

Review

Imidazole: Synthesis, Functionalization and Physicochemical Properties of a Privileged Structure in Medicinal Chemistry

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Abstract: Imidazole was first synthesized by Heinrich Debus in 1858 and was obtained by the reaction of glyoxal and formaldehyde in ammonia, initially called glyoxaline. The current literature provides much information about the synthesis, functionalization, physicochemical characteristics and biological role of imidazole. Imidazole is a structure that, despite being small, has a unique chemical complexity. It is a nucleus that is very practical and versatile in its construction/functionalization and can be considered a rich source of chemical diversity. Imidazole acts in extremely important processes for the maintenance of living organisms, such as catalysis in enzymatic processes. Imidazole-based compounds with antibacterial, anti-inflammatory, antidiabetic, antiparasitic, antituberculosis, antifungal, antioxidant, antitumor, antimalarial, anticancer, antidepressant and many others make up the therapeutic arsenal and new bioactive compounds proposed in the most diverse works. The interest and importance of imidazole-containing analogs in the field of medicinal chemistry is remarkable, and the understanding from the development of the first blockbuster drug cimetidine explores all the chemical and biological concepts of imidazole in the context of research and development of new drugs.

Keywords: imidazole; synthesis; medicinal chemistry; drug discovery

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1. The Chemistry of Imidazole

Imidazole **1** (Figure 1) was first synthesized by Heinrich Debus in 1858, but since the 1840s, several imidazole derivatives have been discovered. Its synthesis started from the use of glyoxal **2** and formaldehyde **3** in ammonia, producing imidazole **1** as a final product, which was initially called glyoxaline (Figure 2) [1,2]. This synthesis, despite producing relatively low yields, is still used to create C-substituted imidazoles.



Figure 1. Structure of imidazole **1** with its respective numbering and resonance hybrids.

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