Hiroshima University Doctoral thesis

Fabrication of paper-based microfluidic devices using a laser beam scanning technique

（レーザービーム走査法を用いたペーパーマイクロ流体デバイスの作製）

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Main Thesis

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Abstract

This thesis describes a novel method for fabricating paper-based microfluidic devices using a laser beam scanning technique. Cellulose chromatography papers were treated with octadecyltrichlorosilane (OTS) to make them entirely hydrophobic. A photoacid generator (CPI-410S) was soaked into the paper, and irradiated with a 405-nm laser beam to induce acid generating reactions. Since the silyl ether bond between cellulose and OTS was cleaved by the hydrolysis reaction, the photo-irradiated area changed to hydrophilic. By scanning the laser beam using a Galvo mirror system, arbitrary shaped hydrophilic patterns were successfully created on the paper in 50 μm resolution. To the best of our knowledge, this is the first report on the fabrication of hydrophilic channels in the OTS-treated paper using photo-induced acid generation processes coupled with the laser beam scanning technique. Quantification of nitrite was demonstrated with the paper device made by this method.

Chapter 1

General Introduction

1.1. Brief history of paper analytical devices

The paper-based microfluidic analytical device (μ-PAD) has been attracted great interest since it possesses beneficial characteristics such as easy-to-use, biocompatible, inexpensive, and so on.[1-3] Therefore, it is considered that the μ-PADs are especially important to use in developing countries where the expensive equipments are rare to use because of the finance issues.

In 2007, Whitesides who first proposed the modern system for the PDA used photolithography to create the hydrophilic/hydrophobic contrast on a chromatography paper.[4] In this treatment, UV-sensitive polymer photoresist (SU-8 2010) was soaked in a chromatography paper and then polymerized by UV light through a photomask. After the uncured photoresist was removed with a proper solvent, the resultant hydrophobic polymer walls act as a chemical-resistant barriers within it a trace amount of urine solution containing protein and glucose flows to the test areas for biological assays. This method was later modified by Whitesides and co-workers using less expensive epoxy negative photoresist[5] and SC photoresist.[6] Unlike conventional materials, such as glass,[7] silicon[8] etc., the liquid flows swiftly in the hydrophilic patterns on the paper due to capillary action without any supporting force. This is one of the important features that spreads the application of μ-PAD to the various fields of science and technology.

As results, there are many fabrication techniques for μ-PADs. The representative examples are wax printing,[9-13], polydimethylsiloxane (PDMS) printing, inkjet etching,[14], plotter printing,[15] plasma oxidation,[16,17] laser cutting,[18] and flexographic printing.[19] However, most of these methods, are based on the generation of the hydrophobic barrier on the paper and the opposite treatment that enables us to draw the hydrophilic patterns directly on the paper is still very rare. Moreover, techniques such as UV-lithography and plasma treatment require the use of expensive equipment controlled precisely in the lab. The knife-plotting technique requires a specially customized patterning equipment and some other techniques also require undesirable postprocessing procedures to create μ-PADs. The limitation of the minimum achievable hydrophilic channel and hydrophobic barrier sizes and the use of special type of chemicals like harsh chemical etchants or inks are other important issues to be solved.

1.2. Purpose of the thesis

Organosilanes are hydrophobizing agents affordable in price applicable to many compatible substrates. Among them, alkyltrichlorosilanes with long hydrocarbon tail groups have been widely applied to functionalize a wide range of inorganic and organic materials such as silicon wafers,[20] stainless steels,[21] aluminum plates,[22] and papers.[23-25] Compare to the other organosilanes, alkyltrichlosilanes offer relatively fast covalent coupling reaction rates without pre-hydrolysis steps, which are, for example, necessary for trialkoxysilanes.[26] The length of the hydrocarbon tail group in these reagents can be varied from a single methyl group to more than 30 carbon atoms. Recently, He et al. succeeded in creating hydrophilic channels in hydrophobic paper, which made of cellulose fibers chemically coupled with octadecyltrichlorosilane (OTS), by irradiating deep UV light with O_3 through a photomask.[27]

This report motivated us to develop a novel μ-PAD fabrication technique using a laser beam scanning. Cellulose silyl ethers can be cleaved also by acid treatment. Photoacid generators are organic compounds that can generate protons upon photo-irradiation. Spirk et al. have reported that desilylation of trimethylsilyl cellulose was induced by UV light irradiation in the presence of *N*-hydroxynaphthalimide as a photoacid generator.[28] Therefore, it should be possible to fabricate hydrophilic channels directly in alkylsilane-treated paper by irradiating a laser beam in the presence of the photoacid generator.

