1. Introduction

Gas-liquid organic reactions, such as oxidation by O₂, are generally clean reactions with environmentally friendly characteristics because no heavy metals are used as reactants and no gaseous substances are released[1,2]. These reactions require high frequency of contact between the gaseous reactants and the dissolved reactants. High-pressure reaction conditions are often used in industry to increase the solubility of the gaseous reactants. Consequently, gas-liquid reactions may be avoided because of the many safety issues and need for larger reactors, despite the potential for green chemistry. Therefore, more efficient and more compact reaction systems operating under milder conditions are desirable for gas-liquid organic reactions.

Fine bubbles are micro-nano bubbles of 100 μm or less diameter in liquid. Fine bubbles have various specific characteristics due to their size, such as huge specific surface areas, lower floating speed, self-pressurization, crushing by self-pressurization, radical generation caused by crushing, and supersaturated dissolution of gas[3-6]. Various applications of fine bubbles have been attempted in the fishery, agriculture, and washing fields to make good use of these specificities, and practical uses have been developed[7-15].

Introduction of gaseous reactants as fine bubbles into gas-liquid organic reactions is expected to increase the collision frequency of reactant molecules due to higher dissolution of fine bubbles in the liquid phase, improve the contact surface area with the liquid phase, and lengthen the residence time of bubbles. These advantages will shorten the reaction time and reduce the pressure of the reaction, so improve safety and reduce the need for large-scale equipment.

Accelerating some gas-liquid organic reactions was confirmed by applying the properties of fine bubbles[16-18]. Application of fine bubbles to organic reactions may dramatically improve the reaction efficiency, but few studies have investigated this aspect[16-18]. Studies of gas-liquid reactions that introduce reactive gases as fine bubbles propose significant themes that should be examined from various angles, e.g., types of reactions, associated reactive gas species, and the relationship between generation methods of fine bubbles and reactions.

Almost all gas-liquid organic reactions using fine bubbles investigated so far involve pressurized dissolution process in the generation of fine bubbles. The pressure dissolution method generates fine bubbles as follows. Pressurization of the system in the gas-liquid equilibrium state saturates the dissolved gas. Return of the system to atmospheric pressure supersaturates the dissolved gas. Under atmospheric pressure, gas that cannot be dissolved is generated as fine bubbles.

We have newly constructed a fine bubble reactor...
using a gas-liquid two-phase flow (swirl) fine bubble generator\(^\text{19}\). The gas is introduced into the liquid phase and is disrupted into fine bubbles by the gas-liquid shear induced by the swirling action of the liquid. This process does not require pressurization, and fine bubbles can be obtained with a simpler reactor. Therefore, gas-liquid reactions carried out using our reactor occur due to formation of fine bubbles predominantly under the condition of gas-liquid shear.

The present study used oxidation of benzaldehyde to benzoic acid with molecular oxygen as the model reaction to verify the effect of generating O\(_2\) fine bubbles (Fig. 1). This reaction is optimal as a model because the oxidation reaction automatically proceeds with O\(_2\) at room temperature and atmospheric pressure, and as benzoic acid is an industrially important raw material for various products. Oxidation reactions using O\(_2\) fine bubbles have been reported academically only by Mase et al.\(^\text{16}\). In this report, using the fine bubbles obtained by the pressure dissolution method, a remarkable effect of accelerating the oxidation of primary alcohols into aldehydes in the presence of copper/2,2,6,6,-tetramethyl-1-piperidinyloxyl (TEMPO) catalysts was obtained. Our study examined the effect of fine bubbles generated by the swirling liquid flow method without the pressurization process, and the oxidation reaction species that has never been investigated introducing fine bubbles.

2. Experimental

2.1. Fine Bubble (FB) Reactor and Reaction Method

Figure 2(a) shows a schematic view of the reactor system that incorporates a gas-liquid two-phase flow (swirl) fine bubble generator (Sakamoto-Giken Inc.). The reaction solution is cyclically drawn into the fine bubble generator (1) using a pump (2). Simultaneously, (1) is supplied with O\(_2\) from the gas cylinder (3) with the flow rate controlled by a flowmeter (4). Fine bubbles are generated in (1) by gas-liquid two-phase flow. The introduction of O\(_2\) as fine bubbles into the reaction solution using this reactor is referred to here as the FB method.

