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The Van Leusen Imidazole Synthesis is used to Synthesise Imidazole-Based Medicinal Molecules

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Opinion

In medicinal chemistry, imidazole and its derivatives are one of the most important and universal heterocycles. These compounds demonstrate a wide range of significant pharmacological or biological actions due to their unique structural properties, and they are frequently explored and used by pharmaceutical companies for medication discovery. The van Leusen reaction based on Tosylmethylisocyanides (TosMICs) is one of the most appropriate techniques for synthetizing imidazole-based pharmaceutical compounds, and it is becoming more popular due to its benefits. Using the van Leusen immobilisation method, we discuss current achievements in the chemical synthesis and bioactivity of imidazole-containing therapeutic small molecules in this study.

The imidazole ring is a five-membered, nitrogen-containing heterocyclic scaffold that is extensively found in natural goods and pharmaceutical compounds. Furthermore, imidazole-based heterocyclic compounds, which play an important role in medicinal chemistry, have been used to treat a variety of disorders, and novel derivatives for medicinal application are being developed. It is favorable for imidazole groups to mix with numerous receptors and enzymes in biological systems, through diverse weak contacts, resulting in a range of biological activities, due to the unusual structural characteristic of imidazole scaffold with a worthy electron-rich property. Currently, a slew of imidazole-containing compounds with significant therapeutic promise have been widely employed to treat a variety of ailments, including antibacterial, antifungal, anti-inflammatory, antiviral, anti-parasitic, anticancer, antihistaminic, and enzyme inhibition. Imidazole and its derivatives are used in a wide variety of medical applications. Pharmaceutical chemists and chemical synthesis researchers have been paying attention to the synthesis of the imidazole-skeleton small molecule due to the considerable pharmacological or biological activities and immense medicinal utility of imidazole-based molecules. However, a simple and effective method for constructing the imidazole heterocyclic skeleton is still required. Several conventional procedures for synthesising this ring molecule in the laboratory have been developed in recent decades, including van Leusen imidazole synthesis, Debus-Radziszewski imidazole synthesis, Wallach imidazole synthesis, and so on. The van Leusen imidazole synthesis based on TosMICs, which is the cycloaddition reaction, is well-known as one of the most convenient and attractive protocols for the preparation of imidazole-based small molecules, due to excellent advantages such as simple manipulation, easily obtained raw materials, and a wide range of substrates, which has been developed. At room temperature, TosMIC, one of the most important reactants, offers a number of advantages, including being a stable solid, odourless, and colourless. This reagent is also known as van Leusen's reagent because it was first introduced and used in organic synthesis by the Dutch professor van

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Leusen in 1972. TosMIC and its derivatives have long been recognised as one of the most important building blocks in the synthesis of nitrogen heterocyclics, particularly in the creation of imidazole-based heterocycles.

As a result, this study will highlight the progress of imidazole-based molecular synthesis using the van Leusen imidazole synthesis, which is based on TosMICS from 1977. This review paper is likely to provide new options for finding a reasonable design for imidazole-containing medications that are less toxic and more bioactive. In a proton solvent, TosMIC and aldimine undergo a base-induced cycloaddition reaction, whereas the effects of R1 and R2 on the production of were qualitatively examined. It was discovered that 1,4,5-trisubstituted imidazoles could be made from -tosylbenzyl isocyanate and -tosylethyl isocyanate. The van Leusen imidazole synthesis is called for the several advantages of this reaction. The van Leusen imidazole synthesis involves a [3+2] cycloaddition reaction from aldimines followed by a reaction with TosMICs, which contain reactive isocyanide carbons, active methylene, and leaving groups like C2N1 "3-atom synthon." Under a base situation, the cyano moiety can be a slow cycloaddition to polarise a double bond. The elimination of p-TosOH produces the intermediate 4-tosyl-2-imidazoline, which is then followed by the elimination of p-TosOH, which is negative to the acquired 1,5-disubstituted imidazoles, to yield the target 1,4,5-trisubstituted imidazoles. Based on an eight-step reaction, the known D-xylo-pentodialdose was reported to lead to imidazo-L-xylo-piperidinose derivatives. A van Leusen reaction was used to obtain the imidazole-base molecule as a vital step in this method, TosMIC was converted into an imidazole derivative via the van Leusen process. Finally, the target product, which is a bicyclic azasugar and a glycosidase inhibitor, was obtained by removing the protective group. The 1,4,5-trisubstituted imidazole was produced, and it showed robust interaction with p38 MAP kinase, a recently discovered protein kinase that plays a role in inflammatory regulation. A novel and simple approach based on the reaction of a -ketoaldimine with aryl-substituted TosMIC reagents was used to obtain 1,4,5-trisubstituted imidazole. It was proposed in an in situ active and gentle method for manufacturing multisubstituted imidazoles from an aryl-substituted TosMIC and a produced imine in one pot. The imine was made in situ from a 40% aqueous solution of pyruvaldehyde and amine, while the ketone was made in DMF with aryl-substituted TosMIC and K2CO3, yielding 75%.

In conclusion, an increasing number of imidazole-containing drugs with lower toxic, better efficacy, superior pharmacokinetic characteristics, effective pathologic probes, and diagnostic agents would be used as a result of in-depth research and application in imidazole-based medicinal chemistry and progress in other disciplines such as cell biology, molecular biology, pharmacology, and organic chemistry. This has the potential to make significant contributions to the protection of humanity's health. As a result, the van Leusen imidazole synthesis based on TosMICs will become increasingly important in the design and synthesis of bioactive molecules as clinic medications. To change the imida, we may concentrate on adjusting the various aldimine groups and TosMIC derivatives in the van Leusen reaction. Above all, the limitless potentiality of van Leusen imidazole synthesis in medicinal chemistry has been demonstrated.