Synthesis of Biaryl, Arylamine and Aryl Ketone Compounds Using a Commercially Available Air- and Moisture-Stable Palladium Catalyst

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Received 1 August 2003

Abstract: A commercially available palladium complex bearing a N-heterocyclic carbene (NHC) was used in gram-scale synthesis of three compounds, a biaryl, an arylamine and an aryl ketone. The syntheses were performed in catalytic fashion using a Suzuki–Miyaura, a Buchwald–Hartwig and a ketone arylation reaction protocol. These three reactions were carried out using the same palladium pre-catalyst.

Key words: N-heterocyclic carbene, palladium, cross-coupling, ketone arylation, Suzuki–Miyaura coupling, aryl-amination

Palladium-mediated cross-couplings have become a very important method for the formation of carbon–carbon and carbon–heteroatom bonds. Traditionally, these couplings have used phosphorus-based ligands to enhance performance, but recently the use of N-heterocyclic carbene (NHC) has shown to be competitive with previous methods. The use of NHC as transition-metal ancillary ligand has been shown as beneficial in a number of catalytic transformations ranging from olefin metathesis to alkene hydrogenation. The NHC themselves have even proven as efficient organic catalysts in transesterification reactions. In this contribution, we wish to report the use of a single well-defined palladium catalyst bearing a NHC, (IPr)Pd(allyl)Cl (1), capable of mediating the formation of gram-scale amounts of products in three popular palladium-mediated catalytic reactions: ketone arylation, aryl amination and Suzuki–Miyaura coupling. The pre-catalyst 1 proves to be a very versatile, air- and moisture stable compound.

The use of NHC-modified catalysts has grown substantially over recent years. This trend is principally due to the isolation of a stable NHC by Arduengo and by observations detailing beneficial properties imparted by the NHC to catalytic systems. It is well known that tertiary phosphine ligands are susceptible to thermal P–C bond degradation and air oxidation resulting in the formation of phosphine-oxides. The NHCs are more stable to oxygen than tertiary phosphines, allowing easier handling and in some cases the ability to do catalysis in air. Complexes bearing NHCs display greater thermal stability than those bearing phosphine ligands, making it possible to heat the NHC complexes to higher temperatures rendering feasible reactions that require higher temperatures.

We have recently reported the synthesis of a well-defined palladium system, (NHC)Pd(allyl)Cl (1), that has shown high activity in a number of different catalytic systems involving simple aryl-substituted as well as heterocyclic-substituted coupling partners. The initial research conducted on this system mainly involved screening of activity across different catalytic transformations. If these methods are to be used by synthetic chemists or in an industrial setting, they must be carried out on a larger scale. We were interested in examining this issue and discuss here three such gram-scale transformations.
In palladium-mediated C–C and C–N bond formation reactions, the present system displays high activity even with traditionally difficult substrates, namely aryl chlorides. Through an increased electron donation originating from the NHC, the palladium center is easily capable of activating the ‘inert’ C–Cl bond. Reactions involving activation of C–Br and C–I bonds can also be mediated by I.

Gram-scale syntheses were carried out using three different systems. The first to be tested was the synthesis of a biaryl molecule through an ent systems. The first to be tested was the synthesis of a biaryl molecule through an ent systems. The first to be tested was the synthesis of a biaryl molecule through an ent systems. The first to be tested was the synthesis of a biaryl molecule through an ent systems. The first to be tested was the synthesis of a biaryl molecule through an...


(7) Complex 1 is now commercially available from Strem Chemicals Inc.


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