

Recent progress on photoreactions in microreactors*

Yoshihisa Matsushita^{1,‡}, Teijiro Ichimura², Nobuko Ohba²,
Shinji Kumada², Kosaku Sakeda², Tadashi Suzuki², Hideki Tanibata³,
and Toshiaki Murata⁴

¹*Department of Chemistry and* ²*Department of Chemistry and Materials Science, Tokyo Institute of Technology, 2-12-1 Ohokayama, Meguro, Tokyo 152-8551, Japan;* ³*Mitsui Engineering & Shipbuilding Co., Ltd., Tokyo, Japan;* ⁴*Mitsui Zosen Plant Engineering Inc., Tokyo, Japan*

Abstract: A microreaction system for organic photoreactions was developed, and the processes of diastereo-differentiating photosensitized reaction, photocatalytic oxidation and reduction of organic compounds, and amine N-alkylation were examined in microspace. These model reactions proceeded very rapidly with considerably large photonic efficiencies because of some distinct properties of microreactors for photoreactions, such as higher spatial illumination homogeneity and better light penetration through the entire reactor depth, and large surface-to-volume ratio in comparison with large-scale batch reactors. These results suggest feasibility of microreaction systems on organic photoreactions.

Keywords: photochemistry; photocatalyst; endocrine disrupters; spectroscopy; asymmetric reaction.

INTRODUCTION

Recently, microchannel reactors have attracted much attention and there has been rapid growth in the development of microreaction technology. There are many reports on thermally driven reactions using the benefits attributed to the characteristics of microspace, such as short molecular diffusion distance, fast mixing, extremely effective heat exchange, and laminar flow [1–4]. On the other hand, to the best of our knowledge, photochemical reactions conducted in microreactors have been much less reported [5–10].

A photochemical reaction is initiated when absorption of a photon by a molecule results in an electronically excited state. Since the electronic structure and the nuclear configuration of the excited molecule will be different from those in the ground state and the excited molecule possesses quite high internal energy, photochemical reaction may generate photoproducts that cannot be formed through thermally driven reactions in the ground state.

Photochemical reactions carried out in microreactors can be expected to exhibit some advantages, such as higher spatial illumination homogeneity and better light penetration through the entire reactor depth, in comparison with those conducted in large-scale reactors. Therefore, we are studying organic photoreactions in microreactors [11,12]. In the first place, we will describe our results on asymmetric photoreactions in this report.

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[‡]Corresponding author

A microreactor is attractive for catalytic reactions because of its large surface-to-volume ratio. We also examined photocatalytic reactions in microreactors. Study of light-induced electron-transfer reactions on semiconductor catalyst has become one of the most attractive research areas in photochemistry. Wide varieties of organic reactions were successfully examined by using semiconductor photocatalyst [13,14]. It has been widely accepted that the illuminated specific surface area of photocatalyst within a reactor is the most important design parameter of photocatalytic reactors. Thus, we have developed a photocatalytic microreaction system which has considerably large surface area per unit volume. We will report the study on the photocatalytic oxidation and reduction of organic compounds, and amine N-alkylation processes in a microreactor with immobilized photocatalytic TiO_2 .

EXPERIMENTAL

Photoreactions were carried out in microreactors made of quartz or Pyrex which has a microchannel of 100–500 μm width, 20–500 μm depth, and 50–100 mm length. The microchannel was inscribed on a flat plate by micromilling, laser ablation, or wet etching process [15]. The microchannel was covered with a quartz plate, and sample solutions were introduced into the microreactor with a syringe pump. The microreactor was photoirradiated by a KrF excimer laser (308 nm, 2 Hz, 15 ns pulse duration), a XeCl excimer laser (308 nm, 2 Hz, 15 ns pulse duration), an OPO laser excited with the third harmonic of a Nd^{3+} : YAG laser (10 Hz, 4 ns pulse duration), a low-pressure Hg lamp (40 W), or an array of UV light-emitting diodes (UV-LEDs, 365 nm). A schematic experimental set-up is shown in Fig. 1. Reaction products were analyzed by gas chromatography or thermal lens spectroscopy. Decay kinetics of excited molecules was examined by means of transient absorption spectroscopy. An experimental set-up for transient absorption spectrum measurement has been described elsewhere [16].

