JACS
ARTICLES

Published on Web 07/01/2010

Dual-Channel Microreactor for Gas−Liquid Syntheses

Chan Pil Park† and Dong-Pyo Kim*,†,‡

National Creative Research Center of Applied Microfluidic Chemistry, and Graduate School of Analytical Science and Technology, Chungnam National University, Daejeon, 305-764, South Korea

Received March 30, 2010; E-mail: dpkim@cnu.ac.kr

Abstract: A microreactor consisting of two microfluidic channels that are separated by a thin membrane is devised for intimate contact between gas and liquid phases. Gas flowing in one microchannel can diffuse into the liquid flowing in the other microchannel through the thin membrane. An oxidative Heck reaction carried out in the dual-channel (DC) microreactor, in which gaseous oxygen plays a key role in the catalytic reaction, shows the significant improvement that can be made over the traditional batch reactor and the conventional segmental microreactor in terms of yield, selectivity, and reaction time. It also allows independent control of the flow of the gaseous reagent. The proposed DC microreactor should prove to be a powerful tool for fully exploring gas−liquid microchemistry.

Introduction

Microfluidic systems have opened up new concepts and offered several attractive possibilities for organic chemists.[1] These systems have been applied in various standard organic reactions, and new chemistry in microreactors has also been reported. Such systems are advantageous in providing increased surface-to-volume ratio, rapid mass- and heat-transfer, enhanced process safety, and diminished waste. Moreover, the chemical reactions in the confined microscale space can be completed in a short time, and the result can be related to mass production.

The chemical reactions between gas and liquid phases have traditionally been carried out in batch systems (Figure 1a). The contact area between the two phases is quite small relative to the reaction volume. This contact area per reaction volume decreases with increasing reaction volume, and as a result the reaction rate in a scaled-up reactor would be sharply decreased due to the reduced contact area relative to the volume. The gas diffusion into the liquid phase has generally been enhanced by vigorous stirring, high pressure, supercritical conditions, or additional means such as ultrasonic waves. The approach taken in microdevices to enhance the contact between the two phases was to utilize segmented flow of gas and solution in the "monochannel" (MC) reactor (Figure 1b).[2] We visualized that contact of gas−liquid phases in dual parallel microchannels is a way of maximizing the contact area between the two phases (Figure 1c). Furthermore, exact control of gas flow into the reaction system is very difficult in monochannel microreactors but might be improved in dual parallel microchannels. This conceptual approach has not been attempted for microchemical reactions that require intimate contact between two phases.

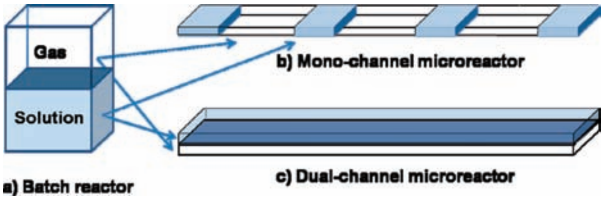


Figure 1. Comparative illustration of various modes of contact area between gas and liquid phases.

The porosity of poly(dimethylsiloxane) (PDMS) has been used in microfluidic systems related to the fields of analytical chemistry and biology, such as in the deoxygenation of solutions, the sensing of gases, oxygenation, and devices for cell culture.[3] However, the PDMS materials were rarely tried for organic reactions, and the oxygen permeability of PDMS was not considered useful in organometallic chemistry. Herein,

---

† National Creative Research Center of Applied Microfluidic Chemistry.
‡ Graduate School of Analytical Science and Technology.

(1) For reviews and books, see: (a) Yoshida, J. I.; Nagaki, A.; Yamada, T. *Chem.—Eur. J.* **2008**, *14*, 7450–7459. (b) Wiles, C.; Watts, P. *Eur. J. Org. Chem.* **2008**, 1655–1671. (c) Fukuyama, T.; Rahman, M. T.; Sato, M.; Ryu, I. *Synlett* **2008**, 151–163. (d) Ahmed-Omer, B.; Brandt, J. C.; Wirth, T. *Org. Biomol. Chem.* **2007**, *5*, 733–740. (e) Mason, B. P.; Price, K. E.; Steinbacher, J. L.; Bogdan, A. R.; McQuade, D. T. *Chem. Rev.* **2007**, *107*, 2300–2318. (f) *Microreactors in Organic Synthesis*; Wirth, T., Ed.; Wiley-VCH: Weinheim, 2008. (g) *Handbook of Micro Reactors*; Hessel, V., Schouten, J. C., Renken, A., Wang, Y., Yoshida, J. I., Eds.; Wiley-VCH: Weinheim, 2009.