To verify the effectiveness of the FB method, the following two procedures were examined: the aeration method in which the reaction proceeds by bubbling O\(_2\) gas into the reaction solution with a controlled flow rate (AR method, Fig. 2(b)), and the balloon method in which the reaction is allowed to proceed in an O\(_2\) atmosphere (BL method, Fig. 2(c)). All reaction methods were carried out with stirring (400 rpm) at (5) in Fig. 2. Both O\(_2\) introduction methods were used for autoxidation of benzaldehyde substrate (20 mmol) with pure O\(_2\) gas in acetonitrile solvent (50 mL).

All reagents were special grade (FUJIFILM Wako Pure Chemical Corp.). The FB, AR, and BL methods used 20 mmol of benzaldehyde and 2.50 g of o-dichlorobenzene (internal standard) per 50 mL of solvent (acetonitrile). The conversion and yield of the reaction were monitored by gas chromatography using a SHIMADZU GC-2014 equipped with a hydrogen-flame ionization detector (FID) and a 30 m capillary column Restek Rxi® 5Sil MS.

2.2. Existence Evaluation of FB and the Degree of Dissolved O\(_2\)

Microbubbles were observed using a KEYENCE VW-6000 Motion Analyzing Microscope with 100× magnification. Oxygen fine bubbles were generated in 1 L of acetonitrile. Acetonitrile was placed in a glass container with a flat side surface, and then oxygen fine bubbles were generated in the solvent. The fine bubbles were observed by recording a video with a microscope from the outside of the container.

The oxygen saturation in the organic solvent (aceto-
nitrile) was measured using an Iijima B-506 DO meter under atmospheric pressure. Aeration was performed on 1 L of acetonitrile at a O₂ flow rate of 20 mL/min, and after the dissolved oxygen was apparently saturated, this was defined as the 100 % standard. Then, N₂ aeration was performed, and the point at which the dissolved oxygen amount did not change was set to t = 0. Subsequently, oxygen was introduced by the FB method and AR method, and the time change of the dissolved O₂ amount was measured.

3. Results and Discussion

3.1. Oxidation of Benzaldehyde with O₂ Fine Bubbles

Oxidation of benzaldehyde was compared using the FB method, the AR method, and the BL method, with the O₂ flow rate fixed at 20 mL/min, and the results assessed after 6 h. Conversion of benzaldehyde and the yield of benzoic acid were remarkably improved 6 h after the start of the reaction (Table 1, Runs 1-3).

Figure 3 shows the time course of the conversion of benzaldehyde, and Fig. 4 shows the time course of the yield of benzoic acid. The reaction rate of benzaldehyde was significantly increased with the FB method compared to the other two methods (Fig. 3). The reaction time for a conversion rate of 90 % was approximately five times shorter for the FB method compared to the aeration method and approximately nine times shorter compared to the balloon method. A similar trend was observed for the yield (Fig. 4). Specifically, the FB method achieved significant improvement in the benzoic acid production rate compared to the other two methods.

The final yields of all methods converged to almost the same level. Specifically, the final selectivity was approximately 80 % for all methods. The improvement in the benzoic acid production rate using the FB method was dominated by the improvement in the conversion. Thus, the yield after 6 h shown in Table 1 was mainly affected by the reaction rate, and the involvement of the selectivity was less significant.

Generally, benzaldehyde oxidation with O₂ occurs in three steps²⁰⁻²⁴, as shown in Fig. 5: (i) formation of peroxide 2 by the free radical chain reaction of benzaldehyde 1, (ii) production of tetrahedral adduct 3 by nucleophilic addition of peroxide 2 to the remaining benzaldehyde, which resembles the Criegee intermediate observed in the Bayer-Villiger reaction, and (iii) formation of 2 moles of benzoic acid 4 from rearrangement of 3 by hydrogen transfer (path a) or formation of 1 mole of benzoic acid 4 and 1 mole of formate 5 from rearrangement of 3 by an aryl group transfer from the aldehyde (path b). Thus, the reaction rate of the first step

| Run | Method | O₂ flow rate [mL/min] | Yield [%, d) | Conversion [%] |
|-----|--------|----------------------|--------------|----------------|
| 1   | FB     | 20                   | 77.8         | 96.9           |
| 2   | AR     | 20                   | 39.7         | 36.0           |
| 3   | BL     | –                    | 27.8         | 40.3           |
| 4   | FB     | 4                    | 67.3         | 85.7           |
| 5   | AR     | 4                    | 33.8         | 46.1           |
| 6   | FB     | 100                  | 82.2         | 96.8           |
| 7   | AR     | 100                  | 37.7         | 53.0           |

a) O₂ introduction method. b) Yield of benzoic acid. c) Conversion of benzaldehyde. d) Determined by GC analyses.

