Synthesis of photochromic diarylethenes using a microflow system†

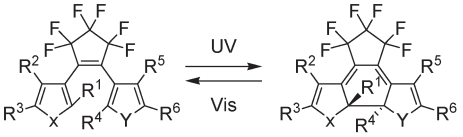
Yousuke Ushiogi,[a] Tomoyuki Hase,[b] Yoshiharu Iinuma,[b] Atsushi Takata[b] and Jun-ichi Yoshida*[c]

Received (in Cambridge, UK) 13th February 2007, Accepted 26th April 2007
First published as an Advance Article on the web 9th May 2007
DOI: 10.1039/b702277h

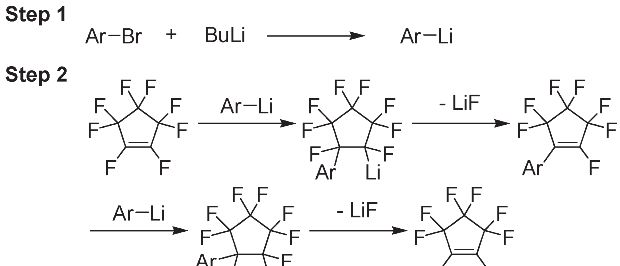
An effective method for the synthesis of photochromic diarylethenes based on microflow systems has been developed, and the synthesis of unsymmetrical diarylethenes which is difficult to achieve using conventional macro batch systems, has been accomplished.

Diarylethenes have received significant research interest from both academia and industry, because some of them exhibit remarkable changing of color by reversible switching of two distinct isomers (photochromism), which is accomplished by absorption of different colors of light as exemplified by Scheme 1.[1]

The most promising photochromic diarylethene candidates include 1,2-diarylhexafluorocyclopentenes, which have been synthesized by the reaction of aryllithium compounds with octafluorocyclopentene in a batch reactor at low temperatures such as −78 °C in order to avoid undesirable side reactions (Scheme 2).[2] The requirement of such low temperatures, however, has been an obstacle to industrial-scale applications. Herein we report that the synthesis of diarylethenes can be accomplished at or above 0 °C using a microflow system[3,4] by virtue of effective temperature and residence time control.[5]



Scheme 1



Scheme 2

The first step of the synthesis of diarylethenes is the halogen–lithium exchange reaction of an aryl bromide with butyllithium. The reaction should be carried out at low temperatures such as −78 °C because aryllithium compounds are often unstable and decompose at higher temperatures. In the next step, the aryllithium compounds are allowed to react with octafluorocyclopentene. Usually, two mol of the aryllihitum compound react with one mol of octaflurocyclopentene presumably *via* the two-fold addition–elimination sequence to give the desired diarylethenes (Scheme 2). Therefore, the method is suitable for the synthesis of symmetrical diarylethenes.

We constructed a microflow system consisting of two T-shaped micromixers and two microtube reactors shown in Fig. 1.[6] We chose to use stainless steel as a material for the mixers and reactors because of high heat-exchange ability and mechanical strength from a viewpoint of industrial applications.[6c] In the first mixer **M1**, a solution of an aryl bromide and a solution of butyllithium were mixed, and the mixture was allowed to react in the first microtube reactor **R1**. The resulting aryllithium was mixed with octafluorocyclopentene in the second micromixer **M2** and the mixture was allowed to react in the second microtube reactor **R2**. The temperature of the whole system was controlled using a cooling bath.

The reaction temperature was optimized using 3-bromo-2-methyl-5-phenylthiophene as an aryl bromide. As shown in Fig. 2, the yield of the desired diarylated product **1** increased with the temperature presumably because the reaction rate increased with the temperature. The highest yield was obtained at 0 °C. Above 0 °C, the yield decreased significantly probably because of the decomposition of the aryllithium intermediate. It is noteworthy that the reaction in a macro-scale batch system at 0 °C gave a complex mixture. Low temperatures such as −78 °C are essential for the success of the reaction in a macro-scale batch system.

