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Imidazole-Based Pharmaceutical Molecules are Synthesized Using the Van Leusen Imidazole Synthesis

George Bell*

Department of Organic Chemistry, Hampshire College, Hampshire, UK

***Corresponding author:** George Bell, Department of Organic Chemistry, Hampshire College, Hampshire, UK; E-mail: George_Bell@yahoo.com

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Abstract

One of the most significant and common heterocycles in medicinal chemistry is imidazole, along with its derivatives. Due to their distinctive structural characteristics, these compounds exhibit a wide range of major pharmacological or biological activities, and pharmaceutical companies routinely research and employ them to create new medications. Due to its advantages, the van Leusen reaction based on tosyl Methylisocyanides (TosMICs) is one of the most suitable methods for synthesizing imidazole based medicinal molecules. In this paper, we review recent developments in the chemical synthesis and bioactivity of imidazole-containing medicinal small molecules using the Van Leusen immobilization approach.

***Keywords:** Leusen reaction; Imidazole; Heterocyclic molecules; Bioactivity; Molecules*

Description

The nitrogen-containing, five-membered heterocyclic scaffold known as the imidazole ring is widely present in both natural products and medicinal molecules. In addition, novel derivatives for medicinal use are being created, and imidazole-based heterocyclic molecules, which are significant in medicinal chemistry, have been utilised to treat a number of illnesses. Due to the peculiar structural feature of the imidazole scaffold with a worthy electron-rich quality, imidazole groups are able to mix with a variety of receptors and enzymes in biological systems, through a variety of weak connections, resulting in a range of biological activities. Currently, a plethora of imidazole-containing compounds have been widely used to treat a variety of illnesses, including antibacterial, antifungal, antiinflammatory, antiviral, antiparasitic, anticancer, antihistaminic, and enzyme inhibition. These compounds also show substantial therapeutic promise.

The imidazole heterocyclic skeleton still needs to be built, though, and a straightforward and efficient approach is still needed. In the past few decades, several traditional techniques for synthesising this ring molecule in the lab have been established, including the Wallach imidazole synthesis, the Debus-Radziszewski imidazole synthesis, and the van Leusen imidazole synthesis. Due to excellent benefits like straightforward manipulation, readily available raw materials, and a broad range of substrates that have been developed, the van Leusen imidazole synthesis based on TosMICs, which is the cycloaddition reaction, is well-known as one of the most practical and alluring protocols for the preparation of imidazole based small molecules. One of the most significant reactants, TosMIC, has a lot of benefits at room temperature, including being a stable solid and being colourless and odourless. Because it was invented and first employed in organic synthesis by the Dutch professor van Leusen in 1972, this reagent is also known as van Leusen's reagent. Long acknowledged as one of the most crucial building blocks in the synthesis of nitrogen heterocyclics, particularly in the production of imidazole based heterocycles, tosMIC and its derivatives are.

As a result, this study will demonstrate how the van Leusen imidazole synthesis, which is based on TosMICS from 1977, has advanced imidazole based molecular synthesis.

This article will probably offer fresh perspectives on how to develop less harmful and more bioactive imidazole containing drugs. TosMIC and aldimine underwent a base-induced cycloaddition process in a proton solvent, however the effects of R^1 and R^2 on the synthesis of were fundamentally different examined. It was discovered that -tosylbenzyl isocyanate and -tosylethyl isocyanate may be used to create 1,4,5-trisubstituted imidazoles. For the many benefits of this process, the van Leusen imidazole synthesis is used. The [3+2] cycloaddition reaction from aldimines is followed by a reaction with TosMICs, which have active methylene, reactive isocyanide carbons, and leaving groups like

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C2N1 "3-atom synthon." The cyano moiety can be a delayed cycloaddition to polarise a double bond in a base environment. The target 1,4,5-trisubstituted imidazoles are produced by eliminating p-TosOH, which is negative to the obtained 1,5-disubstituted imidazoles. This process first forms the intermediate 4-tosyl-2-imidazoline. The known Dxylo-pentodialdose was reported to result in imidazo-L-xylo-piperidinose derivatives after an eight-step reaction. As a crucial step in this approach, the van Leusen reaction was employed to produce the imidazole-base molecule. TosMIC was then transformed into an imidazole derivative. Finally, the protecting group was removed to yield the desired product, a bicyclic azasugar and a glycosidase inhibitor. It was possible to create the 1,4,5-trisubstituted imidazole, and p38 responded to it strongly.