Accelerated Saponification of Methyl Dodecanoate with Aqueous Sodium Hydroxide Solution in the Presence of Alcohols in a Silicone Rubber Tube as a Flow-Type Reactor

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Saponification of methyl dodecanoate with an aqueous sodium hydroxide solution in the absence and presence of alcohols was studied using a tubular reactor made of silicone tube to elucidate effects of alcohol addition on the saponification. The reaction rates of saponification were accelerated significantly when alcohols were dissolved in methyl dodecanoate and the rates were increased in the order: without alcohol $\ll$ ethanol $<$ propanol $<$ butanol. The rates in all cases obeyed the Nernst diffusion rate equation, and the values of apparent diffusion constant, k_a, that were determined from the slope of Nernst plots were increased in the above order, indicating that diffusion of sodium ion in the aqueous solution into the mixture of methyl dodecanoate and alcohol was much easier than that to methyl dodecanoate without alcohol. The values of k_a increased with increase in the amount of butanol both in the tubular reactor and in a beaker (batch system). The thickness of the diffusion layer, δ, decreased with increase in the amount of butanol in the saponification in the tubular reactor, suggesting that the increase in k_a in the saponification in the presence of butanol in the tubular reactor can be explained by decrease in values of δ.

Development of novel technologies for a sustainable world is needed to resolve serious environmental and energy problems. The substitution of organic solvents for water in organic syntheses has attracted much attention from the point of view of eco-friendly production of chemicals.[1–4] A water solvent is also very useful for practical use because water is safe, cheap, and chemically stable. However, organic compounds are often hydrophobic. Therefore, most studies on organic synthesis in a water solvent have focused on the development amphiphilic catalysts such as a phase-transfer catalyst,[5,6] amphiphilic catalyst-anchored polymers[7–10] and a Lewis-acid catalysts that are stable in water.[11,12] An optimal catalyst is generally present for each reaction and there is no catalyst that is almighty for some reactions. It is hence essential for practical use to develop an optimal catalyst for each reaction. Another way to apply a water solvent to organic syntheses is the development of a novel reactor having a large diffusion constant in a two-phase reaction between a water solvent and hydrophobic reactant(s). There have been some studies on a micro-reactor in the two-phase reaction,[13–16] but the high cost of the micro-reactor itself limits its application to the production of expensive chemicals such as medicinal chemicals, because the micro-reactor is made by using advanced technologies and is used under a high pressure. There have been few studies on novel reactors other than a micro-reactor.

We have developed a long tubular reactor using a cheap and mass-produced tube made of silicone rubber. We already reported that saponification of some kinds of fatty acid methyl ester with aqueous alkali hydroxide solution was accelerated significantly by using a long tubular reactor and that the apparent diffusion constant of alkali cation in the aqueous solution to the methyl esters was increased 300–500 times more than those in a batch system.[17,18]

It is known that addition of a solubilizer such as an alcohol to the reaction mixture of water and hydrophobic reagents often promotes the reaction rate in a batch system. We attempted to apply the tubular reactor to saponification of fatty acid methyl esters with aqueous sodium hydroxide solution in the presence of alcohols as a model of two-phase reaction and to elucidate the effects of addition of alcohols on saponification in the tubular reactor. It was found that the addition of alcohols significantly increased the reaction rate of saponification in the tubular reactor as well as in the batch-type reactor. In this paper, we show that (1) the saponification of methyl dodecanoate with sodium hydroxide (NaOH) in the presence of alcohols also obeyed the Nernst diffusion rate equation and that its rate-controlling step was diffusion of sodium cation into the mixture of methyl dodecanoate and alcohol, (2) a larger apparent diffusion constant was obtained in the presence of alcohols, and (3) alcohols dissolved in methyl dodecanoate decreased the thickness of the diffusion layer formed between the ester phase and the aqueous phase.

Experimental

Materials. Commercial and reagent-grade methyl dodecanoate, sodium hydroxide (NaOH), ethanol, propanol, butanol, hexane, and biphenyl were used without further purification. Distilled water was used as a solvent of NaOH. Commercial tubes made of silicone rubber with an inner diameter of 1.7 mm were supplied by ARAM Corporation, Osaka.