In this study, we used a derivative of triarylsulfonium salts (CPI-410S) as a photoacid generator, which is used as photoinitiators for cationic polymerization.[29] By scanning a 405-nm laser beam using a Galvo mirror system, arbitrary shaped hydrophilic patterns were successfully created on the OTS-treated paper. To the best of our knowledge, this is the first report on the fabrication of hydrophilic channels in the OTS-treated paper using photo-induced acid generation processes coupled with the laser beam scanning technique. Furthermore, quantification of nitrite was demonstrated with the paper device made by this method.

Chapter 2

Experimental

2.1. Materials

CPI-410S was supplied by San-Apro Ltd. and used without further purification. The structure of CPI-410S was shown in the Supporting Information, Figure S1. OTS and Acid Red 1 were purchased from Sigma Aldrich-Merck Co. Dimethyl sulfoxide, chloroform, *n*-hexane, and ethanol were purchased from Wako Pure Chemicals Co. Ltd. and used without further purification. Water was purified by reverse osmosis and deionization prior to use (Merck Millipore, Milli-Q Integral 3).

2.2. Fablication of μ-PADs

The procedure of our μ-PAD fablication was schamitically illustrated in Figure 1. Cellulose chromatography papers (Advantec Co., Ltd.) were immersed in 0.1% (v/v) OTS n-hexane solution for 5 min at room temperature. The papers removed from OTS solution were rinsed with n-hexane and ethanol and dried in air. Subsequently, the OTS-treated papers were immersed in chloroform and 5 % (w/w) CPI-410S DMSO solution for 1 and 2 min, respectively. A diode laser (405 nm, 300 mW, Changchun New Industries Optoelectronics Technology Co., Ltd., MDL-III-405-300,) and a Xe lamp (150 W, Hamamatsu photonics K.K., L2274) were used as excitation light sources for CPI-410S. A Galvo mirror system (Thorlabs, Inc., GVS002) was used to scan the laser beam. More detail explanation will be given in the following chapter.

