11
Development and Scale-up of a Microreactor Pilot Plant Using the Concept of Numbering-up

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11.1
Introduction

Micromachining technologies have recently been applied to designing miniaturized devices for synthetic applications, that is, microreactors [1, 2]. A microreactor is a device that enables chemical reactions to be performed on a microliter 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 control precisely 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 reactions including the Friedel–Crafts monoalkylation reaction [5], the Grignard reaction [6] and the Sonogashira coupling reaction [7]. Even the production scale has been touched upon; some of the first examples to be released were polymerization [8] and nitroglycerine production [9] using a pilot plant.

In the studies mentioned above, the production scale was relatively small and the number of stacked microreactors was not very large. However, the expected production scale using microreactors has subsequently increased significantly. It is therefore very important to control the large number of microreactors involved. Accordingly, the objectives of the present study were to develop a pilot plant using the numbering-up of 20 microreactors and to control uniformly the parallel flows of the pilot plant.

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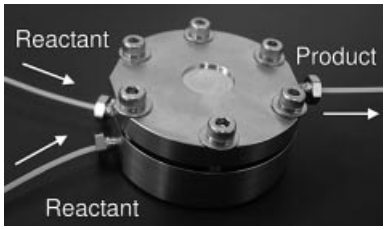


Figure 11.1 Overview of microreactor.

11.2 Microreactor Unit

11.2.1 Configuration

An overview of our microreactor is shown in Figure 11.1. The microreactor is divided into a lower case with two inlet fittings, a microchannel chip and an upper case with one outlet fitting. The microchannel chip is made from quartz glass. Two kinds of liquids flow from the circumference to the center in a multilayer state and they are mixed in the gradually narrowing microchannel. The height of the channel was 150 μm and the minimum width of the channel was 25 μm. The lower and upper cases are made from Hastelloy-C276 with corrosion resistance. The thermocouple was set up in the channel wall neighborhood of the upper cases.

A schematic of a microreactor unit is shown in Figure 11.2. Upstream from the microreactor is a preheating unit and downstream is a unit for adjusting the reaction time. A polytetrafluoroethylene (PTFE) tube 500 μm in diameter is rolled in outside the cylinder in both units. The microreactor can be used for many kinds of chemical reactions by adjusting the preheating and reaction times.

11.2.2 Chemical Performance Evaluation

The targeted chemical reaction of a performance evaluation using the microreactor unit is the consecutive reaction as shown in Eqs. (11.1) and (11.2):

$$A + B \rightarrow P_1 \tag{11.1}$$

$$P_1 + B \rightarrow P_2 \tag{11.2}$$

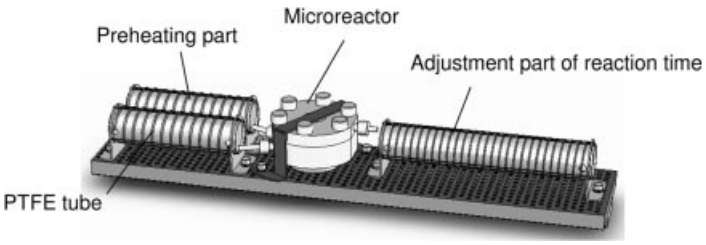
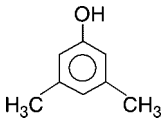
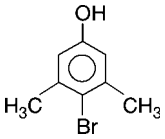
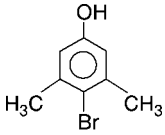
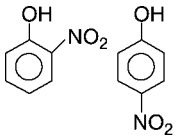
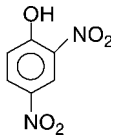
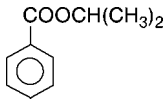
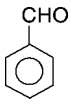
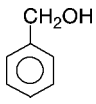


Figure 11.2 Schematic of microreactor unit.

Table 11.1 Details of consecutive reactions using the microreactor unit.

Reaction	Reactant A	Reactant B	Main product P_1	By-product P_2
Bromination		Br_2		
Nitration		HNO_3		
Hydride reduction		$[(CH_3)_2CHCH_2]_2$ AIH		

where A and B are reactants, P_1 is the main product and P_2 is the by-product. The main product P_1 that is monosubstituted is formed in the first stage and the by-product P_2 that is disubstituted is formed in the second stage. We conducted the following three consecutive reactions: bromination of dimethylphenol with bromine [10], a nitration reaction of phenol with nitric acid [11] and a reductive reaction of diisobutylaluminum hydride [12], as shown in Table 11.1. Figure 11.3 shows a comparison of the yield of the main product between conventional batch and microreactor operation. It is found that the yield of the main product is improved by a maximum of 40% by using the microreactor .

