, broad, NH). *Anal.* Calcd. for $C_{16}H_{11}ON_3S$: C, 65.50; H, 3.78; N, 14.32. Found: C, 65.04; H, 3.97; N, 14.17.

Reaction of 2-Methyl-4-chloro-5(*o*-aninophenylthio)-3(2*H*)-pyridazinone (VIII) with 10% Sodium Hydroxide——1.0 g of VIII was heated in 20 ml of 10% NaOH at 150° for 50 hr. After cooling, the orange crystals precipitated were collected by filtration, washed well with H_2O and taken up with $CHCl_3$.

The insoluble substance was recrystallized from DMF to give 0.2 g of 2-methyl-10*H*-benzo(*b*)pyridazino-(4,5-*e*)(1,4)thiazine-1(2*H*)-one (X) as orange needles, mp 300° (decomp.), identical in IR and NMR spectra with an authentic sample.[7] The soluble part in $CHCl_3$ was concentrated and the residue was recrystallized from EtOH to give 0.4 g of 3-methyl-10*H*-benzo(*b*)pyridazino(4,5-*e*)(1,4)thiazine-3(4*H*)-one (IX) as orange needles, mp 216—217°, identical in IR and NMR spectra with an authentic sample.[7]

The alkaline mother liquor was acidified with dil. HCl. The precipitated solid was collected and recrystallized from MeOH to give 0.15 g of 2-methyl-4-hydroxy-5(*o*-aminophenylthio)-3(2*H*)-pyridazinone (XI) as colorless needles, mp 186°. IR (nujol) cm^{-1}: 3460, 3360, 1620. NMR (DMSO-d_6) τ: 3.30 (1H, s, C_3-H). *Anal.* Calcd. for $C_{11}H_{11}O_2N_3S$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.14; H, 4.71; N, 16.98.

After removal of XI, the acidic solution was extracted with $CHCl_3$. The $CHCl_3$ extract was concentrated to give 0.05 g of 2-methyl-4(*o*-aminophenylthio)-5-hydroxy-3(2*H*)-pyridazinone (XII) as colorless prisms, mp 167—169°. IR (nujol) cm^{-1}: 3350, 3250, 1620. NMR (DMSO-d_6) τ: 2.30 (1H, s, C_3-H). *Anal.* Calcd. for $C_{11}H_{11}O_2N_3S$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.07; H, 4.82; N, 16.50.

The aqueous solution was concentrated to dryness under reduced pressure and the residue was recrystallized from $CHCl_3$ to give 0.04 g of 4-chloro-5-hydroxy-3(2*H*)-pyridazinone (XIII) as colorless needles, mp 243—244°, identical in IR and NMR spectra with an authentic sample.[8]

Thermal Cyclization of XI and XII to IX and X——a) 10 mg of XI was heated at 250° for 5 min without solvent. After cooling, the reaction mixture was recrystallized from MeOH to give 1 mg of IX as orange needles, mp 216°, identical in IR spectrum with the specimen obtained above.

b) 10 mg of XII was heated at 250° for 3 min without solvent. After cooling, the reaction mixture was recrystallized from MeOH to give X as orange needles, mp 300° (decomp.), identical in IR spectrum with the specimen obtained above.

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Influence of Operational Variables on Vibro-milling of Silica Sands

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Vibro-milling is much more effective than ball-milling for production of fine powders and practically used in the industrial field. But the detailed mechanism of vibro-milling has not been clarified yet.

In this paper, influence of operational variables on the rate of an increase of the surface area of silica sands by vibro-milling was investigated.

Experimental

The material used was silica sands (Type 3) purchased from Kokusan Kagaku Co., whose true density was 2.65 g/cm^3.