(2) For representative reports, see: (a) Wang, N.; Matsumoto, T.; Ueno, M.; Miyamura, H.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2009**, *48*, 4744–4746. (b) Miller, P. W.; Long, N. J.; de Mello, A. J.; Vilar, R.; Audrain, H.; Bender, D.; Passchier, J.; Gee, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 2875–2878. (c) Rahman, M. T.; Fukuyama, T.; Kamata, N.; Sato, M.; Ryu, I. *Chem. Commun.* **2006**, *21*, 2236–2238. (d) Rebrov, E. V.; Klinger, E. A.; Berenguer-Murcia, A.; Sulman, E. M.; Schouten, J. C. *Org. Process Res. Dev.* **2009**, *13*, 991–998.

(3) The parallel contacting between gas and liquid was tried in the chemical- and bio-engineering field. See: (a) Choudhary, V. R.; Gaikwad, A. G.; Sansare, S. D. *Angew. Chem., Int Ed* **2001**, *40*, 1776–1779. (b) de Jong, J.; Verheijden, P. W.; Lammertink, R. G. H.; Wessling, M. *Anal. Chem.* **2008**, *80*, 3190–3197. (c) Lemke, E. A.; Gambin, Y.; Vandelinder, V.; Brustad, E. M.; Liu, H. W.; Schultz, P. G.; Groisman, A.; Deniz, A. A. *J. Am. Chem. Soc.* **2009**, *131*, 13610–13612. (d) Timmer, B. H.; Olthuis, W.; Van den Berg, A. *Lab Chip* **2004**, *4*, 252–255. (e) Ohira, S. I.; Toda, K. *Lab Chip* **2005**, *5*, 1374–1379. (f) Vollmer, A. P.; Probstein, R. F.; Gilbert, R.; Thorsen, T. *Lab Chip* **2005**, *5*, 1059–1066. (g) Walker, G. M.; Ozers, M. S.; Beebe, D. J. *Biomed. Microdevices* **2002**, *4*, 161–166. (h) Lam, R. H. W.; Kim, M.-C.; Thorsen, T. *Anal. Chem.* **2009**, *81*, 5918–5924. (i) Aota, A.; Nonaka, M.; Hibara, A.; Kitamori, T. *Angew. Chem., Int. Ed.* **2007**, *46*, 878–880.

10.1021/ja102666y

Figure 2. Segmented flow of gas bubbles and liquid slugs in the monochannel microreactor (Inlet part).

we report a dual-channel microreactor in which a thin gas-permeable membrane is sandwiched between two PDMS slabs, the engraved microchannel in each of the slabs facing the other microchannel across the thin PDMS membrane. The microchannel in one of the slabs is used for liquid flow, while the other microchannel across the thin membrane is used for gas flow. This arrangement of dual channels (DC) provides a considerably higher contact area between gas and liquid than the batch or MC microreactor. The three-layered PDMS microreactor with dual-channel structure was readily prepared by facile soft lithography and used for organic chemical reactions without problematic swelling. In particular, the oxidative Heck reaction was thoroughly explored using the dual-channel microreactor. The results demonstrated that it is a highly promising reaction system for achieving significantly improved reaction yields and selectivities in a short time, due to sufficient contact between dissolved Pd catalyst and oxygen gas for generating the active Pd(II) species. To the best of our knowledge, this membrane-assisted microfluidic system is reported for gas−liquid organic chemical reactions for the first time.

