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PREDICTION OF CHEMICAL REACTION YIELD IN A MICROREACTOR AND DEVELOPMENT OF A PILOT PLANT USING THE NUMBERING-UP OF MICROREACTORS

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ABSTRACT

The chemical reaction yield was predicted by using Monte Carlo simulation. The targeted chemical reaction of a performance evaluation using the microreactor is the consecutive reaction. The main product P1 is formed in the first stage with the reaction rate constant *k1*. Moreover, the by-product P2 is formed in the second stage with the reaction rate constant *k2*. It was found that the yield of main product P1 was improved by using a microreactor when the ratio of the reaction rate constants became *k1/k2* >1. To evaluate the Monte Carlo simulation result, the yields of the main products obtained in three consecutive reactions. It was found that the yield of the main product in cased of *k1/k2* >1 increased when the microreactor was uesd. Next, a pilot plant involving the numbering-up of 20 microreactors was developed. The 20 microreactor units were stacked in four sets, each containing five microreactor units arranged. The maximum flow rate when 20 microreactors were used was 1×10^4 mm^3/s, which corresponds to 72 t/year. Evaluation of the chemical performance of the pilot plant was conducted using a nitration reaction. The pilot plant was found to capable of increasing the production scale without decreasing the yield of the products.

INTRODUCTION

Micromachining technologies have recently been applied to designing miniaturized devices for synthetic applications, i.e., microreactors (1,2). A microreactor is a device that enables chemical reactions to be performed on a micro-litre scale(3, 4). The potential advantages of using a microreactor, rather than a conventional reactor (batchwise in stirred vessels), include better control of reaction conditions, improved safety, and improved yield. “Better control of reaction conditions” refers to the ability to precisely control the temperature of the reactor, a direct result of the reactor's extremely high surface-to-volume ratio. The improved safety results from the reactor's extremely small size: if a reaction does 'run away' (i.e., exotherm out of control), then the resulting heat generation increase should not be a threatening amount. Improved yield has been reported in the following reactions: the Friedel-Crafts monoalkylation reaction (5), Grignard reaction (6), Sonogashira coupling reaction (7), etc. Even the production scale has been touched upon; some of the first examples to be released were polymerization (8) and nitroglycerin (9) using a pilot plant.

However, most past researches focused mainly on the experimental results. Moreover, the production scale was relatively small, and the number of stacked microreactors was not very large. Accordingly, the objectives of the present study are to predict the yield of chemical reactions when a microreactor is used and to develop a pilot plant using the numbering-up of 20 microreactors that can increase the production scale.

MONTE CALRO SIMULATION

To predict the conditions for improving reaction yield in a microreactor, the relationship between a chemical reaction and a molecular was analysed by Monte Carlo simulation. **Figure 1** shows the computational area of the Monte Carlo simulation for a microreactor with width L. The areas enclosing each particle, m^2 (where m is the side length of the computational square) were arranged in a two-dimensional area ($L \times L$). **Figure 2** shows the movement rule and the boundary condition governing the particles. A random number was generated every Δt seconds, and the particles were moved L/m by L/m with the