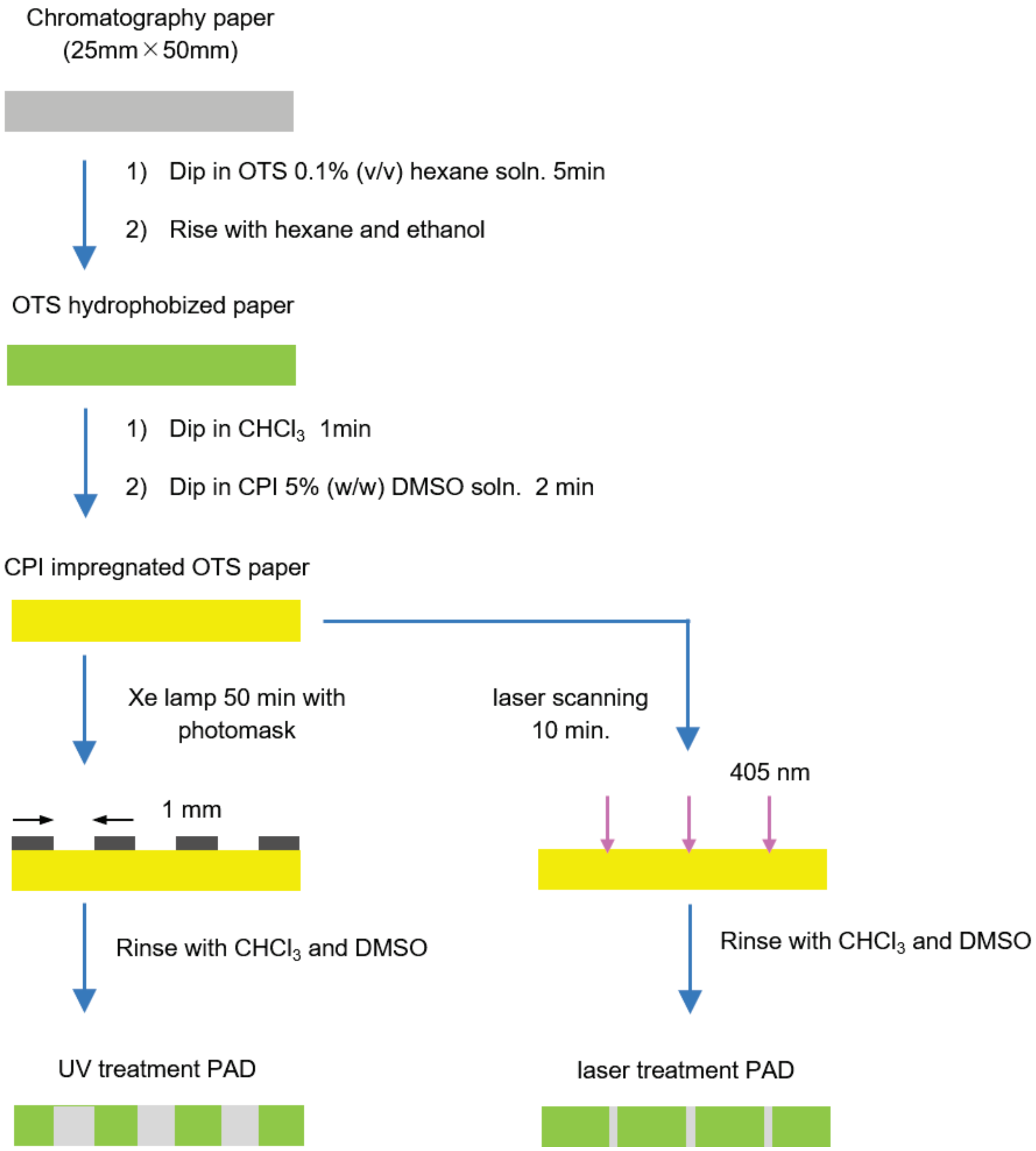

Figure 1. A schematic illustration of μ-PAD fabrications proposed in this study.

Chapter 3

Results and discussion

3.1. Time dependence of the contact angle of a water droplet during photoirradiation

In the present study, hydrophilic-hydrophobic patterns on papers were created by two steps. First, cellulose chromatography papers were treated with OTS to make them entirely hydrophobic. Second, hydrophilic patterns were created by the hydrolysis of the silyl ether bond between cellulose and OTS, which was triggered by the photoinduced acid generation reaction of CPI-410S.

In order to confirm that the CPI-410S can remove OTS in the paper under photoirradiation, the contact angle of a water droplet was investigated. Time dependence of the contact angle of a water droplet during photoirradiation is shown in Figure 2. In this experiment, in order to irradiate the entire surface of the paper with light, UV-visible light from a xenon lamp was used instead of the 405-nm laser beam.

