ORGANIC

UNDERGRADUATE EXPERIMENT

Monitoring a Suzuki Coupling with Benchtop NMR Spectroscopy

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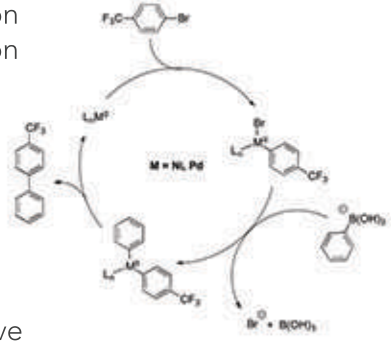
INTRODUCTION

Catalysts are crucial in synthetic chemistry. These substances either lower the activation energy associated with, or provide an alternate reaction pathway to effectively increase the rate of reaction.[1] Additionally, catalysts, by definition, are not consumed within a synthetic transformation, and can participate multiple times (from thousands to millions) throughout the reaction. This mechanistic pathway is often referred to as a catalytic cycle. A plethora of industrial processes such as polymerization,[2] olefin metathesis,[3] as well as hydrogenation[4] rely on such catalysts.

The Suzuki cross-coupling reaction, typically catalyzed by expensive palladium catalysts, is an industrially relevant reaction between organoboron compounds and organohalides that results in the formation of a new C–C bond.[5] More recently, four-coordinate nickel-based complexes have been shown to be effective catalysts for the Suzuki cross-coupling reaction.[6] There is significant interest in these nickel(II) catalysts given its availability and cost (table 1), and favourable reactivity, *i.e.*, stability to air and moisture in the solid form, and facile synthesis from $NiCl_2{\cdot}6H_2O$ and the appropriate phosphine.



Scheme 1. Catalytic cycle

Table 1. Representation of cost and abundance of palladium and nickel

Metal	Cost per 10 gram (USD)	Worldwide Annual Production (1 000 kg)
Pd	368.17	82
Ni	0.12	2 000 000

In this experiment, adapted from an ACS Journal of Chemical Education article published by Thananatthanachon and Lecklider,[7] two dichlorophosphinenickel(II) compounds were synthesized. They were subsequently used to catalyze a Suzuki cross-coupling reaction between phenylboronic acid and 1-bromo-4-(trifluoromethyl)benzene. The progress of the reaction was conveniently monitored by ^{19}F NMR spectroscopy on a NMReady-60 and used to assess the catalytic activity of the synthesized catalysts.

PROCEDURE

Synthesis of $NiCl_2(PR_3)_2$ Complexes

A reflux condenser was attached to a 2-neck 50-mL round bottom flask and purged with an inert gas for approximately 5 minutes. $NiCl_2{\cdot}6H_2O$ (0.240 g, 1.01 mmol) was added to the flask and dissolved in 4 mL of ethanol. Triphenylphosphine (0.556 g, 2.10 mmol) was then added and the reaction was heated to reflux for 1 hour under an insert atmosphere. After cooling to room temperature, the green solid was collected via filtration and washed with EtOH/ether to give $NiCl_2(PPh_2)_2$ (0.422 g, 64 %). $NiCl_2$(DPPE) was synthesized in a similar manner and isolated as an orange solid (0.333 g, 62 %).

Suzuki Cross-Coupling Reaction Catalyzed by $NiCl_2(PR_3)_2$ Complexes

A reflux condenser was attached to a 2-neck 50-mL round bottom flask and the glassware was purged with an inert gas for approximately 5 minutes. To the flask, 10 mmol of K_3PO_4 (2.120 g), 5 mmol of 1-bromo-4-(trifluoromethyl)benzene (**1**, 1.125 g), 7.5 mmol of phenylboronic acid (**2**, 0.915 g), and 10 mol % (with respect to **1**) of the nickel catalyst ($NiCl_2(PPh_2)_2$: 0.327 g; $NiCl_2$(DPPE): 0.264 g) was added along with 25 mL of *t*-amyl alcohol. The reaction mixture was then heated to reflux under an inert atmosphere. At specific time points (1 hr, 2 hr, 3 hr, and 12 hr), 0.7 mL aliquots of the reaction mixture were collected for analysis on the NMReady-60PRO instrument.