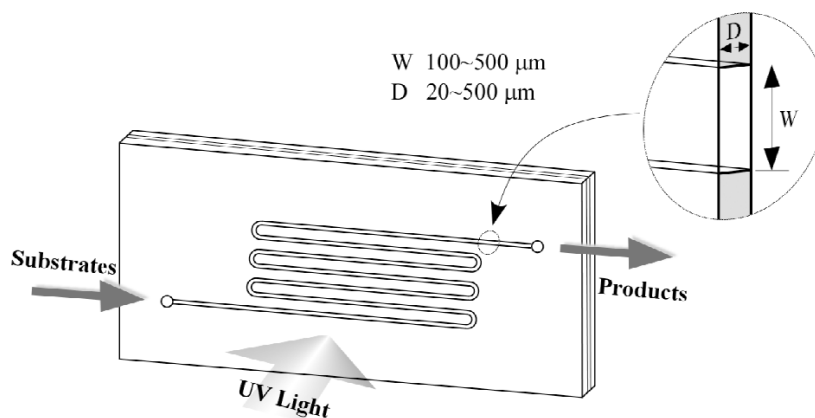


Fig. 1 Schematic view of typical experimental set-up.

RESULTS AND DISCUSSION

Asymmetric photosensitized addition of methanol to (*R*)-(+)-limonene

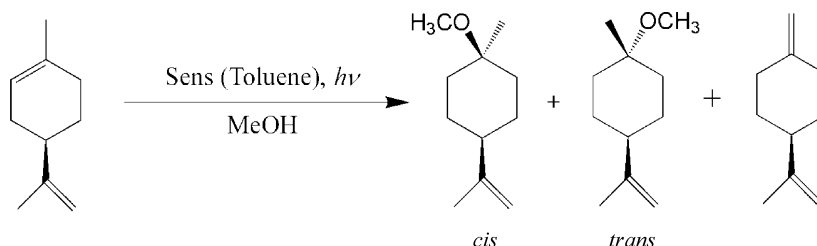
The chirality of molecules is crucial to the action of biological system, and the development of new methodology to control this property has been an important target of a number of researches. Numerous efforts have been devoted to thermally driven and enzymatic asymmetric synthesis. On the other hand, the area of photochemical asymmetric synthesis is still relatively new, although it has already been shown to possess several advantages over its thermal and enzymatic counterparts [17–20]. Therefore,

we are examining asymmetric photoreactions in microreactors. In this report, we will show the results on diastereo-differentiating photosensitized addition of methanol to (*R*)-(+)-limonene.

The photoreaction (Scheme 1) gives three major products [20], i.e., *cis*- and *trans*-4-isopropenyl-1-methoxy-1-methylcyclohexane (*cis* and *trans*) and exocyclic isomer (*exo*). The diastereomeric excess (de) value is defined as follows

$$de = ([trans] - [cis]) / ([trans] + [cis]) \quad (1)$$

where [*trans*] and [*cis*] denote the concentration of the *trans*- and the *cis*-isomers of the methanol adducts, respectively.



Scheme 1 Diastereo-differentiating photosensitized addition of methanol to (*R*)-(+)-limonene.

A methanol solution of (*R*)-(+)-limonene (25 mM) and toluene (10 mM) as a sensitizer was fed into the microreactors of 300 and 20 μm optical path length. As a control experiment, the reaction was also carried out in a quartz batch cell of 3 mm optical path length and 1 ml volume. Figures 2a and b indicate the yields of photoproducts and the conversion of (*R*)-(+)-limonene obtained by a 40-W Hg lamp excitation. In the batch cell, the yield of the *cis*- and *trans*-isomers increased linearly with the irradiation time up to 20 min, and the increasing rate hit a plateau at a longer irradiation time, whereas the yield in the microreactor increased linearly and more quickly during the irradiation period examined up to 135 s.