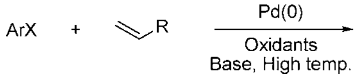
Results and Discussion

1. Relative Contact Area between Gas and Liquid Phases in Various Reaction Systems. At first, we were interested in the relative contact area between the two phases for the three types of reaction systems shown in Figure 1. Typical monochannel (MC) microreactors with discontinuous contact between alternating gas bubbles and liquid slugs have a segmented flow mode of gas−liquid contact, similar to that found in two immiscible liquids in a capillary microreactor, which would yield a larger contact area than a batch system (Figure 2).[4]

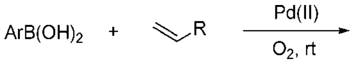
In the MC microreactor (length, 120 cm; height, 85 μm; width, 300 μm; inlet width, 100 μm), narrowed inlets were designed to minimize the gap between the bubbles because the contact area is proportional to the gap thickness (see Figure 2S in the Supporting Information). Moreover, to maximize the contact area, we regulated the feed rates of solution (DMF) and gas (oxygen) and the outlet pressure. However, it was not possible to get a gap narrower than 300 μm because the bubbles easily combined or collapsed with the narrower gaps. Fine control of a steady flow rate in a multiphase microfluidic system is also difficult to achieve due to the presence of a combination of the viscous solution and virtually nonviscous oxygen gas. The volume of the MC microreactor was 30.6 μL (85 μm × 300 μm × 120 cm), and the calculated contact area between the gas bubble (1200 μm long) and liquid slug (300 μm) was 0.408 cm^2 (120 cm/1500 μm × 2 × 300 μm × 85 μm). The maximum contact area-to-volume ratio in the MC microreactor was 13.3 cm^{-1}.

On the other hand, the dual-channel (DC) microfluidic system separated by a highly gas-permeable thin PDMS layer is designed to give a high contact area (Figures 3 and 4).[5] The solution channel is parallel with the gas channel for continuous contact between the gas and the liquid through the thin membrane, which facilitates permeation of the gas into the liquid and prevents the flow from breaking into a segmented flow of gas and liquid. Typically, the contact area between the dual channels was 3.6 cm^2 for the identical channel volume of 30.6 μL, yielding a maximum contact area-to-volume ratio of 117.6 cm^{-1} in the DC microreactor, which is almost an order of magnitude larger than the ratio of 13.3 cm^{-1} for the MC microreactor. In particular, it is worth noting that both microreactors have a much larger contact area to volume ratio than the value of 3.20 cm^{-1} for the cubic-shaped batch system [$\{a^{1/3} \times a^{1/3}\}/\{a^{1/3} \times a^{1/3} \times a^{1/3}\}$, a (reaction volume) = 30.6 μL] and the value of 0.33 cm^{-1} for the NMR tube (in a 0.6 mL reaction volume).[6] Therefore, it is anticipated that the relatively large contact area between the two channels would facilitate rapid gas diffusion from the gas channel to the solution channel through the gas-permeable PDMS layer. A 45 μm thin PDMS membrane layer was placed between the two PDMS microchannels (length, 120 cm; height, 85 μm; width, 300 μm). A thinner PDMS membrane layer (20 μm) was also tested; however, it gave poor results because the membrane deformed due to the large pressure difference between the gas and liquid channels.

2. Oxidative Heck Reaction in Various Reaction Systems. Palladium (Pd) catalysts frequently encountered in the traditional batch reactions have widely been used for miniature chemical systems with continuous flow. A heterogeneous Pd system with nanoparticles immobilized on the microchannel inner surface or supported on a block copolymer was shown to be highly efficient in hydrogenation, Suzuki−Miyaura, Sonogashira, and other reactions.[7] Moreover, packed-bed systems, ionic liquid assisted systems, catalytic membrane reactors, and homogeneous catalytic systems have also been studied.[2c,4,8]



(1)



(2)

Compared with the original Heck reaction (eq 1), the Pd-catalyzed oxidative Heck reaction is recently receiving much attention in synthetic chemistry for its ability to form C−C

---

(4) Ahmed-Omer, B.; Barrow, D. A.; Wirth, T. *Tetrahedron Lett.* **2009**, *50*, 3352–3355.

(5) The preparation procedure of the DC microreactor was described in the Supporting Information (Figure 1S).

(6) The contact area to volume ratio depends on the shape and volume of the reactor. As the simulation for a reaction with narrow contacting area between gas and liquid, a reaction in the NMR tube was tried (Table 2).