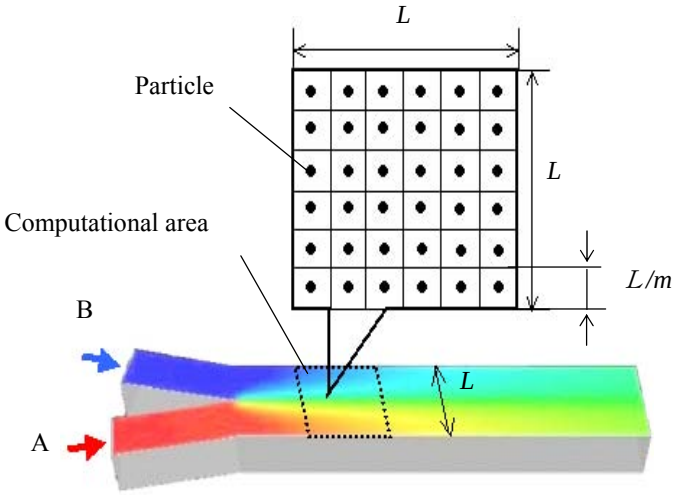


Fig.1 Computational area of Monte Carlo simulation

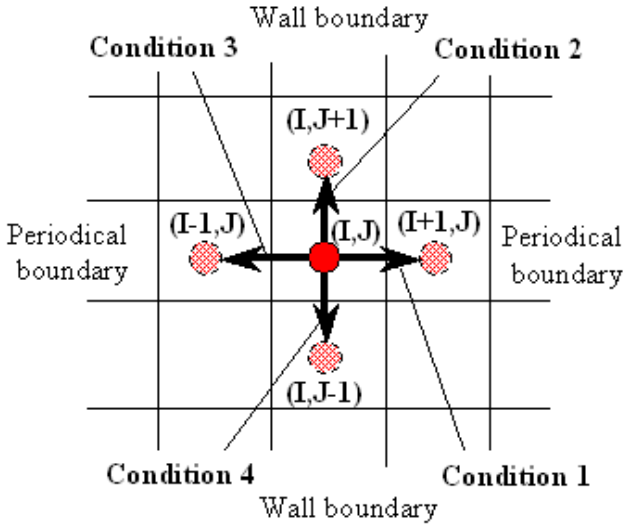


Fig.2 Movement rule of particles

movement rule given by Eqs. (1)–(4) below. After the integer part of the random number, *Irad*, was divided by four, the remainder was used for determining the moving direction of the particle at the position of (I,J)

Condition 1

$$\mathrm{MOD}(Irad,4)=0 \Rightarrow \mathrm{P(I,J)}\rightarrow\mathrm{P(I+1,\ J\ \ )} \quad (1)$$

Condition 2

$$\mathrm{MOD}(Irad,4)=1 \Rightarrow \mathrm{P(I,J)}\rightarrow\mathrm{P(I\ \ ,\ J+1)} \quad (2)$$

Condition 3

$$\mathrm{MOD}(Irad,4)=2 \Rightarrow \mathrm{P(I,J)}\rightarrow\mathrm{P(I\text{-}1,\ J\ \ )} \quad (3)$$

Condition 4

$$\mathrm{MOD}(Irad,4)=3 \Rightarrow \mathrm{P(I,J)}\rightarrow\mathrm{P(I\ \ ,\ J\text{-}1\ )} \quad (4)$$

where the MOD function returns the remainder from the division of the first argument by the sec- ond argument. The targeted chemical reaction in the microreactor is the consecutive reaction given by Eqs. (5) and (6):

$$\mathrm{A} + \mathrm{B} \xrightarrow{k1} \mathrm{P1} \quad (5),$$

$$\mathrm{P1} + \mathrm{B} \xrightarrow{k2} \mathrm{P2} \quad (6),$$

where A and B are reactants, P1 is the main product, P2 is the by-product, *k1* is the reaction-rate constant of the first stage, and *k2* is the reaction-rate constant of the second stage. Main product P1, mono-substitution, is formed in the first stage; by-product P2, di-substitution, is formed in the second stage.

As the initial condition for the Monte Carlo simulation, the particles of reactant-A and reactant-B (where the number of particles are $m^2/2$, respectively) were randomly arranged in the computational area ($L\times L$). When the particles of reactant-A collide n_1 times with the particles of reactant-B and form main product P1, reaction-rate constant *k1* is defined by Eq. (7). Moreover, when the particles of main product P1 collide n_2 times with the particles of reactant-B and become by-product P2, reaction-rate constant *k2* is defined by Eq. (8).

$$k1 = 1/(n1\,\Delta t) \quad (7)$$

$$k2 = 1/(n2\,\Delta t) \quad (8)$$

Moreover, non-dimensional Damkohler Number *Da*, namely, the ratio of the characteristic time of the molecular diffusion and the chemical reaction t_d/t_c, is defined as shown in Eqs. (9)–(11):

$$Da = t_d / t_c = m/2n \quad (9),$$

$$t_d = m\Delta t/2 \quad (10),$$

$$t_c = n1\,\Delta t \quad (11),$$

where t_d is the characteristic time of molecular diffusion, and t_c is the characteristic time of the chemical reaction.

