

EXPERIMENT 7

Iridium Catalyzed Functionalization of C-H Bonds

REFERENCES

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SAFETY RECOMMENDATIONS

[Ir(cod) OMe]₂: Causes skin irritation, Causes serious eye irritation, May cause respiratory irritation.

Bis(Pinacolato)diborane (B₂Pin₂): May be harmful if inhaled, May cause respiratory tract irritation. May cause skin and eye irritation.

bipyridine (bpy): Causes skin irritation, Causes serious eye irritation, May cause respiratory irritation.

1-Chloro-3-fluorobenzene: Causes skin irritation, Causes eye irritation, Specific target organ toxicity.

2,6 dichloropyridine: Toxic if swallowed

INTRODUCTION

For years chemists have been fascinated by reactions that transform C-H bonds, which despite their ubiquity are relatively inert. In 1825 Faraday reported that benzene and nitric acid react,¹ but Mitscherlich was the first to determine that nitrobenzene was the product in 1834.² In the intervening years, electrophilic aromatic substitution (EAS) has evolved as the workhorse for aromatic functionalization. For example, approximately 2.8 million tons of nitrobenzene was produced by benzene nitration in 2000.³

The regioselectivities for EAS are governed by the number, type, and relative placement of substituents in the aromatic system. As systematized by Holleman,⁴ arene substituents fall into two classes: (i) *ortho,para*-directors that typically activate the aromatic system to electrophilic substitution and (ii) *meta*-directors that operate by virtue

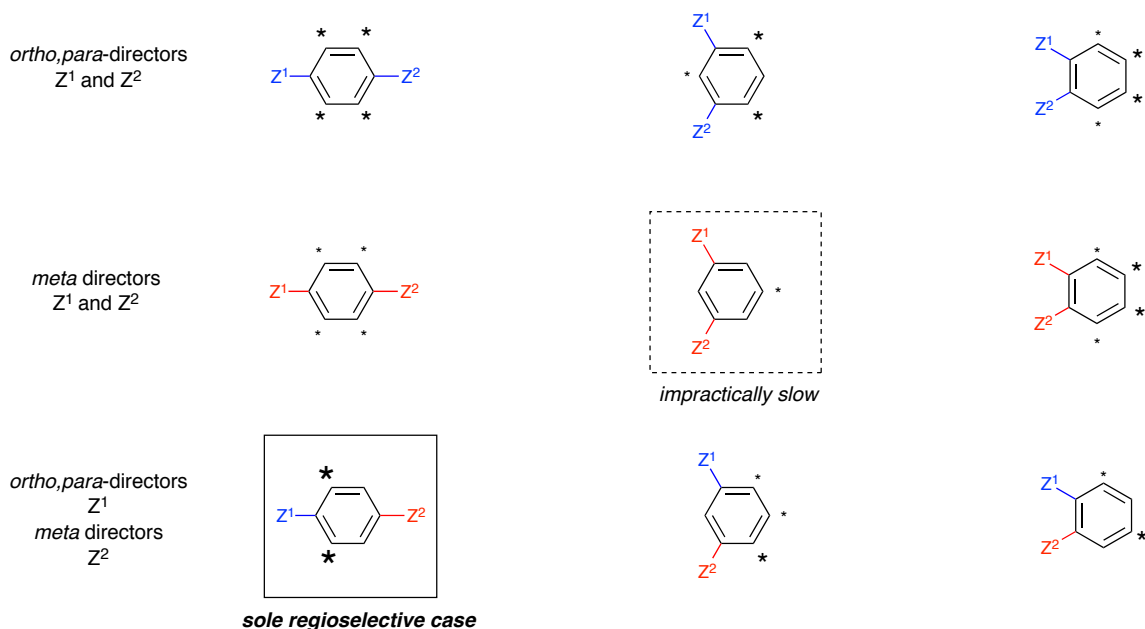


Figure 1. Predicted regioselectivities for electrophilic aromatic substitutions of disubstituted benzenes.

of *ortho,para* deactivation. When an aromatic system possesses more than one substituent, directing effects can work in concert or opposition to afford single products or isomeric mixtures, respectively. In this context, the limitations of EAS can be appreciated if one considers the regiochemical outcomes that can be expected for 9 possible permutations of a disubstituted benzene possessing *ortho,para* and/or *meta*-directors (Figure 1). **Only 1 of 9 combinations offers well-defined regioselectivity via EAS.**

In 1995, an issue of the Accounts of Chemical Research was dedicated to Linus Pauling, a visionary who influenced modern chemistry and a Nobel Laureate in Chemistry and Peace. The issue was entitled “Holy Grails in Chemistry” and leaders in their fields contributed overviews on various topics. One of these involved metal-mediated transformations of C–H bonds.⁵

In 1965, Chatt reported reactions where a highly reactive transition metal complex cleaved C–H bonds to form stable products with metal-carbon and metal-hydrogen bonds.⁶ Despite the fact that transition metal complexes have long been utilized in catalysis, only a handful of examples of catalytic transformations had been reported between Chatt’s discovery and the end of the 20th century.

Over the past decade, this has changed dramatically. In this module, you will prepare Ir catalysts and use them in catalytic reactions where C–H bonds are converted to C–B bonds.⁷ The originally proposed mechanism for the catalytic cycle is shown in Scheme 1.⁸ This chemistry is noteworthy in that it provides the simplest possible synthesis of organoboron compounds, which are used extensively in the cross-coupling reactions that were recognized by the 2010 Nobel Prize in chemistry.⁹

PROCEDURE

Borylation of 1-chloro-3-fluorobenzene

In your Schlenk flask, add [Ir(cod)(OMe)]₂ (10 mg, 1.5 mol %) and 3 mL of dry THF. While your flask is under Nitrogen add 127 mg (0.5 mmol) of B₂Pin₂ and stir the mixture for 15 minutes. Then add 4.8 mg (3 mol %) of bpy and stir it for about a minute. As soon as you

add the bpy ligand the mixture will turn brown. Lastly, add 135 mg (1.03 mmol) of 1-Chloro-3-fluorobenzene, heat the reaction for 1 h at 80 °C. While heating, the reaction mixture will become dark red-brown. Use rotary evaporation to remove solvent. Calculate the yield of the reaction, and take a crude ^1H NMR.

Monoborylation of 2,6-dichloropyridine

In a three-neck round bottom flask equipped with nitrogen adaptor, add $[\text{Ir}(\text{cod})(\text{OMe})_2]$ (10 mg, 1.5 mol %) and 3 mL of dry THF. While your flask is under Nitrogen add 254 mg (1 mmol) of B_2Pin_2 and stir the mixture for 15 minutes. Then add 4.7 mg (3 mol %) of bpy and stir it for about a minute. As soon as you add the bpy ligand the mixture will turn brown. Lastly, add 147 mg (1 mmol) of 2,6-dichloropyridine, heat the reaction for 1h at 60 °C. While heating, the reaction mixture will become dark red-brown. Use rotary evaporation to remove solvent. Calculate the yield of the reaction, and take a crude ^1H NMR.

In your report, address the following points:

1. Write balanced reactions for all of the reactions you perform.
2. Assign your NMR spectra and discuss any trends in chemical shifts.
3. In your report, include the catalytic cycle and include: all the products, oxidation states and reaction types (oxidative addition, reductive elimination etc).
4. What methods need to be made to the experimental methods to perform a diborylation of the substrate?