Supplementary Material (ESI) for Chemical Communications

Supplementary Information

Low Pressure Pd-Catalyzed Carbonylations in an Ionic Liquid Using a Multiphase Microflow System

Md. Taifur Rahman, Takahide Fukuyama,* Naoya Kamata, Masaaki Sato, and Ilhyong Ryu*
Department of Chemistry, Graduate School of Science, Osaka Prefecture University,
Sakai, Osaka 599-8531, Japan
Tel and Fax: +81-72-254-9695
E-mail: ryu@c.s.osakafu-u.ac.jp

1.1 General.

The ionic liquid [BMIm]PF_6, used in this work, was synthesized according to the literature method.[1] The palladium carbene complex **A** was synthesized according to our procedure published elsewhere.[2] Other reagents were used as purchased. The product was confirmed by ^{1}H, ^{13}C NMR, and GC-MS. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL JMN-AL400 spectrometer in $CDCl_3$ operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C measurements. All the products are known compounds and the spectral data are in accordance with the corresponding literature values.[3,4]

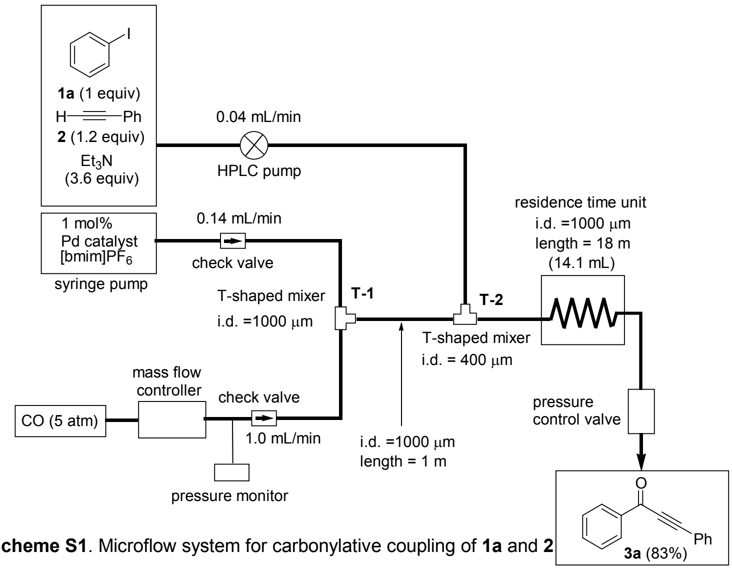
1.2. Continuous microflow apparatus for carbonylation.

The continuous microflow system was comprised of two T-shaped micromixers (i.d. = 1000 μm and 400 μm), residence time unit (stainless tube, i.d. = 1000 μm, length = 18 m), three gas/liquid feed stainless tube and an outlet. Carbon monoxide was delivered to the first micromixer at a constant rate through a mass flow controller from a CO gas cylinder. The pressure of the system was controlled by a pressure control valve, connected to the tail of the residence time unit, and was monitored by a pressure monitor. A palladium catalyst solution in [BMIm]PF_6 was introduced at the other inlet of the first micromixer through a check valve by means of a pressure durable syringe pump, which can be used under high pressures (Furue Science Co. Ltd., Microfeeder JP-H). A mixture of substrates and reactants was introduced through an HPLC pump (JASCO Co. Ltd., PU-2080 Plus) to the second micromixer, where the mixture was mixed with the catalyst solution and the CO. The mixture was then passed through the residence time unit and the pressure control valve, and collected and analyzed by NMR.

Typical experimental procedures:

2.1 Microflow carbonylative Sonogashira coupling reactions.

The reaction of iodobenzene (**1a**) with phenylacetylene (**2**) and CO (Scheme S1): A Pd carbene complex **A** (0.07 mmol, 40 mg) was dissolved in [BMIm]PF_6 (17 mL) and then placed in a syringe, which was then attached to a syringe pump. The system was pressurized with CO (5 atm) by means of the pressure control valve. The flow rate of CO was controlled at 1.0 mL/min by the mass flow controller. The solution of 1 mol% of Pd catalyst in [BMIm]PF_6 (flow rate = 0.14 mL/min) and CO (5 atm, flow rate = 1.0 mL/min) were mixed in the first T-shaped micromixer T-1 (i.d. = 1000 μm). A mixture of iodobenzene (**1a**, 1.48 g, 7 mmol), phenylacetylene (**2**, 855 mg, 8.4 mmol), Et_3N (2.5 g, 25 mmol), and *p*-methoxyanisole as an internal standard, was introduced at a flow rate of 0.04 mL/min through a HPLC pump and mixed with the ionic liquid/CO mixture in a second T-shaped micromixer T-2 (i.d. = 400 μm). The whole reaction mixture (comprising of the ionic liquid, CO gas and the substrates) was then fed into the