PREDICTION OF CHEMICAL REACTION YIELD

Table 1 lists the conditions of Monte Carlo simulation in case of the ratio of reaction rate constants *k1/k2=3.* **Figure 3** shows the time series based Monte Carlo simulation in case of the ratio of reaction rate constants *k1/k2=3.* The normalized molar concentrations of reactant-A, reactant-B, the main product P1, and the by-product P2 are shown, respectively in Fig.3. After 2.5 seconds, the chemical reaction is finished. The yield Y1 of the main product P1was calculated as shown in Eq. (12):

$$Y1 = [P1] / ([A]+ [P1] +[P2]) \qquad (12)$$

where [A], [P1], and [P2] are the molar concentrations of reactant-A, the main product P1, and the by-product P2, respectively, at the end of the reaction.

Table 1 Conditions of Monte Carlo simulation

Channel width L [μm]	100
Division number m	24
Coefficient of molecular diffusion D [m^2/s]	10^{-9}
Collision number criterion n_1	25
Collision number criterion n_2	75
Ratio of reaction rate constants $k1/k2$	3
Time interval Δt [s]	8.7×10^{-3}
Number of steps	300

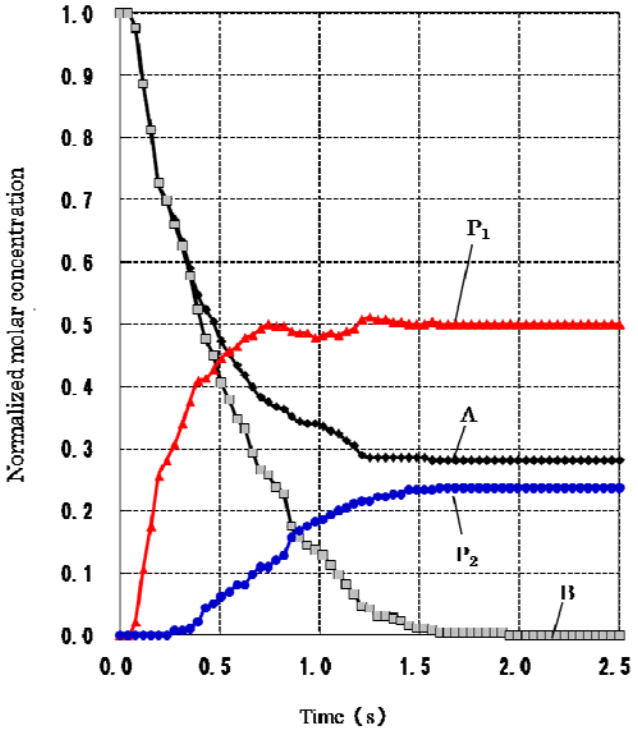


Fig.3 Time series based Monte Carlo simulation in case of the ratio of reaction rate constants *k1/k2=3*

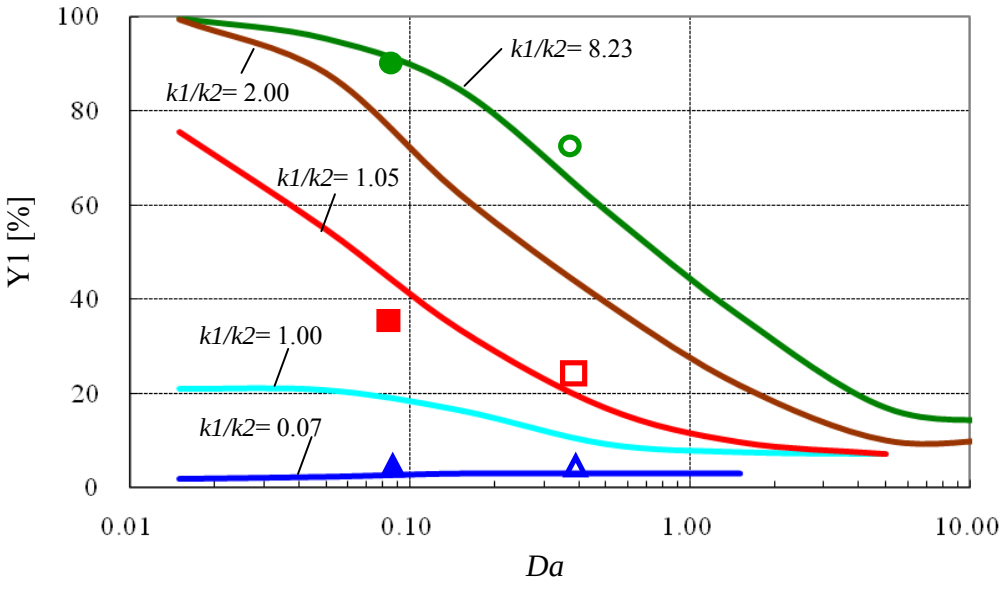


Fig.4 Relationship between the Damkohler Number *Da* and the yield of main product P1
● : Nitaration reaction by Microreactor, ○ : Nitration reaction by batch
■ : Hydride reduction by Microreactor, □ : Hydride reduction by batch
▲ : Grignard reaction by Microreactor, △ : Grignard reaction by batch

