Process Intensification Using a Two-Phase System and Micromixing for Consecutive and Reversible Reactions

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This study aimed to find reaction conditions that improve the yield of target intermediate products, using a two-phase system and a microspace for first-order consecutive and reversible reactions. As a result, the yield of target products with a two-phase system can be surpassed by that of a single-phase system through selecting the organic phase such that the partition coefficient of the raw material to the aqueous phase is large, and that of the target product to the organic phase is also large. In addition, the volume ratio of two phases and the liquid–liquid interfacial area are also important factors for improving the target product yield. In a microspace, the microfluid segments can be designed both arbitrarily and precisely, and thus it is possible to control the interfacial area and mass transfer rates accurately. Utilization of a microspace can play a significant role in intensifying a two-phase system. © 2009 American Institute of Chemical Engineers *AIChE J,* 55: 1505–1513, 2009

Keywords: two-phase reaction, microreactor, rate analysis of multiple reactions, selectivity of reaction

Introduction

Many chemical reactions are accompanied by side reactions, which often produce undesired by-products. Developing processes that produce higher yields of target products provides numerous benefits to the environment as well as cost reductions. To improve the product yield, we need to accurately evaluate the reaction rates and the mass transfer rates and then select proper reaction apparatus, mixing methods, and reaction systems (homogeneous or heterogeneous).[1]

In general, liquid-phase chemical reactions are often initiated by mixing two liquids. A liquid–liquid two-phase system, which can extract intermediate products to a separate phase and inhibit further reactions, or shift equilibrium in a desired direction, can improve the yield of intermediate products.[2,3] Higashimura et al. conducted phenol dimerization in a two-phase reaction system using a batch reactor and successfully improved the dimer selectivity by inhibiting further polymerization reactions through the rapid extraction of dimers produced in the aqueous phase to the oil phase.[4] A two-phase system, where two immiscible or poorly soluble liquids are generally dispersed as minute droplets by mixing, includes microspaces inside the minute droplets, which enhance the interfacial areas. In addition, a two-phase system enables control of the reaction and mass transfer rates.

In recent years, many investigations have been conducted using these microspaces. In a microspace, an orderly laminar flow can be formed, owing to low Reynolds numbers as represented by a parallel flow in a Y-shape microchannel (Figure 1) and a segmented flow. Therefore, microfluid segments can be designed both arbitrarily and precisely.[5] For example, for a Y-shape flow, the liquid–liquid interfacial area, the volume ratio of the two liquids, and the residence time can be changed arbitrarily by varying the channel width, channel depth, and contact length. Hisamoto et al. and Smirnova et al. successfully demonstrated a phase transfer

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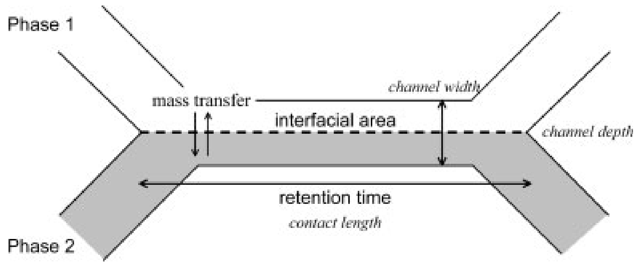


Figure 1. Precise control of operating factors by device design (Y-shape microchannel).

diazocoupling reaction using a two-phase system on a microchip.[6,7] In these reactions, rapid phase transfer of the starting material and the produced chemical species across the liquid–liquid interface played an important role in realizing both a fast chemical reaction and the isolation of the produced chemical species. In addition, the large specific interfacial area and short molecular diffusion distance played important roles in extracting the main product from the aqueous phase to the organic phase, which avoided the undesirable side reaction. Thus, using the microspace can lead to process intensification of a two-phase reaction system accompanied by mass transfer.

Although many investigations have been conducted on two-phase systems, few reports have discussed the conditions under which a two-phase system can be effective in improving the selectivity of a target product, compared with a single-phase system. Unlike macroscale mixing, precise control of mass transfer is possible by utilizing a well-designed microspace, thus simulation results can be accurately replicated. This study aimed to find the reaction conditions that improved the selectivity of target products using a two-phase system and a microspace for first-order consecutive and reversible reactions.

Theoretical Consideration

We considered both single- and two-phase systems of consecutive and reversible reactions, shown in Figure 2, and assumed that the reaction components are completely mixed. We also assumed that the organic and aqueous phases in the two-phase system are immiscible, and considered the partition equilibrium and mass transfer between the two phases. The reaction was conducted by mixing an organic phase containing raw material A with an aqueous phase. A is extracted to the aqueous phase and the reaction proceeds only in the aqueous phase. R and B, produced in the reaction, are extracted to the organic phase or converted to S by a subsequent reaction. The mass balance equations are shown later. The target product is set to R for consecutive reaction, and we considered conditions where the maximum concentration of R_{or}, $C_{Ror,max}$, which is extracted to the organic phase in a two-phase system, surpasses the maximum concentration, $C_{R,max}$, obtained in a single-phase system. We also considered the reaction times required to obtain the maximum concentration, τ_{max} (single-phase system) and τ'_{max} (two-phase system). In addition, the target product is set to B for the reversible reaction; the equilibrium concentration of B_{or}, $C_{Bor,e}$, which is extracted to the organic phase in a two-phase system, surpasses the maximum concentration, $C_{B,e}$, obtained in a single-phase system. We also considered the reaction time when the equilibrium is attained as well as the consecutive reaction.