Analysis of the Aliquots with the NMReady-60

Approximately 0.7 mL of each aliquot was transferred to an NMR tube and the ^{19}F NMR spectrum (spectral width = 50 ppm, spectral center = -63 ppm, number of points = 4096, number of scans = 64) was acquired using proton lock so that sample preparation and the use of deuterated solvents was not required. The observed ^{19}F resonances were integrated to monitor the progress of each reaction along with calculating the percent conversion and the turnover number of the catalyst.

RESULTS

^{19}F NMR (56 MHz, *t*-amyl alcohol):

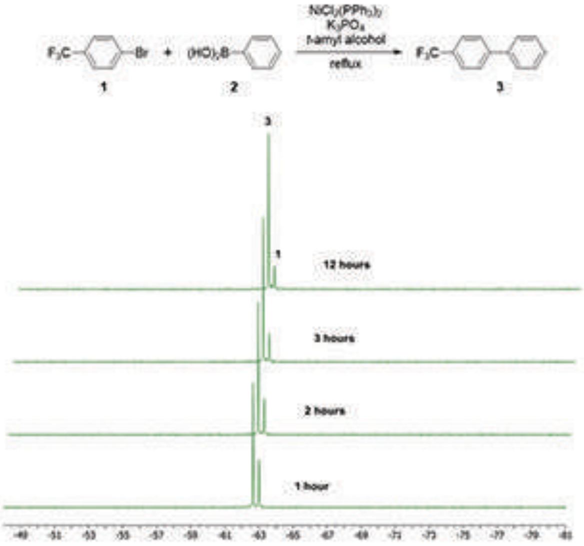


Figure 1. Stacked plot of ^{19}F NMR spectra to prepare 4-(trifluoromethyl)biphenyl catalyzed by $NiCl_2(PPh_3)_2$.

DISCUSSION

As seen in figure 1, the ^{19}F NMR spectra of the reaction aliquots displayed two singlets. The signal at -62.7 ppm was assigned to the product, 4-(trifluoromethyl)biphenyl (**3**), while the signal at -63.0 ppm was attributed to 1-bromo-4-(trifluoromethyl)benzene (**1** It is readily apparent that the signal for **1** decreases over time, as the reaction progresses with the concomitant increase in the peak for **3**. While the coupled product was formed selectively with both catalysts, $NiCl_2$(DPPE) was shown to be the more active catalyst. As seen in table 2, after 12 hours the reaction catalyzed by $NiCl_2(PPh_3)_2$ had a percent conversion of 82 %, while a 94 % conversion was found with $NiCl_2$(DPPE).

Table 2. Percent conversion over time of the Suzuki Cross-Coupling Reactions Catalyzed by $NiCl_2(PPh_3)_2$ & $NiCl_2$(DPPE).

Time (hr)	$NiCl_2(PPh_3)_2$ (%)	$NiCl_2$(DPPE) (%)
1	67	74
2	74	83
3	79	93
12	82	94

Another metric to gauge the catalytic activity of the two catalysts is the turnover number (abbreviated as TON). The TON is defined as the number of times a catalyst goes through the catalytic cycle before it becomes deactivated and is calculated by dividing the moles of substrate by the moles of catalyst multiplied by the % yield of the product. In this case the TON of $NiCl_2(PPh_3)_2$ is 8.2 while it was calculated to be 9.4 for $NiCl_2$(DPPE), consistent with the higher activity of $NiCl_2$(DPPE) compared to $NiCl_2(PPh_3)_2$

CONCLUSIONS

In this experiment two nickel complexes were prepared and subsequently used as catalysts in the Suzuki cross-coupling reaction. Due to the presence of the trifluoromethyl group in the reactant and product, the progress of the reaction was easily monitored by ^{19}F NMR spectroscopy with the NMReady-60PRO instrument. Furthermore, quantitative data, % conversion and TON, were extracted from the spectra collected which allowed for a direct comparison of the catalytic activity of the two nickel catalysts.

REFERENCES

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DATA ACCESSIBILITY

The data can be processed directly on the NMReady-60 and printed and/or exported directly to a USB or networked file where it can be worked up using third party NMR processing software.

For additional ideas of how to incorporate the NMReady-60™ benchtop NMR spectrometer into undergraduate laboratories please see:

1) Chemosensors and ^{19}F NMR Spectroscopy
2) Isomerization of Mo complexes via ^{31}P NMR Spectroscopy
3) Aldol Condensation

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