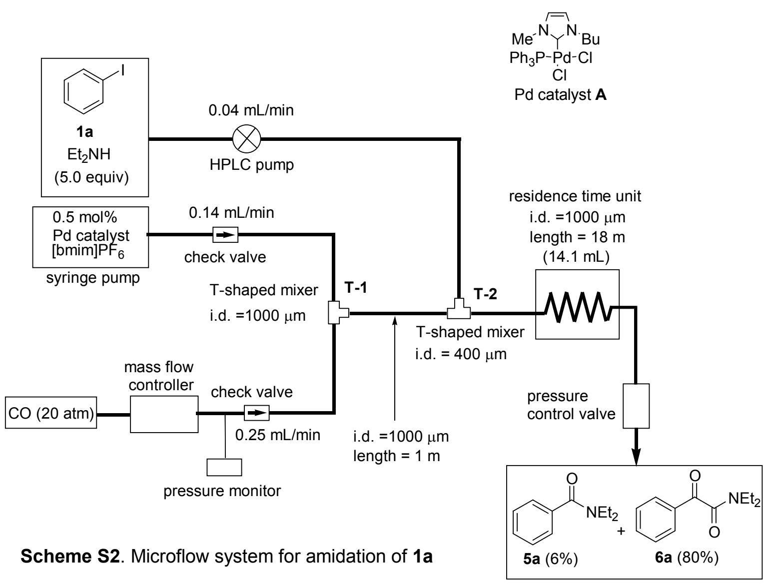


Scheme S1. Microflow system for carbonylative coupling of **1a** and **2**

residence time unit, which was immersed in an oil bath, and heated at 120 °C. The time needed for the reaction mixture to travel through the residence time unit was expressed as the residence time (12 min). The mixture of products was collected from the outlet. The reaction mixture eluted during the first 20 min was discarded and the following portion was collected for a 10 min period. The product was extracted with ether (5 x 5 mL). The product was confirmed by ^1H, ^{13}C NMR, and GC-MS. The yield was determined by ^1H NMR (based on the iodobenzene used) and calculated from the internal standard added.

2.2 Microflow amidation reactions.

The reaction of iodobenzene (**1a**) with diethylamine and CO (Scheme S2): The amidation reactions of aryl iodides were carried out by a similar protocol and by using the same apparatus as is described for the carbonylative Sonogashira coupling reactions. Here in the amidation reactions, 0.5% solution of Pd carbene complex **A** in $[BMIm]PF_6$ was used. The system was pressurized with CO (20 atm) by means of the pressure control valve. The solution of 0.5 mol% of Pd catalyst in $[bmim]PF_6$ (flow rate = 0.14 mL/min) and CO (20 atm, flow rate = 0.25 mL/min) were mixed in the first T-shaped micromixer T-1 (i.d. = 1000 μm). A mixture of iodobenzene (**1a**, 2.89 g, 14 mmol), Et_2NH (5.17 g, 70 mmol), and 1-chlorotetradecane as an internal standard, was introduced at a flow rate of 0.04 mL/min through a HPLC pump and mixed with the ionic liquid/CO mixture in a second T-shaped micromixer T-2 (i.d. = 400 μm). The whole reaction mixture was then fed into the residence time unit, which was immersed in an oil bath, and heated at 80 °C. The residence time for this reaction is 34



Scheme S2. Microflow system for amidation of **1a**

min. The mixture of products was collected from the outlet. The reaction mixture eluted during the first 20 min was discarded and the following portion was collected for a 10 min period. The products were extracted with ether (5 x 5 mL). The products were confirmed by ^{1}H, ^{13}C NMR, and GC-MS. The yield was determined by ^{1}H NMR (based on the iodobenzene used) and calculated from the internal standard added.

2.3 Autoclave carbonylative Sonogashira coupling reactions.

In a glass liner of a 50 mL autoclave Pd carbene complex **A** (0.01 mmol, 5.8 mg, 1.0 mol%) was dissolved in [BMIm]PF_6 (3.0 mL). To this was added a mixture of iodobenzene (**1a**, 204 mg, 1.0 mmol), phenylacetylene (**2**, 123 mg, 1.2 mmol), Et_3N (364 mg, 3.6 mmol), and *p*-methoxyanisole as an internal standard. The autoclave was closed, purged three times with 10 atm of carbon monoxide, pressurized with 5 or 3 atm with CO, and then heated at 120 °C for 1 h. Excess CO was discharged at room temperature. The product was extracted with Et_2O (5x5 mL). The combined extract was concentrated and the yield was determined by ^{1}H NMR (based on the iodobenzene used) and calculated from the internal standard added.

2.4 Autoclave amidation reactions.

In a glass liner of a 50 mL autoclave Pd carbene complex **A** (0.013 mmol, 7.7 mg, 0.5 mol%) was dissolved in [BMIm]PF_6 (2.0 mL). To this was added a mixture of iodobenzene (**1a**, 543 mg, 2.66 mmol), Et_2NH (973 mg, 13.3 mmol, 5 equiv), and 1-chlorotetradecane as an internal standard. The autoclave was closed, purged three times with 20 atm of carbon monoxide, pressurized with 20 atm with CO, and then heated at 80 °C for 5 h. Excess CO was discharged at room temperature. The product was extracted with Et_2O (5x5 mL). The combined extract was concentrated and the yield was determined by ^{1}H NMR (based on the iodobenzene used) and calculated from the internal standard added.

2.5 Controlled carbonylative Sonogashira coupling reaction in an autoclave.

The reactions were carried out according to the procedure as in section 2.3 and by using the same glass liner and autoclave to maintain dimensional integrity of the reactor. In each run individual molar concentrations of the catalyst, substrates and reagent were same e.g., 1 mol% of catalyst containing solution of [BMIm]PF_6 (3.0 mL, 4.5 mL and 6.0 mL in each run) was taken along with an identical molar concentrations of the substrates and reagent (0.33 M of **1d**, 0.4 M of **2** and 1.19 M of Et_3N in each run) and 1,4-dimethoxybenzene as an internal standard. The yields were determined by ^1H NMR and calculated from the internal standard added.

References:

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