Consecutive reaction

Single-Phase System. Mass balance of the reaction

$$\frac{dC_A}{dt} = -k_1 C_A \tag{1}$$

$$\frac{dC_R}{dt} = k_1 C_A - k_2 C_R \tag{2}$$

$$\frac{dC_S}{dt} = k_2 C_R. \tag{3}$$

Two-Phase System. Partition equilibrium and mass balance between two phases

$$V_{or} C_{A,or} + V_{aq} C_{A,aq} = V_{or} C^{eq}_{A,or} + V_{aq} C^{eq}_{A,aq} \tag{4}$$

$$V_{or} C_{R,or} + V_{aq} C_{R,aq} = V_{or} C^{eq}_{R,or} + V_{aq} C^{eq}_{R,aq} \tag{5}$$

$$C^{eq}_{A,or} = H_A C^{eq}_{A,aq} \tag{6}$$

$$C^{eq}_{R,or} = H_R C^{eq}_{R,aq} \tag{7}$$

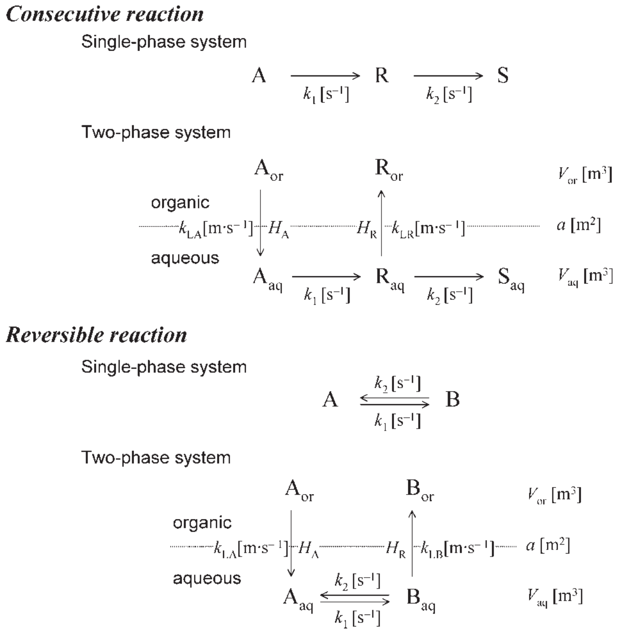


Figure 2. Models of consecutive and reversible reactions.

Mass balance of the reaction

$$\frac{dC_{\mathrm{A,or}}}{dt} = -\frac{1}{V_{\mathrm{or}}} k_{\mathrm{LA}} a\left(C_{\mathrm{A,or}} - C_{\mathrm{A,or}}^{\mathrm{eq}}\right) \tag{8}$$

$$\frac{dC_{\mathrm{A,aq}}}{dt} = \frac{1}{V_{\mathrm{aq}}} k_{\mathrm{LA}} a\left(C_{\mathrm{A,or}} - C_{\mathrm{A,or}}^{\mathrm{eq}}\right) - k_1 C_{\mathrm{A,aq}} \tag{9}$$

$$\frac{dC_{\mathrm{R,aq}}}{dt} = k_1 C_{\mathrm{A,aq}} - k_2 C_{\mathrm{R,aq}} - \frac{1}{V_{\mathrm{aq}}} k_{\mathrm{LR}} a\left(C_{\mathrm{R,aq}} - C_{\mathrm{R,aq}}^{\mathrm{eq}}\right) \tag{10}$$

$$\frac{dC_{\mathrm{R,or}}}{dt} = \frac{1}{V_{\mathrm{or}}} k_{\mathrm{LR}} a\left(C_{\mathrm{R,aq}} - C_{\mathrm{R,aq}}^{\mathrm{eq}}\right) \tag{11}$$

$$\frac{dC_{\mathrm{S,aq}}}{dt} = k_2 C_{\mathrm{R,aq}}. \tag{12}$$

Reversible reaction

Single-Phase System. Mass balance of the reaction

$$\frac{dC_{\mathrm{B}}}{dt} = -\frac{dC_{\mathrm{A}}}{dt} = k_1 C_{\mathrm{A}} - k_2 C_{\mathrm{B}} \tag{13}$$

Two-Phase System. Partition equilibrium and mass balance between two phases

$$V_{\mathrm{or}} C_{\mathrm{A,or}} + V_{\mathrm{aq}} C_{\mathrm{A,aq}} = V_{\mathrm{or}} C_{\mathrm{A,or}}^{\mathrm{eq}} + V_{\mathrm{aq}} C_{\mathrm{A,aq}}^{\mathrm{eq}} \tag{14}$$

$$V_{\mathrm{or}} C_{\mathrm{B,or}} + V_{\mathrm{aq}} C_{\mathrm{B,aq}} = V_{\mathrm{or}} C_{\mathrm{B,or}}^{\mathrm{eq}} + V_{\mathrm{aq}} C_{\mathrm{B,aq}}^{\mathrm{eq}} \tag{15}$$

$$C_{\mathrm{A,or}}^{\mathrm{eq}} = H_{\mathrm{A}} C_{\mathrm{A,aq}}^{\mathrm{eq}} \tag{16}$$

$$C_{\mathrm{B,or}}^{\mathrm{eq}} = H_{\mathrm{B}} C_{\mathrm{B,aq}}^{\mathrm{eq}} \tag{17}$$

