Chicago Discovery Solutions, LLC
23561 W. Main Street
Plainfield, IL 60544 U.S.A.
Telephone: 1-815-609-2071

New Advances in Green Technologies:

Synthesizing new drug candidates using greener methodology – a long-standing problem with a big impact on pharmaceutical business

As a company involved in technology development, we at Chicago Discovery Solutions are constantly on the lookout for new solutions that have broad implications for chemists. Our investigations have moved us to address the environmental impact of organic reactions, in particular, the traditional cross-coupling reaction of carbon-carbon bonds.

The formation of carbon-carbon bonds by transition metal-catalyzed direct functionalization of C–H bonds has recently emerged as a greener alternative. Despite the improvements in catalytic efficiency that allows reactions to proceed under milder conditions or lower catalyst loadings, this type of transformation still suffers from a major limitation with regards to the reaction medium.

Traditional cross-coupling reactions regularly use *N*-methylpyrrolidinone (NMP), dimethylformamide (DMF) or dimethylacetamide (DMAc) as reaction solvents. These solvents are undesirable because of their toxicity and high boiling points. Recent efforts have been made to execute these reactions in a greener, more environmentally acceptable media. A review published in *Green Chemistry* (1) summarizes the contributions made in this direction during the past few years.

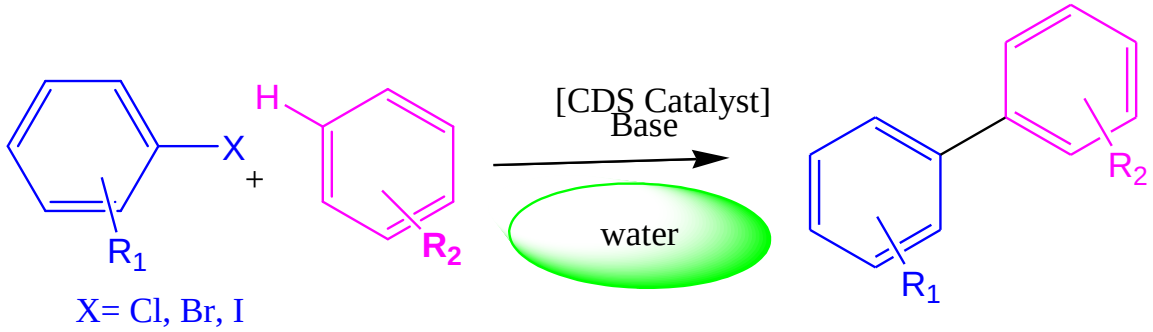

Figure 1. CDS' successful examples of direct arylation reactions in a water medium at atmospheric pressure (no need for sealed tube/ pressure reactor conditions)

One environmentally benign solvent that has commanded much attention in this arena is water. At CDS, we have developed a catalyst that performs C-H activation in water at atmospheric pressure. All attempts to do this type of transformations have been in sealed tube conditions commonly known as pressure reactors. We have several successful examples of direct arylation of hetero aromatics in water (Figure 1). Most importantly, by eliminating the need for pressure reactors and additives in the reaction such as detergents, our reaction conditions are far more cost effective, safer and generate less waste.

Our technology is applicable to a broad range of drug molecules containing aromatic functional groups, which are by far the most essential pharmacophore for medicinal

chemistry and drug development (2). Our technology positions us well to fill the gap in environmentally friendly methodologies in medicinal chemistry and drug development.

World is paying increased attention to organic waste produced by chemical enterprise and organic solvents play a considerable role in this regards (3). Small molecule pharmaceuticals have among the highest E factors in the chemical industry, in the range of 25 to 200. Fine-chemicals. Pharmaceutical industry requires more steps in synthesis and higher purity which results in higher waste and higher E factor. Most of the waste is inorganic salt by products and organic solvents (CEN ACS Org , 21, April 2013). Organic solvents account for 80% of the waste generated during typical pharmaceutical processing according to data presented to ACS Green Chemistry Institute's pharmaceutical roundtable.

ACS Green Chemistry Institute's pharmaceutical roundtable viewed developing alternative to traditional organic solvents as a critical step towards safer and more sustainable pharmaceutical manufacturing.

As a company, we are dedicated to developing new environmentally friendly technologies in the area of pharmaceutical research. Our goal is to reduce the environmental impact of synthetic Chemistry. If you would like us to assist with improving your research program, please contact us at sales@chicagodiscoverysolutions.com.

References:

1. Fischmeister and Doucet. *Green Chem.*, 2011, **13**, 741-753
2. Constable et al. *Green Chem*., 2007, **9**, 411-420
3. R.A. Sheldon. Green Chem. 2007, 9 (12), 1273