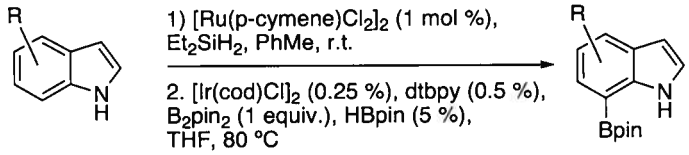
Iridium-Catalyzed, Silyl-Directed C-H Borylation of Nitrogen-Containing Heterocycles

Daniel W. Robbins and John F. Hartwig

The indole framework is a common structural feature of many biologically active molecules, including hormones, natural products and pharmaceuticals. Although there are many methods and strategies for the synthesis of substituted indoles, strategies for the selective functionalization of the indole skeleton are less common. Among these strategies, few selectively functionalize the 7-position of the indole scaffold. We report a one-pot, Ir-catalyzed, silyl-directed C-H borylation of indoles at the 7-position that proceeds with good yields. The scope of this method has been expanded to encompass a variety of indole substrates. We also demonstrate that the 7-boryl indole products can be converted to 7-aryl and 7-halo indoles. The Ir-catalyzed, silyl-directed C-H borylation has been applied to several other nitrogen heterocycles, including phenoxazine, phenothiazine and tetrahydroquinoline. The utility of this methodology is highlighted by the one-pot synthesis of members of the pyrrolophenanthridone class of alkaloid natural products.



Chemical and Biological Studies into the Anti-Cancer Properties of Cribrostatin 6

Mirth T. Hoyt and Paul J. Hergenrother

Cribrostatin 6 is an isoquinoline quinone marine natural product isolated from a *Cribrochalina* sponge by Pettit *et al.* in 2003. Although many cancer therapies contain quinones, none of them share the fused heterocycle structure of cribrostatin 6; thus, we began to examine cribrostatin 6 as an anti-cancer agent with novel chemical structure and possible novel cytotoxic mechanism. Here we show that cribrostatin 6 induces apoptotic cell death in cancer cells in a cell cycle arrest independent manner while producing reactive oxygen species (ROS). Also, quiescent cells and vincristine resistant leukemia cells are effectively killed by cribrostatin 6. These interesting phenotypes have provoked further experiments investigating a ROS induced cell death mechanism using a variety of biochemical and chemical biology techniques, and pave the way for evaluation of cribrostatin 6 in pre-clinical models of cancer.