Mass balance of the reaction

$$\frac{dC_{\mathrm{A,or}}}{dt} = -\frac{1}{V_{\mathrm{or}}} k_{\mathrm{LA}} \cdot a\left(C_{\mathrm{A,or}} - C_{\mathrm{A,or}}^{\mathrm{eq}}\right) \tag{18}$$

$$\frac{dC_{\mathrm{A,aq}}}{dt} = \frac{1}{V_{\mathrm{aq}}} k_{\mathrm{LA}} \cdot a\left(C_{\mathrm{A,or}} - C_{\mathrm{A,or}}^{\mathrm{eq}}\right) - k_1 C_{\mathrm{A,aq}} + k_2 C_{\mathrm{B,aq}} \tag{19}$$

$$\frac{dC_{\mathrm{B,aq}}}{dt} = k_1 C_{\mathrm{A,aq}} - k_2 C_{\mathrm{B,aq}} + \frac{1}{V_{\mathrm{aq}}} k_{\mathrm{LB}} \cdot a\left(C_{\mathrm{B,or}} - C_{\mathrm{B,or}}^{\mathrm{eq}}\right) \tag{20}$$

$$\frac{dC_{\mathrm{B,or}}}{dt} = \frac{1}{V_{\mathrm{or}}} k_{\mathrm{LB}} \cdot a\left(C_{\mathrm{B,or}} - C_{\mathrm{B,or}}^{\mathrm{eq}}\right) \tag{21}$$

Results and Discussion

Consecutive reactions

Single-Phase System. The maximum concentration of R, $C_{\mathrm{R,max}}$, and the reaction time when the maximum concentration is obtained, τ_{max}, were obtained as analytical solutions by solving the Eqs. from 1–3. C_{A0} is the concentration of the reaction initiation ($t = 0$) and the initial concentrations of R and S are 0.

$$\frac{C_{\mathrm{R,max}}}{C_{\mathrm{A0}}} = \left(\frac{k_1}{k_2}\right)^{k_2/(k_2 - k_1)} \tag{22}$$

$$\tau_{\mathrm{max}} = \frac{\ln(k_1/k_2)}{k_2 - k_1} \tag{23}$$

Two-Phase System. The following are the results of numerical analysis, which were classified according to the mass transfer rates of A and R.

Chemical reaction rate control regime (rapid extraction of both A and R): When both A and R are rapidly extracted, the phase equilibrium between the organic and aqueous phases is consistently maintained, and the mass transfer constants, k_{LA} and k_{LR}, have infinite values. The maximum concentration of $\mathrm{R_{or}}$, $C_{\mathrm{Ror,max}}$, and the reaction time when $C_{\mathrm{Ror,max}}$ is obtained, τ'_{max}, are provided by Eqs. 24 and 25 by substituting Eqs. 26 and 27, which indicate the apparent reaction rates, k'_1 and k'_2, into Eqs. 22 and 23, and considering the partition between the two phases. C_{A0} is the initial concentration ($t = 0$) of the raw material A supplied to the organic phase, and the initial concentrations of R and S in both the organic and aqueous phases are 0.

$$\frac{C_{\mathrm{Ror,max}}}{C_{\mathrm{A0}}} = \left(\frac{k'_1}{k'_2}\right)^{k'_2/\left(k'_2 - k'_1\right)} \Bigg/ \left(1 + \frac{1}{H_{\mathrm{R}} \cdot V_{\mathrm{r}}}\right) \tag{24}$$

$$\tau'_{\mathrm{max}} = \frac{\ln\left(k'_1/k'_2\right)}{k'_2 - k'_1} \tag{25}$$

$$k'_1 = \frac{k_1}{1 + H_{\mathrm{A}} \cdot V_{\mathrm{r}}} \tag{26}$$

$$k'_2 = \frac{k_2}{1 + H_{\mathrm{R}} \cdot V_{\mathrm{r}}} \tag{27}$$

The volume ratio, V_{r} ($= V_{\mathrm{or}}/V_{\mathrm{aq}}$), between the organic and aqueous phases was set to 1, and the maximum concentration of R, $C_{\mathrm{R,max}}$ and $C_{\mathrm{Ror,max}}$, and the reaction time ratio, $\tau'_{\mathrm{max}}/\tau_{\mathrm{max}}$, at various values of partition coefficients, H_{A} and H_{R}, are plotted vs. the reaction rate ratio k_2/k_1, in Figures 3

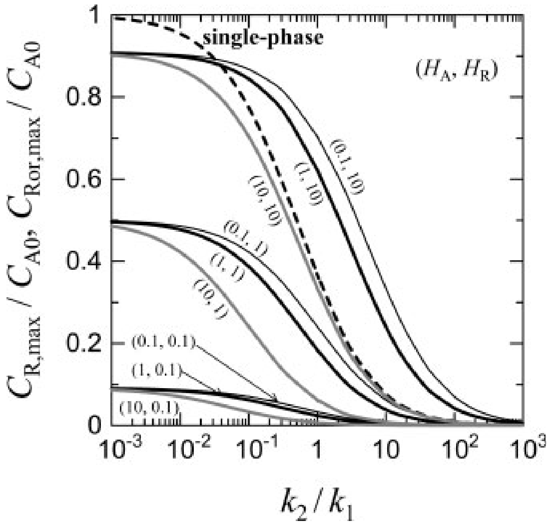


Figure 3. The maximum concentration vs. the reaction rate ratio (V_r = 1, consecutive reaction).

