

8.8.2 C–H Functionalization

The development of new methods for transition metal-mediated C–H bond functionalization has received significant interest in recent years in the context of heterocyclic synthesis.⁶⁴ The C–H functionalization approach toward C–N bond formation offers a potential advantage over the more traditional metal-mediated approaches that require more highly functionalized (e.g., aryl halide) starting materials. The synthesis of benzimidazoles *via* C–H functionalization approaches has received only limited attention to date. Nevertheless, the initial reports show that this is a promising new area for continued investigation, and further applications toward drug synthesis will likely emerge in due course. Brasche and Buchwald have described a copper-mediated C–H insertion method for intramolecular *N*-arylation of phenyl amidines.⁶⁵ The optimized conditions involve treatment of an *N*-phenylamidine with $\text{Cu}(\text{OAc})_2$ (15 mol%) and acetic acid in DMSO at 100 °C under an oxygen atmosphere. (The authors report that catalytic activity was also observed under an air atmosphere, but product formation was considerably slower.) A variety of functionalized 2-aryl benzimidazoles was accessed using this approach.

