SUPPORTING INFORMATION

"GREEN" SUZUKI-MIYAURA CROSS-COUPLING: AN EXCITING MINI-PROJECT FOR CHEMISTRY UNDERGRADUATE STUDENTS

Student Handout

Week #1: 4-methoxybiphenyl synthesis via the Suzuki-Miyaura cross-coupling reaction

Add phenylboronic acid (1.5 mmol), 4-iodoanisole (1.0 mmol), Pd/C 10 wt. % loading (15 mg, 1.4 mol% of Pd), K_2CO_3 (2.0 mmol), and 8 mL of dimethylformamide (DMF) into a 25 mL bottom flask. Connect the bottom flask into the reflux condenser of the adapted domestic microwave oven and begin heating for an assigned time (30, 45, 50, 60, or 90 min). Discontinue heating when to project reaction mixture in reflux condenser. Wait for the mixture to cool, and heat it again. After the reaction time is complete, the mixture should be stored in air at room temperature until the next class.

Week #2: TLC analyzes and purification of the 4-methoxybiphenyl product

Determine the Rfs of compounds **1**, **2**, **3** and the reaction mixture via TLC techniques using silica gel chromatoplate 60 F_{254} and the eluent, ethyl acetate/hexane in a 1:1 ratio (revealed with UV light). To confirm the 4-methoxybiphenyl formation, transfer the contents of the bottom flask into a 250 mL separation funnel. Wash the bottom flask with 20 mL of diethyl ether, and transfer the solution to the separation funnel. Add aqueous NaOH (1 M, 5 mL) and extract the lower phase. Afterwards, wash with brine (2 x 5 mL) and dry the organic layer over $MgSO_4$. Filter and concentrate the solution in vacuum to obtain the 4-methoxybiphenyl product.

Week #3: Characterization of the 4-methoxybiphenyl product

Determine the product melting range (mp 81-83.5 °C) and mass chromatogram via GC-MS.

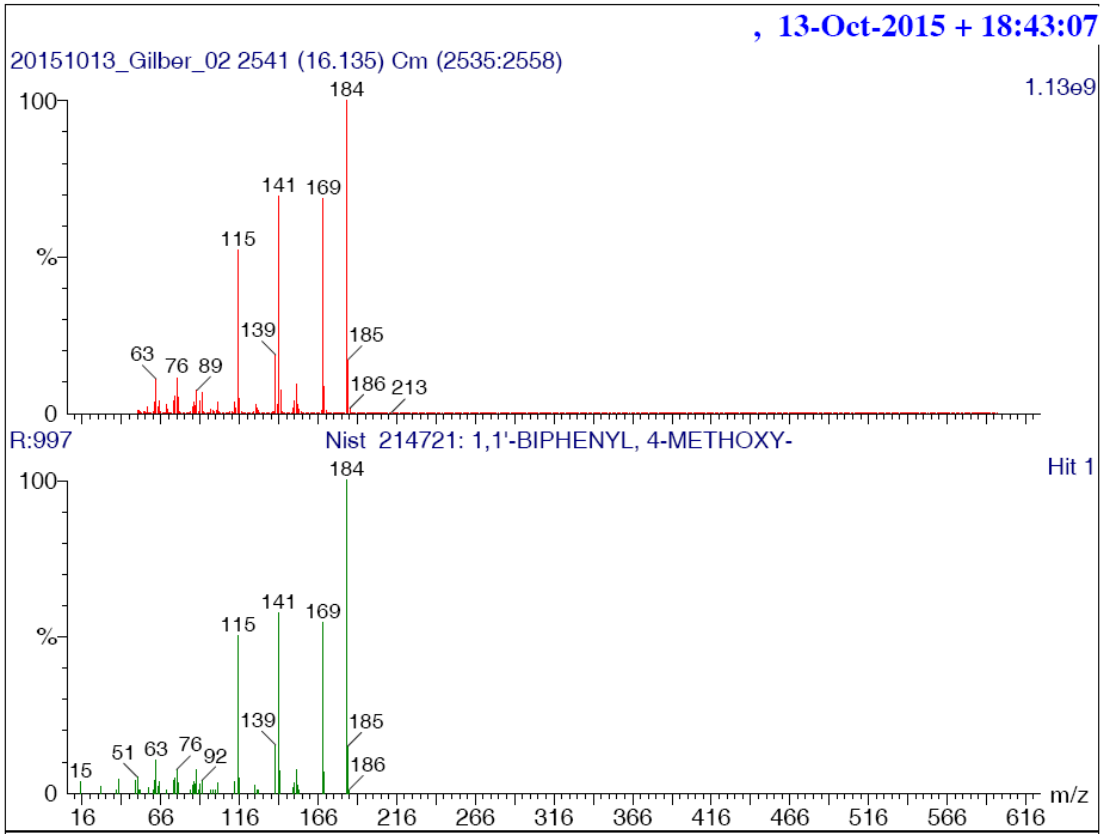
HAZARDS

DMF, ethyl acetate, hexane, and diethyl ether are flammable. NaOH is corrosive. 4-iodoanisole is harmful if inhaled. The 4-methoxybiphenyl, biphenyl (by-product), and potassium carbonate are irritants. A small amount of a by-product is generated during the proposed catalytic reaction (Suzuki-

Miyaura cross-coupling) that is of low toxicity to the students. All experiments are conducted with students wearing eye protection, lab coats, nitrile gloves, and fume hoods (for harmful reagents).

Instructor's Notes

1. GC-MS analysis was performed on a GC/MS Shimadzu QP-5050 (EI, 70 eV). As an example below is the result obtained by Group 4.



4-Methoxybiphenyl. White solid, mp 81–83.5 ºC. GC–MS (IE, 70 eV) m/z (%): 184 (100, M^+), 141 (69), 169 (68), 115 (52), 139 (18), 185 (17), 76 (11), 63 (10).

2. Phenylboronic acid (CAS number 98-80-6), 4-iodoanisole (CAS number 696-62-8), Pd/C 10 wt. % loading (CAS number 7440-05-3), and potassium carbonate (CAS number 584-08-7) were purchased from Sigma-Aldrich (Brazil). Ethyl acetate (CAS number 141-78-6), hexane (CAS number 110-54-3), diethyl ether (CAS number 60-29-7), sodium hydroxide (CAS number 1310-73-2), and magnesium sulfate (CAS number 7487-88-9) were purchased from VETEC (Brazil). DMF (CAS number 68-12-2) was purchased from Synth (Brazil). All chemicals were used without further purification.

Laboratory Report

To familiarize the students with the format of scientific papers, the reports were required to be presented using the *Organic Letters* template (available for download at the *Organic Letters* website). The criteria for evaluation of the report were: (i) presentation according to the template, (ii) detailed description of the experiment, (iii) interpretation of the results obtained and correlation with the current literature, and (iv) the use of technical vocabulary.

The mechanism of the Suzuki-Miyaura reaction and a comparison between the results obtained by the students compared with those reported by other research groups are the key elements of the practical lab report.