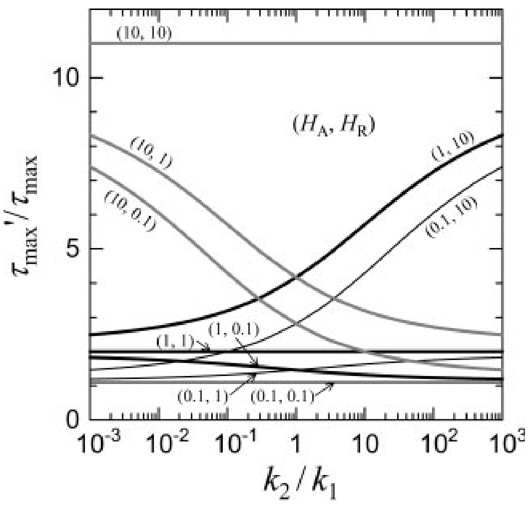


Figure 4. The reaction time ratio vs. the reaction rate ratio (V_r = 1, consecutive reaction).

and 4, respectively. Figure 3 shows that, when H_A is small and H_R is large, the two-phase system yield of R is above that of a single-phase system. In a two-phase system, when k_2/k_1 is larger than 1, selecting the organic phase, such that H_A is small and H_R is large, has a remarkable affect. Figure 4, however, shows that the reaction time, τ'_{max}, when the highest yield of R can be obtained, is greater than that for a single-phase system. In particular, the reaction time, τ'_{max}, is significantly larger than that of a single-phase system, when k_2/k_1 is larger than 1, H_A is small and H_R is large. Figures 5a,b show the concentration of each component with time for both single- and two-phase systems, respectively, when $V_r = 1$, $H_A = 0.1$, $H_R = 10$, $k_1 = 0.1\ s^{-1}$, and $k_2 = 0.1\ s^{-1}$.

Figures 6 and 7 show $C_{Ror,max}$ and τ'_{max}/τ_{max}, respectively, vs. the reaction rate ratio k_2/k_1, when H_A is 0.1 and V_r is varied. Figure 6 indicates that a large V_r increases the yield of R substantially and leads to yield improvements. In addition, Figure 7 also shows that when V_r is large, τ'_{max}/τ_{max} becomes large.

Mass-transfer control regime 1 (only A is rapidly extracted and R is mass-transfer limited): Next, we consider the condition when only A is rapidly extracted and R is mass-transfer limited (the mass transfer constant of k_{LR} is finite). Figures 8 and 9 show $C_{Ror,max}$ and τ'_{max}/τ_{max} vs. the reaction rate ratio k_2/k_1 when H_A and H_R are 0.1 and 10, respectively. Figure 8 shows that when k_{LR} exceeds 0.01 m s^{-1}, $C_{Ror,max}$ is approximately the same and overlaps the value when both A and R are rapidly extracted. When k_{LR} decreases, $C_{Ror,max}$ increases and τ'_{max}/τ_{max} also increases. Figure 12a shows the concentration of each component with time in the reaction when $V_{or} = V_{aq} = 10^{-3}\ m^3$, $H_A = 0.1$, $H_R = 10$, $k_1 = 0.1\ s^{-1}$, $k_2 = 0.1\ s^{-1}$, $k_{LR} = 10^{-4}\ m\ s^{-1}$, $a = 1\ m^2$. Here, the average droplet diameter of the dispersion phase can be calculated at 0.6 mm when the liquid–liquid interfacial area a equals 1 m^2.

Mass-transfer control regime 2 (only R is rapidly extracted and A is mass-transfer limited): Similarly, we consider the condition when only R is rapidly extracted and A is the

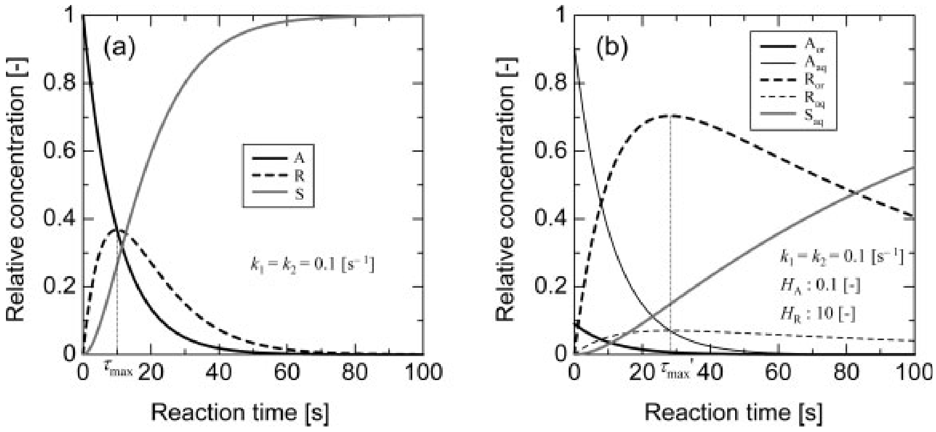


Figure 5. The concentration of each component with time both (a) single- and (b) two-phase systems when both A and R are rapidly extracted.

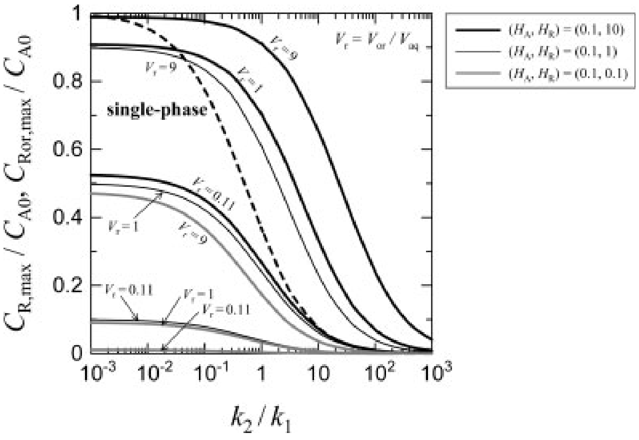


Figure 6. The maximum concentration vs. the reaction rate ratio (H_A = 0.1, consecutive reaction).

mass-transfer limited (the mass transfer constant of k_{LA} is finite). Figures 10 and 11 show $C_{Ror,max}$ and τ'_{max}/τ_{max} vs. the reaction rate ratio k_2/k_1 when H_A and H_R are 0.1 and 10, respectively. Figure 10 shows that when k_{LR} exceeds 0.001 m s^{-1}, $C_{Ror,max}$ is approximately the same and overlaps that the values when both A and R are rapidly extracted. When k_{LR} decreases, $C_{Ror,max}$ increases and τ'_{max}/τ_{max} also increases, similar to when only A is rapidly extracted. Compared to the situation when only A is rapidly extracted, k_{LR} appears to influence the maximum yield of R to a greater degree than k_{LA}. Figure 12b shows the concentration of each components with time in the reaction when $V_{or} = V_{aq} = 10^{-3}$ m^3, $H_A = 0.1$, $H_R = 10$, $k_1 = 0.1$ s^{-1}, $k_2 = 0.1$ s^{-1}, $k_{LA} = 10^{-4}$ m s^{-1}, and $a = 1$ m^2.