Saponification. In a typical run, NaOH (20 mmol) was dissolved in 5.0 cm^3 of distilled water. A peristaltic pump (Cole

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Palmer Masterflex 7553-70) was used to separately supply the aqueous NaOH solution (aq NaOH) and an equivalent volume ($5.0\,\mathrm{cm}^3$) of methyl dodecanoate (corresponding to 20 mmol) to each silicone rubber tube with inner diameter of 1.7 mm. The two tubes were connected with a Y-type joint made of polypropylene and the two liquids were mixed at the Y-type joint. The mixture was introduced from the third port of the joint to main tubes with the same inner diameter and various lengths (25–125 cm) heated in a water bath adjusted to 333 K. The reaction mixture that flowed out from the tubular reactor was quickly cooled at 273 K to avoid further saponification. Saponification of methyl dodecanoate (20 mmol) containing alcohol (ethanol, propanol, or butanol, 5.0–20 mmol) with an equivalent volume of aq NaOH (20 mmol) was also carried out by the above same procedure. Each flow rate of aq NaOH and the methyl dodecanoate–alcohol mixture was $14.4\,\mathrm{cm}^3\,\mathrm{min}^{-1}$ within 0.25% change to attain a constant Reynolds number. The flow rate gave a mixed flow of aqueous and oil phases in the narrow tubular reactor. Reaction rates were measured in an initial period to minimize surfactant effects of reaction product (sodium dodecanoate) on diffusion of sodium ion, because it was well known that a soap promoted the saponification of oils and fats with aq NaOH and that the reaction mixtures began to be homogenized and to increase their viscosities when the saponification proceeds to high conversion. The methyl dodecanoate unreacted in the reaction mixture was immediately extracted twice with hexane, and the amounts of the ester were determined: the amounts of the unreacted methyl dodecanoate were corrected by using the distribution ratio of methyl dodecanoate between hexane and reaction mixture. The extracted methyl dodecanoate was determined by GC as a calibration of biphenyl. Reaction time (t) was defined by the quotient of the tube volume to the total flow rate.

Saponification of methyl dodecanoate with aq NaOH in a beaker was also carried out at the same temperature for comparison with that in the tubular reactor at the same temperature. In this case, stirring time is defined as reaction time. The methyl dodecanoate unreacted in the reaction mixtures was analyzed by the same procedures as those described above.

Results and Discussion

Effect of Addition of Various Alcohols on Saponification of Methyl Dodecanoate with aq NaOH in a Tubular Reactor. Results of saponification of methyl dodecanoate (20 mmol) with aq NaOH (20 mmol) in the presence of various alcohols (5 mmol) in an initial period using the tubular reactor are shown in Figure 1. Results of saponification in the absence of alcohol are also shown in the figure for comparison. The results clearly show that the reaction rate of saponification in the tubular reactor was significantly accelerated by addition of alcohols. The reaction rate of saponification in the presence of alcohols was increased in the order of ethanol < propanol < butanol. We previously reported that diffusion of alkali ion into fatty acid methyl ester was the rate-controlling step in the saponification of methyl ester with alkali hydroxide in the absence of alcohol.[17,18] Therefore, the data in Figure 1 were plotted according to the Nernst diffusion rate equation:[19,20]

$$\ln(C_0/C_t) = k_a \cdot t \tag{1}$$

where k_a, t, C_0, and C_t are apparent diffusion constant, reaction time, initial concentration of aq NaOH, and concentration of NaOH at t, respectively. Logarithm of the ratio of C_0 to C_t vs. t is shown in Figure 2, and a linear relationship was observed between the logarithm and t in the presence of alcohols (ethanol, propanol, and butanol) as well as in the absence of alcohol. These results indicate that the saponification in the presence of alcohols also obeyed eq 1, which was derived on the basis of the assumption that the diffusion process was the rate-controlling step, in all cases independent of the type of alcohol. Therefore, in the presence of alcohol, diffusion of sodium ion in the aqueous phase into the mixture of methyl dodecanoate and alcohol was the rate-controlling step in the saponification with aq NaOH as well as in the saponification in

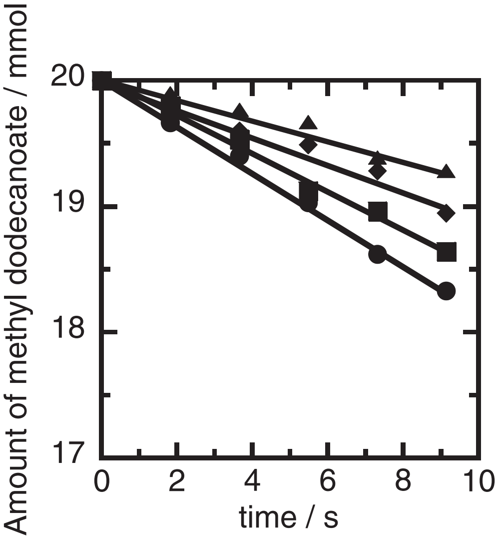


Figure 1. Saponification of methyl dodecanoate (20 mmol) in the absence of alcohol (triangles) and in the presence of 5.0 mmol of ethanol (diamonds), propanol (squares), and butanol (circles) with equivalent volumes of aqueous sodium hydroxide (20 mmol) solutions in silicone tubes having various lengths and an inner diameter of 1.7 mm at 333 K with each flow rate of $14.4\,\mathrm{cm}^3\,\mathrm{min}^{-1}$. Reaction time in tubes was defined by the quotient of the tube volume to the total flow rate.

