

ARYLATION USING DIARYLIODONIUM SALTS

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December 8th, 2014

INTRODUCTION

The site-selective introduction of aryl groups to a complex organic molecule is a useful technique for the synthesis of both natural and unnatural products. When imagining synthetic disconnects involving aryl groups, the delivery of an aryl electrophile is typically more challenging than the delivery of an aryl nucleophile, owing to the inherent limitations of S_NAr reactions. Diaryliodonium salts offer an alternative approach to facile delivery of an aryl electrophile (Figure

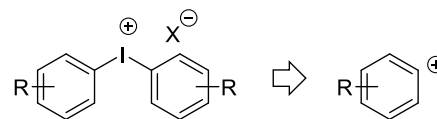


Figure 1. A diaryliodonium salt functions as an aryl electrophile equivalent.

1). These salts are hypervalent iodine(III) reagents of the form $Ar_2I^+X^-$ which are highly electrophilic species.^{1,2} Such reagents can be used to arylate a wide variety of nucleophiles under mild conditions.

SYNTHESIS

Numerous methods exist for the preparation of diaryliodonium salts.^{1,3} Commonly, commercially available iodine(III) reagents are combined with arenes or arylsilanes under acidic conditions to afford the desired species.^{1,3} Alternatively, preparation of a vinyl iodine(III) species from ICl_3 and acetylene and subsequent reaction with an aryllithium generates diaryliodonium salts under basic conditions.^{1,3} More recently, highly efficient one-pot procedures have been developed for the synthesis of symmetrical and unsymmetrical iodonium salts from aryl iodides and arylboronic acids using *m*-CPBA as an oxidant.⁴

ARYLATION OF HETEROATOM AND CARBON NUCLEOPHILES

In one early application, Beringer and coworkers demonstrated a synthesis of anisole by deprotonation of methanol and subsequent reaction with diaryliodonium bromide.⁵ In addition to alcohols, diaryliodonium salts react with carboxylic acids to form aryl esters. It was later shown that nitrogen and even carbon nucleophiles are arylated with these reagents.^{1,5,6} Reaction of carbonyl compounds with a suitable base and a diaryliodonium salt leads to α -arylation. This process has been made enantioselective by using a copper catalyst with a chiral ligand.^{7,8}

ARYLATION OF ARENES AND OLEFINS

Diaryliodonium salts can be used in place of aryl iodides in traditional cross-coupling reactions. The oxidative addition step is more facile in the former case, which can allow for milder reaction

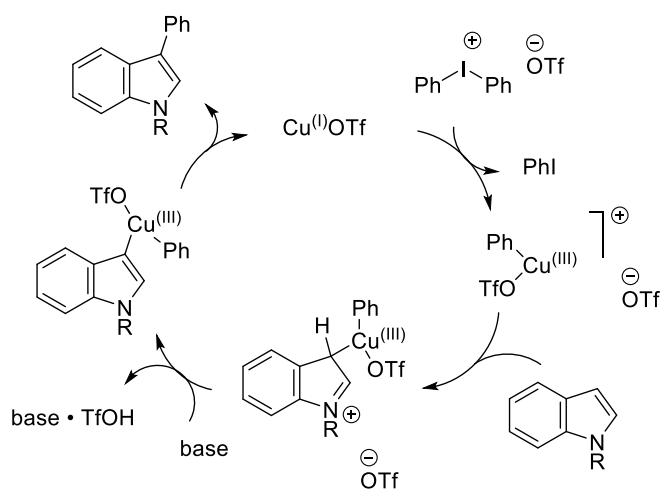


Figure 2. Proposed mechanism of Gaunt's indole arylation. attack by an arene or olefin in a Friedel-Crafts type process, generating a transient cationic intermediate. This intermediate is re-aromatized by base, and subsequent reductive elimination forms a new carbon-carbon bond and regenerates the copper(I) catalyst. This method has proven useful in a highly site-selective arylation of indoles¹⁰ (Figure 2) and in promoting tandem cascade reactions in the arylation of terminal olefins.¹¹ A similar method developed by Sanford and coworkers employs a palladium catalyst and often leads to different site-selectivities than those observed with copper.¹²

SUMMARY

Diaryliodonium salts are used for the mild arylation of a wide variety of functional groups, including heteroatom nucleophiles, carbon nucleophiles, olefins, and arenes. The incorporation of diaryliodonium salts into copper or palladium-catalyzed electrophilic metallation pathways allows for remarkably site-selective arylations under exceptionally mild conditions.

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