Mass-transfer control regime 3 (both A and R are mass-transfer limited): Figure 13 shows the concentration of each component with time in the reaction when $V_{or} = V_{aq} = 10^{-3}$ m^3, $H_A = 0.1$, $H_R = 10$, $k_1 = 0.1$ s^{-1}, $k_2 = 0.1$ s^{-1}, $k_{LA} = k_{LR} = 10^{-4}$ m s^{-1}, and $a = 1$ m^2. The maximum yield of R is lower and τ'_{max}/τ_{max} longer when either A or R are rapidly extracted.

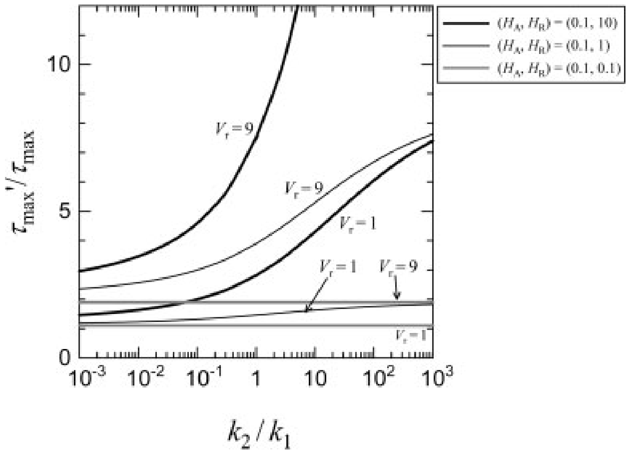


Figure 7. The reaction time ratio vs. the reaction rate ratio (H_A = 0.1, consecutive reaction).

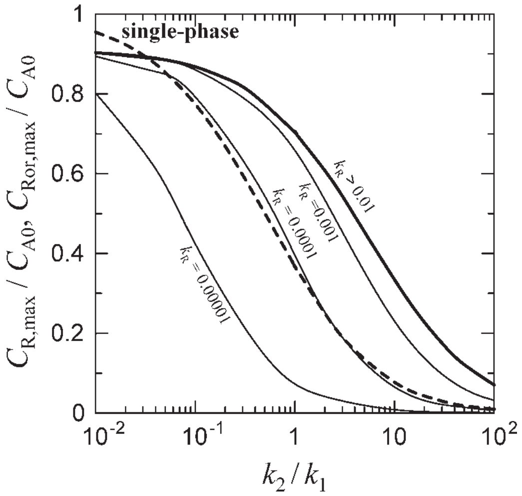


Figure 8. The maximum concentration vs. the reaction rate ratio when only A is rapidly extracted and R is mass-transfer limited (H_A = 0.1, H_R = 10).

Reversible reactions

Single-Phase System. When the equilibrium reaction rate is set to $X_{A,e}$, Eqs. 28 and 29 are true by solving Eq. 13.[3] C_{A0} is the initial concentration (t = 0) and the initial concentration of B is 0. $C_{B,e}$ is the equilibrium concentration of B, which is the target product.

$$\frac{C_{B,e}}{C_{A0}} = X_{A,e} = \frac{k_1}{k_1 + k_2} \tag{28}$$

$$-\ln\left(1 - \frac{X_A}{X_{A,e}}\right) = \frac{k_1}{X_{A,e}} \tag{29}$$

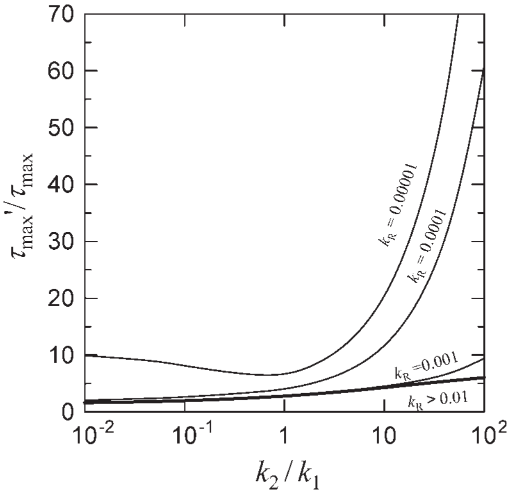


Figure 9. The reaction time ratio vs. the reaction rate ratio when only A is rapidly extracted and R is mass-transfer limited (H_A = 0.1, H_R = 10).

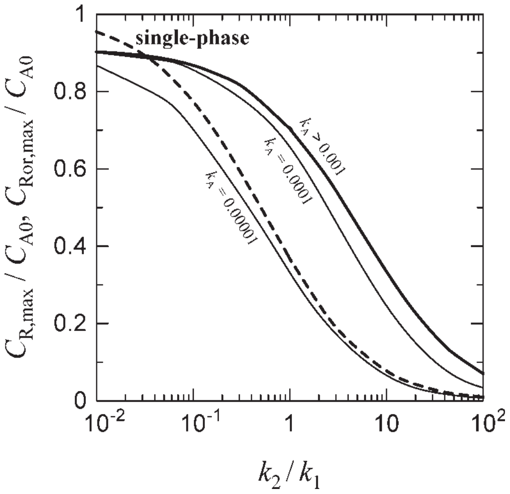


Figure 10. The maximum concentration vs. the reaction rate ratio when only R is rapidly extracted and A is mass-transfer limited (H_A = 0.1, H_A = 10).