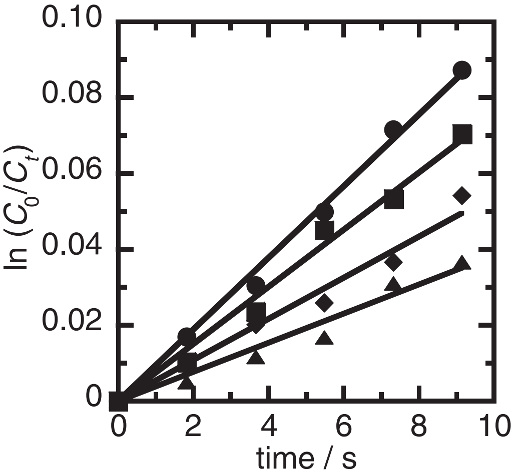


Figure 2. Plots of $\ln(C_0/C_t)$ vs. reaction time using various tubular reactors. Symbols are the same as those used in Figure 1.

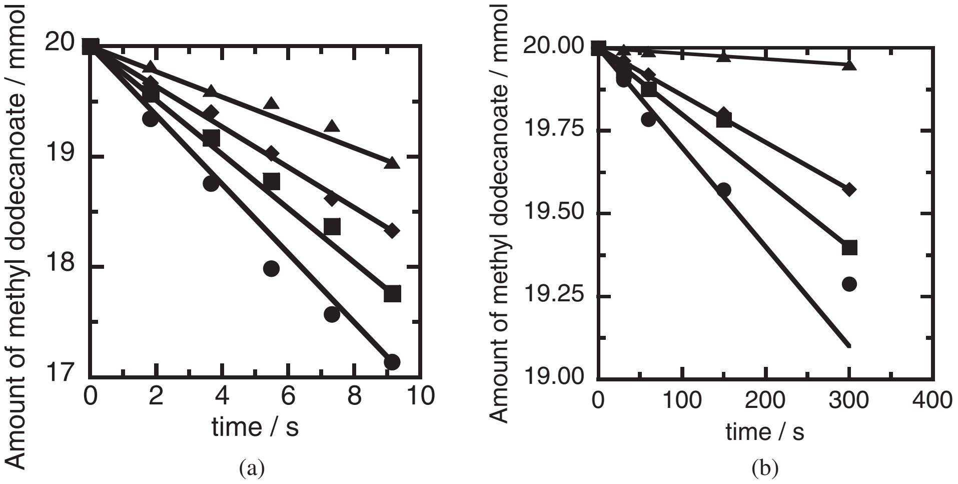


Figure 3. Saponification of methyl dodecanoate (20 mmol) in the absence (triangles) and presence of 5 mmol of butanol (diamonds), 10 mmol of butanol (squares), and 20 mmol of butanol (circles) with equivalent volumes of aqueous sodium hydroxide (20 mmol) solutions in (a) tubes having various lengths and an inner diameter of 1.7 mm at 333 K and (b) beakers. Reaction time in tubes was defined by the quotient of the tube volume to the total flow rate.

the absence of alcohol. In addition, we previously reported that the values of k_a in the tubular reactor system were proportional to the inner surface area of hydrophobic silicone tube.[17] The slope of the Nernst plot shown in Figure 2 represents k_a. The values of k_a were determined to be $0.0038\,s^{-1}$ in the absence of alcohol and 0.0053, 0.0075, and $0.0094\,s^{-1}$ in the presence of ethanol, propanol, and butanol, respectively, indicating that addition of alcohol (5 mmol, corresponding to 20 mol %) drastically increased k_a. Therefore, the large increase in k_a was attributed to the larger reaction rate in the saponification in the presence of alcohol using the tubular reactor. The value of k_a in the presence of butanol was ca. 2.5-times larger than that without butanol. The results indicate that diffusion of sodium ion in the aqueous solution into the mixture of methyl dodecanoate and alcohol was much easier than that into methyl dodecanoate without alcohol and that the diffusion of sodium ion was affected by the type of alcohol dissolved in methyl dodecanoate. The values of k_a were increased with increase in the carbon number of alcohol, i.e., ethanol < propanol < butanol. It is expected that hydrophobicity of the alcohols increased in this order due to increase in the alkyl chain. These results suggest that hydrophobicity of alcohols as solubilizers is one of the important factors for increasing k_a in saponification of methyl dodecanoate with aq NaOH in the presence of alcohols in the tubular reactor.