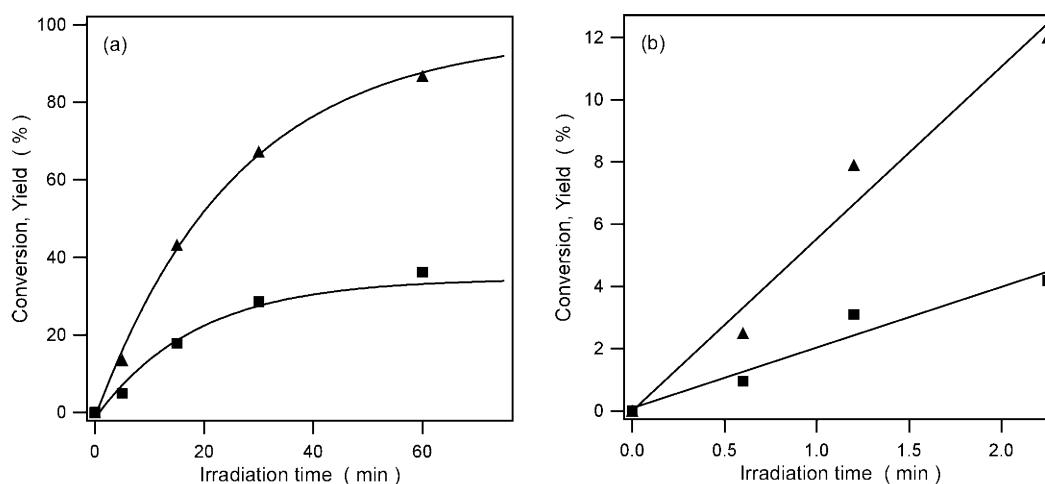


Fig. 2 The yield of *cis*- and *trans*-isomers (square), and conversion of (*R*)-(+)-limonene (triangle) in the batch cell of 3-mm optical path (a), and in the microreactor of 300 μm optical path (b) excited with a 40-W low-pressure Hg lamp.

To our surprise, the yield of *cis*- and *trans*-isomers against the photon number absorbed by the sensitizer per second, namely, photon efficiency, in the microreactor was much higher than that in the batch cell. The photon efficiency is defined as follows

$$\text{Photon efficiency} = [\text{number of product molecules}]/[\text{number of absorbed photons}]$$

The number of absorbed photon was evaluated from the light power (J/s) at 253.7 nm of the Hg lamp, the irradiation time controlled by the flow rate, and the absorbance of the sample solution, which was calculated from the absorption coefficient at 253.7 nm and concentration of the photosensitizer toluene in methanol and the light path length. In the microreactors of 300- and 20- μm optical path length, the photon efficiencies were 0.11 and 0.29, respectively, while it was 0.059 in the batch cell (Table 1). The *de* values in the microreactors and the batch cell were also examined. We obtained slight but certain increase of the *de* value by using the microreactors. The *de* value was increased up to 30.6 % *de* by 36-s irradiation in the microreactor while the value in the batch cell was 28.6 % by the irradiation of 15 min.

Table 1 Photon efficiency, formation rate constants for *cis* (k_{cis}) and *trans* (k_{trans}) isomers, and *de* values of photosensitized addition of methanol to (*R*)-(+)-(*Z*)-limonene in a batch cell and microreactors.

Reactor	Size (width \times optical path length)	Photon efficiency	Formation rate constants		
			$k_{trans}/10^8 \text{ M}^{-1}\text{s}^{-1}$	$k_{cis}/10^7 \text{ M}^{-1}\text{s}^{-1}$	<i>de</i> /%
Batch cell	10 \times 3 mm	0.059	0.29	1.6	28.7
Microreactor	500 \times 300 μm	0.11	0.55	2.9	30.6
Microreactor	200 \times 20 μm	0.29	1.4	7.4	30.0

To clarify the origin of the difference in *de* observed in the microreactor vs. the batch cell, the reaction rate constants for the *cis*- and *trans*-isomer formation were estimated. The quenching rate constants of triplet toluene by (*R*)-(+)-limonene were determined by the transient absorption measurements. We successfully obtained the formation rate constants of the *cis* (k_{cis}) and *trans* (k_{trans}) isomers by using the steady-state approximation of the concentration of triplet toluene and the quenching rate constants. The ratio of the formation rate of the *cis* and *trans* isomers (k_{cis}/k_{trans}) in the microreactors became slightly smaller than that in the batch system, and the difference of the k_{cis}/k_{trans} values obviously results in the higher *de* value in the microreactor.