Two-Phase System. ***Chemical reaction control regime (rapid extraction of both A and B):*** The equilibrium concentration of B_{or}, $C_{B,e}$, can be expressed in Eq. 30 using Eqs. 26 and 27. In addition, when the reaction rate X'_A is defined as in Eq. 32, Eq. 29 changes into Eq. 31, using the equilibrium reaction rate $X'_{A,e}$. C_{A0} is the initial concentration (t = 0) of the raw material A supplied to the organic phase, and the initial concentration of B in both the organic and aqueous phases is 0.

$$\frac{C_{Bor,e}}{C_{A0}} = \frac{k'_1}{k'_1 + k'_2} \Big/ \left(1 + \frac{1}{H_R \cdot V_r}\right) \tag{30}$$

$$-\ln\left(1 - \frac{X'_A}{X_{A,e}{}'}\right) = \frac{k_1 t}{X_{A,e}{}'} \tag{31}$$

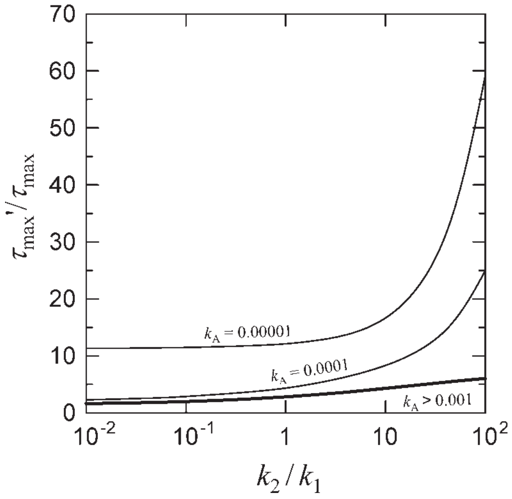


Figure 11. The reaction time ratio vs. the reaction rate ratio when only R is rapidly extracted and A is mass-transfer limited (H_A = 0.1, H_R = 10).

$$X'_A = \frac{C_{Bor}V_{or} + C_{Baq}V_{aq}}{C_{A0}V_{or}} \tag{32}$$

The volume ratio, V_r, between an organic and aqueous phase is set to 1, and the equilibrium concentration of B, $C_{B,e}$ and $C_{Bor,e}$, and the reaction time ratios, τ'_e/τ_e, at various values of partition coefficients H_A and H_R are plotted vs. the reaction rate ratio k_2/k_1, as shown in Figures 14 and 15, respectively. Figure 14 shows that when H_A is small and H_R is large, the yield of B in a two-phase system is greater than that in a single-phase system. In a two-phase system, when k_2/k_1 is larger than 1, selecting the organic phase, such that H_A is small and H_R is large, has a remarkable affect. Figure 15, however, shows that the reaction time, τ'_e, when equilibrium is attained, is greater than that for a single-phase system. In particular, τ'_e is significantly larger than τ $_e$, when k_2/k_1 is larger than 1, H_A is small and H_B is large.

Figures 16 and 17 show $C_{B,e}$ and τ'_e/τ_e vs. the reaction rate ratio k_2/k_1 when H_A is 0.1 and V_r is varied. Figure 16 indicates that a large V_r increased the yield of B

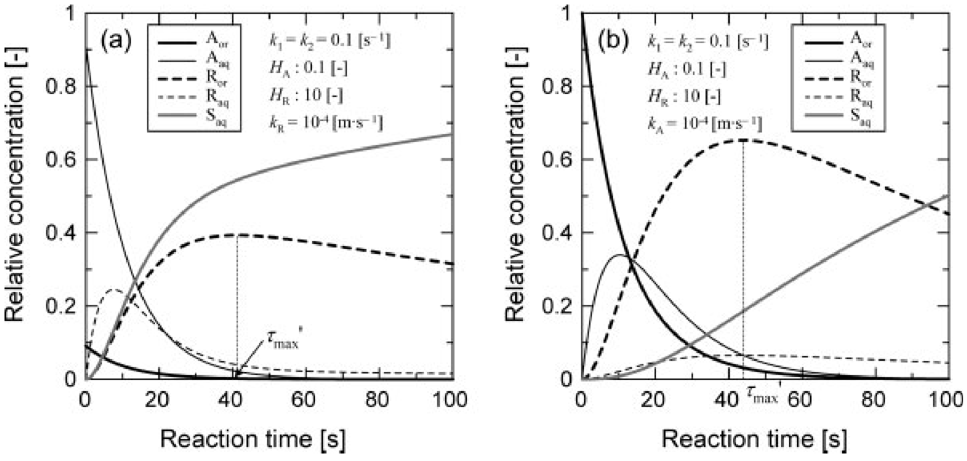


Figure 12. The concentration of each component with time (a) when only A is rapidly extracted and (b) when only R is rapidly extracted.

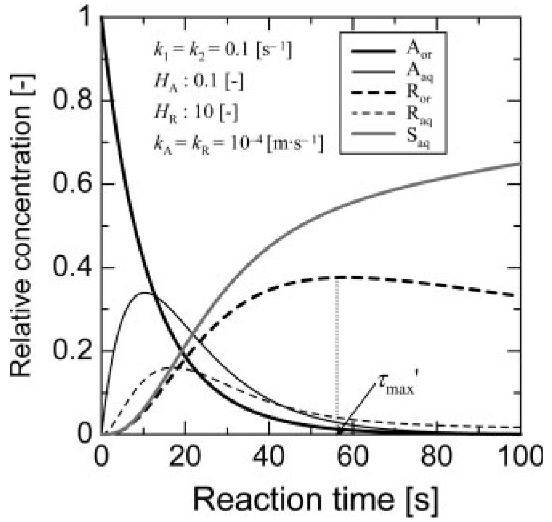


Figure 13. The concentration of each component with time when both A and R are mass-transfer limited.

substantially, leading to improvement of the yield. In addition, Figure 17 also shows same tendency of the consecutive reaction: when V_r is large, τ_e'/τ_e becomes large.