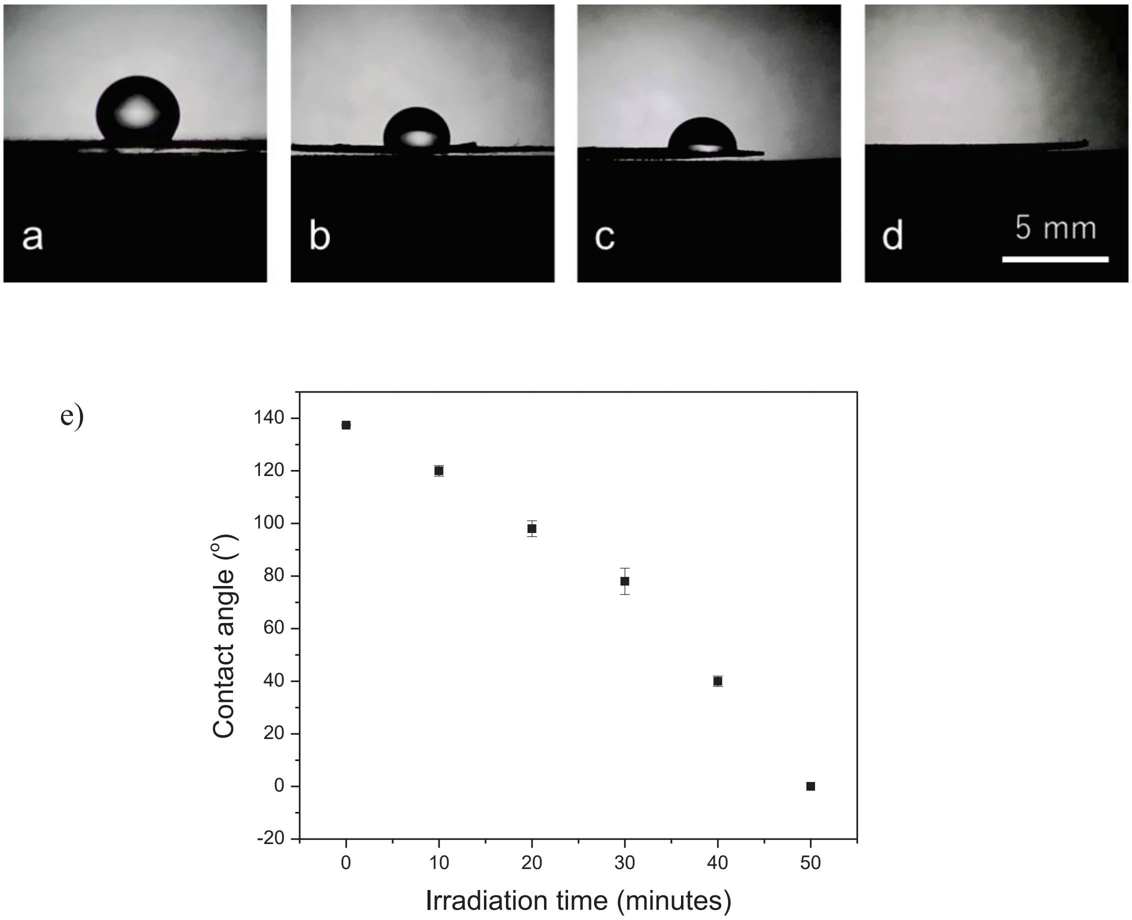

Figure 2. Change in contact angle of water droplets on OTS-treated paper in the presence of CPI-410S. The paper was illuminated with a Xe lamp for (a) 0, (b) 20, (c) 40, and (d) 50 min, respectively. e) the dependence of the contact angles on the irradiation time. (a) (b) (c) (d) adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

As shown in Figure. 2, the OTS-treated paper was hydrophobic, and the contact angle of the water droplet was approximately 137°. When CPI-410S was dipped in the paper and irradiated with light, the contact angle decreased with increasing of irradiation time of light as shown in Figure 4. When the light irradiation time was 50 min, the contact angle of the water droplet became 0°. This result clearly shows that the hydrophobic paper has turned into a completely hydrophilic one. Generally, triarylsulfonium salts are used for photoinitiators of cationic polymerization, but we demonstrated for the first time that they can also be used for a photoinduced hydrolysis reaction in the paper treated with OTS.

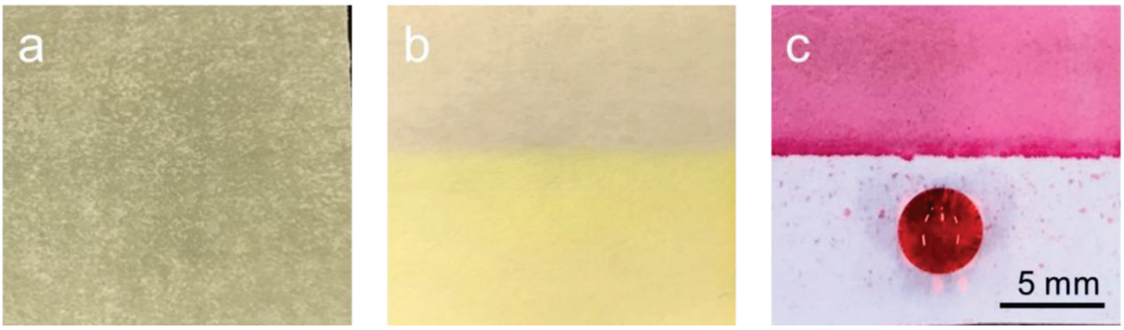

Figure 3. The images display photographs of the OTS-treated paper taken, (a) immediately after pulling out from DMSO solution of CPI-410S, (b) after photoirradiation for 50 min, (c) after rinsed with chloroform and DMSO and put aqueous Acid Red 1 droplets, respectively. This figure adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

3.2. Hydrophilic-hydrophobic contrast on the paper treated with OTS

To fabricate hydrophilic channels on OTS-treated papers, it is necessary that only the light-irradiated area becomes hydrophilic. Prior to the laser scanning experiment, the hydrophilic-hydrophobic contrast at the boundary between the light-irradiated and the non-irradiated area was examined by using a photomask. Figure 3 (a) is a photograph of an OTS-treated paper immediately after pulling out from the DMSO solution of CPI-410S. Since CPI-410S has an absorption band at around 400 nm, the entire paper has a light-yellow color. The lower half of the paper was masked with black paper and illuminated with light from a xenon lamp.

