Laccase in Organic Synthesis and its Applications (2008)

A Dissertation by Suteera Witayakran

Abstract: Laccase (benzenediol:oxygen oxidoreductase, EC 1.10.3.2), a multi-copper-containing oxidoreductase enzyme, is able to catalyze the oxidation of various low-molecular weight compounds, specifically, phenols and anilines, while concomitantly reducing molecular oxygen to water. Moreover, due to their high stability, selectivity for phenolic substructures, and mild reaction conditions, laccases are attractive for fine chemical synthesis. In this study, new green domino syntheses were developed by conducting reactions in an aqueous medium, an environmentally-friendly solvent, and using laccase as a biocatalyst.

The first study presents a work on the synthesis of naphthoquinones in the aqueous medium. Herein, laccase was used to oxidize o- and p-benzenediols to generate o- and p-benzoquinones in situ. These quinones then underwent Diels-Alder and oxidation reactions to generate napthoquinone products. This reaction system can yield naphthoquinones in up to 80% yield depending on the structure of the starting hydroquinone and diene. The next part of this thesis reports the cascade synthesis of benzofuran derivatives from the reaction of catechols and 1,3-dicarbonyl compounds via oxidation-Michael addition in the presence of laccase and $Sc(OTf)_3$/SDS in an aqueous medium. Depending on the substrates, one-pot yields of benzofurans averaged 50-79%. In the absence of $Sc(OTf)_3$, these yields decreased to 45-65%. Hence, the use of Lewis acid was critical for efficient synthesis of the desired compounds. From an environmental concern, this system still produced a hazardous waste from the transition metal catalyst. Therefore, the development of alternative methodologies to replace the lanthanide metal catalyst in this synthesis is a high priority to enhance the overall green chemistry aspect. As a consequence, lipase was used as a catalyst to replace Sc(OTf)3 for the synthesis of benzofuran derivatives. The laccase/lipase co-catalytic system provides the benzofuran products in a good yield. In addition, this catalytic system was also able to catalyze the reaction of anilines and catechol.

Besides its application in organic synthesis, laccase also has an application in fiber modification. Therefore, in the last part of this thesis, laccase was applied to the modification of high-lignin softwood kraft pulp. This modification demonstrates the potential of laccase-facilitated grafting of amino acids to high lignin content pulps to improve their physical properties in paper products which resulted from the increase of carboxylic acid group of the fibers. A unique two-stage laccase grafting protocol was developed. Fibers were first treated with laccase, followed by grafting reactions with amino acids. The bulk acid group content was measured, and a variety of amino acids, including glycine, phenylalanine, serine, arginine, histidine, alanine, and aspartic acid, were examined. The effects of laccase dosage and amino acids on fiber modification were studied. In this study, histidine provided the best yield of acid groups on pulp fiber and was used in the preparation of handsheets for physical strength testing. Laccase-histidine-treated pulp showed an increase in the strength properties of the resulting paper.