

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

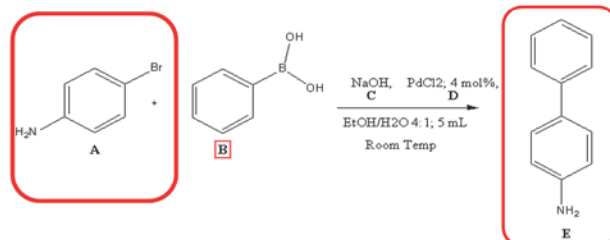
Isocratic at 0.2 mL/min 50% water/MeOH containing 0.1% formic acid

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

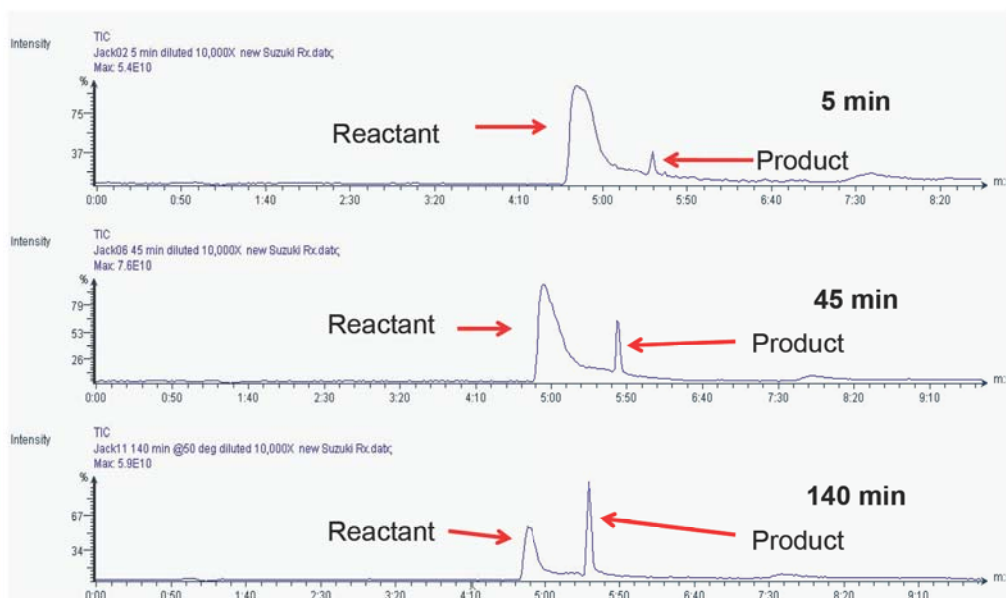


	A	B	C	D	E
CxHy	C ₆ H ₆ BrN	C ₆ H ₇ BO ₂	NaOH	PdCl ₂	C ₁₂ H ₁₁ N
MW (g/mol)	171	122	40	176	169
Moles	0.005	0.005	0.0065	0.005 (0.04)	0.005
Grams	0.855	0.61	0.26	0.035	0.845
mg.	855	610	260	35	845
Sp. Gr.*	-	↓	-	-	-

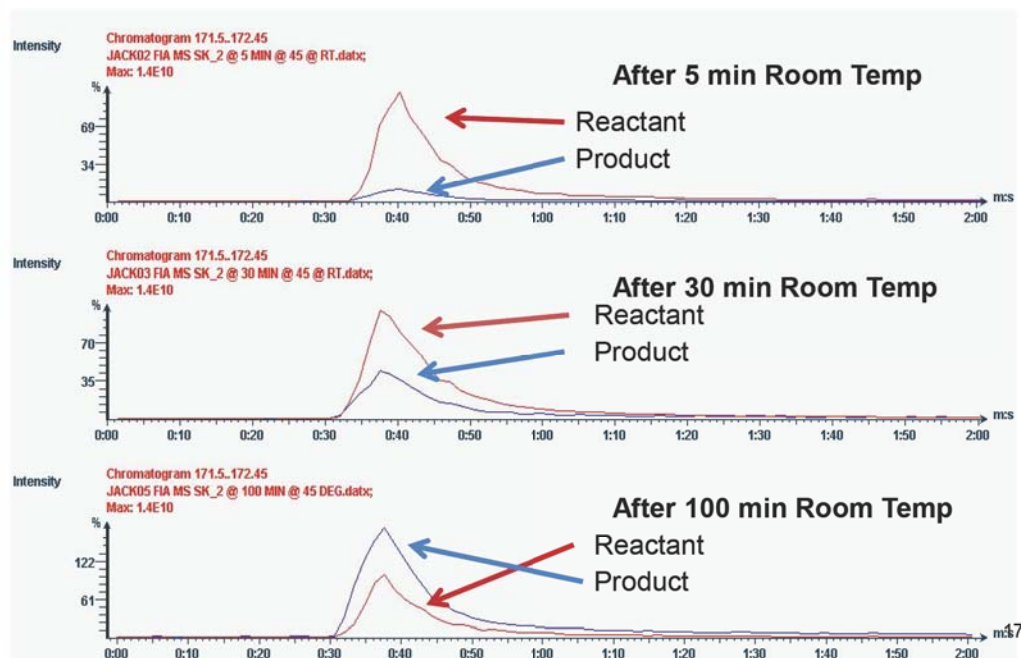
FN: Suzuki Rx to p-aminobiphenyl.cdx

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