The balls used were ceramic balls of true density of 2.35 g/cm^3 and of diameter between 1.4 cm and 3.0 cm, ceramic balls of true density of 3.65 g/cm^3 and of diameter between 1.0 cm and 4.0 cm, stainless steel balls of true density of 8.29 g/cm^3 and of diameter of 0.5 cm and stainless steel balls of true density of 7.50

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[1] Location: *1-5-8, Hatanodai, Shinagawa-ku, Tokyo.*

g/cm^3 and of diameter of 1.3 cm. Various amounts of balls and silica sands were inserted in a stainless steel mill in capacity of 3100 ml and the mill was vibrated in amplitude of 5 mm and in frequency between 200 cpm and 800 cpm. The surface area of a vibro-milled sample was measured by the air permeability method.[2]

Result and Discussion

The rate of an increase of the surface area of silica sands decreased gradually with the lapse of the vibro-milling time. But at the first stage of vibro-milling, linear relation was applied between the surface area of silica sands and the vibro-milling time (Fig. 1). It was reported in the previous paper that equation (1) applied well to ball-milling of thirty-two kinds of organic and inorganic powders.

$$dS/dt = k_1 \exp(-k_2 S) \qquad (1)$$

S; The surface area of the sample ball-milled for t hours. Parameter k_1 is identical with dS/dt for the sample whose surface area is negligibly small. Parameter k_2 was considered to be concerned in a decrease of dS/dt due to coherency of particles caused by an increase of the surface area by ball-milling. The value of k_2 for ball-milling of silica sands was very small.[3] Probably k_2 for vibro-milling of silica sands is very small and the tangent of the straight line obtained by the plot of the surface area of silica sands versus vibro-milling time, k, is identical with k_1 at the first stage of vibro-milling.

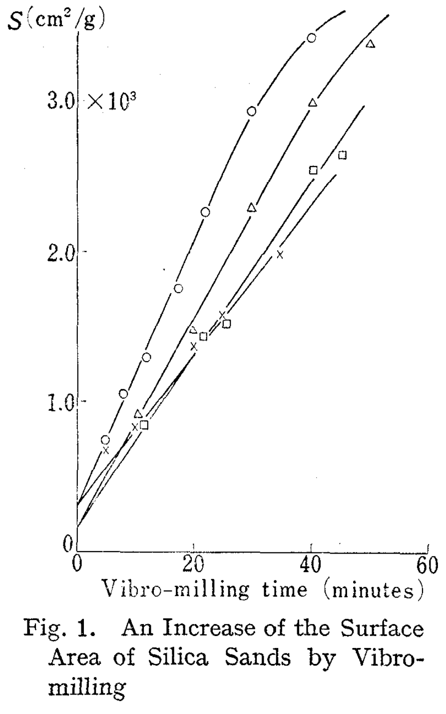

Fig. 1. An Increase of the Surface Area of Silica Sands by Vibro-milling

frequency of a vibro-mill; 650 cpm
stainless steel balls; $\rho_b=7.50$, $d_b=1.3$ cm, $J_b=0.63$
○: $J_s=0.31$, ×: $J_s=0.61$
ceramic balls
□: $\rho_b=3.65$, $d_b=4.0$ cm, $J_b=0.22$, $J_s=0.062$
△: $\rho_b=2.35$, $d_b=1.5$ cm, $J_b=0.34$, $J_s=0.062$

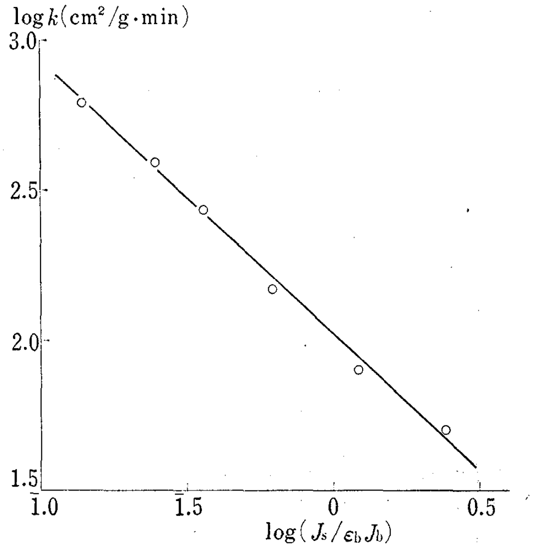

Fig. 2. Influence of the Apparent Volume of Silica Sands inserted in a Mill on k

frequency of a vibro-mill; 650 cpm
stainless steel balls; $\rho_b=7.50$, $d_b=1.3$ cm, $J_b=0.63$