In order to test the applicability of the present method, various diarylethenes were synthesized using the corresponding aryl

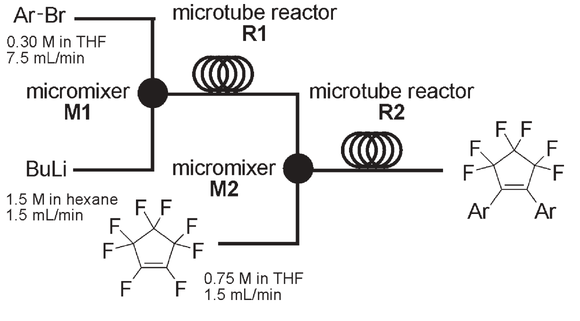


Fig. 1 Synthesis of symmetrical diarylethenes using the microflow system.

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[a] *The Research Association of Micro Chemical Process Technology (MCPT) in Kyoto, Kyoto University, Kyoto, 615-8530, Japan*
[b] *Yamada Chemical Co., Ltd., Minami-ku, Kyoto, 601-8105, Japan*
[c] *Department of Synthetic Chemistry and Biological Chemistry, Graduate School of Engineering, Kyoto University, Nishikyo-ku, Kyoto, 615-8510. E-mail: yoshida@sbchem.kyoto-u.ac.jp; Fax: +81-75-383-2727; Tel: +81-75-383-2726*

† Electronic supplementary information (ESI) available: Experimental section. See DOI: 10.1039/b702277h

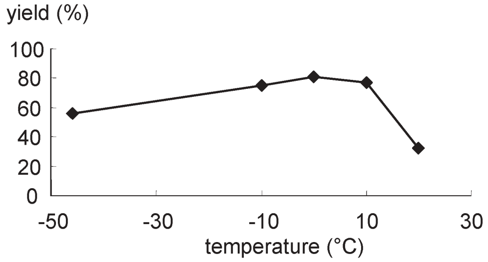


Fig. 2 Temperature effect for the synthesis of diarylethene **1** in the microflow system (residence time, **R1**: 3.4 s, **R2**: 2.9 s).

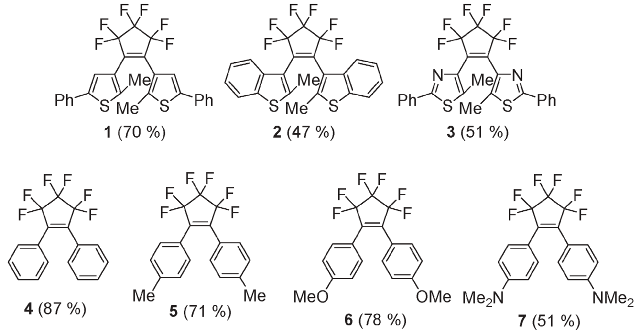
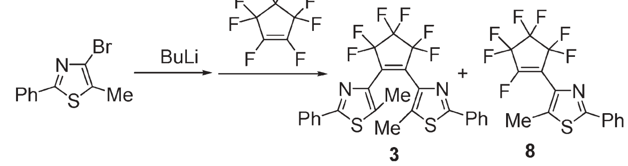


Fig. 3 Synthesis of diarylethenes from aryl bromides and octafluorocyclopentene (isolated yields) using the microflow system at 0 °C.

bromide and octafluorocyclopentene at 0 °C in the microflow system and the results are summarized in Fig. 3. Although the yield depends on the nature of the aryl group, the results indicate that the use of microflow systems serves as a powerful method for synthesis of diarylethenes of various structures (**1**–**7**).

