

Controlled Growth of Monodisperse Silica Spheres in the Micron Size Range¹

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A system of chemical reactions has been developed which permits the controlled growth of spherical silica particles of uniform size by means of hydrolysis of alkyl silicates and subsequent condensation of silicic acid in alcoholic solutions. Ammonia is used as a morphological catalyst. Particle sizes obtained in suspension range from less than 0.05 μ to 2 μ in diameter.

In many experimental studies which involve the use of colloidal suspensions of matter in form of hydrosols and aerosols, it would be desirable to have the suspended phase consisting of homogeneous particles of uniform shape and size. Such monodisperse particulate suspensions offer many experimental and theoretical advantages. They not only facilitate easy calibration procedures for analytical equipment, but also simplify data reduction, evaluation and interpretation of experiments designed to elucidate physicochemical properties or physiopathological effects of colloids and aerosols. The results would no longer be biased by parameters of size and shape distributions.

Some monodisperse suspensions of particles in the colloidal size range are available in form of spheres of organic high polymers (1). In the aerosol field, they are primarily used as model substances and for calibration purposes. Generators producing monodisperse particle clouds from soluble or volatile materials are used in various aerosol studies

and have been described in the literature (2). However, no successful attempt has been made to generate monodisperse suspensions of silica particles. A commercial form of highly disperse silica produced by combustion of silicon tetrachloride in a hydrogen torch (3) consists of primary silica spheres of sizes below 0.1 μ , but they are aggregated to coarse and irregular clusters which cause a very poorly defined state of suspension.

The following investigation was made to explore the possibilities of producing monodisperse suspensions of silica spheres in the colloidal size range. Such material can be used in both hydrosol and aerosol studies. It will be of particular interest to investigators in the medical field because of its known cytotoxicity and inhalation hazard.

The experiments were based on the fact that silica particles can be produced by chemical reaction of tetraesters of silicic acid (tetraalkyl silicates) with certain solutions. In 1956, Kolbe (4) described the formation of silica particles by reacting tetraethyl silicate in alcoholic solution with water in the presence of certain bases. With very pure reactants he observed in several cases a slowly proceeding reaction leading to the formation of uniform spherical silica

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particles. In an attempt to duplicate these findings, many of our experiments resulted in gel formation and only in a few cases did the electron micrographs show particles of ellipsoidal shape and a size range near 0.08μ . Then, a systematic study of the reaction parameters was made and after some drastic changes of the experimental conditions, quasi-monodisperse suspensions of silica spheres of sizes up to 2μ were finally obtained within less than an hour and the reaction no longer required extremely pure reactants.

EXPERIMENTAL

Reagents

Methanol, ethanol, *n*-propanol and *n*-butanol used as solvents were of analytic reagent quality.

Tetraesters of silicic acid (tetraalkyl silicates) were either supplied in technical grade (methyl, ethyl) or prepared by reacting silicon tetrachloride and alcohol (*n*-propyl, *n*-butyl, *n*-pentyl). All esters were redistilled before used in the experiments.

Ammonia (anhydrous, 99.99%) from a tank was passed through a drying column filled with sodium hydroxide pellets and bubbled through the alcohol at 0°C . Concentrations obtained were about $8 M$ in methanol, $5 M$ in ethanol, $3 M$ in *n*-propanol, *n*-butanol and *n*-pentanol.

Ammonium hydroxide, $26^{\circ}\text{B}\acute{\text{e}}$., U.S.P., was used as supplied. Titrations indicated an ammonia concentration of $14.2 M$.

Instruments

Electron microscopes Zeiss EM 9 and Philips EM 100 B and particle size analyzer Zeiss TGZ 3 were used.

Procedures

Throughout the investigation, ammonia was used as the catalyst causing the formation of spherical particles. In many cases, it was applied by adding saturated alcoholic solutions of ammonia to the reaction vessel. In other cases, particularly when high ammonia concentrations were desired, saturated ammonium hydroxide solution was used and the water content was taken into account.