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2) E. Suito, M. Arakawa, and M. Takahashi, *Kogyo Kagaku Zasshi*, **59**, 307 (1956).
3) A. Ikekawa, K. Imagawa, T. Omori, and N. Kaneniwa, *Chem. Pharm. Bull.* (Tokyo), **19**, 1027 (1971).

1) Influence of the Apparent Volume of Silica Sands inserted in a Mill on Parameter *k*

The ratio of the apparent volume of the sample in a mill in loose packing to the capacity of a mill, J_s, is represented by equation (2), where ε_s is the porosity of the sample in loose packing, W_s is the total weight of the sample in a mill, ρ_s is the true density of the sample and V_m is the capacity of a mill.

$$J_s = W_s/\rho_s(1-\varepsilon_s)V_m \qquad (2)$$

The ratio of the apparent volume of balls in a mill in loose packing to the capacity of a mill, J_b, is represented by equation (3), where ρ_b is the true density of the balls, ε_b is the porosity of balls in loose packing and W_b is the total weight of the balls in a mill.

$$J_b = W_b/\rho_b(1-\varepsilon_b)V_m \qquad (3)$$

Then, the ratio of the apparent volume of the sample in loose packing to the volume of the space between balls in a mill is equal to $J_s/\varepsilon_b J_b$. In case of ball-milling of sulfadimethoxine and white alundum, k_1 was small when $J_s/\varepsilon_b J_b$ was larger than 1.0.[4] The porosity of the powder of large particles in loose packing is approximately equal to 0.4, and the porosity increases and approaches to 1.0 with a decrease of the particle size.[5] Here, ε_b is assumed to be 0.4 and ε_s is assumed to be 0.6. In case of vibro-milling of silica sands, k was approximately inversely proportional to the 0.9 th power of J_s and apparent difference was not observed between the relation of k to J_s in case of $J_s/\varepsilon_b J_b$ below 1.0 and the relation in case of $J_s/\varepsilon_b J_b$ above 1.0 (Fig. 2).

2) Influence of J_b on *k*

When J_s was constant, k was proportional to J_b, as shown in Fig. 3. When $J_s/\varepsilon_b J_b$ was constant, k was proportional to the 0.16 th power of J_b. In this case, equation (4) is applied.

$$J_b^{0.16}(J_s/\varepsilon_b J_b)^{-0.90} = (\varepsilon_b/J_s)^{0.90} J_b^{1.06} \qquad (4)$$

It is considered from Fig. 3 and equation (4) that k is approximately proportional to J_b.

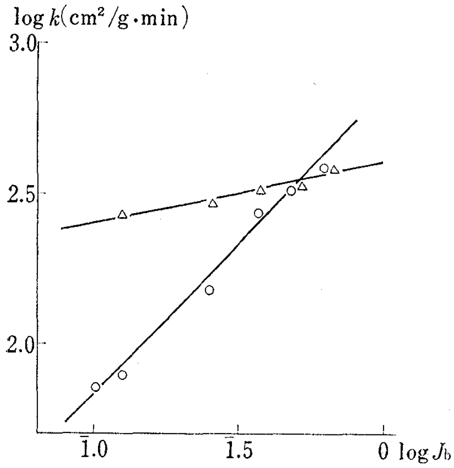

Fig. 3. Influence of J_b on k

frequency of a vibro-mill; 650 cpm
stainless steel balls; ρ_b=7.50, d_b=1.3 cm
○: J_s=0.062, △: $J_s/\varepsilon_b J_b$=0.25