Effect of the Amount of Butanol Dissolved in Methyl Dodecanoate on Saponification with aq NaOH. In the previous section, it was shown that butanol exhibited the greatest effect on saponification of methyl dodecanoate with aq NaOH in the tubular reactor. In this section, the effect of the amount of butanol dissolved in methyl dodecanoate on saponification with aq NaOH is described. Results of saponification of methyl dodecanoate in the presence of various amounts of butanol in an initial period using the tubular reactor are shown in Figure 3a. For comparison, saponification in a beaker system under the same conditions was also examined and the results are shown in Figure 3b. When saponification was carried out in a beaker, the reaction mixture was separated immediately into aqueous and ester phases. The saponification rates both in the tubular reactor and in the beaker were increased with increase in the amount of butanol dissolved in methyl dodecanoate. Logarithms of the ratio of C_0 to C_t vs. t in the tubular reactor and in the beaker are shown in Figures 4a and 4b, respectively. A linear relationship was observed between the logarithm and t in all cases, i.e., both in the tubular reactor and in the beaker, and independent of the amount of butanol. These results indicate that saponification in the presence of butanol obeyed eq 1 independent of the type of reactor and of the amount of butanol dissolved in methyl dodecanoate. From the slopes in Figures 4a and 4b, the values of k_a under various conditions were determined and are summarized in Table 1. The values of k_a were increased both in the tubular reactor and in the beaker with increase in the amount of butanol.

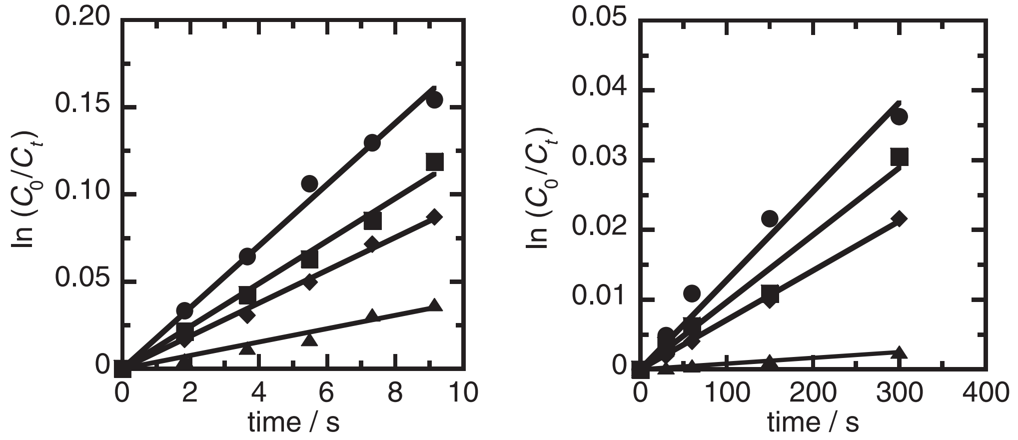
In our previous study, we examined saponification of three kinds of fatty acid methyl esters (octanoate, decanoate, and dodecanoate) with aqueous solutions of alkali hydroxides (NaOH and potassium hydroxide) in the absence of alcohol using the tubular reactor[17,18] and determined the diffusion constant (D) using eq 2:[21]

$$k_a = (DS)/(V\delta) \qquad (2)$$

where S, V, and δ represent contact interface area, volume of ester, and thickness of the diffusion layer, respectively. It was found that D increased with decrease in the carbon number of fatty acid methyl esters and that the value of D was proportional to the reciprocal of viscosity of methyl ester. This correlation was explained by the Stokes–Einstein equation:

$$D = (kT)/(6\pi\eta r) \qquad (3)$$

where, k, T, η, and r are Boltzmann constant, absolute temperature, viscosity of ester, and radius of Na^+, respectively. In the present study, values of viscosity of the mixtures of methyl dodecanoate and butanol were decreased with increase in the amount of butanol dissolved and are shown in Table 2. Assuming that the linear correlation between D and the



(a)

(b)

Figure 4. Plots of ln(C_0/C_t) vs. reaction time using (a) tubular reactors and (b) beakers. Symbols are the same as those used in Figure 3.

