Review Article

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Propargylic ureas as powerful and versatile building blocks in the synthesis of various key medicinal heterocyclic compounds

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ABSTRACT

This review article is an attempt to highlight the most important contributions toward the synthesis of various nitrogen-containing heterocyclic compounds from corresponding propargylic ureas through regio- and chemoselective 5-*exo-dig* and 6-*endo-dig* modes of N- and O-cyclization reactions. The review is divided into three major sections. In the first section we only focus on 5-exo-dig N-cyclization fashion. In the second section 5-*exo-dig* O-cyclization is described. The third section is devoted to 6-*endo-dig* N- and O-cyclizations.

1. Introduction

Heterocyclic compounds are the special class of organic compounds that contain a ring structure containing atoms in addition to carbon, such as nitrogen, oxygen or sulfur, as part of the ring [1]. These compounds constitute a common structural unit of most of the currently marketed drugs [2]. Over 90% of new drugs contain at least one heterocyclic (especially nitrogen-containing ring) fragment in their structures [3]. Interestingly, of the top five US small molecule drug retail sales in 2014, four are or contain *N*-heterocycle fragments in their overall structure (Figure 1) [4]. Although many synthetic approaches are reported to make this special class of organic compounds [5], still there is a demand for new methods. The intramolecular cyclization of heteroatom-containing acetylenic compounds has emerged as an effective and general synthetic route to the construction of various heterocyclic systems in an atom- and step-economic manner. This methodology is one of the most useful tools to create new carbon–heteroatom bonds both in the academic laboratory and in industry [6]. Propargylic urea derivatives are one of the most specific classes of heteroatom containing alkynes having diverse reaction patterns. These compounds not only can undergo regio- and chemoselective 5-*exo-dig* and 6-*endo-dig* *N*-cyclization reactions to provide synthetically and biologically important 1*H*-imidazol-2(3*H*)-one and 2,4-dihydropyrimidin-2(*1H*)-one derivatives, respectively, but also can undergo regioselective 5-*exo* and 6-*endo* modes of *O*-cyclization reactions to produce corresponding oxazolidin-2-imine and 3,4-dihydro-1,3-oxazin-2-imines, respectively (Figure 2).

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