Da was varied from 0.01 to 10.0, and the ratio of the reaction-rate constants, *k1/k2*, (i.e., *n2/n1*) was varied from 0.1 to 10.0. **Figure 4** shows the relationship between *Da* and the yield Y1 of the main product P1. Using a microreactor instead of a conventional batch method corresponds to decreasing width *L*, that is, decreasing *Da*, as shown in Eq. (9). It was found that the yield Y1 of the main product P1 was improved by using the microreactor when $k1/k2 > 1$. On the other hand, it was found that the yield Y1 of the main product P1 was not improved by using the microreactor when $k1/k2 < 1$.

VALIDATION BY EXPERIMENT

To validate the Monte Carlo simulation results described above, experiments using either a microreactor or a conventional batch method were conducted. **Figure 5** shows an overview of our microreactor. The microreactor is divided into a lower case with two inlet fittings, an upper case with one outlet fitting, and a micro channel chip between the upper and the lower cases. The lower and upper cases are made of corrosion-resistant Hastelloy-C276. The thermocouple is set up in the neighborhood of channel walls neighborhood of the upper case. **Figure 6** shows the microchannel chip, which is made of quartz glass and which has a diameter of 42 mm. Two kinds of liquids flow (Reactant-A and Reactant-B) from the edge to the center in a multilayer state, and they mix in the gradually narrowing microchannel. The height of the channel is 150μm, and the minimum width of the channel is 250 μm (10).

Figure 7 shows a laboratory experimental setup using the conventional batch reactor. The conventional batch vessel containing reactant-A was placed in the constant-temperature bath, and reactant-B was added into the batch vessel as its contents were stirred.

Table 2 lists the details of the three kinds of consecutive reactions. **Table 3** lists the experimental results, namely, reaction rate constant *k1/k2* and yield of main product. The experimental results were agreement with the simulation results as shown with the symbols in Fig. 4 (11,12). As shown with the triangular symbols in the figure, in the case of the Grignard reaction, the yield of the main product was not improved when $k1/k2<1$. On the other hand, as shown by the squares and circles, in the case of reductive reaction of diisobutylaluminium hydride and nitration reaction, the yield was improved when $k1/k2>1$.