(7) For representative reports on microreactors using immobilized Pd catalysts, see: (a) Kobayashi, J.; Mori, Y.; Okamoto, K.; Akiyama, R.; Ueno, M.; Kitamori, T.; Kobayashi, S. *Science* **2004**, *304*, 1305–1308. (b) Kirschning, A.; Solodenko, W.; Mennecke, K. *Chem.−Eur. J.* **2006**, *12*, 5972–5990. (c) Baxendale, I. R.; Griffiths-Jones, C. M.; Ley, S. V.; Tranmer, G. K. *Chem.−Eur. J.* **2006**, *12*, 4407–4416. (d) Kawanami, H.; Matsushima, K.; Sato, M.; Ikushima, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 5129–5132. (e) Mennecke, K.; Cecilia, R.; Glasnov, T. N.; Gruhl, S.; Vogt, C.; Feldhoff, A.; Vargas, M. A. L.; Kappe, C. O.; Kunz, U.; Kirschning, A. *Adv. Synth. Catal.* **2008**, *350*, 717–730. (f) Shore, G.; Morin, S.; Organ, M. G. *Angew. Chem., Int. Ed.* **2006**, *45*, 2761–2766.

(8) (a) Uozumi, Y.; Yamada, Y. M. A.; Beppu, T.; Fukuyama, N.; Ueno, M.; Kitamori, T. *J. Am. Chem. Soc.* **2006**, *128*, 15994–15995. (b) Yamada, Y. M. A.; Watanabe, T.; Torii, K.; Uozumi, Y. *Chem. Commun.* **2009**, 5594–5596.

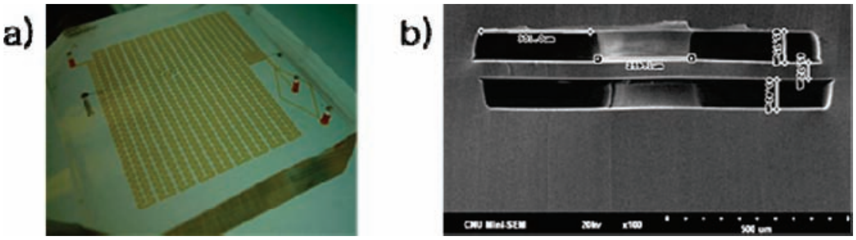


Figure 3. Dual-channel microreactor. (a) Optical image with 45 μm PDMS membrane layer between two fabricated PDMS channels (length, 120 cm; height, 85 μm; width, 300 μm). (b) The cross-section view of the corner of the dual-channel microreactor.

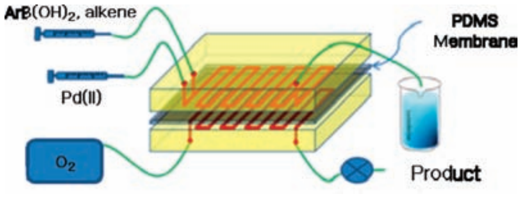
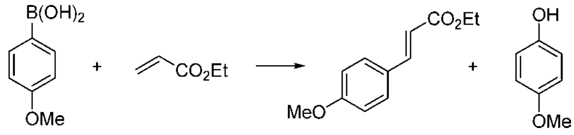


Figure 4. Schematic of the dual-channel microchemical system.

Table 1. Oxidative Heck Reactions in a DC Microreactor[a]



entry	gas (injection rate)	heck	alcohol
1	O_2 (10 μL/min)	25%	1%
2	O_2 (20 μL/min)	65%	5%
3	O_2 (25 μL/min)	74%	7%
4	O_2 (30 μL/min)	79%	7%
5	O_2 (35 μL/min)	78%	6%
6	N_2 (30 μL/min)	5%	0%
7	air (30 μL/min)	13%	1%

[a] Standard reaction conditions: DMF, rt, 5 mol % of $Pd(OAc)_2$, 5 mol % of [2,2′]-bipyridinyl, 0.5 μL/min injection rate (reagents: 1.0 M solution). The ^{1}H NMR yields were recorded using an external capillary standard.

bonds between various aryl carbons and alkene carbons with relatively mild reaction conditions and high reaction yields and without the need for an additional base and expensive organic/inorganic oxidants (eq 2).[9] The push for environmentally friendly processes and highly efficient methods has created a demand for the use of molecular oxygen as a terminal oxidant.[10] On the other hand, the introduction of a gaseous reactant has caused scale-up problems such as long reaction time and side product formation. These problems are expected to be resolved through the sufficient contact between dissolved Pd catalyst and oxygen gas that is now made possible with the dual microchannels. It is noted that the oxygen is needed to regenerate the active Pd(II) species.[9d,11]