After photoirradiation for 50 min, the photo-irradiated part and the photo-masked part were different in color as shown in Figure 3(b). The photochemical reaction of triarylsulfonium salts is very complicated, and various reaction processes have been proposed in the literature.[16] The heterolytic cleavage of triarylsulfonium gives phenyl cation and diphenyl sulfide as shown in Figure 4. Therefore, the color change of the paper indicates that the photolysis of CPI-410S proceeded in the upper parts. After the photoirradiation, the paper was rinsed with chloroform and DMSO to wash out the CPI-410S, and both the upper and lower parts of the paper became colorless. To investigate the hydrophilic or hydrophobic properties, aqueous droplets containing Acid Red 1 were dropped on the upper and lower parts of the paper, respectively. As shown in Figure 3 (c), it was clearly visible that a hydrophilic-hydrophobic boundary was formed between the light-exposed part and the photo-masked part. This result clearly indicates that the change from hydrophobic to hydrophilic nature of the OTS-treated paper was caused by the photochemical reaction with CPI-410S.

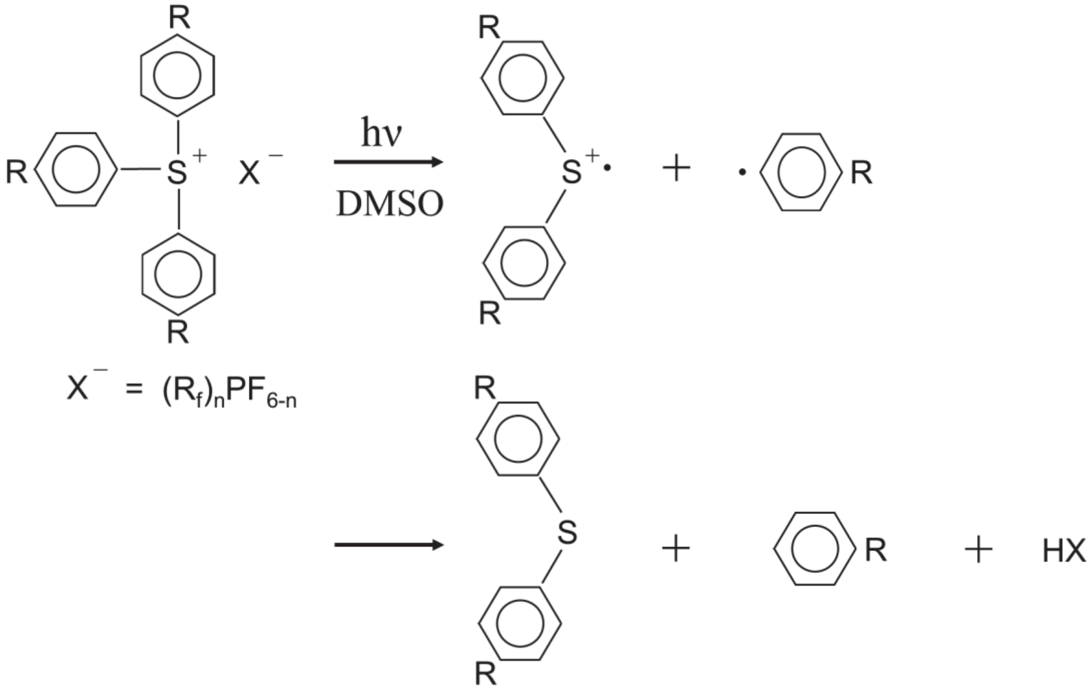

Figure 4. Photolysis of triphenylsulfonium salts. This figure adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

3.3. Hydrophilic patterns fabricated on the paper treated with OTS by the laser beam scanning technique

As described in the previous section, using CPI-410S as a photoacid generator, the photoirradiated area on the OTS-treated paper becomes hydrophilic. Therefore, by using a laser beam as a light source for the photochemical reaction and scanning the beam to draw an arbitrary spatial pattern on the paper, it should be possible to fabricate hydrophilic channels directly on the OTS-treated paper without using a photomask. To demonstrate this idea, using a computer-controlled Galvo mirror system, a 405-nm laser beam was scanned in a star pattern on the OTS-treated paper containing CPI-410S as shown in Figure 5.

