

A Highly Reactive, General and Long-Lived Catalyst for Palladium-Catalyzed Amination of Heteroaryl and Aryl Halides

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A systematic study of the scope, applications, and relationship between ligand structure and catalyst activity for a highly efficient and selective class of catalysts for the coupling of primary nitrogen nucleophiles with heteroaryl and aryl chlorides, bromides and iodides will be described. These catalysts contain sterically hindered chelating alkylphosphines linked by the ferrocenylethyl backbone of the Josiphos ligand structure. In the presence of this catalyst, aryl and heteroaryl halides react with many primary nitrogen nucleophiles in high yields with part-per-million quantities of palladium precursor and ligand. Many reactions of primary amines with both heteroaryl and aryl halides occur to completion with 0.0005-0.01 mol % catalysts. This combination of palladium and ligand also catalyzes the reactions of hydrazones and benzophenone imine with low loadings of palladium and ligand.

Furthermore, this catalyst has enabled selective synthesis of primary anilines from aryl halides and ammonia directly for the first time. The aryl palladium amido intermediate in this process was synthesized, and this complex reductively eliminates primary aryl amine.

Systematic structure-reactivity studies have indicated that the high reactivity of the catalyst originates from the ligand's rigid conformation and tight binding to palladium. This tight chelation prevents phosphine substitution by nitrogen-bearing substrates.

Thus, these complexes constitute a fourth-generation catalyst for the amination of aryl halides, whose activity complements catalysts based on monodentate phosphines and carbenes.

