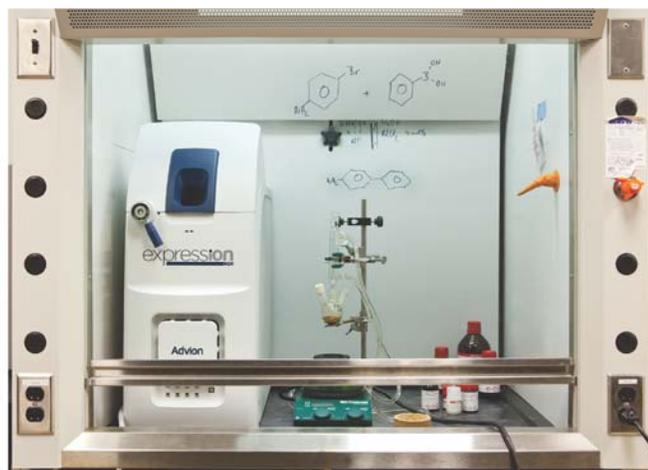


# Real-time monitoring of Suzuki reaction using Compact Mass Spectrometry via LC/MS and Flow Injection (FI)/MS

## Introduction

Medicinal chemists are routinely faced with personally synthesizing over a hundred new chemical entities (NCE's) each year for testing as future pharmaceutical drug candidates. The goal is to prepare a high yield, relatively pure product via an optimized synthetic route. TLC and LC/UV/MS are routinely used to monitor and guide these reaction outcomes. In most cases the LC/UV/MS technology is only available through a central core facility or via shared open access of systems. A preferred alternative is a personal small LC/MS system located in a hood adjacent to the synthetic reaction apparatus. This note describes such an LC/CMS system used to monitor and optimize a Suzuki coupling reaction.



## Application

We demonstrate a novel compact single quadrupole mass spectrometer for hood-based applications in the analysis of chemical reactions employing either LC/MS or flow injection analysis (FIA).

## Materials and Methods

HPLC System:

Shimadzu SCL-10A System controller

HPLC pumps (2): LC10AD

HPLC column: 2.1 mm x 50 mm Phenomenex Luna 5 micron C-18

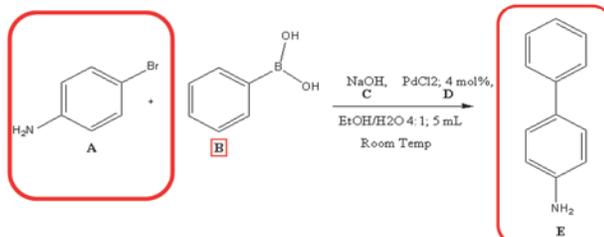
Isocratic at 0.2 mL/min 50% water/MeOH containing 0.1% formic acid

FIA: Simply remove the HPLC column and inject the reaction mixture into the same flowing mobile phase

Mass spectrometer: **expression** CMS

Ionization: Ion Spray, Pos Ions

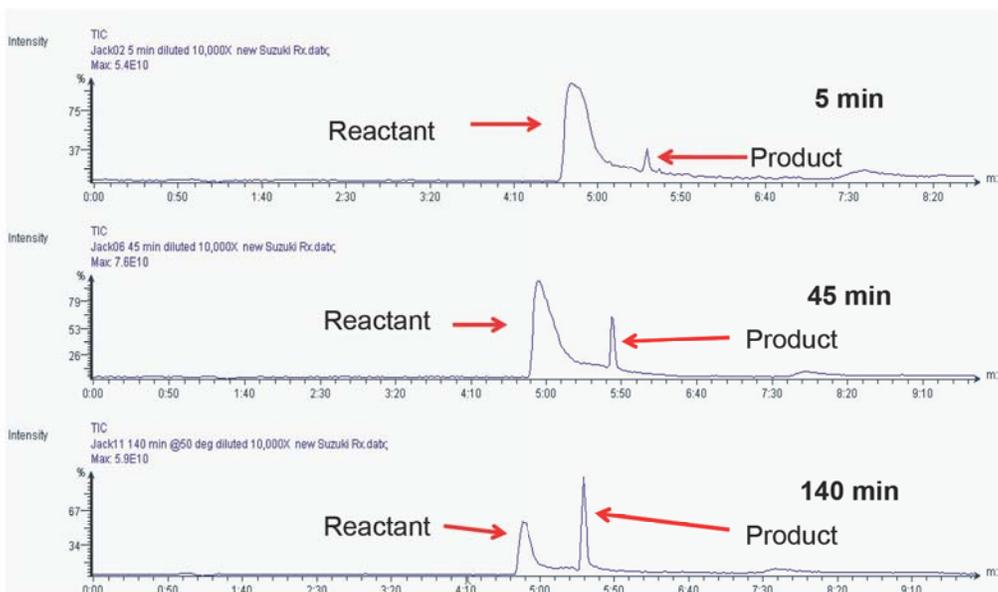
## Suzuki Reaction to prepare p-Aminobiphenyl



