Manganese-catalyzed Benzylic C(sp^3)—H Amination for Late-stage Functionalization

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Reactions that directly install nitrogen into C—H bonds of complex molecules are significant because of their potential to immediately change the chemical and biological properties of a given molecule. While selective intramolecular C—H amination reactions are known, intermolecular C—H amination reactions with high reactivity and selectivity are scarce. Achieving high levels of reactivity while maintaining excellent site-selectivity and functional group tolerance remains a frontier challenge for intermolecular C—H amination. We report a novel manganese perchlorophthalocyanine catalyst [Mn(ClPc)] for a highly site-selective intermolecular benzylic C—H amination of bioactive molecules and natural products. In the presence of Brønsted or Lewis acid, the [Mn(ClPc)]-catalyzed C—H amination demonstrates unprecedented tolerance for 3° amine, pyridine, and benzimidazole functionalities. Contrary to analogous C—H amination systems, mechanistic studies suggest that C—H cleavage is the rate-determining step of the reaction.

The Design and Synthesis of an ARH3 Reporter Substrate and its Applications to a High-throughput Screen

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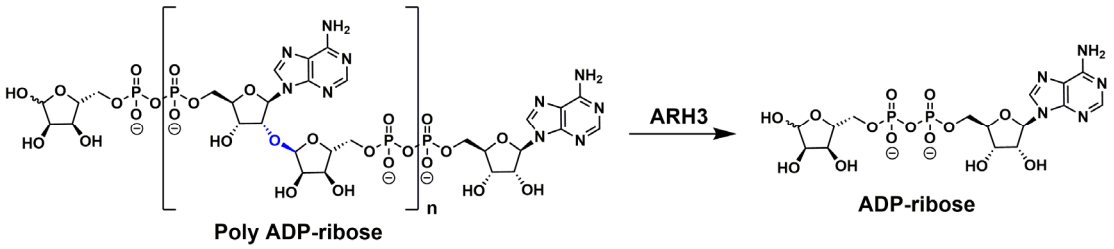
Poly ADP-ribosylation is a post-translational modification of proteins involved in a myriad of cellular functions, chief among them DNA damage repair and cell death. Poly ADP-ribosylation is catalyzed by poly (ADP-ribose) polymerases (PARPs) and reversed by PAR-degrading enzymes, poly (ADP-ribose) glycohydrolase (PARG) and a more recently described adenosine ribosyl hydrolase 3 (ARH3). Herein we describe the design and synthesis of a novel reporter substrate for the glycohydrolytic activity, and its applications to a high throughput screen to identify ARH3 inhibitors.



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