The oxidative Heck reaction was carried out in the DC microreactor (Figure 4). The two DMF solutions of reagent and Pd(II) catalyst were injected into the top channel, and the injection rates were set at 0.5 μL/min (Table 1). The O_2 gas was supplied from the bottom inlet in a precisely controlled manner by varying the flow rate. In the case of an O_2 injection rate of 40 μL/min, bubbles formed due to supersaturation of the O_2 in the solution channel, which in turn generated a discontinuous flow (the segmented flow) as in the MC microreactor. However, 10 and 20 μL/min injection rates gave low reaction yields and caused liquid to leak from the solution channel. Eventually, 30 μL/min was found to be suitable for preventing supersaturation in the solution channel and leaking of solution between channels. Furthermore, we found that an injection rate over 30 μL/min did not increase the reaction yield and selectivity any more as seen in Table 1. Under the reaction conditions, neither a blackish tint due to a precipitated Pd(0) deposit[12] nor channel deforming was detected even for 2 days of continuous running or repeated use. The lack of deformation indicates the compatibility of the PDMS microchannel with the solvent (DMF), which was confirmed by a recent study showing only negligible swelling with DMF.[13] The reactions under dried air and nitrogen gas were also tested, which led to a poor result or stoichiometric reaction by palladium acetate. For comparison, we also tried a coaxial microfluidic system developed by Kobayashi and co-workers under fast gas flow and slow liquid flow.[7a] However, it was not appropriate for the oxidative Heck reaction because a fast gas flow carried away the volatile alkenes (acrolein, ethyl acrylate) from the solution.[14]

In the small-scale batch system 1 of the oxidative Heck reaction (Table 2), the extended reaction period (reaction time 12 h) yielded a relatively low reaction selectivity, inevitably generating a significant amount of aryl alcohol as a side product. The H_2O_2 generated as an alternative byproduct caused the decomposition of boronic acid and oxidation of some ligands, hence excess addition of boronic acid was generally required for the high reaction yields. Insufficient contact between the dissolved Pd catalyst and oxygen gas further retarded the conversion of Pd(0) species to active Pd(II), resulting in a much delayed reaction, which in turn caused high production of side products during the extended reaction time. However, both systems of the MC microreactor and DC microreactor significantly suppressed the formation of the aryl alcohol. In the MC microreactor, total conversions in the range of 67−72% resulted with 53−59% yields of Heck product and only 6−8% of aryl alcohol in 30 min of reaction time.

---

(9) (a) Stahl, S. S. *Angew. Chem., Int. Ed.* **2004**, *43*, 3400–3420. (b) Yoo, K. S.; Yoon, C. H.; Jung, K. W. *J. Am. Chem. Soc.* **2006**, *128*, 16384–16393. (c) Yoo, K. S.; Park, C. P.; Yoon, C. H.; Sakaguchi, S.; O'Neill, J.; Jung, K. W. *Org. Lett.* **2007**, *9*, 3933–3935. (d) Gligorich, K. M.; Sigman, M. S. *Chem. Commun.* **2009**, 3854–3867.

(10) Punniyamurthy, T.; Velusamy, S.; Iqbal, J. *Chem. Rev.* **2005**, *105*, 2329–2363.

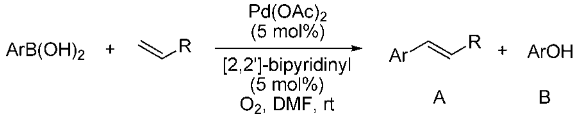
(11) For the detailed reaction mechanism, see the Supporting Information.

(12) XPS spectra for the channel surface of the used DC microreactor show that there is no significant deposition of Pd(0) species.

(13) Lee, J. N.; Park, C.; Whitesides, G. M. *Anal. Chem.* **2003**, *75*, 6544–6554. PDMS has a good transparency in UV-visible regions, chemical inertness. A fabrication is easy and requires low cost, compared to that for microfluidic materials (e.g., glass and silicon). For solvent compatibility at elevated temperature (60 °C), see the Supporting Information (Table 1S).

(14) In the Kobayashi device, gas over 20 equiv amount should be used to conduct an efficient result.

