Using a somewhat different C–H functionalization approach to benzimidazoles, Punniyamurthy and co-workers have explored the conversion of *N*-benzyl bisarylhydrazones to 2-aryl-*N*-benzyl-benzimidazoles.[66] This conversion is optimally achieved using stoichiometric $Cu(OTf)_2$ in toluene at 110 °C. (This transformation was also reported using catalytic $Cu(OTf)_2$ (20 mol%) under an oxygen atmosphere, albeit in lower yield). This reaction likely proceeds via a copper-amidine intermediate analogous to the intermediate accessed by Brasche and Buchwald in their direct intramolecular arylation of *N*-aryl amidines.

8.9 Alternative Cyclization Approach Toward Benzimidazoles: Process Route Toward BYK405879

In the vast majority of cases, benzimidazole syntheses begin with a functionalized benzene intermediate, which may undergo additional functionalization prior to cyclization to the desired benzimidazole target. Webel, Palmer, and co-workers at Nycomed have recently reported a novel process route toward BYK405879, a drug candidate for treatment of "acid-related diseases."[67] Their unconventional approach of building the benzimidazole from an appropriately functionalized imidazole was designed to provide scale-up advantages over the previous, more conventional medicinal chemistry route. In this new process route, (1,2-dimethyl-1*H*-imidazol-5-yl)methanol undergoes a hypochlorite-TEMPO oxidation to the corresponding aldehyde, which is telescoped without isolation to a subsequent Stobbe condensation with diethyl succinate. This product is again telescoped without isolation to the cyclization reaction, in which acetic anhydride is employed to promote the dehydrative aromatization to the desired benzimidazole. This benzimidazole can be converted via a 4-step reaction sequence to BYK308944, a key intermediate in the synthesis of BYK405879.