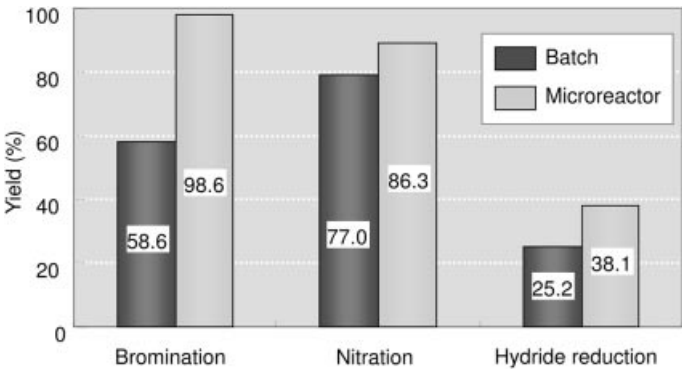


Figure 11.3 Comparison of the yield of the main product between conventional batch and microreactor operation.

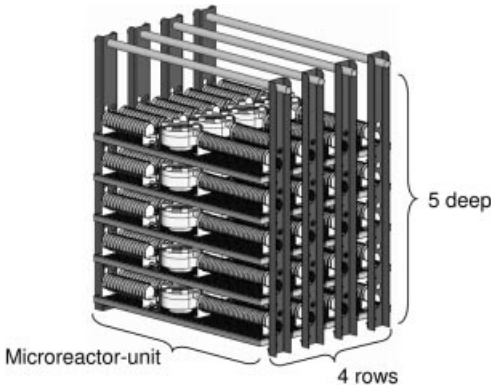


Figure 11.4 Numbering-up structure.

11.3 Pilot Plant

11.3.1 Numbering-up

Figure 11.4 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.

A schematic of a pilot plant is shown in Figure 11.5. The pilot plant was 1500 mm wide, 900 mm long and 1500 mm high. Figure 11.6 shows the internal structure of the pilot plant in which 20 microreactors were set up in a constant-temperature bath. The inside of the pilot plant has a lower and upper step structure and it is composed of a flow control system, temperature and reaction control system and monitoring system. The flow control system consisted of non-pulsatile pumps and tanks in the lower step and electromagnetic valves and needle valves in the upper step. The withstand

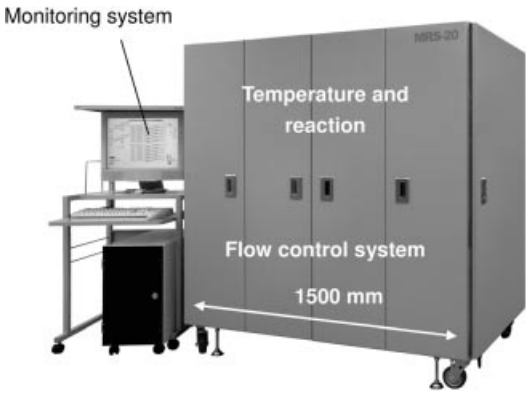


Figure 11.5 Schematic of pilot plant.

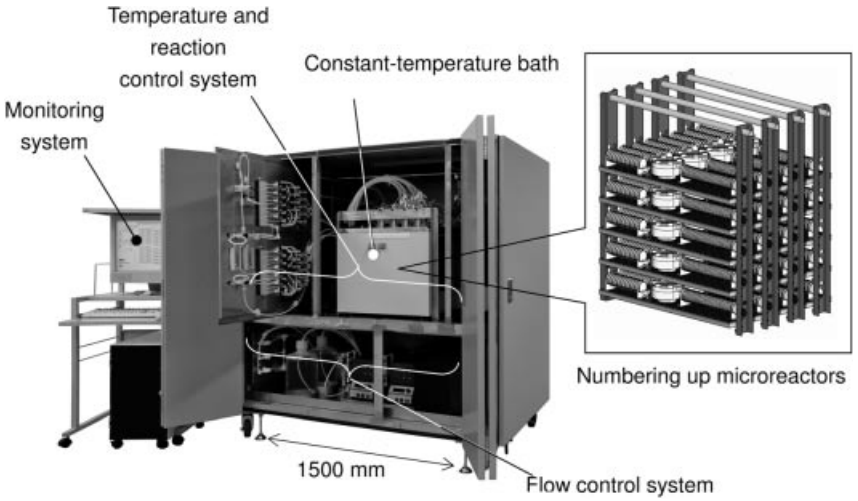


Figure 11.6 Internal structure of pilot plant.

pressure of the flow control system was 0.35 MPa. The temperature and reaction control system consisted of the 20 microreactors in the constant-temperature bath. A monitoring system as shown in Figure 11.7 was used to observe and control the flow rates, pressures and temperatures .

