**N-Bromosuccinimide Catalyzed Three Component One-Pot Efficient Synthesis of 2,4,5-Triaryl-1H-imidazoles from Aldehyde, Ammonium Acetate, and 1,2-Diketone or α-Hydroxyketone**

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**Abstract.** A simple, green, and efficient method for the synthesis of 2,4,5-triaryl-1H-imidazoles using N-bromosuccinimide (NBS) as a catalyst under solvent-free condition is described. The major advantages of the present method are: high yields, less reaction times, solvent-free conditions, easy purification of the products, environmental friendliness, and convenient operation.

**Key words:** 2,4,5-Triaryl-1H-imidazoles, aldehydes, ammonium acetate, 1,2-diketone, α-hydroxyketone, N-bromosuccinimide.

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**Introduction**

In 1858 Debus reported the reaction between glyoxal and ammonia, a reaction that pioneered a novel synthetic route to imidazole [1]. Over the century, the importance of imidazoles in biological system has attracted much interest due to their chemical and biochemical properties. Compounds with imidazole ring system have many pharmacological properties and can play important role in biochemical processes [2-3]. For example, it is reported that substituted imidazoles can act as glucagon receptor agonists [4], inhibitors of P38 MAP kinase [5], B-Raf kinase [6], plants growth regulators [7], antibacterial [8], antitumour [9], therapeutic agents [10] and also pesticide [11]. In recent years, substituted imidazoles are substantially used in ionic liquids [12-15], that has been given a new approach to “Green Chemistry”. The potency and wide applicability of the imidazole pharmacophore can be attributed to its hydrogen bond donor-acceptor capability as well as its high affinity of metals which are present in many protein active sites [16]. Because of their wide range of pharmacological activity, industrial and synthetic applications, the synthesis of imidazoles has received considerable attention, and many articles have appeared. Japp and Radziszewski proposed the first synthesis of the imidazole core in 1822, starting from 1,2-dicarbonyl compounds aldehydes and ammonia, to obtain 2,4,5-triphenyl-1H-imidazole [17-18]. Subsequently, many other synthesis of this important heterocycle have been published, for example, hetero-Cope rearrangement [19], four-component condensation of arylglyoxals, primary amines, carboxylic acids and isocyanides on wasp resin [20], reaction of N-(2-oxo)-amides with ammonium trifluoroacetate [21], 1,2-aminalcohols in the presence of PCl₅ [22].

In spite of various methods for the synthesis of 2,4,5-triaryl-1H-imidazoles, generally, these compounds synthesized by three components cyclocondensation of 1,2-diketone or α-hydroxyketone with an aldehyde and ammonium acetate [23]. Various reagents can catalyze this reactions, such as: H₃PO₄·12MoO₃·24H₂O, KH₃PO₄, [24] catalyst-free under microwave irradiation [25-26], ionic liquid (1-n-butyl and 1,3-di-butyl imidazolium salts) [27], ceric (IV) ammonium nitrate (CAN) [28], Eu(OTf)₃ [29], zeolite HY/SiO₂ [30], ZrCl₄ [31], Yb(OTf)₃ [32], NiCl₂·6H₂O [33], sodium bisulfate [34], iodine [35], sulphuric acid [36], oxalic acid [37], silica sulphuric acid [38], acetic acid [39], L-proline [40], PEG-400 [41], Cu(TFA)₂ [42], p-TSA/TBAI [43], (NH₄)₆MoO₂⁴·4H₂O [44], InCl₃·6H₂O [45], Zr(acac)₄ [46], heteropolyacid [47] and uranyl nitrate hydrate [UO₂(NO₃)₂·6H₂O] supported on acidic alumina [48]. However, many of these methods suffer from longer reaction times, unsatisfactory yields, acidic media, difficult workup, excessive use of reagents and catalyst. It is therefore important to find more convenient methods for the preparation of these compounds.

**Results and Discussion**

N-Bromosuccinimide (NBS) (Fig. 1) has gained interesting attraction in recent years due to economic and environmentally considerations [49-54]. This catalyst is generally inexpensive and easily available, which can conveniently be handled and...
removed from the reaction mixture. Thus, making a simple and eco-friendly experimental procedure is still strongly desired for the synthesis of these important heterocyclic compounds.

As a part of our program, seeking at development new methodologies for the preparation of heterocyclic compounds containing nitrogen [55-60] herein, we wish to describe a new and convenient protocol for the synthesis of 2,4,5-triaryl-1H-imidazoles via a multicomponent reaction of aldehydes, 1,2-diketone or α-hydroxyketone, and ammonium acetate in the presence of N-bromosuccinimide under solvent-free conditions (Scheme 1).

Initially, we investigated the ability of this catalyst for examining the reaction of 4-chlorobenzaldehyde, 1,2-diketone and ammonium acetate. After initial screening of amounts for NBS, solvents and reaction temperature, we obtained that use of 15 mol% NBS at 120 °C under solvent-free conditions produced 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole after 45 min, in 92% yield (entry1). Notably, the desired product could not be obtained under similar reaction conditions, even after a long time (120 min) in the absence of the catalyst (entry 6).

Subsequently, to examine the efficiency and applicability of this protocol, the reaction was extended to other substituted benzaldehydes under solvent-free conditions. Importantly for the ultimate goal of applying this reaction in a diversity-generating strategy, this broad generality extends to the 1,2-diketone substrate as well (Table 1).