The following observation for 4-bromo-5-methyl-2-phenylthiazole demonstrates a striking advantage of the microflow system (Scheme 3). The batch reaction at −78 °C gave monoarylated compound **8** as a major product even with the use of two equivalents of the aryllithium reagent. The elimination of LiF from the first adduct (Scheme 1) seems to be slow at −78 °C presumably because of nitrogen coordination to Li. LiF elimination seemed to take place during the work-up. In order to synthesize diarylated compound **3**, monoarylated compound **8** was isolated and then was subjected to the second reaction with the aryllithium at −78 °C. In the case of the microflow system, however, the reaction gave diarylated compound **3** as the major product in one step. The result can be attributed to a higher temperature (0 °C) for the microflow system, where the aryllithium intermediate survived within a short residence time and the LiF elimination took place spontaneously. The present observations suggest a new potentiality of microflow systems; *sequential transformations, which require quite different temperatures in the case of macro batch systems, can be achieved at the same temperature by virtue of short residence time inherent in microflow systems*.



		3	8
Batch System	-78 °C, 1 h + 2h	10 %	52 %
Microflow System	0 °C, 3.4 s + 5.7 s	51 %	11 %

Scheme 3

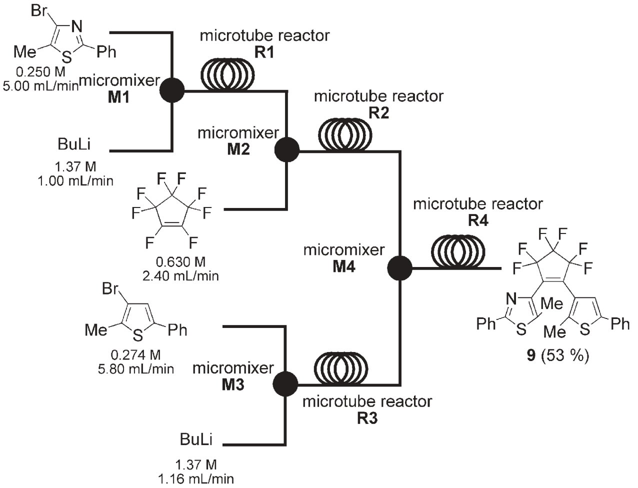


Fig. 4 Synthesis of unsymmetrical diarylethene **9** using the microflow system.

It is also noteworthy that the monoarylated product can be obtained selectively in the microflow system by employing one equivalent of the aryllithium. Thus, selective synthesis of unsymmetrical diarylethenes can be easily accomplished using two different aryl bromides sequentially. Fig. 4 illustrates the synthesis of unsymmetrical diarylethene **9** (53% yield). The ring-closed isomer of **9** obtained by photo-irradiation exhibited a different color from those of the corresponding symmetrical compounds **1**[7] and **3**[8] (Fig. 5). The result indicates a possibility of fine-tuning of physical properties by introducing different heteroaromatic substituents on the alkene framework by taking advantage of the microsystem.

In conclusion, we have developed an effective method for the synthesis of photochromic diarylethenes using microflow systems, which enables reactions at much higher temperatures. Successful synthesis of unsymmetrical diarylethenes[9] using two different aryl bromides in one flow speaks well for the potential of microflow systems in making new functional materials, which are otherwise difficult to synthesize in a conventional way. Because several micro chemical plants at pilot scale have already been built,[6c,10] this process seems to be easily transformed to the system in an industrial scale by scaling-up and continuous operation. Further

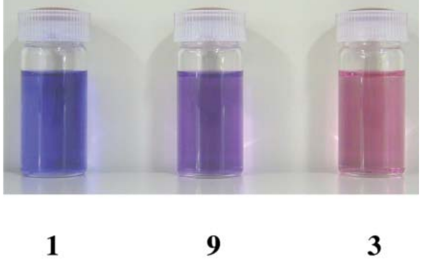


Fig. 5 Colors of the ring-closed isomers of diarylethenes.

work aiming at synthesis of various diarylethenes using microflow systems in laboratory and industrial scales is currently in progress.

The authors are grateful to a Grant-in-aid for Scientific Research and the Project of Development of Microspace and Nanospace Reaction Environment Technology for Functional Materials of NEDO for partial financial support.

We dedicate this paper to the late Professor Yoshihiko Ito in honor of his outstanding contribution to synthetic chemistry and organometallic chemistry.

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