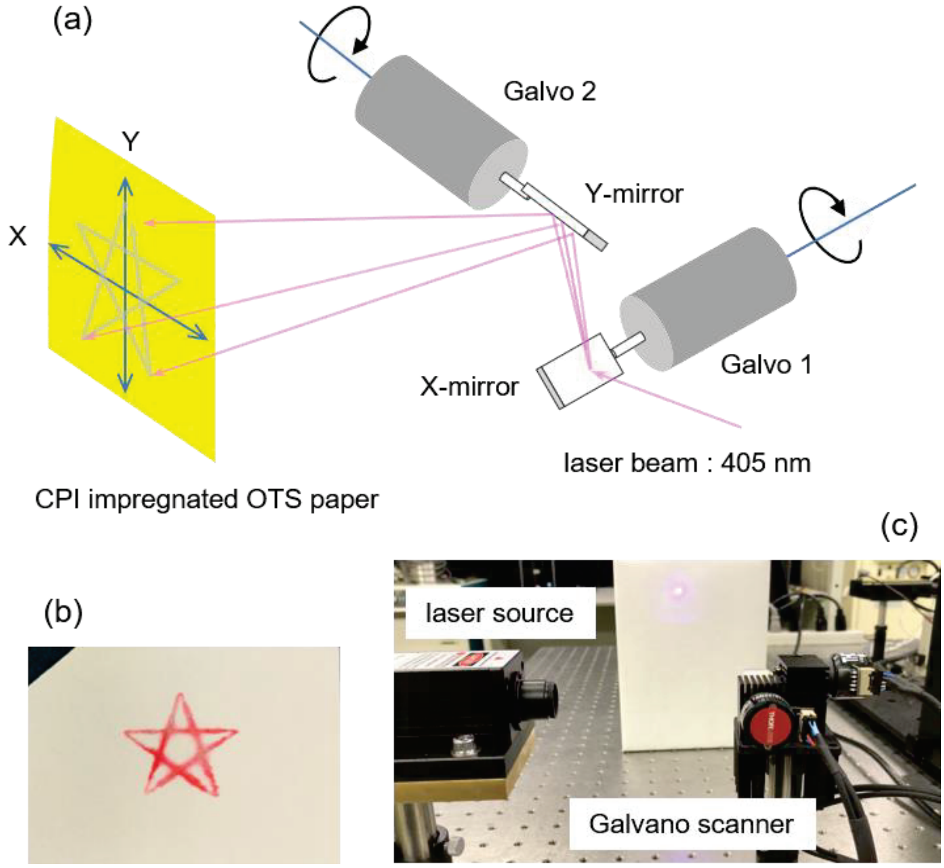

Figure 5. (a) Schematic illustration of a laser beam scanning with a Galvo mirror system, (b) star-like shape hydrophilic channel fabricated by laser beam scanning, and (c) a picture of our optical system. This figure adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

The continuous wave laser beam of 300 mW was loosely focused and scanned at a speed of 10 mm/s for 50 minutes on the paper. Then, the paper was rinsed with chloroform and DMSO to wash out the CPI-410S, and a pale-yellow star appeared on the paper (Figure 6 (a)). The width of the channel observed by an optical microscope was about 50 μm. When a water droplet containing Acid Red 1 was dropped on one vertex of the star, the aqueous solution spread along the channels via capillary forces as shown in Figure 6 (a) and (b). As shown in Figure 6(c), the width of the red-colored line observed under an optical microscope was approximately 400 μm. This indicates that while the aqueous solution was flowing through the hydrophilic channel, it diffused in the lateral direction. To the best of our knowledge, this is the first report on the fabrication of hydrophilic channels in the OTS-treated paper using photo-induced acid generation processes coupled with the laser beam scanning technique.

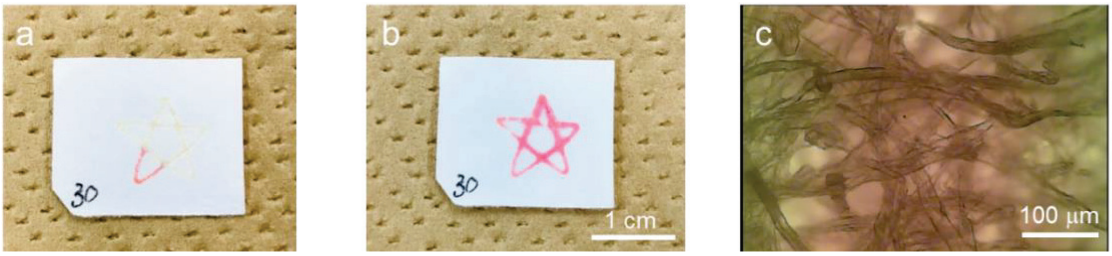

Figure 6. The images display photographs of a star-shaped hydrophilic channel in OTS-treated paper. An Acid Red 1 solution immersed in a part of the channel (a), in the entire channel (b), respectively. (c) The red-colored line observed under an optical microscope. This figure adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