Mass-transfer control regime: When either A and B (or both) are mass-transfer limited, the equilibrium concentration of B_{or}, $C_{Bor,e}$, can be calculated by Eq. 30, despite mass transfer between the two phases. Unlike the consecutive reaction, the equilibrium concentration, $C_{Bor,e}$, is not influenced by mass transfer rates between the two phases. Meanwhile, the smaller the mass transfer rate, the longer the reaction time when the equilibrium is attained, as was true for consecutive reaction.

Effects of the two-phase system and process intensification

Table 1 summarizes the simulation results on single- and two-phase reaction systems. The yield of target products with a two-phase system can be surpassed by that of a single-phase system under certain conditions of both consecutive and reversible reactions. The most important operating factor is the partition relations of a raw material and a target product between the organic and aqueous phases. For both consecutive and reversible reactions, the organic phase must be selected such that the partition coefficient of the raw material to the aqueous phase (reaction phase) is large, and that of the target product to the organic phase is also large.

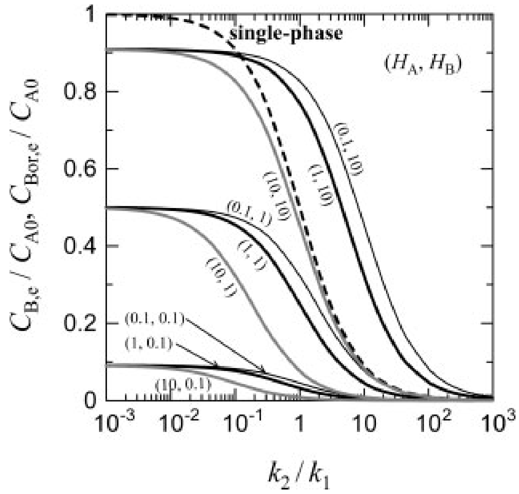


Figure 14. The maximum concentration vs. the reaction rate ratio (V_r = 1, reversible reaction).

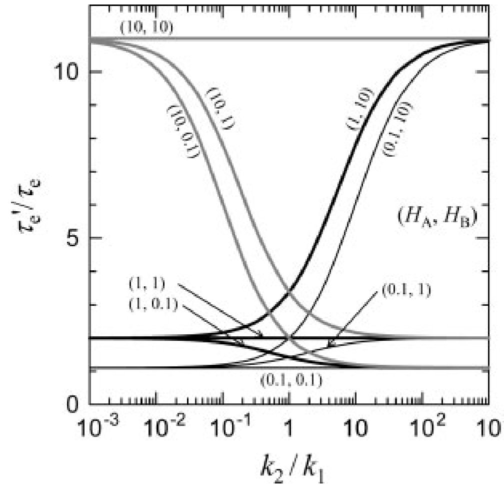


Figure 15. The reaction time ratio vs. the reaction rate ratio (V_r = 1, reversible reaction).

Next, the mass transfer to the partition equilibrium state must be as rapid as possible. The operating parameters maximizing the mass transfer effectively are the volume ratio of organic and aqueous phases, V_r, and the liquid–liquid interfacial area a. Increasing V_r enhanced the extraction of target products, which improve the yield. In addition, an increase in the liquid–liquid interfacial area a is equivalent to an increase in the mass transfer rate from the viewpoint of mass balance, and approaches the reaction-limited condition, contributing to an improved yield. Meanwhile, the reaction time of a two-phase system increases compared with a single-phase system. Controllability of the reaction can be improved by adopting a two-phase system when the reaction

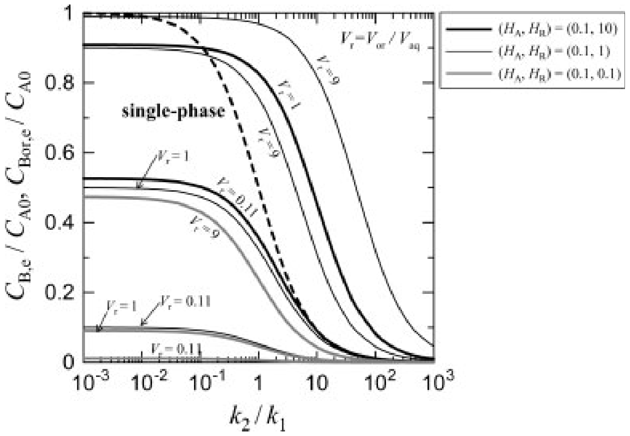


Figure 16. The maximum concentration vs. the reaction rate ratio (H_A = 0.1, reversible reaction).

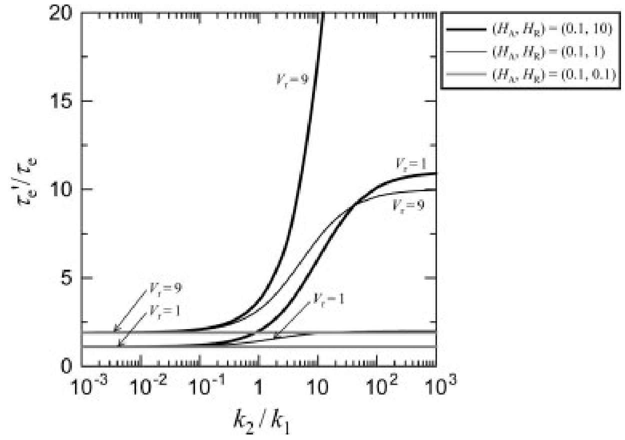


Figure 17. The reaction time ratio vs. the reaction rate ratio (H_A = 0.1, reversible reaction).

