

**Paper-Based Colorimetric Sensor System for the High-Throughput Screening of Ir-catalyzed C-H Borylation**Han-Sung Kim<sup>1</sup>, Min Sik Eom<sup>2</sup>, Min Su Han<sup>2\*</sup>, and Sunwoo Lee<sup>1\*</sup><sup>1</sup>Chonnam National University, South Korea<sup>2</sup>Gwangju Institute of Science and Technology (GIST), South Korea

Many C-H activation methodologies have been developed in the last decades and are used in the pharmaceutical and materials industry. Among them, C-H borylation is one of the most useful reaction methods, because the products are not only easily transformed to other functional groups, but also react with the coupling partners. The most general method is the reaction of a substrate with bis(pinacolato)diboron ( $B_2Pin_2$ ) or pinacolborane (HBpin) in the presence of an Ir-catalyst. To determine the suitable parameters for a substrate, considering large numbers of combination of parameters, it is important to use an efficient high-throughput screening (HTS) assay that can rapidly identify the outcome. Automated analysis instruments have been commonly used as HTS tools in metal-catalyzed transformations. However, they have several drawbacks such as the need for expensive instruments and at least several minutes to analyze one sample. To address these issues, we developed a simple and general HTS assay for C-H borylation. A paper-based colorimetric sensor system (PBCSS) was developed to analyze the amount of  $B_2Pin_2$  and applied as a high-throughput screening protocol in Ir-catalyzed C-H borylation. First, ninety-six ligands were screened for the borylation of benzene, and then twelve of them were selected and tested for five substrates. These reaction mixtures were spotted in the PBCSS, showing a blue-violet color in the presence of residual  $B_2Pin_2$  in an Ir-catalyzed reaction library. The value of the gray scale of each reaction was obtained from these colored spots and converted to the extent of conversion of  $B_2Pin_2$ . The extents of conversion of  $B_2Pin_2$  obtained from the PBCSS showed good correlation with those obtained from gas chromatography analysis. In addition, the modified conversions that removed the false-positive hits caused by the decomposition of  $B_2Pin_2$  using blank data showed high correlation with the yield of products. Based on these results obtained from the PBCSS, the best condition for each substrate was selected. And this PBCSS has several advantages: 1) The preparation method is very simple and inexpensive, 2) It is readily accessible because only a paper and scanner are needed, 3) It gives fast and accurate extent of conversion of  $B_2Pin_2$  by qualitative analysis using visual color change and quantitative conversions using a grayscale image, 4) The use of blank data removes the wrong information caused by the false-positive hits.

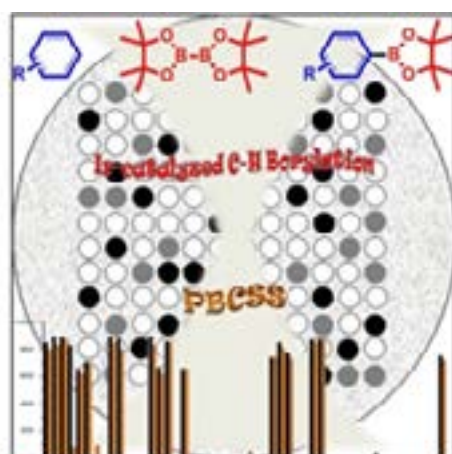


Figure 1. Paper-Based Colorimetric Sensor System for the HTS of Ir-catalyzed C-H borylation.

#### Recent Publications

1. Kim H-S, Eom MS, Han MS, Lee S (2017) Paper-based colorimetric sensor system for high-throughput screening of C-H borylation. *Chem. Eur. J.* 23:6282-6285.
2. Eom MS, Noh J, Kim H-S, Yoo S, Han MS, Lee S (2016) High-throughput screening protocol for the coupling reactions of aryl halides using a colorimetric chemosensor for halide ions. *Org. Lett.* 18:1720-1723.
3. Jung E, Kim S, Kim Y, Seo SH, Lee SS, Han MS, Lee, S (2011) A colorimetric high-throughput screening method for palladium-catalyzed coupling reactions of aryl iodides using a gold nanoparticle-based iodide-selective probe. *Angew. Chem. Int. Ed.* 50:4386-4389.
4. Kim S, Jung E, Kim MJ, Pyo A, Palani T, Eom MS, Han MS, Lee S (2012) A simple, fast, and easy assay for transition metal-catalyzed coupling reactions using a paper-based colorimetric iodide sensor. *Chem. Commun.* 48:8751-8753.
5. Pyo A, Kim S, Kumar MR, Byeun A, Eom MS, Han MS, Lee S (2013) Palladium-catalyzed hydrodehalogenation of aryl halides using paraformaldehyde as the hydride source: high-throughput screening by paper-based colorimetric iodide sensor. *Tetrahedron Lett.* 54:5207-5210.

#### Biography

Han-Sung Kim was born in Seoul, South Korea. He obtained his B.S. from Chongnam National University in 2008. After completed his M.S. (2016) from the Department of Chemistry at the Chonnam National University, he commenced his Ph.D. under supervision of Prof. Sunwoo Lee in the same university. And he worked at POSTECH as a researcher (2013-2014). His research interests include development of high-throughput screening method for the coupling reactions and their applications.

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