Design and Synthesis of Teraryl-based α-Helix Mimetics

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Protein-protein interactions (PPIs) play a crucial role in the function and regulation of biological systems. The number of binary PPIs in the human body is estimated to be more than 300 000 and many of them are associated with diseases. Modulation of PPIs represents a new promising strategy for drug discovery and the first PPI inhibitors have already reached clinical trials.[1,2] An α-helix is the most abundant secondary structural motif within PPIs and therefore represent an ideal starting point for the design of mimetics.[3,4] Our focus is the design and synthesis of a library of α-helix mimetics based on a teraryl scaffold, which act as small molecule inhibitors of PPIs and are able to mimic the side chains of an α-helix in positions *i*, *i*+3, *i*+7 and eventually in additional positions. Based on our previous work the teraryl scaffolds are assembled in a modular and flexible synthesis of aryl building blocks via Suzuki-Miyaura cross-coupling reactions (Figure 1).[5,6]

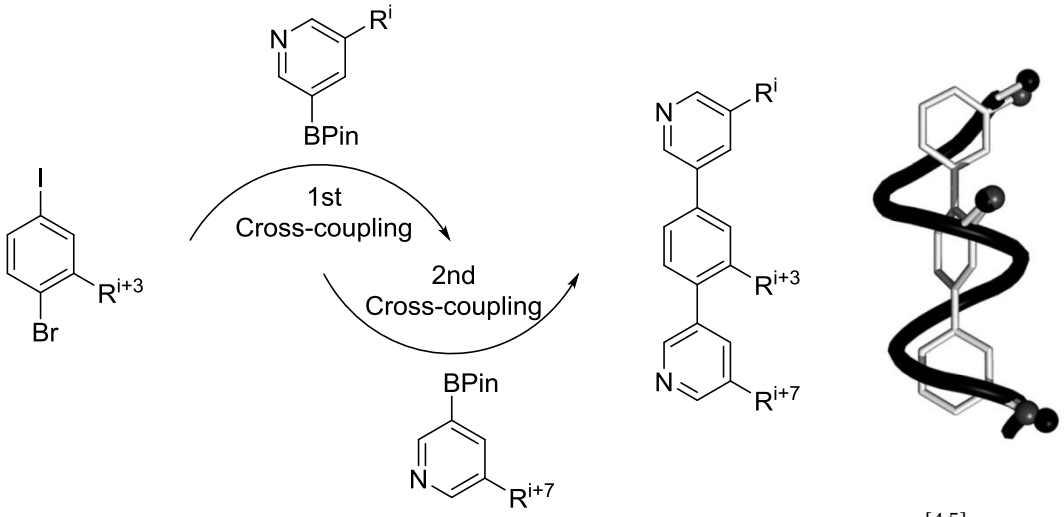

Figure 1. Synthesis of α-helix mimetics via Suzuki-Miyaura coupling.[4,5]

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