3.4. Quantitative analysis of nitrite

Finally, the paper-based microfluidic device prepared by the present method was applied to the quantitative analysis of nitrite ion (NO_2^-) using the Griess reaction, in which red color appears due to the reaction of NO_2^- with sulfanilamide and *N*-(1-naphthyl) ethylenediamine.[30,31] The reaction scheme of Griess reaction was shown in Figure 7.

As shown in Figure 8, six linear hydrophilic channels were fabricated. An aqueous solution (3 μl) containing 50 mM sulfanilamide, 0.33 M citric acid, and 10 mM *N*-(1-naphthyl) ethylenediamine sulfanilamide was permeated in each channel, and dried in an oven at 40 °C for 10 min. Standard solution was prepared by dissolving $NaNO_2$ in water, and 0.25 μl of standard solutions with different concentrations were dropped on the end of each channel. As shown in Figure 8, the length of the red colored area increased with increasing NO_2^- concentration. Although the color contrast at the forefront is slightly obscure, this preliminary experiment might suggest the possibility of quantitative analysis of NO_2^- based on the length of the red colored area.

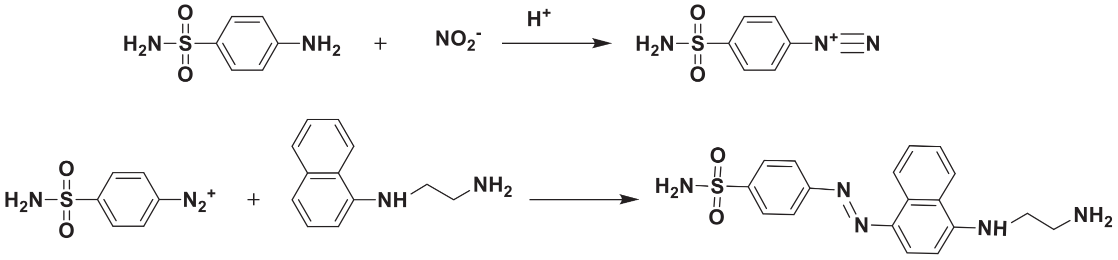

Figure 7. Reaction scheme of Griess reaction

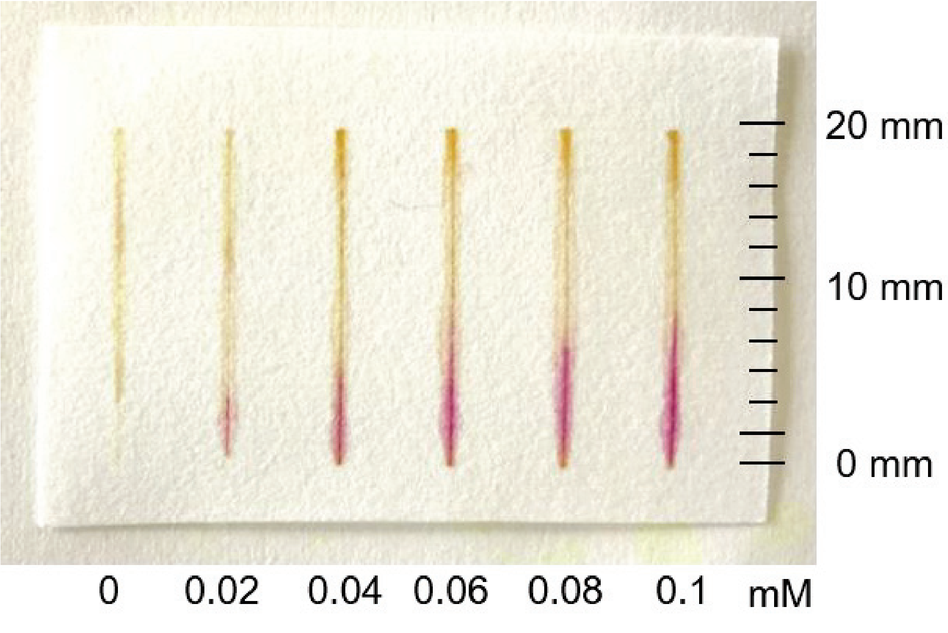

Figure 8. NO_2^- concentration dependence of the length of the colored region. This figure adapted with permission from HIEP. D. H; Tanaka. Y; Matsubara. H; Ishizaka. S. *Anal. Sci. Advanced online publication June 19, 2020*. Copyright (2020) Japan society for Analytical Chemistry.