Fig. 3 Time Dependence Curves for the Conversion of Benzaldehyde for the FB, AR (both 20 mL/min of O₂ flow rate), and BL Methods

Fig. 4 Time Dependence Curves for the Yields of Benzoic Acid from FB, AR (both at 20 mL/min of O₂ flow rate), and BL Methods
involving O\textsubscript{2} (as fine bubbles) was probably specifically improved compared to other steps without the use of molecular oxygen. On the other hand, the triplet state is the ground state for O\textsubscript{2}. Therefore, oxidation of triplet state O\textsubscript{2} to the singlet state organic molecule is generally unlikely to occur. In general, even in the oxidation of aldehyde species, O\textsubscript{2} addition as the first step is the rate-determining step, and the rate constant is smaller than the other steps\textsuperscript{23,24}. This study suggests that the rate-determining first step was significantly promoted by fine bubbles, which greatly contributed to the improvement of the overall reaction rate.

3.2. Effect of Promoting O\textsubscript{2} Dissolution by Fine Bubbles

The amount of O\textsubscript{2} in the reaction solution is important to know. At present, we cannot determine the amount of O\textsubscript{2} in 50 mL of reaction solution with our equipment. However, the degree of O\textsubscript{2} saturation in the organic solvent can be estimated on the liter scale. The relative amount of dissolved O\textsubscript{2} introduced by the FB method was compared with the amount of saturated O\textsubscript{2} dissolved by the AR method as the standard of 100 \% saturation in 1 L of acetonitrile (Fig. 6). Generally, the dissolved amount of gas in water solvent is supersaturated if fine bubbles are present\textsuperscript{41}. No such supersaturation phenomenon has been observed in organic solvents, but we confirmed the supersaturation of dissolved O\textsubscript{2} in the presence of fine bubbles in acetonitrile. This supersaturation was not caused by the artificial pressurization but by the presence of fine bubbles in the reaction solution under atmospheric pressure. This supersaturated effect of dissolved O\textsubscript{2} is likely to have a significant effect on improving the reaction rate. Since 1 L of acetonitrile became supersaturated in approximately 10 min, supersaturation can occur even faster in a 50 mL reaction solution, and may be sufficiently faster than the reduction rate of benzaldehyde, so that the reaction system always maintains supersaturation of O\textsubscript{2}. Acetonitrile saturated with O\textsubscript{2} contains 4.32 $\times$ 10\textsuperscript{-4} of dissolved oxygen as a mole fraction\textsuperscript{25}. Oxygen supersaturation is approximately 160 \% in the presence of fine bubbles, so that approximately 13 mmol/L of O\textsubscript{2} is always present in a dissolved state.

3.3. Relationship between O\textsubscript{2} Flow Rate and Conversion

The effects of fine bubbles were also verified at other O\textsubscript{2} flow rates (Table 1, Runs 4-7). The FB method exhibited remarkable promotion of the reaction even at flow rates of 4-mL/min and 100-mL/min compared with the AR method, as with the 20-mL/min flow rate. In our reactor, at 100-mL/min flow rate, visible bubbles of the order of millimeters or more (non-fine bubbles) appeared together with fine bubbles (Fig. 7(a)). At 20 mL/min flow rate, visible bubbles were reduced (Fig. 7(b)), and at 4-mL/min flow rate, the reaction solution was almost visually transparent (Fig. 7(c)). However, fine bubbles on the order of micrometers (microbubbles, with a diameter of 1 to 100 \textmu m) in acetonitrile were confirmed using a microscope (Fig. 8). However, the fine bubble observation method used in our study could observe only micro-sized objects within the 100 $\times$ magnification field of view and matching the set focus. Our method measured only microbubbles slightly inside the inner wall of the container. Therefore, our observation of multiple bubbles at the same time was unexpected. Microparticles are true spheres with transparent central parts as the observed characteristics\textsuperscript{7,26,27}. In our study, particles other than fine
bubbles were not introduced, so our observations captured the characteristics of fine bubbles. If the particles are solid impurities, the center is not transparent. Therefore, we concluded from the present results that microbubbles were present in the organic solvent. Figure 9 shows the relationship between the O2 flow rate and the conversion of benzaldehyde with the FB method. Higher the O2 flow rate caused faster benzaldehyde reaction rate, but did not change the conversion as much as the O2 flow rate. Therefore, increased amount of introduced O2 did not increase the reaction rate correspondingly; as the degree of increase in the reaction rate reached the limit. Ultra-fine bubbles (nano-scale fine bubbles) that cannot be visually observed are present in transparent aqueous solvent, and ultra-fine bubbles have been measured by various methods\(^7\). Very few research reports discuss the existence of ultra-fine bubbles in organic solvents. The presence of H\(_2\) ultra-fine bubbles in various organic solvents was first evaluated recently for the time by Mase et al. In the same report, observation results for O2 ultra-fine bubbles in ethyl acetate were obtained. Therefore, ultra-fine bubbles were likely in the reaction solution containing the fine bubbles in our present study. Therefore, at a 100-mL/min flow rate, despite the larger volume of O2 introduced, micro bubbles and non-fine bubbles with a relatively small specific surface area contributed significantly to the gas volume. If the reaction rate was improved by supersaturated dissolved O2 and/or ultra-fine bubbles with a large specific surface area, the reaction rate was not significantly improved at the 100-mL/min O2 flow rate compared to the other two O2 flow rates.