At the beginning of each series of tests, pure alcohol or alcohol mixtures, saturated alcoholic ammonia solution, ammonium hydroxide, and water were mixed in Erlenmeyer flasks with ground stoppers or in rubber sealed injection bottles in the desired concentrations of ammonia and water. Actual ammonia contents were measured by withdrawing small samples and titrating with $1 N$ hydrochloric acid. Total water contents were computed by adding up the fractional amounts introduced by the components. Subsequently the alkyl silicate was added and the flasks were mounted either on a shaker or in a water bath under ultrasonic vibration. Some tests were made while the solution was agitated by a magnetic stirrer. Either way of agitation was effective and kept the particles in suspension after they had formed.

The total amount of solution in each test varied between 50 and 110 ml. One large scale experiment with 2 liters of solution gave the same result as a test with 80 ml of a solution containing the same concentrations of solutes.

Except for the initial exploratory tests at low concentrations, the condensation reaction generally started within 10 min. This could easily be observed, because, after an invisible hydrolytic reaction forming silicic acid, the condensation of the supersaturated silicic acid was indicated by an increasing opalescence of the mixture starting 1–5 min after adding the tetraalkyl silicate. After this initial phase, the transition to a turbid white suspension occurred regularly within a few more minutes.

As a standard procedure, samples for electron microscopic investigation were taken after 120 min, although a series of samples taken at different times from the same test solution indicated that particles sometimes reach their final size after about 15 min. All sampling for size determination was done by dipping electron microscopic carrier grids covered with Formvar films into the suspension, subsequently putting them on filter paper to remove excessive solution from the grid, and taking electron micrographs of the particles retained on the film.

Random micrographs of the samples com-

prising between 100 and 1000 particles were evaluated by means of a semiautomatic particle size analyzer. The cumulative distribution curve of the particles was recorded

in logarithmic size increments and plotted on log-probability paper. The median projected diameter and, in some cases, the approximate logarithmic standard deviation were taken from the graph.

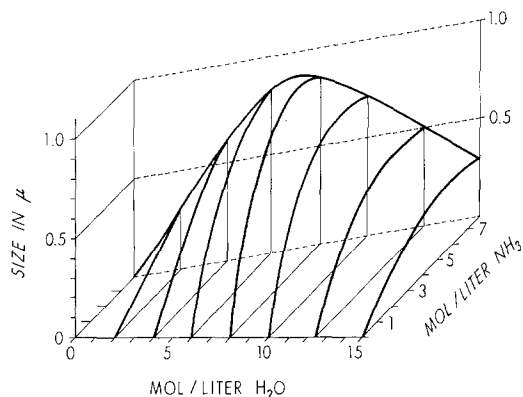


FIG. 1. Final particle sizes as obtained by reacting 0.28 mole/liter of tetraethyl silicate with various concentrations of water and ammonia in ethanol.

RESULTS AND DISCUSSION

For the different alcoholic solvents, reaction rates were fastest with methanol, slowest with *n*-butanol. Likewise, final particle sizes obtained under comparable conditions were smallest in methanol and biggest in *n*-butanol. However, there was a tendency toward wide size distributions with the higher alcohols. Methanol-butanol mixtures in a ratio of 1:1 provided more uniform big particles.

A similar relationship with regard to reaction rates and particle sizes was found when comparing results with different alkyl silicates. Fastest reactions (less than 1 min) and smallest sizes (less than 0.2 μ)