The enhancement of stereoselectivity and the drastic increase of the photon efficiency in the microspace were probably brought by the distinct properties of microreactors on photoreactions, high spatial illumination homogeneity, and excellent light penetration throughout the reactor. Moreover, in the microflow system, the residence time of the substrate is very short and the reaction vessel does not retain the reaction products. These facts may prevent sequential side reactions [20] and increase the quantum yield of the photoreaction.

Fabrication of photocatalytic microreactors

Most research on photocatalytic reactions has been carried out using dispersed powders in conventional batch reactors. A separation step of the powders is required after the reaction, and the dispersed powders prevent the light penetration through the entire reactor depth. Though systems with immobilized catalyst can avoid the step, they tend to have low interfacial surface areas. Thus, we have developed photocatalytic microreactors with an immobilized TiO_2 layer.

The bottom and side walls of the microchannel were coated with a thin layer of TiO_2 by using a sol-gel process. A solution of titanium tetraisopropoxide $[\text{Ti}(-\text{O}-\text{iso}-\text{C}_3\text{H}_7)_4\text{-acetylacetone}]$, NDH-510C; Nippon Soda Co. Ltd., TiO_2 concentration: 0.5 M] was spin-coated on the microchannel surface and then calcinated at 770 K for 2 h in air. The crystalline phase of the thin layer was evaluated to be nearly identical anatase form by means of X-ray diffraction analysis. Particles of Pt as a cocatalyst were loaded on the TiO_2 layer for the study of photocatalytic N-alkylation of amines by using a photodeposition method. An aqueous solution of 0.1 mM chloroplatinic acid (H_2PtCl_6) and 1 M methanol was loaded into a microchannel with immobilized TiO_2 and irradiated with an Hg lamp.

The illuminated specific surface areas per unit of liquid of the microreactors with a microchannel of 25, 100, 300, and 500 μm in depth were calculated to be 5.4×10^4 , 1.4×10^4 , 7.3×10^3 , and $6.0 \times 10^3 \text{ m}^2/\text{m}^3$, respectively, without taking into account of roughness of the photocatalyst surface. Thus, the microreactors with immobilized photocatalyst have much larger values of illuminated specific surface area of photocatalyst than typical conventional batch reactors [21]. An atomic force microscopy (AFM) image of an inner wall of the photocatalytic microreactor is shown in Fig. 3. To make use of the advantages of the miniaturized reaction vessel, a light source of minimal space and lower photon cost is suitable for the microreaction system. Thus, we employed UV-LEDs for the excitation light source of photocatalyst.