Chapter 4

Conclusion

As demonstrated in this study, we achieved the fabrication of hydrophilic channels in the OTS-treated paper using photo-induced acid generation processes coupled with the laser beam scanning technique. Since the photoacid generators are used as photoinitiators for cationic polymerization, various photoacid generating compounds have been developed and widely used in industry so far. The method is very versatile, since similar experiments are expected to be possible with photoacid generators other than CPI-410S. Furthermore, since only the photo-irradiated area becomes hydrophilic, it would be possible to make paper-based microfluidic devices by irradiating light through a photomask on the OTS-treated papers containing photoacid generators. In this study, we employed the laser beam scanning methods to create hydrophilic channels on the OTS-treated papers. Using the loosely focused laser beam as an excitation light source, the hydrophilic channels were successfully created on the paper in 50 μm resolution. The minimum width of the hydrophilic channels approximately corresponds to the diameter of the spot of the laser beam on the paper. The channel width is one of the important factors governing the velocity of liquid flow via capillary forces. To improve the contrast of color change in the quantitative analysis of NO_2-, the flow rate dependence of the Griess reaction will be discussed in future studies. We are convinced that the photo-induced acid generation processes coupled with the laser beam scanning technique will be a versatile method to fabricate paper-based microfluidic devices.

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Supporting Information

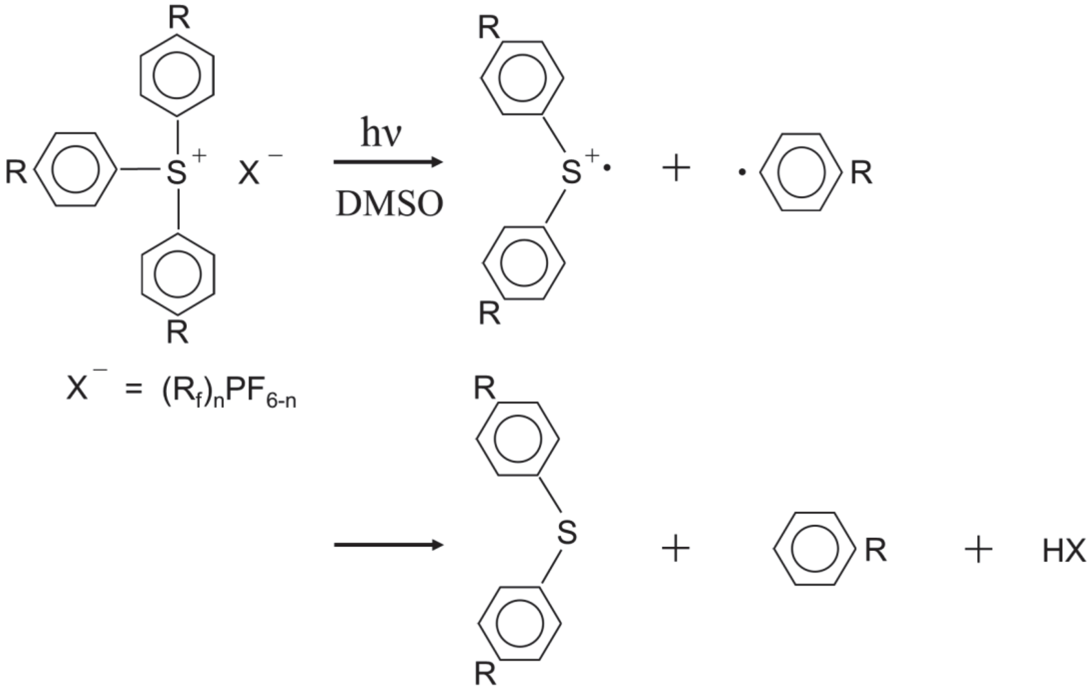

Figure S1 Photolysis of triphenylsulfonium salts