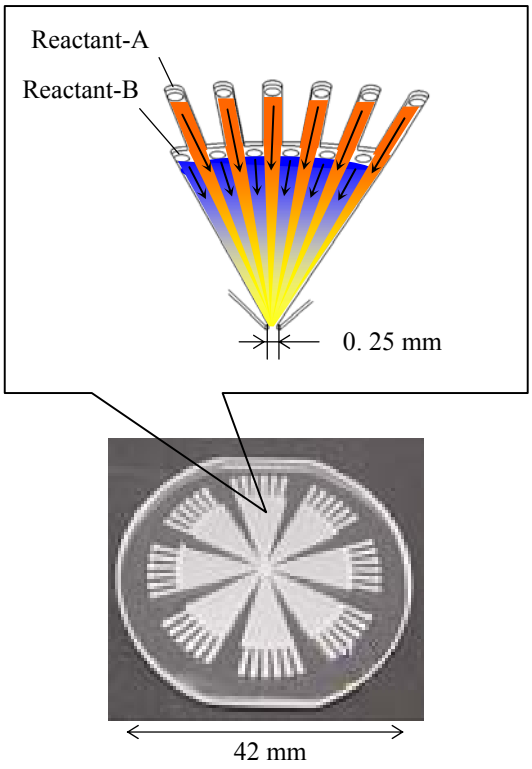


Fig. 6 Overview of a micro-channel chip

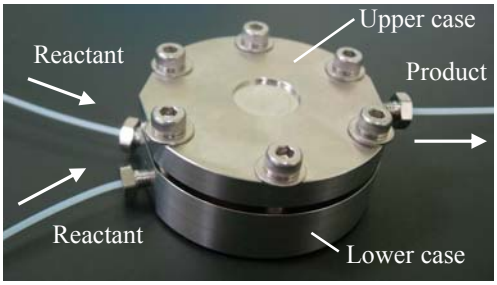


Fig. 5 Overview of a microreactor

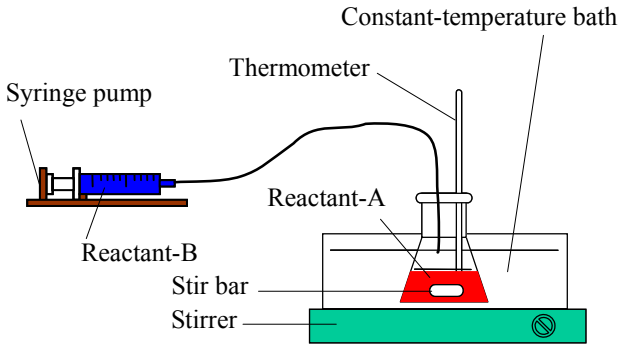


Fig. 7 Laboratory experimental setup using a conventional batch reactor

Table 2. Detail of consecutive reactions

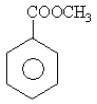
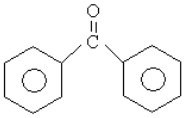
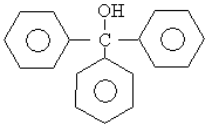
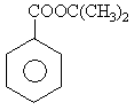
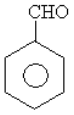
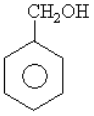
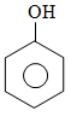
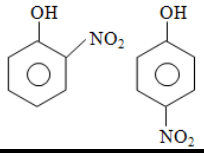
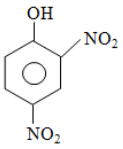
Reaction	Reactant		Main product	By-product
	A	B	P1	P2
Grignard		PhMgBr		
Hydride reduction		$[(CH_3)_2CHCH_2]_2AlH$		
Nitration		HNO_3		

Table 3. Experimental results

Reaction	*k1/k2*	Yield of main product (%)	
		Conventional batch	Microreactor
Grignard	0.07	3.3	3.8
Hydride reduction	1.05	25.2	38.1
Nitration	8.23	77.0	86.3

PILOT PLANT

Figure 8 shows a structure of a pilot plant that involves the numbering-up of microreactors. The pilot plant was 1500 mm wide, 900 mm long, and 1500 mm high. Figure 8(a) shows the internal structure of the pilot plant, in which 20 microreactors were set up in a constant-temperature bath. Figure 8(b) illustrates the numbering up structure, in which 20 microreactor units are arranged in parallel like a computer blade server. The microreactor units are stacked five deep and in four rows. The inner side of the pilot plant has step structure with a lower step and an upper step, and it is composed of a flow control system, temperature and reaction control system, and monitoring system. **Figure 9** shows a block diagram of the pilot plant that involves the numbering-up of microreactors. The flow control system consisted of two nonpulsatile pumps (Nihon Seimitsu Kagaku, Ltd.) and tanks in the lower step and electromagnetic valves and needle valves in the upper step. The flow control system could withstand pressures up to 0.35 MPa. Twenty thermocouples were set up in each microreactor and one thermocouple was set up in the constant-temperature bath. Moreover, two flow sensors and two pressure sensors were set up in the downstream of each nonpulsatile pump. A pressure sensor was set up upstream of the product tank, as shown in Figure. 9. The monitoring system recorded the flow velocity at two points, the pressure at three points, and the temperature at 21 points (13).

PERFORMANCE EVALUATION

The flow performance of the pilot plant was evaluated using pure water before the chemical performance evaluation was performed. The uniformity of the parallel flows and the flow rate were evaluated over four hours of continuous running. Manifold was set up upstream of each microreactor unit as shown in Figure 9. Moreover, the pressure loss in the tube connected to each microreactor was set to a constant value by using the needle valve. As a result, the parallel flows were uniformly set to an accuracy of ±3%. Moreover, the total maximum flow rate when the 20 microreactors was 1×10^4 mm^3/s, which corresponds to 72 t/year when operated at rates less than 10 h/d for 200 days.