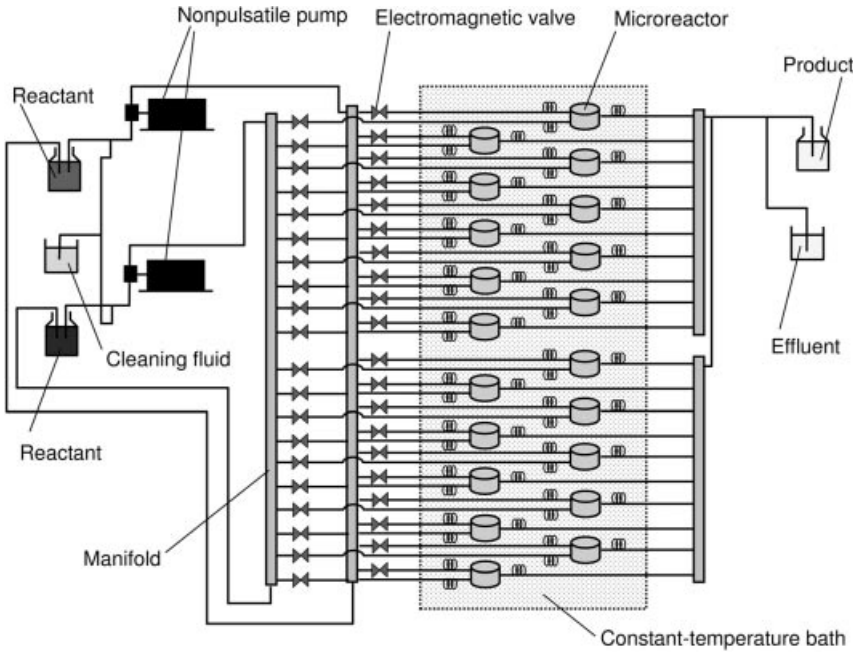


Figure 11.7 Monitoring system of pilot plant.

11.3.2
Flow Performance Evaluation

The performance evaluation of the pilot plant was conducted using pure water before a chemical reaction experiment. First, the pressure losses in all the tubes were uniformly set using the needle valves. The uniformity of the parallel flows and the flow rate were evaluated in 4 h of continuous running. As a result, the parallel flows were uniformly set to an accuracy of ±3%. Moreover, the maximum flow rate using the 20 microreactors was 600 mL min^{-1}, which corresponds to 72 t p.a.

11.3.3
Chemical Performance Evaluation

Nitration is generally used in the field of synthetic chemistry. Accordingly, a nitration reaction of phenol with nitric acid was carried out as a real evaluation using a chemical reaction as shown in Table 11.1. This is a consecutive reaction. The mononitrophenols (*o*- and *p*-nitrophenol) are formed in the first stage and 2,4-dinitrophenol in the second stage.

Two reactants, phenol in water solvent (0.9 mol L^{-1}) and nitric acid solution (15.8 mol L^{-1}), were mixed in the numbering-up microreactors. The reactants and reaction products (mononitrophenols and 2,4-initrophenol) were analyzed by high-performance liquid chromatography (HPLC). Table 11.2 shows the yields of mononitrophenols and 2,4-dinitrophenol. The results of the conventional batch reactor and the results using one microreactor [10] are also shown for comparison.

Compared with the conventional batch, the yield of mononitrophenols is increased by 9.3% by using the microreactor, while the yield of 2,4-dinitrophenol is decreased. Moreover, the results for the pilot plant and the single reactor are almost the same. That is, we confirmed that the pilot plant using 20 numbering-up microreactors was able to increase the production scale without decreasing the yield of the products [13].

Table 11.2 Yield of mononitrophenols and 2,4-dinitrophenol.

	Yield (%)	
Reactor	**Mononitrophenols**	**2,4-Dinitrophenol**
Conventional batch	77.0	7.7
Single microreactor	86.3	2.3
Microreactor system	88.1	1.7

11.4 Conclusion

A pilot plant using 20 numbering-up microreactors was developed. The microchannel chip was made from quartz glass and the case was Hastelloy-C276 with corrosion resistance. The 20 microreactor units were stacked five deep and in four rows like a computer blade server. An experimental evaluation showed that the parallel flows were uniform up to an accuracy of ±3%. The maximum flow rate using the 20 microreactors was 600 mL min^{-1}, which corresponds to 72 t p.a.. Moreover, nitration reaction of phenol with nitric acid was carried out as a real evaluation using a chemical reaction. It was found that the pilot plant using the 20 numbering-up microreactors was able to increase the production scale without decreasing the product yield.

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