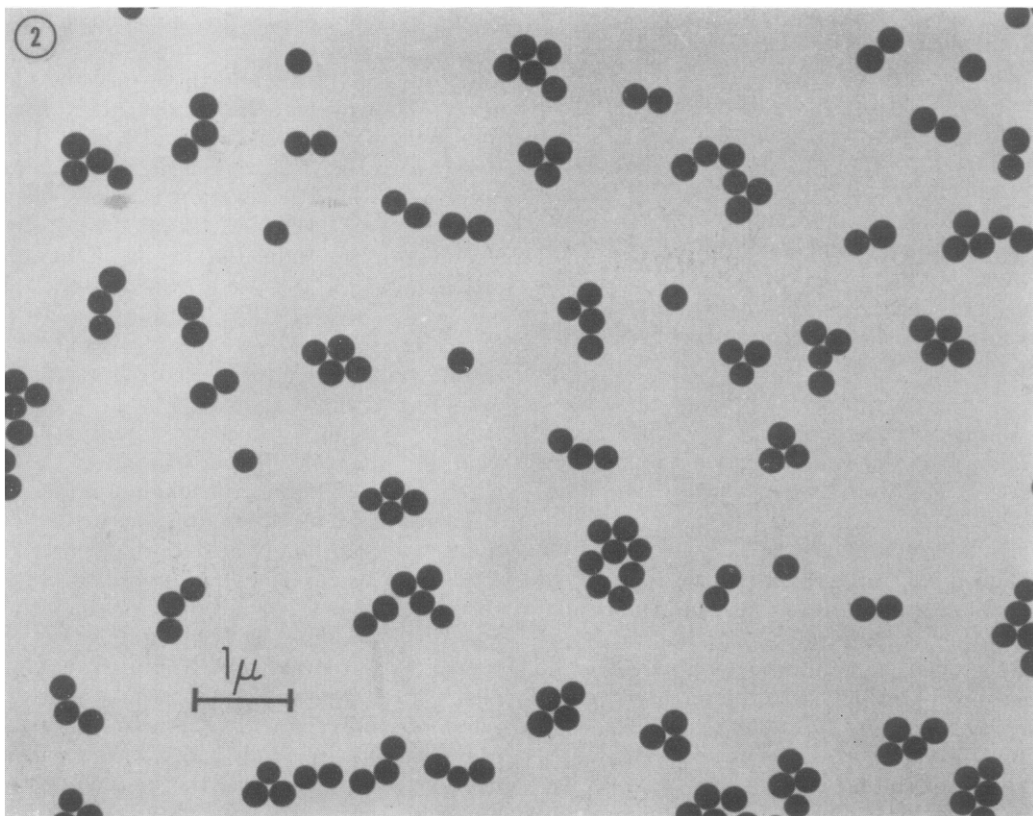


FIG. 2. Electron micrograph of a sample of silica spheres obtained in the ethanol-ethyl ester system.

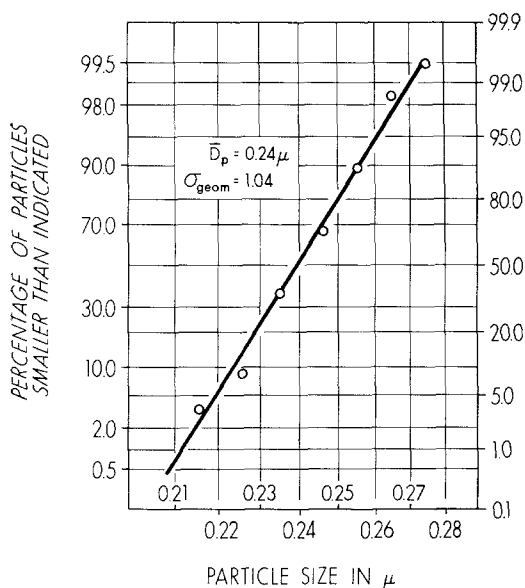


FIG. 3. Log-probability plot of the cumulative size distribution curve of the sample shown in Fig. 2.

were observed with tetramethyl ester, while tetrapentyl ester reacted slowly (up to 24 hours for quantitative condensation) and produced big particles which, in *n*-propanol and *n*-butanol, reached sizes somewhat scattered around 2 μ. More uniform particles were obtained in 1:3 mixtures of methanol-*n*-propanol.

A systematic investigation of the influence of different concentrations of water, ammonia and ester was made with the ethanol-ethyl ester system. The condensation rate depends strongly upon the water content of the system. In the absence of ammonia, the silica flocculated in irregularly shaped particles and no spheres could be observed under the electron microscope. Thus, ammonia apparently influenced the morphology, and created spherical particles whenever it was present during the reaction. An increase in ammonia concentration (up to 8 moles/liter) under otherwise constant experimental conditions caused larger particle sizes. Accordingly, the largest spheres were obtained when the reaction mixture was saturated with ammonia. When the water concentration under these conditions was varied, maximum particle size was obtained at water concentrations around 6