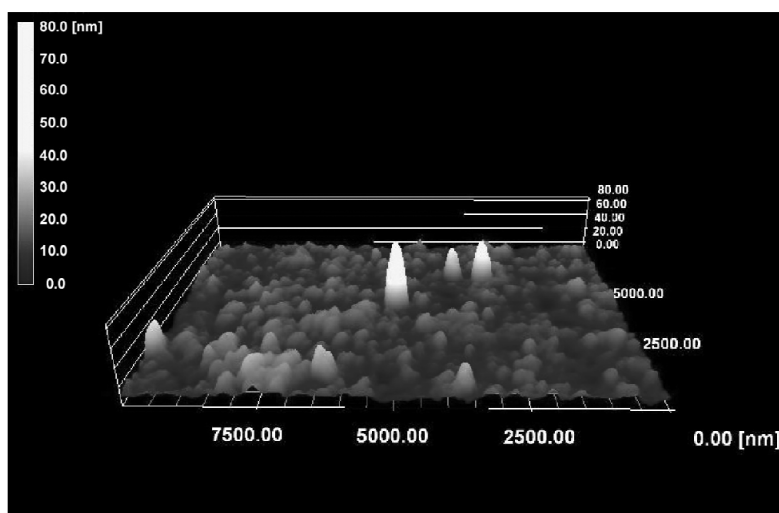
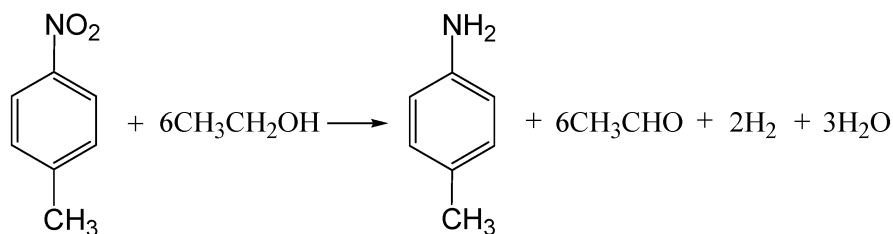


Fig. 3 An AFM image of an inner wall of a microreactor with immobilized photocatalytic TiO_2 particles by sol-gel method.

Photocatalytic oxidation and reduction

Photoexcited semiconductor photocatalyst oxidizes a reactant that donates an electron to the photocatalyst while it reduces a reactant that receives an electron. Photooxidation of organic compounds in aqueous solutions have been fruitfully investigated by using TiO_2 as a photocatalyst, and there are some reports on the photocatalytic reduction process in organic solvents by using conventional batch reactors [14,22]. We examined the photooxidation process of pollutants of the environment such as chlorophenols, bisphenol A, and dimethylformamide in aqueous solutions, and the photoreduction process of aldehydes to their corresponding alcohols, and nitro compounds to their corresponding amino compounds (Scheme 2) in alcoholic solutions [12,23]. Figure 4 indicates some typical results of the photoreduction process in ethanol saturated with nitrogen to form amino compounds and alcohols in a micro-



Scheme 2 Photocatalytic reduction of nitrotoluene.

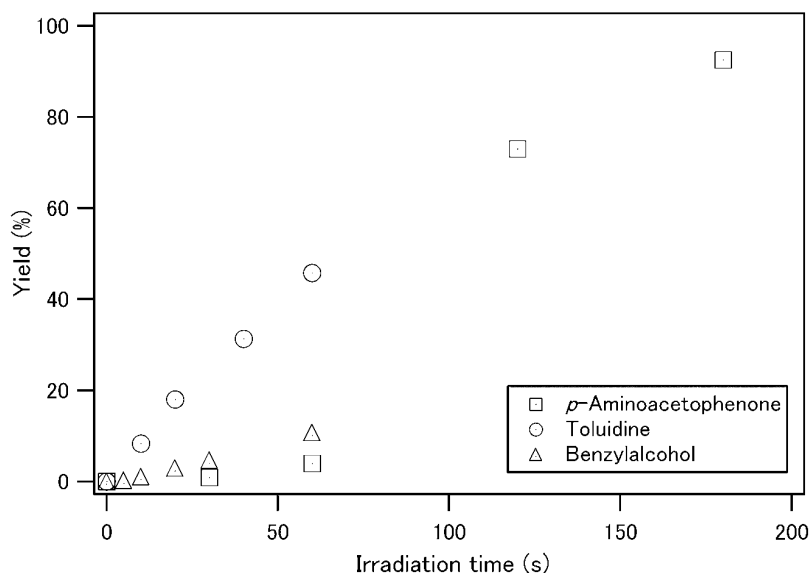


Fig. 4 Photocatalytic reduction of *p*-nitroacetophenone to yield *p*-aminoacetophenone, *p*-nitrotoluene to yield toluidine, and benzaldehyde to yield benzylalcohol. Ethanol solutions of the substrate (0.10 mM) were irradiated by 365-nm UV-LEDs (9.8 mW) in the photocatalytic microreactor of 100 μm in depth.

reactor of 100 μm in depth excited with 365 nm UV-LEDs (9.8 mW). These reduction and oxidation processes proceeded quite quickly in comparison with those conducted in batch reactors.