Table 1. Apparent Diffusion Constant (k_a) in Saponification of Methyl Dodecanoate (20 mmol) with aq NaOH (20 mmol) in a Tubular Reactor and in a Beaker in the Absence and Presence of Butanol

Butanol[a) /mmol	k_a for TR[b) $/10^{-2}\,s^{-1}$	k_a for BR[c) $/10^{-2}\,s^{-1}$
0	0.38	0.00058
5	0.94	0.0071
10	1.2	0.0096
20	1.8	0.013

a) Amount of butanol dissolved in methyl dodecanoate. b) Apparent diffusion constant in tubular reactor. c) Apparent diffusion constant in beaker.

Table 2. Some Parameters of Saponification of Methyl Dodecanoate (20 mmol) with aq NaOH (20 mmol) in a Tubular Reactor in the Absence and Presence of Butanol

Butanol[a) /mmol	η[b) /Pa s	D[c) $/10^{-6}\,cm^2\,s^{-1}$	V[d) $/cm^3$	δ[e) $/10^{-3}\,cm$
0	1.45	0.592	5.0	1.246
5	1.34	0.641	5.2	0.525
10	1.29	0.666	5.6	0.396
20	1.23	0.698	6.4	0.242

a) Amount of butanol dissolved in methyl dodecanoate. b) Viscosity of mixtures of methyl dodecanoate and butanol. c) Diffusion constant determined from linear correlation between D and η^{-1} in saponification of some kinds of fatty acid methyl esters with aq NaOH. Slope in D vs. η^{-1} plot was 8.59×10^{-7} Pa cm^2.[18] d) Volume of mixture of methyl dodecanoate and butanol. e) Thickness of diffusion layer.

reciprocal of viscosity of methyl ester observed in the saponification without alcohol can be applied to the present reaction system, i.e., saponification in the presence of butanol, the values of D of the mixtures of methyl dodecanoate and butanol were calculated from the observed viscosity and are shown in Table 2. The values of D obtained were applied to eq 2, and the values of δ with different contents of butanol were determined and are summarized in Table 2. Here, S was regarded to be nearly equal to the surface of the inner wall of the tubular reactor,[18] because the thin diffusion layer of the mixtures of ester and alcohol expanded parallel to the inner wall. The thicknesses of δ decreased with increase in the amount of butanol dissolved in methyl dodecanoate in saponification in the tubular reactor. This result indicates that the drastic increase in k_a in saponification in the presence of butanol in the tubular reactor can be explained by the decrease in thickness of the diffusion layer. The effect of butanol addition can probably be applied for explanation of the increase in k_a in the beaker.

Conclusion

Effects of the Addition of Various Alcohols on Saponification of Methyl Dodecanoate with aq NaOH in a Tubular Reactor. The saponification rate in the tubular reactor was significantly accelerated by addition of alcohols. Saponification in the presence of alcohols obeyed the Nernst diffusion rate equation in all cases independent of the type of alcohol, and diffusion of sodium ion in the aqueous phase into the mixture of methyl dodecanoate and alcohol was the rate-controlling step in the saponification with aq NaOH as well as the saponification in the absence of alcohol. The values of k_a were determined to be 0.0038 s^{-1} in the absence of alcohol and 0.0053, 0.0075, and 0.0094 s^{-1} in the presence of ethanol, propanol, and butanol, respectively, indicating that addition of alcohol (5 mmol, corresponding to 20 mol %) drastically increased k_a. The results, obtained in this study indicate that diffusion of sodium ion in the aqueous solution into the mixture of methyl dodecanoate and alcohol was much easier than that into methyl dodecanoate without alcohol and that the diffusion of sodium ion was affected by the type of alcohol dissolved in methyl dodecanoate.

Effects of the Amount of Butanol Dissolved in Methyl Dodecanoate on Saponification with aq NaOH. Reaction rates of saponification in the tubular reactor increased with an increase in the amount of butanol dissolved in methyl dodecanoate as did the reaction rates of saponification in the beaker. Saponification in the presence of butanol obeyed the

Nernst diffusion rate equation independent of both the type of reactor and the amount of butanol. The values of k_a increased both in the tubular reactor and in the beaker with increase in the amount of butanol. The thicknesses of δ decreased with increase the amount of butanol in saponification in the tubular reactor. This result indicates that the drastic increase in k_a in saponification in the presence of butanol in the tubular reactor can be explained by the decrease in thickness of the diffusion layer.

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