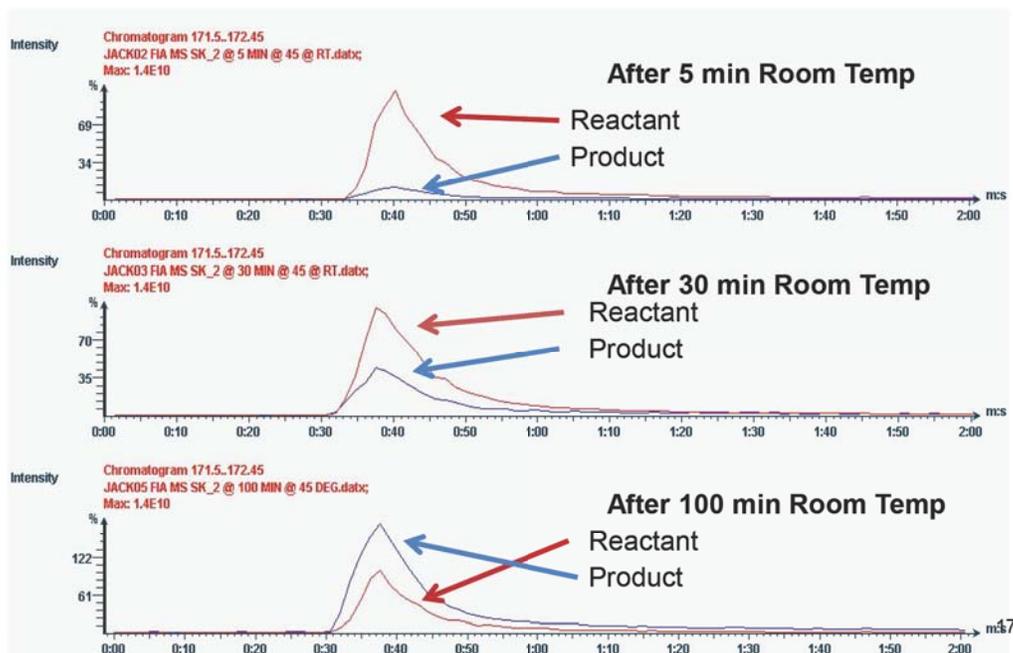
|                   | A       | B       | C      | D            | E       |
|-------------------|---------|---------|--------|--------------|---------|
| <b>ChHy</b>       | C6H6BrN | C6H7BO2 | NaOH   | PdCl2        | C12H11N |
| <b>MW (g/mol)</b> | 171     | 122     | 40     | 176          | 169     |
| <b>Moles</b>      | 0.005   | 0.005   | 0.0065 | 0.005 (0.04) | 0.005   |
| <b>Grams</b>      | 0.855   | 0.61    | 0.26   | 0.035        | 0.845   |
| <b>mg.</b>        | 855     | 610     | 260    | 35           | 845     |
| <b>Sp. Gr.*</b>   | -       | ↓       | -      | -            | -       |

## Results

### LC/CMS Analysis of Suzuki Reaction - Results in 6 minutes



### FIA/CMS of Suzuki Reaction - Results in 1 minute



The goal of a synthetic reaction is to produce a high yield of the desired product in a minimum period of time. Monitoring a reaction mixture over the course of time with a selective detector can allow one to optimize this process. This work describes the use of a new compact single quadrupole compact mass spectrometer (CMS) equipped with electrospray ionization to monitor a representative Suzuki coupling reaction in real-time. The results demonstrate proof-of-principle for this approach for real-time reaction monitoring by observing the increase of the product/reactant ratio over time.

### Advantages

- A fresh new perspective and an alternative to traditional MS products
- Fast answers in space-restricted labs
- Does not compromise your performance requirements or your budgets
- A Mass Spec for the Masses