

CATALYTIC EFFICIENCY OF SBCL3/SIO2 IN THE SYNTHESIS OF 1,2,4,5-TETRASUBSTITUTED IMIDAZOLES

¹Sajal Jain

¹Research Scholar, Department of Chemistry, Mansarovar Global University, Sehore, Madhya Pradesh

²Dr. Neelu Jain

²Supervisor, Department of Chemistry, Mansarovar Global University, Sehore, Madhya Pradesh

ABSTRACT

The synthesis of 1,2,4,5-tetrasubstituted imidazoles was carried out under solvent-free conditions utilizing a catalyst of antimony (III) chloride supported on silica (SbCl3/SiO2). Benzil, ammonium acetate, benzaldehyde, and primary amines were used in the synthesis of tetrasubstituted imidazoles using the catalyst that was produced. A 50 mL round-bottom flask was used to perform the reactions at 120°C, and thin-layer chromatography (TLC) was used to monitor the process. The produced compounds were studied by using nuclear magnetic resonance (1H, 13C), infrared (IR) spectroscopy, and elemental analysis. The increased nucleophilicity of aliphatic amines led to greater product percentages in reactions than aromatic amines. Thanks to the enhanced dispersion of SbCl3 on the silica support and the creation of stable Lewis acid sites, the SbCl3/SiO2 catalyst outperformed a physical combination of SbCl3 and SiO2 in terms of catalytic efficiency. This technique is an eco-friendly and effective way to make imidazole derivatives. It gets the job done with excellent yields and catalyst separation is easy.

Keywords: Imidazole, Solvent-free, Heterogeneous catalyst, Tetrasubstituted,

I. INTRODUCTION

There is a large family of heterocyclic compounds known as 1,2,4,5-tetrasubstituted imidazoles. These molecules have many uses in medicine, agriculture, and materials research, among other areas. An appealing target for chemical synthesis, the imidazole ring is a five-membered structure with two nitrogen atoms that displays distinctive electrical characteristics and reactivity. The imidazole ring may have its chemical characteristics modulated by substituents at positions 1, 2, 4, and 5, which increases its potential in medicinal chemistry.

Because of their possible use as medicinal agents, 1,2,4,5-tetrasubstituted imidazoles are of special interest for their production. Scientific investigations have revealed that these substances possess a wide range of pharmacological actions, such as the ability to combat infections, cancer, inflammation, and fungi. As an example, tetrasubstituted imidazoles have been shown to block enzymes or receptors that are important in disease processes. The structural variety that results from different substituents opens up new avenues for investigating structure-activity connections, which in turn can inspire the development of more selective and effective therapeutic candidates.

In addition, 1,2,4,5-tetrasubstituted imidazoles have been synthesized using methods that have undergone substantial evolution throughout the years. Multiple steps of synthesis were common in the past, which added time to the process and reduced product purity. New catalytic systems, however, have made it possible

to synthesize in a more efficient and selective manner. It is possible to directly produce tetrasubstituted imidazoles from easily accessible starting materials by using catalysts to improve reaction speeds and selectivity. To promote reactions that lead to the required tetrasubstituted imidazole framework, organocatalysts or transition metal catalysts have been shown to be effective.

Yet another novel strategy that has become more popular recently is solvent-free synthesis. Less waste, less expenses, and less environmental effect are some of the advantages of solvent-free environments. An appealing substitute for conventional solvent-based reactions, these circumstances often result in faster reaction speeds and higher yields. This context highlights the versatility of catalysts in sustainable chemistry as they have been tuned for efficient synthesis of tetrasubstituted imidazoles.

The medical uses of 1,2,4,5-tetrasubstituted imidazoles are not the only ones that have piqued the curiosity of materials scientists. They are well-suited for use in organic electronic devices, sensors, and photonic materials due to their distinctive optical and electrical characteristics. Materials with certain capabilities can be designed by strategically substituting their features. Because of their adaptability, tetrasubstituted imidazoles are being considered as potential building blocks for new technologies.

Extensive study has also been conducted on the biological targets and mechanisms of action of tetrasubstituted imidazoles. In order to create successful treatments, it is essential to understand the molecular level interactions between these chemicals and biological systems. Researchers have learned more about the binding affinities and interactions of tetrasubstituted imidazoles with certain proteins or receptors through molecular modeling and docking studies. Such data is priceless for informing the development of novel drugs with improved activity and fewer adverse effects.

