Buchwald et al. report conditions for the Suzuki couplings of di-ortho-substituted aryl halides and boronic acids to generate unsymmetrical tetra-ortho-substituted biaryls. One set of conditions employs a novel ligand (3a or 3b in Scheme 1) and efficiently catalyzes the cross-coupling of substrates with neutral or electron-donating ortho substituents. Another set of conditions uses DPEPhos (Scheme 1) as the ligand and is more effective when the aryl halide substrate contains an ortho electron-withdrawing substituent. The chemistry described provides a remarkably general solution to a previously unsolved problem in cross-couplings, although relatively harsh conditions and high catalyst loadings (4 mol% Pd) are required for reactivity.

Ligand 3 is derived from previously reported biaryl-phosphine ligands which contained substituted phenyl groups or naphthyl groups instead of phenanthracene in the biaryl moiety. In general, 3a outperforms the other biaryl-phosphine ligands in the synthesis of tetra-ortho-substituted biaryls. The authors obtain a crystal structure of 3a/Pd(dba) showing coordination of the ligand through both P and the C9-C10 π-bond of phenanthracene and suggest that this novel coordination is critical to the success of catalyst systems employing 3a. Unfortunately, they do not attempt to characterize the coordination of the ligand under the reaction conditions, so the bidentate coordination seen in the crystal structure cannot be definitely invoked in the catalytic cycle. Nevertheless, this idea can be examined in light of the mechanism for Suzuki couplings.

The basic steps in the catalytic cycle for Suzuki couplings are oxidative addition, transmetalation, and reductive elimination. With very hindered substrates, transmetalation and reductive elimination are probably the most difficult steps. Transmetalation is difficult because both the ArPdBr intermediate and the transmetalating reagent are sterically congested and reductive elimination is difficult because it requires bringing the bulky aryl groups close together so that there is sufficient orbital overlap for bond formation. Competing with the desired pathway is protonolysis of PdAr intermediates. One possibility for the reason ligand 3a is particularly successful with these difficult couplings is presented in Scheme 1. In this model, the Pd-π-bond interaction is weak and reversible, creating an equilibrium between monodentate and bidentate ligand-Pd species through rotation about the P-biaryl bond. This enables the catalyst to exploit the advantages of both modes of coordination throughout the catalytic cycle. Thus, bidentate coordination stabilizes the formation of PdL and thereby promotes oxidative addition. Monodentate ligand coordination promotes transmetalation by making the metal center less sterically encumbered. Finally, bidentate ligand coordination promotes reductive elimination by pushing the two aryl groups closer together.

While it is interesting to speculate on the features of 3a which make it particularly useful for this chemistry, it is clear from the paper that 3a is not the only ligand suited for the formation of tetra-ortho-substituted biaryls. The precursors to 3a with substituted phenyls instead of phenanthracene work well for some substrates. Furthermore, DPEPhos, a known bidentate ligand, is more effective for the transformation when the aryl bromide contains an electron-withdrawing substituent at one of the ortho positions. This indicates that bidentate ligands are viable in the most sterically demanding Suzuki couplings. The authors state that 3a outperforms DPEPhos in direct comparisons (presumably with substrates containing electron-neutral or electron-donating substituents) but they do not provide the data. A thorough comparison of 3a with several bidentate ligands and an attempt to characterize the binding of 3a to Pd under the reaction conditions would be valuable for determining whether there is indeed something special about this ligand and for improving the chemistry.

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