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Oxidative Lactamization of Amino Alcohols: An Overview

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ABSTRACT

Lactams are essential functional groups in a number of pharmacologically and biologically active compounds. They are widely found in many natural products, marketed drugs, as well as in the base of polymeric structures (e.g., polyamides/Nylons). In this context, it is quite important to develop novel and efficient methods for the synthesis of these compounds. Recently, intramolecular dehydrogenative coupling reactions of amino alcohols, which generate only hydrogen as a side product, have emerged as one of the most versatile and powerful synthetic strategies to construct lactam rings. In the present review we will discuss recent advances on this chemistry with the emphasis on the mechanistic aspects of the reactions.

1. Introduction

Lactams are important heterocyclic motifs found in a significant number of natural and non-natural biologically active molecules (Figure 1) [1, 2] and have therefore been widely used as privileged structures and substructures in the drug design processes. They are also monomers of polyamides (Nylons), which are frequently used polymer materials in our everyday life and industry [3]. Although numerous synthetic approaches have been described for the construction of these heterocycles [4], they are often suffering from poor selectivity, intolerance to various functional groups, undesired by-products, and/or low atom economy. Therefore, development of new, efficient, and convenient approaches for the synthesis of titled compounds from simple and easily available starting materials is of considerable attention.

Cross-dehydrogenative coupling, which generally refers to the formation of C(X)–C(X) (X= heteroatom) directly from two C(X)–H bonds with liberation of H_2, has emerged as a very powerful and valuable tool for increasing the structural complexity in organic molecules [5-7].

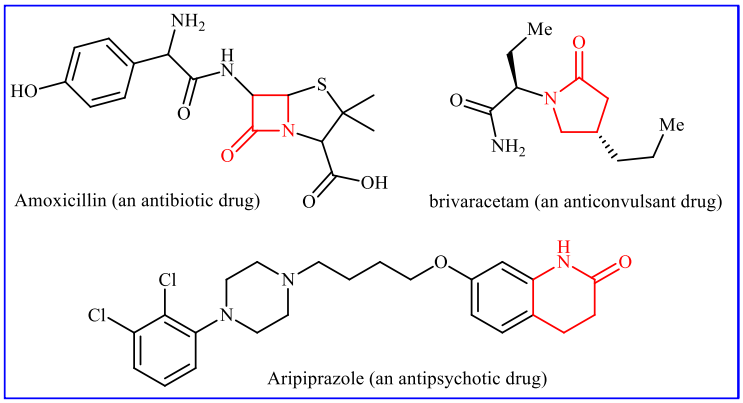

Figure 1. Chemical structure of some of the marketed drugs containing lactam rings

Along this line, dehydrogenative lactam synthesis from amino alcohols has received much attention, because readily available starting materials are used, and H_2, a clean source of energy, is generated as the sole by-product. To the best of our knowledge, a comprehensive review has not appeared on this novel and atom-economical synthetic route of lactams in literature so far. In continuation of our recent works on the synthesis of lactam cores [8, 9] and cross-coupling reactions [10] herein, we will highlight the most important advances and developments on intramolecular cross-dehydrogenative coupling of amino alcohols (Figure 2)