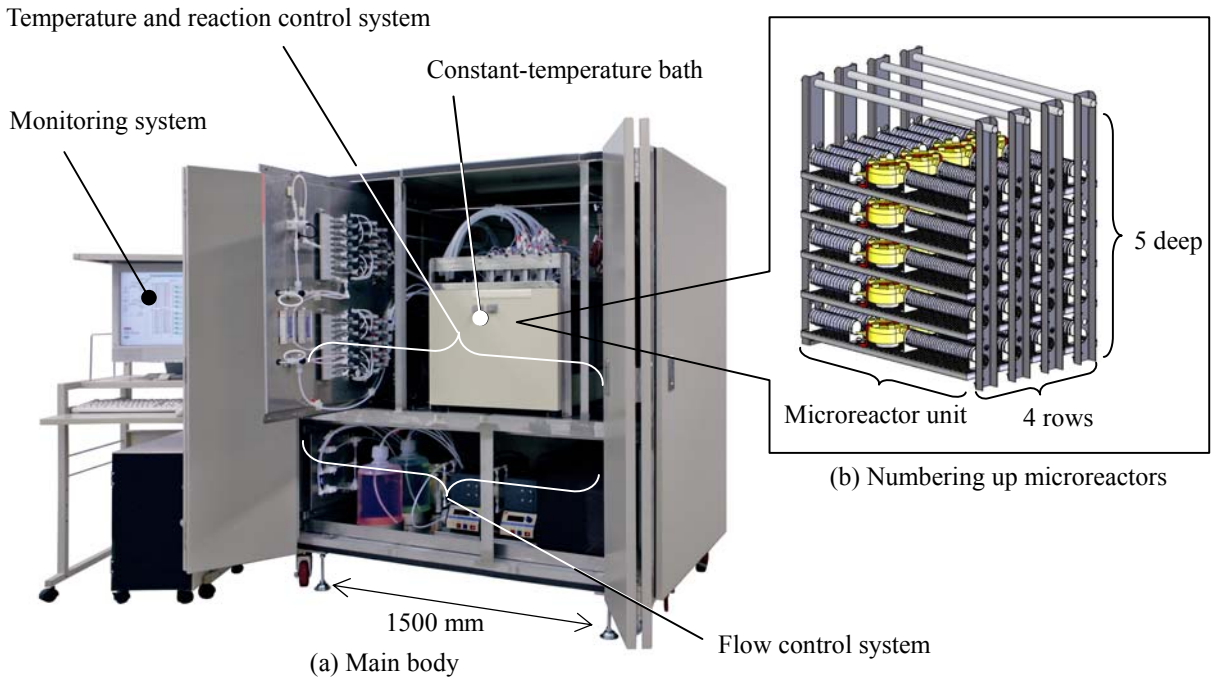


Fig. 8 Structure of the pilot plant involving the numbering-up of microreactors

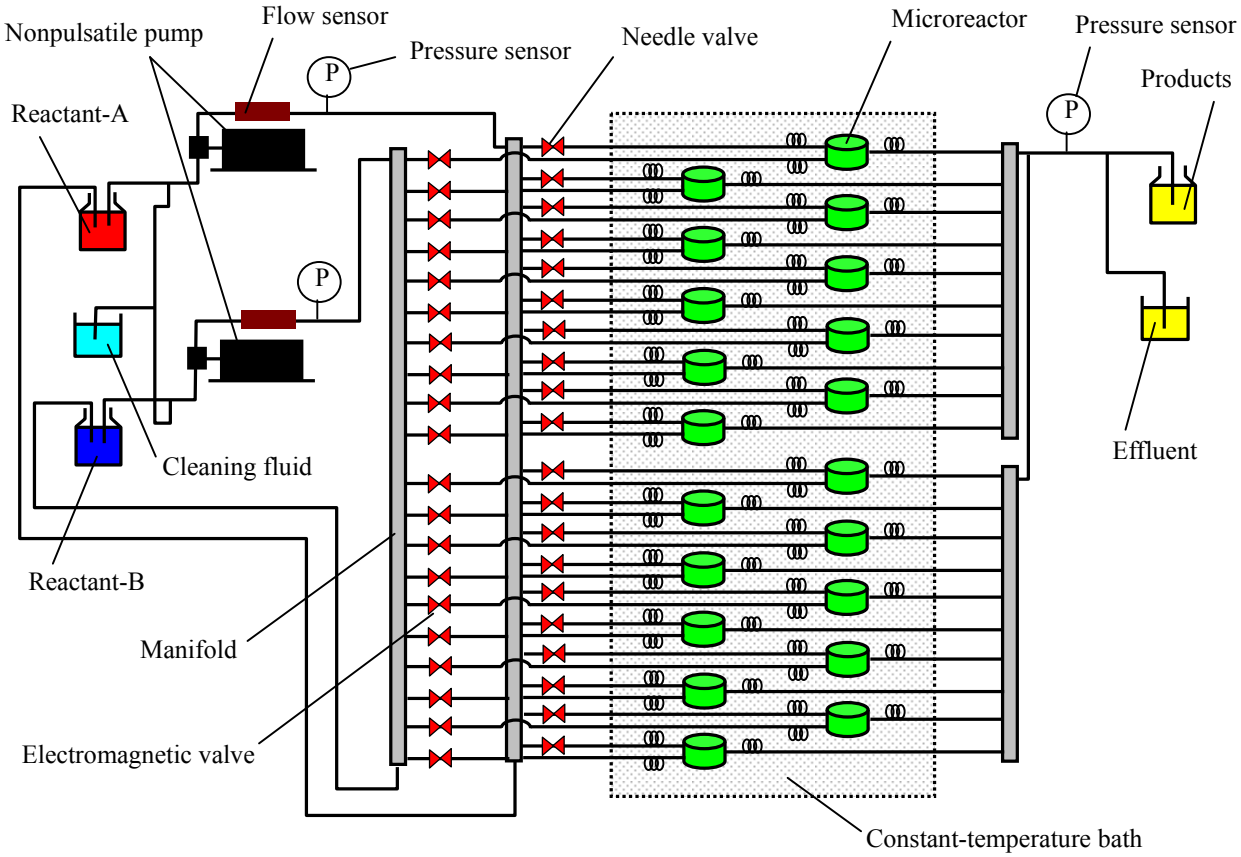


Fig. 9 Block diagram of the pilot plant involving the numbering-up of microreactors

The nitration reaction was selected from among three consecutive reactions to evaluate the chemical performance in the laboratory experiment. Experimental conditions in the pilot plant are similar to these in the case of laboratory experiments involving in the use of one microreactor. The yields of the main product were evaluated at 298.15 K over 0.5 h of continuous running. **Table 7** shows the yield of mono-nitrophenols and 2,4-dinitrophenol. The results of the conventional batch reactor and the results using one microreactor are also shown for comparison. Compared with the conventional batch reactor experiment, the yield of mono-nitrophenols was increased by 9.3% in the microreactor. However, the yield of 2,4-dinitrophenol was decreased. Moreover, the results of the experiments involving the pilot plant and these of the experiment involving microreactor are almost the same. Thus, we confirmed that the pilot plant involving the numbering-up of 20 microreactors, was capable of increasing the production scale without decreasing the yield of the products.

Table 7 Yield of mono-nitrophenols and 2, 4-dinitrophenol

	mono-nitrophenols [%]	2,4 di-nitrophenol [%]
Batch reactor	77.0	7.7
One microreactor	86.3	2.3
Pilot plant	88.1	1.7

CONCLUSION

The chemical reaction yield was predicted by using Monte Carlo simulation. The targeted chemical reaction of a performance evaluation using the microreactor is the consecutive reaction. The main product P1 is formed in the first stage with the reaction rate constant *k1*. Moreover, the by-product P2 is formed in the second stage with the reaction rate constant *k2*. It was found that the yield of main product P1 was improved by using a microreactor when the ratio of the reaction rate constants became *k1/k2* >1. On the other hand, It was found that the yield of main product P1 was not improved even by using a microreactor when the ratio of the reaction rate constants became *k1/k2* <1. To evaluate the Monte Carlo simulation result, the yields of the main products obtained in three consecutive reactions. It was found that the yield of the main product in cased of *k1/k2* >1 increased when the microreactor was uesd.

Next, a pilot plant involving the numbering-up of 20 microreactors was developed. The 20 microreactor units were stacked in four sets, each containing five microreactor units arranged vertically, similar to a computer blade server. The maximum flow rate when 20 microreactors were used was 1×10^4 mm^3/s, which corresponds to 72 t/year. Evaluation of the chemical performance of the pilot plant was conducted using a nitration reaction. The pilot plant was found to capable of increasing the production scale without decreasing the yield of the products.

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