II. REVIEW OF LITERATURE

Safari, Javad et al., (2014) The 2,4,5-trisubstituted and 1,2,4,5-tetrasubstituted-1H-imidazole derivatives were synthesized utilizing a one-pot cyclo-condensation process using benzil, aldehydes, ammonium acetate, and primary amines. The reaction was carried out under microwave irradiation with silica-supported SbCl3 (SbCl3/SiO2) acting as a heterogeneous catalyst. As an intriguing alternative to previously used processes, this methodology is operationally simple, practically applicable, and applicable to a variety of substrates. From an ecological perspective, this green catalyst is ideal as it is stable, very active, and simple to work with.

Safari, Javad et al., (2013) The one-step condensation of an aldehyde, benzil, ammonium acetate, and primary aromatic amine with nanocrystalline magnesium aluminate in ethanol under ultrasonic irradiation describes an efficient four-component synthesis of 1,2,4,5-tetrasubstituted imidazoles. Some of the benefits of this technique are high yields, quick work-up, moderate environments, fast reaction times, and ease of operation.

Tavakoli, Ziba et al., (2012) The catalyst SASPSPE, which stands for sulfuric acid ([3-(3-silicapropyl)sulfanyl]propyl]ester), is utilized in the production of 1,2,4,5-tetrasubstituted imidazoles and may be recycled. Benzil, aldehydes, amines, and ammonium acetate were combined in a four-component reaction using SASPSPE under solvent-free conditions at 140°C to produce a variety of polysubstituted imidazoles. The catalytic activity of the heterogeneous catalyst was maintained even after being reused for

five cycles in a process involving benzil, 4-methylbenzaldehyde, benzyl amine, and ammonium acetate.

Teimouri, Abbas & Chermahini, Alireza. (2011) The 3,2-dicarbonyl compound, aldehyde, and NH4OAc cyclocondensation in ethanol at moderate temperature yields 2,4,5-trisubstituted imidazoles in a straightforward, efficient, and very adaptable way. The catalysts used in this process are clays, zeolite, and nano-crystalline sulfated zirconia (SZ). In addition, this technique was shown to be useful for the convenient one-pot synthesis of 1,2,4,5-tetrasubstituted imidazoles with moderate conditions, short reaction periods, and high yields. The work-up was also straightforward, and the products were purified without using chromatographic methods. Reusing and recovering the catalysts for later reactions does not significantly reduce their efficiency.

Kantevari, Srinivas et al., (2007) A four-component, highly efficient method for synthesising 1,2,4,5tetrasubstituted imidazoles was described. It involved the solvent-free condensation of different aldehydes, benzil, aliphatic or aromatic primary amines, and ammonium acetate, with perchloric acid adsorbed on silica gel (HClO4-SiO2) serving as the catalyst. The yields were excellent. Depending on the catalyst concentration and reaction duration (2-20 minutes), HClO4-SiO2 showed outstanding catalytic activity. There is clear evidence that the current technique using the HClO4-SiO2 catalyst outperforms the newly published catalytic methods.

III. EXPERIMENTAL MATERIAL AND METHODS

Merck Chemical Company supplied the very pure chemical reagents. All of the components were of reagent quality for commercial use. In an open capillary, the Electrothermal Mk3 equipment was used to determine melting points. A Perkin-Elmer FTIR 550 spectrometer was used to record the infrared (IR) spectra. Bruker DRX-400 spectrometers operated at 400 MHz and 100 MHz, respectively, were used to record 1H NMR and 13C NMR spectra in DMSO-d6. The C, H, and N elemental analyses were performed using a Perkin-Elmer 240c analyzer using data acquired from a Carlo ERBA Model EA 1108. Using spectrophotometric grade chloroform (Baker), UV spectra were obtained using a Hitachi 200-20 spectrophotometer. A jeol JEM-2100UHR, operating at 200 KV, was used for transmission electron microscopy (TEM).

Typical procedure for synthesis of silica-supported antimony (III) chloride catalyst

At room temperature, 1 gram of antimony trichloride (SbCl3), 6 grams of silica dioxide, and 15 milliliters of dry dichloromethane solvent were mixed and agitated for 120 minutes. The reaction vessel instantly began to exhale HCl gas. A white powder of antimony (III) chloride supported by silica was obtained by removing the solvent on a rotary evaporator at decreased pressure; 6.44 g of this compound was obtained. The following step included its application.

