Experiment No 6 - Metal Catalyzed Cross-Coupling Reactions

In this lab you will be introduced to one of the most important reactions in modern organic chemistry; the cross-coupling reaction between organic halides and organometallic reagents catalyzed by Palladium for the formation a new C-C bond.

The importance of this set of reactions was recognized in 2010 when the Nobel Prize in chemistry was awarded to Suzuki, Negishi and Heck for ***"for palladium-catalyzed cross couplings in organic synthesis***.

For a comprehensive review on the history and the development of the different types of the reactions:

### **Palladium-Catalyzed Cross-Coupling: A Historical Contextual Perspective to the 2010 Nobel Prize**, [Carin C. C. Johansson Seechurn, Matthew O. Kitching, Dr. Thomas J. Colacot, Victor Snieckus *Angew. Chem. Int. Ed.* **2012**, 51, 5062 – 5085](http://onlinelibrary.wiley.com/doi/10.1002/anie.201107017/abstract).

In this lab you will perform a Cu free Sonogashira type cross-coupling in water between an aryl iodide and an acetylene.



The iodide will be prepared via the Sandmeyer reaction (see procedure below).

The procedure for the Sonogashira coupling can be found in the following article:

**Copper-Free Sonogashira Coupling Reaction with PdCl2 in Water under Aerobic Conditions,** [Bo Liang, Mingji Dai, Jiahua Chen and Zhen Yang, J. Org. Chem. 2005, 70, 391-393](http://pubs.acs.org/doi/abs/10.1021/jo048599z)

Preparation of p-iodonitrobenzene :



In a 200 mL Erlenmeryer flask mix 5 g of ice and 5 mL of water; keep the solution cold using an ice bath (don't let it heat above 5oC). Slowly add 1 mL of concentrated sulfuric acid.

To the mixture, add slowly 0.045 mol of p-nitroaniline and stir until most of the solid is dissolved. In another Erlenmeyer, dissolve 0.045 mol of sodium nitrite in 2.5 mL H2O and cool this solution using an ice bath. Slowly add the sodium nitrite solution to the p-nitroaniline solution, **maintain the temperature below 10oC.**

Prepare a solution of 0.0075 mol of potassium iodide in 7.5 mL of water in a 200 mL Erlenmeyer. Slowly (in portions) pour the diazonium salt solution into the potassium iodide solution, wait for the foaming to subside, and then add another portion.

When the addition is completed and the foaming subsides, cool the Erlenmeyer in an ice bath and collect the solid product formed using Büchner filtration. Recrystallize your product from isopropanol.