moles/liter, while different ester concentrations between 0.02 and 0.50 mole/liter had no significant influence on the particle size. The three-coordinate graph in Fig. 1 represents the general correlation between particle size, water, and ammonia concentration obtained with an ester concentration of 0.28 mole/liter. The actual particle sizes observed varied between 0.05 and 0.90 μ and were uniform in each test. Figure 2 shows an electron micrograph of a sample from this series, and Fig. 3 indicates the cumulative size distribution curve of the same sample as plotted on log-probability paper. The geometric standard deviation derived from the graph is 1.04. This value was quite typical for most of these tests. It indicates that only 5% of the particles differ from the median size by more than 8%.

The generation of particles larger than 1 μ could not be effected with the ethanol-ethyl ester system but required the use of esters of higher alcohols. Various tests with these esters indicated that, under comparable conditions, the condensation reaction slowed down with increasing molecular weight of the ester, while, at the same time, particles of larger size with a fair degree of uniformity were produced. The reaction could be further slowed down by using higher alcohols as solvents. In these cases, however, the median particle size and the spread of the size distribution increased simultaneously. Sometimes the samples also contained two distinctly different particle sizes. Thus, special precautions had to be taken to reduce these adverse effects. To achieve this, isothermal conditions (22°C) and homogeneous particle suspension maintained during the reaction by gentle agitation proved effective.

An extensive investigation was made with tetrapentyl ester. Particles were grown under various conditions by using different component concentrations and several alcohols or alcohol mixtures as solvents.

In the simple ethanol-pentyl ester system, at ester concentrations sufficiently low (≤ 0.2 mole/liter) to provide miscibility over the considered range of water concentrations (≤ 10 moles/liter), the results resembled the pattern given in Fig. 1.

Within this range, the ester concentrations (≥ 0.03 mole/liter) again had little influence on the final size of the particles, but the particles obtained in these tests were definitely bigger than those grown under comparable conditions from ethyl ester. The maximum values obtained for fairly uniform batches of particles were about 1.5μ in diameter. The sample shown in Fig. 4 was grown from 0.2 mole/liter of pentyl ester in a solvent saturated with ammonia and containing 5 moles/liter of water. The median particle size is 1.38μ as derived from the cumulative size distribution curve shown as a log-probability graph in Fig. 5. This graph indicates that the sample consists of two superimposed size distributions; the

more prominent one is close to a log-normal distribution having a geometric standard deviation of 1.08 and covering the upper size range. It comprises about 93% of the particles. This result is quite typical for most of the size distributions obtained in tests designed to produce particles of sizes bigger than 1μ .

At high pentyl ester concentrations, the ester formed a separate phase at the bottom of the reaction vessel, thus providing a substrate reservoir for the hydrolysis proceeding in the upper phase. In this way, continued particle growth up to sizes 3μ in diameter was effected, but apparently, the reservoir was also continuously supplying new condensation nuclei so that the particle