To further probe the feasibility of microreactor in photocatalytic reactions, we investigated the oxidation process of higher-concentration phenol in aqueous solutions as a model of effluent from a factory of semiconductor industry in both the microreactors and a large-scale flow system. The large-scale flow system consists of a circulation pump, a 40-W Hg lamp as an excitation light source of photocatalyst, and photocatalytic water purifier modules (Aquasolution, Ube Industries Ltd.). The module was developed by focusing on photocatalytic property of titania, for instance, oxidizing and decomposing organic substances, and composed of functional ceramic fibers with a gradient surface layer by means of precursor methods using a polycarbosilane. It was reported that many types of organic chemicals and bacteria can be effectively decomposed into CO_2 and water by irradiation of UV light to the module [24]. The cone-shaped photocatalytic fiber (TiO_2 -covered SiO_2 fiber) modules were stacked in a cylindrical reaction chamber of 8 cm diameter and 70 cm length, and excited with the Hg lamp positioned at the center of the reaction chamber.

Figures 5a and b indicate the photodegradation yield of phenol (47 mM) in aqueous solution obtained by using the large-scale photocatalytic water purifier module system and the photocatalytic microreactor of 100 μm channel depth excited with a 365-nm UV-LED array (9.8 mW), respectively.

The photodegradation yield was reached at 17 % by 5 min photoirradiation of the microreactor while the yield was 15 % by 360 min circulation in the large-scale system. Figure 6 shows change of absorption spectra of the solutions in the micro- and large-scale systems. In increasing the irradiation time, coloration of the solution to dark yellow was observed only in the case of the large-scale system. The reaction yields per unit optical power input and time were calculated to be 1.3×10^{-1} mmol/Whr for the microreaction system and 5.3×10^{-4} mmol/Whr for the large-scale system, respectively.

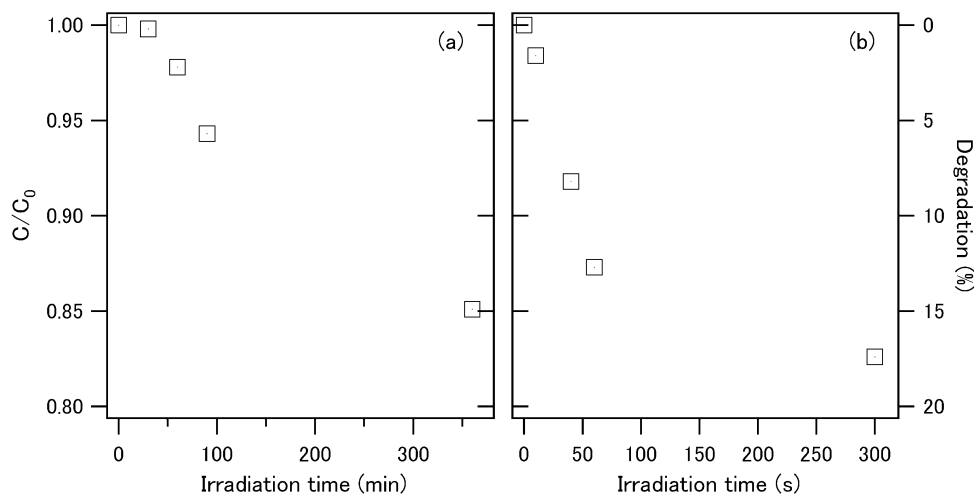


Fig. 5 Photocatalytic degradation of phenol (47 mM) aqueous solution in the large-scale photocatalytic water purifier module system excited with a 40-W Hg lamp (a), and the photocatalytic microreactor of 100 μ m channel depth excited with a 365-nm UV-LED array (9.8 mW).