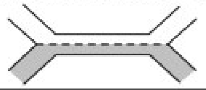
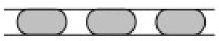
is rapid and completed within milliseconds. Base-catalyzed hydrolysis[8] and liquid-phase hydrogenation[9] under reaction-limited conditions for consecutive reaction and dissolution using enzyme biocatalysts[10] for reversible reactions are examples for which the target product yield is expected to be improved using a two-phase system.

One method for process intensification of a two-phase system is the use of microspaces. In a microspace, the target product yield can be improved by increasing the liquid–liquid interfacial area significantly, which enables to enhance the apparent mass transfer rates between the two phases. Table 2 shows the comparison of specific surface area of microfluid segments (=liquid–liquid interfacial area a/volume of dispersed phase V_d) under macro and microoperations. A large specific surface area, which can be attained under turbulent regime in a macro operation, can be obtained easily by within a microspace. In addition, high controllability of operating factors can be obtained in a microspace under orderly laminar flow conditions. In the case of segmented flow, it has been reported that mass transfer is enhanced more than that expected from increase in interfacial area.[11,12] As mentioned previously, the apparent mass transfer rate is enhanced, approaching the reaction-limited condition, thereby contributing to improved product yields. In addition, designing the microspace precisely, such as a parallel flow in a Y-shape channel, is possible for controlling mass transfer rates and retention times. For rapid reaction systems, improvement of the yield of a target product by sophisticated control of the reaction and separation of the product are possible. Both consecutive and reversible reactions were considered as described earlier, and Figure 18 shows the oxidative polymerization of phenol that we are now considering as an example of consecutive reaction. Phenol dimers are industrially useful, thus we are now trying to improve the dimer selectivity. Oxidative polymerization of phenol using oxidant ($Ce_4(NH_4)_2(NO_3)_6$, CAN) proceeds only in the aqueous phase. It is very difficult to control polymerization reaction so that only dimmers will be produced because dimer and oligomer are much more reactive than the phenol monomer. Experimental results using each reaction system are listed in Table 3. Compared with conventionally used batch reactor using single-phase system, dimer selectivity was improved by micromixing with two-phase system. We are now examining the most appropriate reaction system for enhancing dimer selectivity by selecting more suitable two-phase solvent systems and microdevices. In the future, we try to apply to specific reaction systems including phase-transfer catalysis system based on these results. As described earlier, utilization of a microspace, which enhances mass transfer rate and provides high operability of operating parameters, can play a significant role in intensifying a two-phase system.

Table 1. Comparison Between Single - and Two-Phase Reaction

		Yield of a target product	Reaction time
Consecutive and Irreversible reactions	Single-phase	Depending on the reaction rates. Eqs. 22 and 28	Depending on the reaction rates. Eqs. 23 and 29
	Two-phase	Depending especially on the reaction rates. and the partition relations between two phases. Eqs. 24 and 30	The reaction time becomes longer. Eqs. 25 and 31

Table 2. Comparison Between Macro-and Microoperations

Shape of fluid	Droplet			Parallel flow	Slug
a/V_d[m^{-1}]	4000	8000	20,000	8000	6000 ca.
Droplet size: d_p/ Device geometory	d_p: 1.5 mm Stirred vessel mild mixing	d_p: 750 μm Stirred vessel turbulent regime	d_p:300 μm Micromixer	Y-shaped mocrochannel: 3 cm (length), 250 μm (width), 100 μm (depth)	Segmented flow: 440 μm (tube diameter), 400 μm (slug length)
					
Operation	Macro operation		Micro operation		

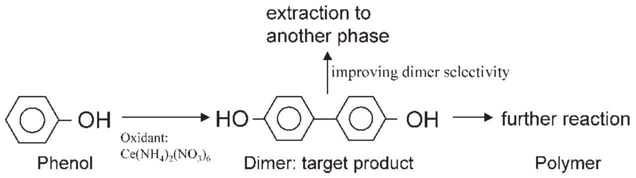


Figure 18. Oxidative polymerization of phenol.

Table 3. Comparison of Experimental Results Using Each Reaction System

Reaction system	Single-phase	Two-phase
Solvents	THF:100 mL (Phenol:4 mmol) Water: 20 mL (CAN: 3.52 mmol)	Ethyl acetate: 100 mL (Phenol: 4 mmol) Water: 20 mL (CAN: 3.52 mmol)
Reactor	Batch reactor (stirred vessel)	Micromixer
Operation pattern	Macrooperation	Microoperation
Dimer selectivity [%]	9.8	49.5

Conclusions

The improvement of yield of a target product by adopting a two-phase system was considered for first-order consecutive and reversible reactions. As a result, the target product yield of a two-phase system can surpass that of a single-phase system when the partition relations between the two phases of a raw material and a target product are selected appropriately. In addition, the volume ratio of the two phases and liquid–liquid interfacial area are important operating factors for improving the yield. The reaction time when the maximum target product yield is attained is greatly increased compared with a single-phase system.

For a consecutive reaction, use of a microspace can contribute to improving the yield of a target product by increasing the liquid–liquid interfacial area and enhancing the apparent mass transfer. For a rapid reaction system, improvement of the target product yield and simultaneous separation of the product are possible, because precise control of retention time is possible. The use of a microspace can play significant roles in intensifying a two-phase system.

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