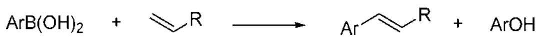
Table 2. Comparative Synthetic Yields of Oxidative Heck Reactions in Two Types of PDMS Microreactors and Two Types of Batch Systems



entry	Ar	R	batch 1^a (A%:B%)^d	batch 2^b (A%)^d	MC^c (A%:B%)^d	DC^c (A%:B%)^d
1	phenyl-	-CO_2Et	69:24	19 (20%)^e	59:6 (72%)^e	82:8 (79%)^f
2	phenyl-	-Ph	67:25	17 (17%)^e	53:8 (67%)^e	79:9 (76%)^f
3	4-bromo-phenyl-	-CO_2Et	64:24		55:7 (69%)^e	79:8 (75%)^f

[a] 12 h reaction, 1.0 mmol of aryl boronic acid, 1.1 mmol of alkene, and 2 mL of DMF in a 10 mL flask. [b] 3 days reaction, 0.3 mmol scale, and 0.6 mL of DMF-d_7 in an NMR tube. [c] 30 min reaction in a microreactor. [d] The ^{1}H NMR yields were recorded using an external capillary standard. [e] Conversion. [f] Isolation yield of Heck product A.

Table 3. Oxidative Heck Reaction of Aryl Boronic Acids with Alkenes in the DC Microreactor



entry	Ar	R	NMR yield (Heck:alcohol)^a	Heck^b
1	phenyl-	-CHO	80%:8%	78%
2	2-naphthyl-	-CHO	77%:10%	75%
3	2-naphthyl-	-CO_2Et	84%:6%	81%
4	2-naphthyl-	-phenyl	80%:10%	78%
5	4-methoxyphenyl-	-CO_2Et	79%:7%	76%
6	4-bromophenyl-	-CO_2Et	85%:7%	82%

[a] Standard reaction conditions: DMF, rt, 5 mol % of $Pd(OAc)_2$, 5 mol % of [2,2′]-bipyridinyl, 30 min reaction in the microreactor. The ^{1}H NMR yields were recorded using an external capillary standard. [b] Isolatied yield of Heck product.

The performance of the DC system was impressive. It should be noted that the DC system improved significantly reaction performance in all terms of yield and the reaction selectivity, which produced yields of 76−85% for the Heck product with about 10:1 selectivity. The highly effective contact between gas and solution phases in the DC microreactor rapidly reactivated Pd(0) species to accelerate the reaction. As a result, the reaction time was reduced to 30 min, and the decomposition of phenyl boronic acid to phenol was minimized (Table 2, entry 1). Similar trends were also observed in the reactions with alternative alkenes and boronic acids (entries 2 and 3). The usefulness of the DC microreactor is more clear when the DC microreactor is compared to a batch system with an extremely small contact area between two phases and a low mixing efficiency in solution. We tested the oxidative Heck reaction in an NMR tube (batch 2), which has only 0.33 cm^{-1} contact area to volume ratio (in 0.6 mL reaction volume). The reaction was still not completed after 3 days. The ^{1}H NMR yield of the Heck product was only 19% and 17%, and black precipitation of Pd(0) was significant. The result simply demonstrates the extreme case that can be encountered in the scaled-up reactor with highly limited contact efficiency. The comparisons show that the membrane-assisted DC microreactor is a powerful microfluidic device for gas−liquid reactions.

3. Various Oxidative Heck Reactions in a Dual-Channel Microreactor. We further demonstrated the efficiency of the DC microreactor with the C−C bond-forming reactions of a variety of alkenes and boronic acids (Table 3). Phenyl boronic acid effectively reacted with acryl aldehyde to produce cinnamaldehyde (entry 1). 2-Naphthyl boronic acid also reacted with acrylic ester, styrene, and acrylaldehyde with even higher yields and excellent selectivity. The oxidative Heck reactions with the use of 4-methoxy- and 4-bromo-phenyl boronic acid further confirmed the reliable chemical performance of the DC microreactor. It is notable that all the reactions produced only (*E*)-configuration Heck products. The product in entry 6 could be further elaborated through a combination with a Suzuki or Sonogashira reaction. It is noted here that the DC microreactor enabled precise injection of required oxygen into the solution phase of boronic acid and alkene. It is significant that the precise control of a gaseous reagent makes it possible to complete a multistep chemical process without unreacted gas remaining at each of the successive steps.