A probable mechanism for the synthesis of 2,4,5-triaryl-1H-imidazoles was proposed in Scheme 2. In this procedure, ammonium acetate can be decomposed into ammonia and acetic acid. Ammonia is the nitrogen source. Since NBS contains bromine atom which are attached to nitrogen, it is very probable that this reagent releases Br⁺ in situ which can conduct as an electrophilic species [48-54]. It can active the carbonyl group (C=O) of aldehyde and decrease the energy of transition state. Br⁺ facilitates the formation of the diimine intermediate [I] that under mild catalysis of NBS (Br⁺) condenses with the carbonyl carbon of the 1,2-diketone followed by dehydration to afford the iso-imidazole which rearranges via a [1,5] sigmatropic shift to the required 2,4,5-triaryl-1H-imidazoles (4a-l).

Using benzoin (1), aromatic aldehydes substrates, and ammonium acetate with NBS as a catalyst, the proposed mechanism includes initial oxidation of Benzoin (2) in the presence of Br⁺ followed by similar mechanism as that for benzil (1) (Scheme 2) [22-47].
Table 1. Synthesis of 2,4,5-triaryl-1H-imidazoles (4a-l) using (15 mol%) N-bromosuccinimide under solvent-free conditions.

<table>
<thead>
<tr>
<th>Products</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
<th>Found</th>
<th>Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>4a</td>
<td>50</td>
<td>65</td>
<td>89</td>
<td>91</td>
<td>274-275</td>
</tr>
<tr>
<td>4b</td>
<td>45</td>
<td>60</td>
<td>92</td>
<td>86</td>
<td>264-265</td>
</tr>
<tr>
<td>4c</td>
<td>55</td>
<td>70</td>
<td>80</td>
<td>74</td>
<td>230-232</td>
</tr>
<tr>
<td>4d</td>
<td>60</td>
<td>75</td>
<td>83</td>
<td>83</td>
<td>188-190</td>
</tr>
<tr>
<td>4e</td>
<td>50</td>
<td>60</td>
<td>86</td>
<td>72</td>
<td>265-267</td>
</tr>
<tr>
<td>4f</td>
<td>60</td>
<td>70</td>
<td>72</td>
<td>68</td>
<td>217-219</td>
</tr>
<tr>
<td>4g</td>
<td>50</td>
<td>75</td>
<td>85</td>
<td>80</td>
<td>250-252</td>
</tr>
<tr>
<td>4h</td>
<td>60</td>
<td>65</td>
<td>72</td>
<td>70</td>
<td>232-233</td>
</tr>
<tr>
<td>4i</td>
<td>60</td>
<td>75</td>
<td>84</td>
<td>70</td>
<td>&gt;300</td>
</tr>
<tr>
<td>4j</td>
<td>50</td>
<td>70</td>
<td>84</td>
<td>80</td>
<td>227-229</td>
</tr>
<tr>
<td>4k</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>228-231</td>
</tr>
</tbody>
</table>
**Conclusion**

In conclusion, the present protocol demonstrates the potential of NBS, as a cheap and readily available reagent, neutral, green and effective catalyst for the synthesis of 2,4,5-triaryl-1H-imidazoles. In this method, complicated operation of pre-separating mixtures is not necessary.

**Experimental**

Solvents, reagents, and chemical materials were obtained from Aldrich (United States), Merck (Germany) and Fluka (Switzerland) chemical companies and purified prior to use. Melting points were determined in open capillary tubes in a Stuart BI Branstead Electrothermal Cat No:1A9200 apparatus and are uncorrected. Nuclear magnetic resonance spectra were recorded on JEOL FX 90Q using tetramethylsilane (TMS) as an internal standard. IR spectra were recorded on a Shimadzu 435-U-04 spectrophotometer (KBr).

**General procedure for the synthesis of 2,4,5-triaryl-1H-imidazoles**

To a stirred mixture of the aromatic aldehydes (3a-r) (1 mmol), benzil or benzoin (1 mmol), ammonium acetate (3 mmol), at room temperature was added N-bromosuccinimide (NBS) (15 mol%) and then temperature was raised to 120°C and maintained for the appropriate time (see Table 2). After completion of the reaction (monitored by TLC) the reaction mixture diluted

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**Table 1. Continue.**

<table>
<thead>
<tr>
<th>Products</th>
<th>Time (min)</th>
<th>Yield (%)</th>
<th>Mp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Benzil</td>
<td>Benzoin</td>
<td>Benzil</td>
</tr>
<tr>
<td>4l</td>
<td>50</td>
<td>60</td>
<td>84</td>
</tr>
<tr>
<td>4m</td>
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<td>75</td>
<td>82</td>
</tr>
<tr>
<td>4n</td>
<td>50</td>
<td>60</td>
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</tr>
<tr>
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<td>80</td>
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</tr>
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<td>45</td>
<td>50</td>
<td>88</td>
</tr>
<tr>
<td>4r</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

*All the isolated products were characterized on the basis of their physical properties and IR, 1H-and 13C-NMR spectral analysis and by direct comparison with authentic materials; †Isolated yields
with EtOH (96%, 5 ml) and stirred for 2 min in 120°C. The solvent evaporated, the resulting solid products were collected and washed with water to give the crude products. Then, recrystallized from EtOH (96%, 5 ml) to afford pure 2,4,5-triaryl-1H-imidazoles (4a-r) to afford pure 2,4,5-triaryl-1H-imidazoles (4a-r).

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