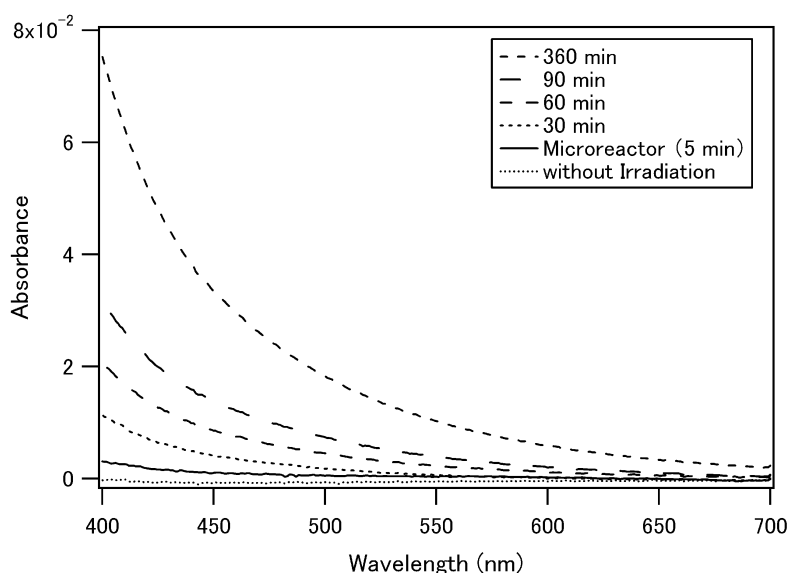
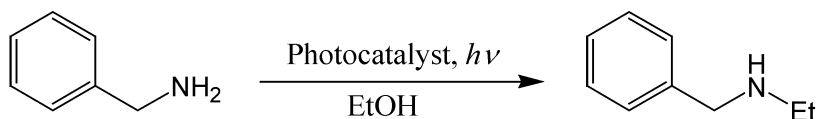


Fig. 6 Change of absorption spectra of phenol aqueous solutions (47 mM) as increasing the irradiation time in the large-scale system. Absorption spectrum of the solution photoirradiated for 5 min in the microreactor of 100 μ m depth is displayed by a solid line.

The much lower reaction efficiency of the large-scale system may be attributed to the fact that the coloration of the sample solution, probably due to polymerization of reaction intermediates, prevented light penetration to deeper inside of the reaction vessel. Actually, accumulation of hydroquinone and catechol, which have been known to be the reaction intermediates of the photocatalytic degradation process of phenol, was observed by means of gas chromatography analysis in the case of the large-scale system, while these compounds were not detectable in the microreaction system. In the microflow system, the residence time of the substrate is very short and the reaction vessel does not retain the reaction products. These facts may prevent the polymerization of reaction intermediates and bring about the increase of reaction efficiency.

Photocatalytic alkylation

It has been known that N-alkylation of aromatic amines proceeds by UV irradiation of Pt-loaded TiO_2 (TiO_2/Pt) suspended in alcoholic solvents (Scheme 3). Ohtani et al. [25] studied the N-alkylation process of amines by the irradiation 400-W high-pressure Hg lamp of TiO_2/Pt . They reported that N-alkylation of benzylamine occurred with the yield up to 84.4 % by 4 h irradiation in ethanol solvent. They also reported that N-alkylation of amines could not be observed by the irradiation of Pt-free TiO_2 .



Scheme 3 Photocatalytic N-ethylation of benzylamine.

The N-alkylation of benzylamine was examined in the photocatalytic microreactor of 300 μm in depth excited with 365-nm UV-LEDs. Observed photocatalytic processes of N-alkylation of aromatic amines by alcoholic solvents in microreactors were considerably different from those in conventional batch reactors. The reaction proceeded very rapidly in the photocatalytic microreactor with immobilized TiO_2/Pt . The N-alkylation in ethanol proceeded within only 150 s to yield 85 % of *N*-ethylbenzylamine from benzylamine [26]. The photonic efficiency, which is defined as the number of reaction product molecules divided by the number of photons of monochromatic light incident inside the window of the microchannel, of the N-alkylation of benzylamine was calculated to be 0.35 %. In contrast to the result in batch reactors, we also successfully observed N-alkylation of aromatic amines by using the microreactor with immobilized Pt-free TiO_2 as well as TiO_2/Pt . The N-alkylation in ethanol proceeded within only 150 s to yield 43 % of *N*-ethylbenzylamine in the microreactor with Pt-free TiO_2 .