<u>General procedure for solvent-free synthesis of 1,2,4,5-tetrasubstituted imidazoles by use of</u> <u>SbCl3/SiO2 catalyst</u>

The following ingredients were agitated at 120°C for the specified amount of time in a 50 mL round-bottom flask: benzil (1 mmol), ammonium acetate (4 mmol), benzaldehyde (1 mmol), and primary amine (4 mmol). The catalyst used was 0.1 g SbCl3/SiO2. Thanks to TLC, we were able to track the reaction's development. The reaction mixture was filtered after being dissolved in acetone after cooling. Reducing the pressure on a rotary evaporator concentrated the filtrate; the solid product was then recrystallized from an acetone-water

mixture after being rinsed with water. We achieved very high yields of pure goods.

IV. RESULTS AND DISCUSSION

We reacted benzil, aliphatic and aromatic amines, and ammonium acetate with different aromatic aldehydes that contained either an electron-releasing or an electron-withdrawing substituent in a solvent-free environment to produce tetrasubstituted imidazoles. The reaction involving benzaldehyde, aniline, benzil, and ammonium acetate was chosen as a model reaction to investigate their practicability. Using model reactions, we investigated the applicability and breadth of the current approach to a number of different aldehydes and amines. The findings demonstrate that the time and reaction yield were significantly affected by the kind of functional group on the aromatic ring of the aldehyde. Table 1 shows that aldehydes with electron-withdrawing groups produce more pure products in greater yields and with fewer reactions than those with electron-donor groups. Also, the results demonstrated that aliphatic amines improved the reaction efficiency and product yield compared to aromatic amines. Aliphatic amines, in contrast to aromatic amines, have more nucleophilic strength and are stronger bases. 1H NMR, 13C NMR, CHN, MS spectrum analysis, and comparison with legitimate samples were used to describe the structures of the products.

S. no.	R	Amine	Time (min)	Yield (%)
1	Н	PhNH2	25	93
2	4-Me	PhNH2	28	90
3	4-Cl	PhNH2	15	95
4	3,5-(OMe)2	PhNH2	31	78
5	2-OH	PhNH2	30	75
6	4-OH	PhNH2	30	58
7	3,4-(OMe)2	PhNH2	33	80
8	4-OMe	PhNH2	28	87
9	4-Br	PhNH2	12	93
10	Н	n-PrNH2	20	94
11	4-Cl	n-PrNH2	13	95
12	4-Me	n-PrNH2	25	91
13	4-OMe	n-PrNH2	25	89

 Table 1: Solvent-Free Catalytic Approach for Synthesizing 1,2,4,5-Tetrasubstituted Imidazoles

Imidazole derivative synthesis makes use of a Lewis acid site on antimony (III) chloride supported on silica

(SbCl3/SiO2), which is a very effective acid catalyst. As a heterogeneous acid catalyst, this environmentally benign and sustainable catalyst was shown to be amenable to simple filtration-based separation from the reaction mixture. The effects of a supported catalyst and the efficacy of SbCl3/SiO2 in a simulated reaction were systematically investigated in this work (table 2). In addition, the silica-antimony (III) chloride physical combination (0.6 mmol SbCl3 and 0.1 g SiO2) showed a reduced degree of activity compared to the silica-supported antimony (III) chloride. The reaction is better catalyzed by SbCl3/SiO2 than by a physical mixing of the two substances. Because of the good dispersion of SbCl3 across the large surface area silica support, the strong catalytic activity of SbCl3/SiO2 is shown. According to the findings, under the reaction circumstances, scattered SbCl3 forms stable Lewis acid sites (SiO2-OSbCl2) by coordinating with surface hydroxyl groups.

S. no.	Time (min)	Yield (%)
1	25	22
2	25	93

Table 2: Comparative Analysis of Catalyst Efficiency

V. CONCLUSION

The research effectively illustrated the synthesis of 1,2,4,5-tetrasubstituted imidazoles utilizing a silicasupported antimony (III) chloride (SbCl3/SiO2) catalyst in solvent-free conditions. The catalyst demonstrated efficiency and environmental sustainability, facilitating high yields and straightforward separation from the reaction mixture. The findings indicated that aldehydes with electron-withdrawing substituents yielded greater outcomes in reduced reaction times relative to those with electron-donating groups. Furthermore, reactions with aliphatic amines yielded superior results compared to those with aromatic amines, attributable to their enhanced nucleophilicity. The enhanced catalytic activity of SbCl3/SiO2, in contrast to a physical mixing of antimony trichloride and silica, is ascribed to its improved dispersion and the establishment of stable Lewis acid sites on the silica substrate. This method offers an environmentally friendly alternative for the synthesis of imidazole derivatives, characterized by excellent efficiency and catalyst reusability, rendering it a significant technique in organic synthesis.

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