Finally, it is plausible that this type of microreactor would be extended to a wide range of gas−liquid reactions carried out at mild temperatures and in polar solvents, including carbonylation with Pd catalysts, gold-catalyzed reductions of nitro compounds,[15] and Pd-catalyzed Saeguesa reactions.[16]

Conclusions

A dual-channel (DC) microreactor has been prepared for gas−liquid reactions in which intimate contact between gas and liquid can significantly enhance reaction yield and selectivity. The dual microchannel reactor that is 120 cm long has been utilized to investigate an oxidative Heck reaction with gaseous oxygen to fully derive the benefits attainable through efficient gas−liquid contact. The DC microreactor has been shown to deliver much improved reaction yield (72−82% isolation yield) and selectivity (7.7:1−13.7:1) in much less reaction time (30 min), compared with a small-scale batch system where the selectivity is 2.7:1−2.9:1 in 12 h of reaction time and with a batch system with an extremely small contact area where the yield (NMR yield) is 17−19% in 3 days of reaction. Although the microreactor was fabricated with PDMS, it can be fabricated with other materials[17] that are more tolerant to solvents and chemicals for wider applications. The microreactor should prove to be a powerful tool for fully exploring reactions and syntheses involving gaseous and liquid reagents.

---

(15) He, L.; Wang, L.; Sun, H.; Ni, J.; Cao, Y.; He, H.; Fan, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9538–9541.

(16) (a) Liu, J.; Zhu, J.; Jiang, H.; Wang, W.; Li, J. *Chem. Asian J.* **2009**, *4*, 1712–1716. (b) Liu, J.; Zhu, J.; Jiang, H.; Wang, W.; Li, J. *Chem. Commun.* **2010**, *46*, 415–417.

(17) We developed novel polymer microfluidic devices with high solvent resistance: (a) Yoon, T. H.; Park, S. H.; Min, K. I.; Zhang, X.; Haswell, S. J.; Kim, D.-P. *Lap Chip* **2008**, *8*, 1454–1459. (b) Kim, B.-Y.; Hong, L.-Y.; Chung, Y.-M.; Kim, D.-P.; Lee, C.-S. *Adv. Funct. Mater.* **2009**, *19*, 3796–3803.

Experimental Section

General Description of the Oxidative Heck Reaction Using the MC Microreactor. In one syringe was loaded a 1 mL DMF-d_7 solution of aryl boronic acid (1.0 mmol) and alkene (1.1 mmol), and in another syringe was loaded a 1 mL DMF-d_7 solution of the Pd(II) complex prepared with 0.05 mmol of $Pd(OAc)_2$ and 0.05 mmol of [2,2′]-bipyridinyl. Oxygen supply was placed in the third inlet. The reaction streams were introduced to the three inlets of the monochannel microreactor through a 25 cm segment of polytetrafluoroethylene (PTFE) tubing. The injection rates of reagent and catalyst varied from 0.2 to 0.5 μL/min, and that of the gas varied from 20 to 200 μL/min. The reaction result was collected in a vial through a segment of PTFE tubing. Reaction yield and selectivity were measured by the ^{1}H NMR analysis using an external capillary standard.

General Description of the Oxidative Heck Reaction Using the DC Microreactor. Three lines for reagent, catalyst, and oxygen were prepared in the same manner as in the MC microreactor. The streams of reagent and catalyst were introduced to the two top-channel inlets through a 25 cm segment of PTFE tubing. The oxygen gas stream was introduced to the inlet of the bottom channel in the same manner as the reagent connections. The injection rates of reagent and catalyst were set at 0.5 μL/min, and that of the gas was set at 30 μL/min. The reaction result was collected in a vial through a segment of PTFE tubing. Reaction yield and selectivity were measured by the ^{1}H NMR analysis using an external capillary standard. The mixtures were purified through extraction with ethyl acetate (EA) from the DMF/water solution and column chromatography.

Acknowledgment. This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MEST) (20100000722).

Supporting Information Available: Experimental details for the preparation of the microreactors and reaction procedure. The solvent compatibility of PDMS at elevated temperature (60 °C). The XPS spectra for a channel surface of the used DC microreactor and ^{1}H NMR and ^{13}C NMR spectral data for isolated Heck reaction products. This material is available free of charge via the Internet at http://pubs.acs.org.

JA102666Y