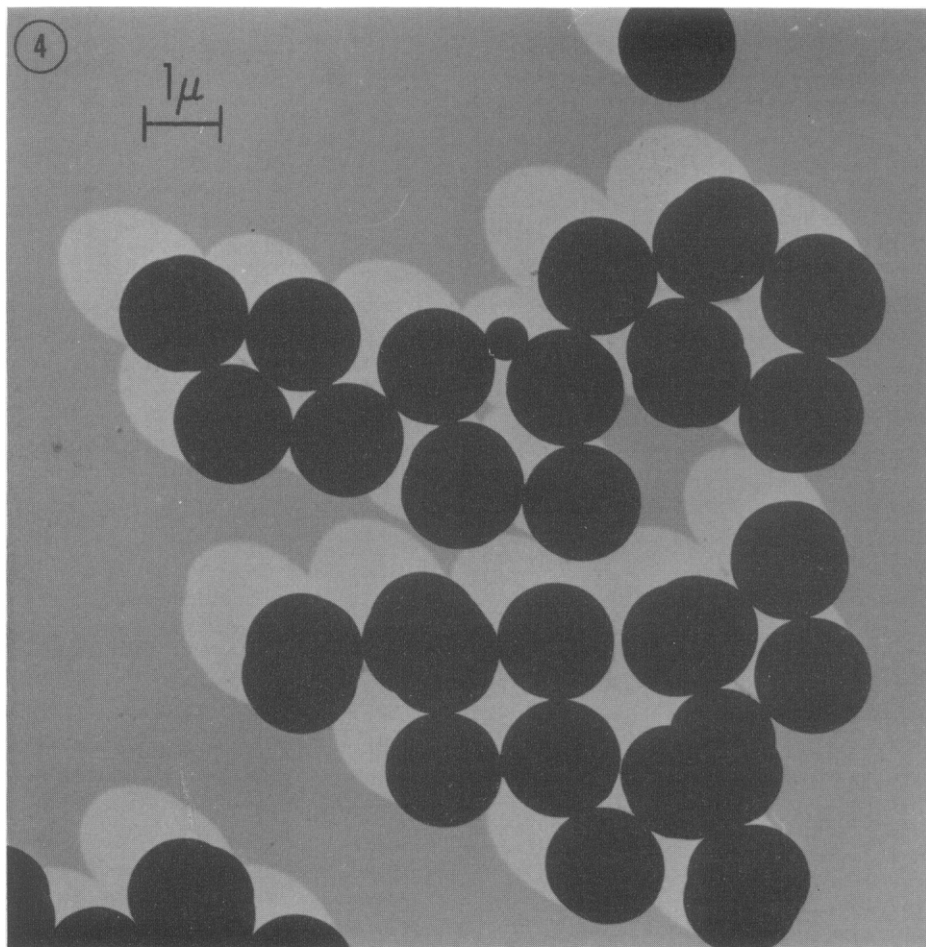


FIG. 4. Electron micrograph of a sample of silica spheres obtained in the ethanol-pentyl ester system.

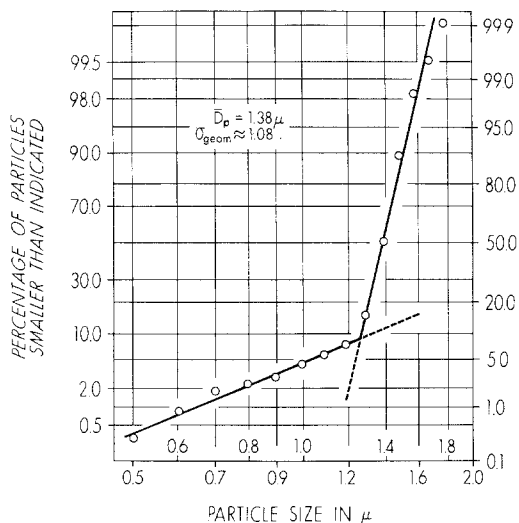


FIG. 5. Log-probability plot of the cumulative size distribution curve of the sample shown in Fig. 4.

sizes in the final dense suspension were no longer approximately uniform. Instead, the sizes were scattered in high count frequencies between values of 0.5 and 3 μ . Emulsifying the ester during the reaction by violent agitation did not significantly improve these results. Tests with higher alcohols or their mixtures with methanol proved to be more effective. While butanol gave particle populations of poor uniformity, the tests with propanol were satisfactory. Maximum particle sizes were obtained at an optimum water content of 5 moles/liter and at high concentrations of ammonia and ester. Under these conditions, median diameters were observed between 1.5 and 2 μ . The best growth of fairly uniform particles of 2 μ diameter was facilitated by using mixtures of methanol with butanol (1:1) and propanol (1:3) as solvents. Figure 6 shows