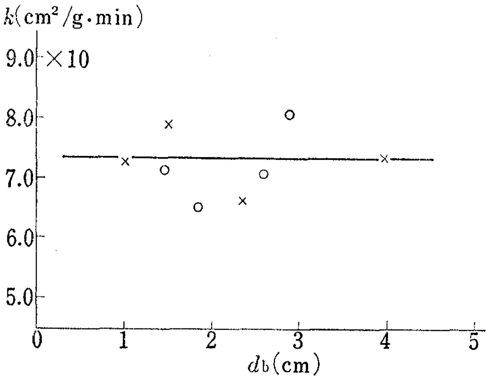

Fig. 4. Influence of the Diameter of Balls on k

frequency of a vibro-mill; 650 cpm, ceramic balls; J_s=0.062

○: ρ_b=2.35, J_b=0.34
×: ρ_b=3.65, J_b=0.22

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3) Influence of the Diameter of Balls on *k*

In case of vibro-milling with balls of an equal size, *k* was influenced little by the diameter of balls, as shown in Fig. 4. When the balls of true density of 2.35 g/cm³ and of diameter of 1.5 cm were mixed with the balls of diameter of 2.5 cm in the ratio by weight of 1: 2 or 2: 1 and the other conditions were the same as those in Fig. 4, the values of *k* were 5.0×10 cm²/g·min and 4.0×10 cm²/g·min, respectively, and smaller than the values in Fig. 4 in case of vibro-milling with balls of an equal size.

4) Influence of the true Density of Balls on *k*

Silica sands were vibro-milled in a mill containing 1.5 kg of stainless steel balls of true density of 7.50 g/cm³ or 8.29 g/cm³ and of diameter of 1.3 cm or 0.5 cm, respectively, or 1.5 kgs of ceramic balls of true density of 2.35 g/cm³ or 3.65 g/cm³ and of diameter of 1.5 cm. The values of *k* in case of J_b of 0.34 were obtained by multiplying *k* by $0.34/J_b$. As shown in Fig. 5, $0.34\,k/J_b$ was proportional to the true density of balls.

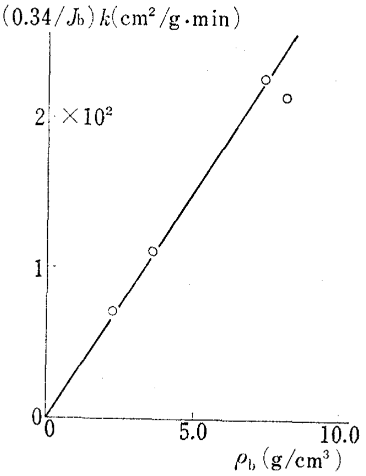

Fig. 5. Influence of ρ_b on *k*

frequency of a mill; 650 cpm, $J_s=0.062$

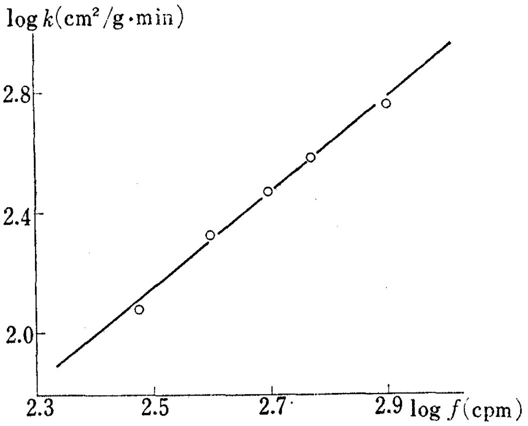

Fig. 6. Influence of the Frequency of a Vibro-mill, *f*, on *k*

stainless steel balls; $\rho_b=7.50$, $d_b=1.3$ cm, $J_b=0.63$, $J_s=0.062$

5) Influence of the Frequency of a Vibro-mill on *k*

As shown in Fig. 6, *k* was proportional to the 1.6 th power of the frequency of a vibro-mill.