It is known that depositing Pt on TiO_2 enhances the photocatalytic activity by serving as an electron sink and consequently slowing charge recombination. Since the electron-hole recombination within the photocatalyst is in competition with the reaction process, the reaction efficiencies must be strongly affected by the surface-to-volume ratio of a photocatalytic reactor. Thus, the photoreaction can proceed rapidly in the microreactor which has a remarkably large surface-to-volume ratio, and the N-alkylation of benzylamine may be observed even in the microreactor without Pt cocatalyst. To further examine the advantages of the microreaction system, the alkylation with TiO_2/Pt was carried out by using UV-LEDs of larger optical power output (450 mW) and a microreactor of 25 μm in depth. The illuminated specific surface areas per unit of liquid of the microreactor was calculated to be $5.4 \times 10^4 \text{ m}^2/\text{m}^3$, which is more than 10 times larger than that of typical batch reactors with dispersed photocatalyst powders [21]. As shown in Fig. 7, the reaction proceeded quite quickly. The concentration of the mono-alkylated product reached a maximum value (65 %) within 5 s irradiation. Further, the formation of *N,N*-di-alkylated product with the yield of 29 % was observed by only 10 s irradiation. A development of the photo-

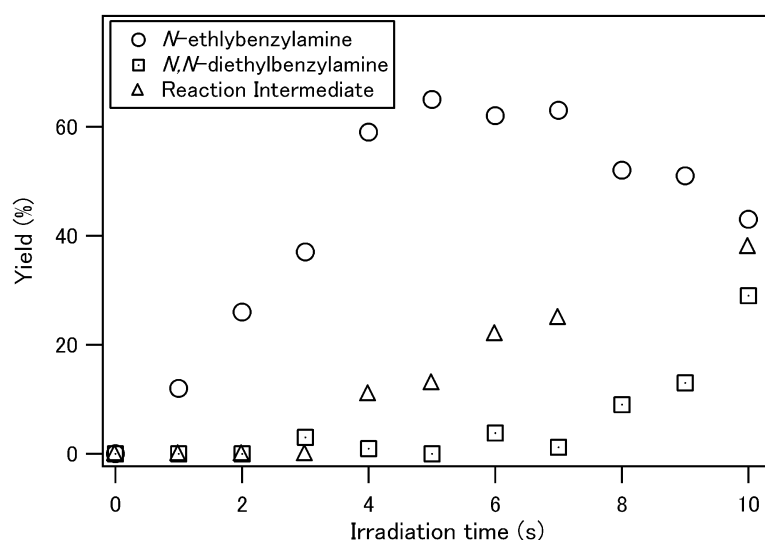


Fig. 7 Photocatalytic N-ethylation of benzylamine (1.0 mM) in the microreactor of 25- μ m depth with immobilized TiO_2/Pt excited by 365-nm UV-LEDs (450 mW).

catalytic microreaction system with multiple microchannels is in progress for the application of the very fast reaction system to the screening process of optimizing photocatalyst and reaction conditions.

CONCLUSION

We examined the feasibility of microreaction system on organic photoreactions. Photosensitized asymmetric reaction, and photocatalytic oxidation, reduction, and amine N-alkylation processes were investigated. These model reactions proceeded very rapidly with considerably large photonic efficiencies.

We are carrying out further experiments to probe the reaction intermediates and reaction kinetics in a microchannel by laser spectroscopy. Optimization of excitation wavelength, irradiation conditions, and design of microchannel are in progress for the establishment of photochemical microreaction systems. The enhancement of reaction yield and selectivity by using the features unique to microspace, for instance, large surface-to-volume, laminar flow, and gas–liquid–solid multiphase flow, and the methodology of the development of microreaction system for the synthesis of high-value-added compounds like pharmaceutical production intermediates will be presented in the forthcoming paper.

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