TABLE I
EXPERIMENTAL ARRANGEMENT, FINAL MEDIAN DIAMETER, AND GEOMETRIC STANDARD DEVIATION OF SILICA SPHERES

Components	Final pH	Test					
		1		2		3	
		\bar{D} (μ)	σ_{geom}	\bar{D} (μ)	σ_{geom}	\bar{D} (μ)	σ_{geom}
10 ml pentyl ester; 10 ml ammonium hydroxide (sat.); 50 ml propanol saturated with NH ₃	12.7	1.53	1.06	1.35	1.06	1.22	1.10
8 ml pentyl ester; 8 ml ammonium hydroxide (sat.)							
50 ml propanol-methanol (3:1) saturated with NH ₃	12.7	1.68	1.07	1.26	1.05	1.30	1.50
50 ml propanol saturated with NH ₃	12.6	1.57	1.07	1.21	1.07	1.35	1.45
6 ml pentyl ester							
6 ml ammonium hydroxide (sat.); 50 ml ethanol	11.8	1.10	1.07	0.42	1.03	0.99	1.09
5 ml ammonium hydroxide (sat.); 50 ml ethanol	11.6	0.57	1.06	0.64	1.14	0.42	1.06
4 ml ammonium hydroxide (sat.); 50 ml propanol-methanol (3:1)	11.4	0.60	1.03	0.63	1.08	0.64	1.10
4 ml pentyl ester							
4 ml ammonium hydroxide (sat.); 50 ml ethanol	11.6	0.29	1.02	0.36	1.05	0.44	1.03
4 ml ammonium hydroxide (sat.); 50 ml propanol-methanol (3:1)	11.5	0.44	1.04	0.66	1.05	0.64	1.06
3 ml ammonium hydroxide (sat.); 50 ml ethanol	11.4	0.25	1.08	0.25	1.06	0.27	1.12
2 ml ammonium hydroxide (sat.); 50 ml ethanol	11.3	0.05	1.07	0.08	1.05	0.08	1.05
2 ml ammonium hydroxide (sat.); 50 ml propanol-methanol (3:1)	11.2	0.11	1.06	0.17	1.07	0.20	1.06

a typical sample as obtained from 0.28 mole/liter tetrapentyl ester reacting with 4.5 moles/liter of water and 4.6 moles/liter of ammonia in a propanol-methanol mixture (3:1). The log-probability plot in Fig. 7 shows that about 20% of the particles are

smaller than indicated by a log-normal distribution relating to the median diameter of 1.93μ and the geometric standard deviation of 1.07.

