

Palladium-Catalyzed Intramolecular C–C Coupling and Selective Hydrodehalogenation of Halogenated Biaryl Acetamides

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ABSTRACT A practical and rapid method is reported for the Pd-catalyzed intramolecular aryl-aryl coupling reaction under mild conditions through hydrodehalogenation, with acetic acid as a hydrogen source. Regioselective products were obtained when halogenated biaryl acetamides bear meta-substituents in the aryl ring. Isotopic labeling reactions are used to establish a direct hydrodehalogenation route by utilizing deuterated acetic acid. The findings provide a new mechanism for intramolecular coupling and hydrodehalogenation of aryl halides.

KEYWORDS Biaryl acetamides, Diphenylamines, Intramolecular aryl-aryl coupling, Hydrodehalogenation, Regioselective, Carbazoles

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INTRODUCTION

Palladium-catalyzed reactions have been widely used in organic synthesis.^[1] Among the studies conducted thus far, carbon–carbon (C–C) or carbon–heteroatom (C–X) bond formations, which are among the most powerful transformations known, have been extensively investigated over the past 30 years.^[2-8] Construction of value-added molecules through C–C or C–X bond formation is extensively adopted in the chemical and pharmaceutical industries, because it can significantly simplify and shorten synthetic routes, and utilize inexpensive, widely available, and recyclable materials.^[9] Intramolecular C–H functionalization, in which heteroatoms act as directing groups and intramolecular nucleophiles, is an ideal process for the construction of heterocyclic architectures.^[10-20] Such heterocyclic molecules, for example, with a skeleton of carbazole, have found many applications such as photoelectrical materials, natural products, and therapeutic agents.^[21-28] As a result, searching for more effective methods for the synthesis of new functional carbazoles has

attracted much attention recently from synthetic chemists worldwide.^[29-37]

Arenes generated from aryl halides are crucial for chemical transformation in organic synthesis.^[38-40] The reduction of a carbon–halogen bond represents a fundamental reaction in organic synthesis that still draws considerable attention.^[41] It has also taken on added significance in light of environmental issues, in particular concerning polychlorinated biphenyls (PCBs), which are known to be health hazards.^[42] New technologies that not only result in aromatic dehalogenation but also provide both economic and environmentally attractive processes remain in demand.^[43] Many new dehalogenation methods using palladium, rhodium, iron, and nickel catalysts have been reported,^[44-50] where palladium is still the most commonly used transition metal for this transformation.^[41-55]

In our previous work on intramolecular oxidative aryl-aryl coupling, a palladium catalyst was employed successfully in the coupling reaction of substituted diphenylamines (**Scheme 1**).^[56] Further to that work, in

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2-Methyl-9H-carbazole (4i, 4j)

Isolated as white solid, yield 88% and 85%. ¹H-NMR (500 MHz, DMSO-d₆) δ: 11.10(s, 1H), 8.04 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.44(d, J = 8.0 Hz, 1H), 7.34-7.30 (m, 1H), 7.26 (s, 1H), 7.13-7.09 (m, 1H), 6.98 (d, J = 8.0 Hz, 1H), 2.47 (s, 1H). ¹³C-NMR (500 MHz, DMSO-d₆) δ: 140.7, 140.2, 135.4, 125.4, 123.0, 120.6, 120.5, 120.3, 120.2, 118.8, 111.4, 111.3, 22.2. HRMS (EI, m/z) M⁺: Calculated for C₁₃H₁₁N: 181.0891; found: 181.0893.

CONCLUSION

A highly practical method has been demonstrated for the palladium-catalyzed intramolecular C–C coupling and hydrodehalogenation of aryl halides. Acetic acid served as the proton source through palladium-centered reductive elimination. The mild reaction conditions tolerated various functional groups and electron-deficient heteroarenes, allowing highly chemoselective reactions in the vicinity of halide, ester, and nitrile substituents. This practical and rapid methodology suggests further applications in the selective dehalogenation of complex molecules and scavenging of environmentally noxious halo aromatics.

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