Alternatively, O2 is more effectively used for the reaction at low O2 flow rates. Figure 10 shows the relationship between the reaction time and the O2 utilization efficiency, \(\eta\)

benzaldehyde reacts per mole of O2,

\[
\eta(t) = \frac{n_{\text{AL}}(t)}{2n_{\text{O2}}(t)} \times 100
\]

where, \(n_{\text{O2}}(t)\) and \(n_{\text{AL}}(t)\) are the amount of oxygen introduced into the reaction system and the amount of benzaldehyde reduced by time \(t\), respectively. \(n_{\text{O2}}(t)\) was estimated as follows, assuming an ideal gas,

\[
n_{\text{O2}}(t) = \frac{pV_{\text{O2}}(t)}{RT}
\]

where \(V_{\text{O2}}(t)\) is the volume of O2 introduced into the reaction system by time \(t\), \(T\) is the absolute temperature, \(R\) is the gas constant, and \(p\) is atmospheric pressure.

According to Fig. 10, \(\eta\) is larger for the FB method than for the AR method at the same flow rate. As expected, \(\eta\) was larger at lower O2 flow rate, and approximately one fourth of the introduced O2 was used for the reaction at the maximum O2 utilization efficiency at a flow rate of 4 mL/min.

4. Conclusion

The present study investigated the effect of fine bubbles on the oxidation of benzaldehyde with O2 as a
model reaction. The product, benzoic acid, was produced efficiently in the presence of fine bubbles. We found that the promotion effect was mainly dominated by the conversion, not the selectivity. The first step of the reaction involving O₂ was predominately accelerated. Additionally, the reaction was promoted even without pressurization, so the characteristics of the O₂ fine bubbles and/or the effect of supersaturation in the presence of the O₂ fine bubbles promoted the reaction. Therefore, improvement in the reaction rate by the introduction of fine bubbles may be observed in a wider range of other types of gas-liquid reactions. Other gas-liquid reaction systems that use fine bubbles will be reported soon elsewhere.

Acknowledgement
This work was supported in part by JST Adaptable and Seamless Technology Transfer Program through Target-driven R&D (VP30218088556) and Kochi Prefectural Industry-academia-government Collaborative Multi-field Utilization Promotion Project.

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要　旨

ファインパブルを使用したベンズアルデヒドの酸素酸化反応の促進

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気-液有機反応に対し、気体反応物をファインパブルとして導入できる新しい旋回流型のファインパブル有機反応装置を開発した。ベンズアルデヒドの分子状酸素による酸化反応をモデル反応として、酸素ファインパブルによる気-液有機反応の反応促進効果を評価した。その結果、O₂ファインパブルを用いることで顕著な反応促進効果が得られることを確認した。この反応促進は選択率の向上よりもむしろ転化率の向上が大きく影響していることが判明した。転化率90％となる反応時間と同じ流量のエアレーション手法と比較すると、約1/5に反応時間が短縮されていた。通常のサイズの泡と比較して体積あたりの表面積が大きい、浮遊速度が遅い、溶媒中のガスの飽和和を保持できる等のファインパブルの持つユニークな特性が転化率向上に大きく影響したと考えられる。

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