Finally, a series of experiments was made under conditions which may be used for

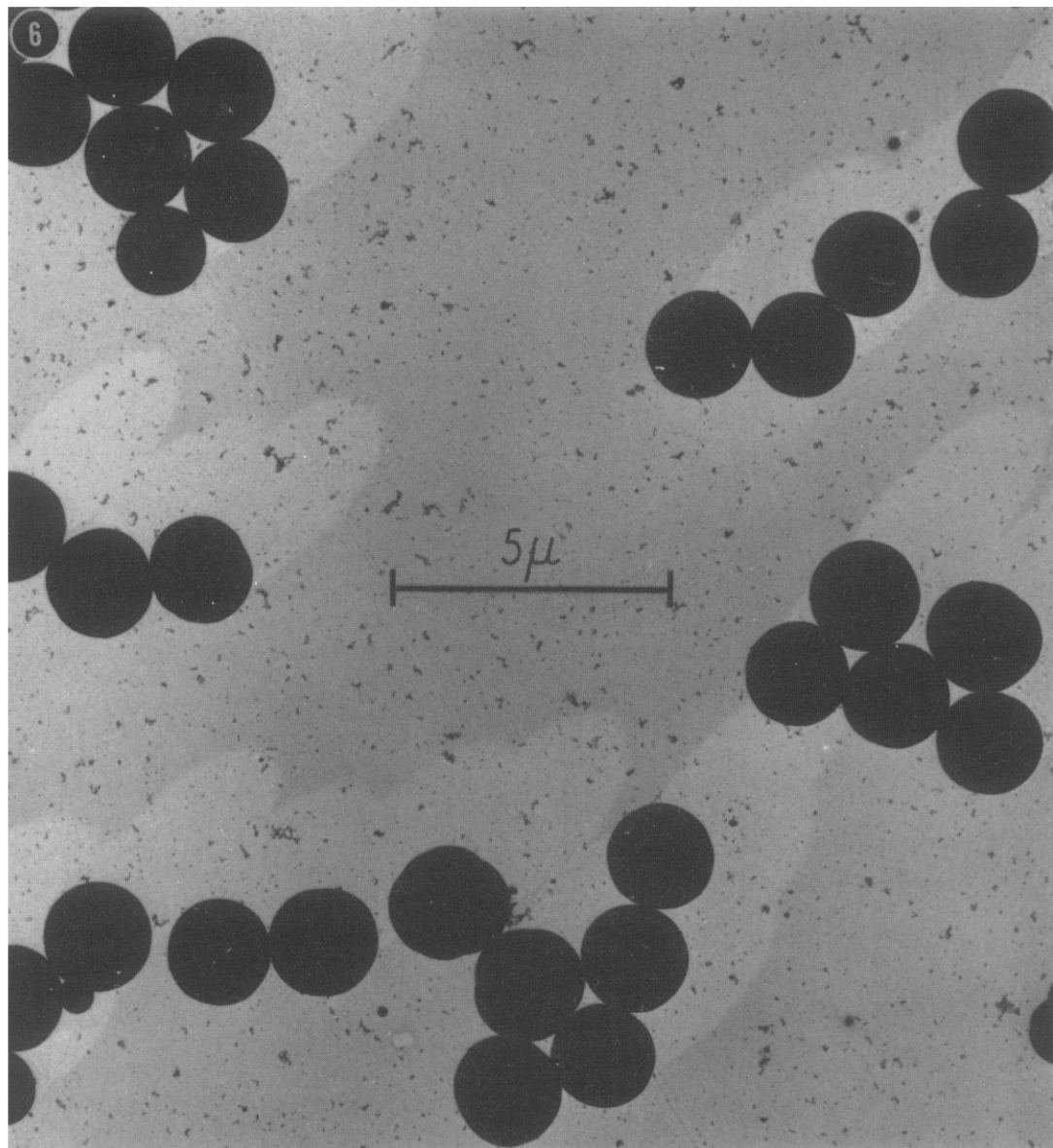


FIG. 6. Electron micrograph of silica spheres obtained by reacting tetrapentyl silicate with 4.5 moles/liter H_2O and 4.6 moles/liter NH_3 in a 3:1 propanol-methanol mixture.

standard procedures in the production of silica spheres of predetermined size in the range of 0.05–2 μ diameter. Table I lists the components for 11 different experimental

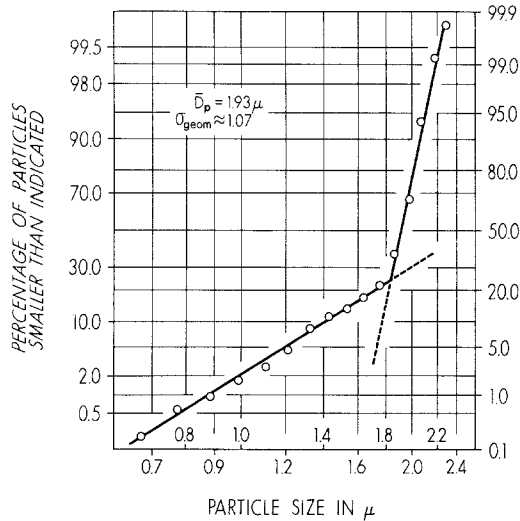


FIG. 7. Log-probability plot of the cumulative size distribution curve of the sample shown in Fig. 6.

arrangements and gives the final particle sizes obtained under these conditions in a number of tests repeated on different days with different reagents. The results indicate that the particle sizes are not precisely reproduced and, occasionally, an unusually high standard deviation of the size distribution is encountered. But, in general, a uniform particle size is predictable from the experimental conditions within a margin of about 30% and the geometric standard deviation of the size distribution remains below 1.10.

REFERENCES

1. BRADFORD, E., AND VANDERHOFF, J., *J. Appl. Phys.* **26**, 864 (1955).
2. FUCHS, N. A., AND SUTUGIN, A. G., In "Aerosol Science" C. N. Davies, ed. pp. 1-27. Academic Press, New York (1966).
3. WAGNER, E., AND BRÜNNER, H., *Angew. Chem.* **72**, 744 (1960).
4. KOLBE, G., "Das komplexchemische Verhalten der Kieselsäure," Dissertation, Jena (1956).