It was shown from the above findings that *k* was represented by equation (5), where *f* was the frequency of a vibro-mill and *K* was a parameter dependent on physical and chemical properties of a sample and so on.

$$k = Kf^{1.6}\rho_b \cdot J_b/J_s^{0.9} = Kf^{1.6}J_s^{-0.1}(\rho_b \cdot J_b/J_s) \tag{5}$$

In the previous paper, in case of ball-milling of sulfadimethoxine and white alundum, k_1 was represented by equation (6) when J_b was between 0.15 and 0.45 and the revolving velocity of a mill was constant.

$$k_1 = K'(J_b^{\alpha'}J_s^{-\beta'})(\rho_b J_b/J_s)^{\gamma} \tag{6}$$

When N/N_c was 0.7 (*N*; the revolving velocity of a mill, N_c; the revolving velocity of a mill when the gravitational force of balls is equal to the centrifugal force given to balls by the revolution of a mill), α' and γ were influenced little by physical and chemical properties of a sample and α' was between 0.8 and 1.1 and γ was approximately 1.0. The value of β' for sulfadimethoxine was 0.4 and the value for white alundum was 0.6.[4] Tanaka reported that the rate of an increase of the surface area by crushing was proportional to the product of

P_c by P_σ, where P_c was the probability of collision between balls and powder particles and P_σ was the probability for powder particles to be crushed by the collision with balls.[6] In the previous paper, $J_b^{\alpha'} J_s^{-\beta'}$ was considered to be related to P_c and $(\rho_c \cdot J_b/J_s)^{\gamma}$ was considered to be related to P_σ.[4] Probably, in equation (5), $\rho_b \cdot J_b/J_s$ is related to P_σ and $J_s^{-0.1}$ is related to P_c, when f is constant. The probability of collision between balls and powder particles is considered to be very high in case of vibro-milling.

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UDC 547.92.057 : 591.05

Marine Sterols. III.[1] Synthesis of Asterosterol, a Novel C_{26} Sterol from Asteroids

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In the preceding paper we reported isolation of asterosterol, a minor C_{26} sterol from the asteroid *Asterias amurensis* and proposed the structure of 22-*trans*-24-nor-5α-cholesta-7,22-dien-3β-ol from spectral data.[1] This sterol was also found in trace amounts in other asteroids and japanese holothurian, *Stichopus japonicus*.[3] Recently, Nomura, Barbier and co-workers suggested occurrence of asterosterol in the tunicate *Halocynthia roretzi*.[4] We could not detect this sterol in another japanese tunicate, *H. aurantium* though it contained 4.4% of 22-*trans*-24-norcholesta-5,22-dien-3β-ol (IV). We now confirm the structure of asterosterol by synthesis through Wittig reaction.

The 20S aldehyde (I) obtained from 5,6-dihydroergosterol acetate[5] was treated in hexane at room temperature with the ylide generated from isobutyltriphenyl phosphonium bromide and butyl lithium and gave a mixture of 22-*trans* and -*cis* isomers (IIa and IIIa) in about 1: 1 ratio (60%). The configuration at C-20 was confirmed as R by ozonolysis of the mixture which gave only the starting 20S aldehyde (I).[6] At higher temperature, I gave mainly IIa and appreciable amount of by-product. It was shown to be 20S isomer of IIa from the fact that Wittig reaction of 1: 1 mixture of 20S and 20R aldehyde gave these two compounds in the same ratio. It showed retention time relative to 20R isomer (IIa) of 1.16 by gas–liquid chromatography (GLC) on 1.5% SE-30 column (1.8 m) at 250°. Interestingly, 20S-22-dehydrocholesterol was reported to show shorter retention time than natural 20R isomer.[7]

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