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One pot multicomponent synthesis of highly substituted imidazoles using tetrabutylammonium peroxy disulfate as a catalyst

Ramesh Nukala[1] · Kumaraswamy Gullapelli[2] · Ramaiah Konakanchi[3]

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Abstract

A fascinating trend in the synthesis of heterocyclic molecules is focused on green chemistry, including efficient reactions and the use of eco-friendly reagents to meet the demands of the pharmaceutical industry due to its many biological activities. In our ongoing efforts to promote new synthetic strategies for preparing heterocyclic compounds in this study. In this work describes a method for the synthesis of tri- and tetra-substituted imidazoles using Tetra butyl ammonium Peroxy disulfate (TBAPDS) as a catalyst. The reaction involves a multi-component condensation of benzoin, aniline, ammonium acetate, and araldehydes in acetonitrile under reflux conditions ~ 2 to 3 h at 60–65 °C. Results found that optimized 20% mole ratio of TBAPDS catalyst to acetonitrile solvent resulted in excellent yields of the desired products (77–96%). The use of TBAPDS as a catalyst in this condensation reaction offers several advantages, including operational simplicity, cost-effectiveness, reusability of the catalyst, and high product yields. To confirm the structures of the newly synthesized compounds, various spectroscopic techniques were employed. Proton-NMR, ^{13}C-NMR, FTIR, and mass spectra were used to analyze and characterize the chemical structures of the synthesized imidazoles. ^{1}HNMR data reveals that all aromatic protons were present in that at chemical shift value δ 6.92–7.89 ppm. Overall, the study highlights a simple and efficient method for the synthesis of tri- and tetra-substituted imidazoles using TBAPDS as a catalyst. The results suggest that this method holds promise for the production of these compounds, offering advantages such as cost-effectiveness and high yields.

Keywords Synthesis · Imidazoles · Tetra butyl ammonium peroxy disulfate · Catalysis

Extended author information available on the last page of the article

Introduction

Multicomponent reactions (MCRs) have indeed garnered significant attention in the field of modern chemistry and pharmacy, primarily due to their efficiency and versatility. These reactions involve the interaction of three or more starting materials in a single reaction flask to generate a product that typically incorporates structural elements from each starting material [1, 2].This approach drastically reduces the time and resources typically needed for complex multi-step syntheses, making it particularly attractive for drug discovery and medicinal chemistry [3–6]. Medicinal chemistry bears a significant responsibility in providing effective treatments for various ailments. The drug discovery process is arduous and full of unexpected challenges, and one of the major goals is to identify and synthesize molecules with specific therapeutic properties. Given the complexity of medicinal chemistry, approaches that streamline the process are highly desirable. MCRs have emerged as a solution, as they offer an efficient, high-throughput method to synthesize a variety of structures, including heterocyclic compounds [7–9].

Multi-Component Reactions (MCRs), which are a very effective approach to chemical synthesis. MCRs involve the simultaneous interaction of three or more starting materials to produce a final product, essentially bypassing the need for intermediate purification steps. This can significantly increase the synthetic efficiency and speed of reaction, making them particularly attractive for pharmaceutical applications [10–12]. In the context of drug discovery, the assembly of scaffolds from smaller fragments is a critical aspect of MCRs. This approach can lead to a novel kind of fragment-based drug discovery, a method in medicinal chemistry where lead compounds are generated by the assembly of smaller, less complex fragments. This can provide a more efficient and rational way to design new drugs, reducing the time and resources required for drug discovery [13–16].

The development of new eco-friendly methodologies in heterogeneous catalyzed organic synthesis has become one of the most favorite areas for researchers since publishing of 12 Principles of Green Chemistry [17, 18].Various heterogeneous methodologies were developed for the synthesis of organic compounds by three or four component reactions by using different catalysts like, sodium benzoate [19], triethylamine [20], amberlyst [21], lemon juice [22], nano MgO [23], NAF[24], L-proline [25], ceriumammoniumnitrate [26], $Zn(ANA)_2Cl_2$ [27], $ZnAl_2O_4$ nanoparticles [28], $NiFe_2O_4@SiO_2$-supported $H_3PW_{12}O_{40}$ [29] cocamidopropylbetaine [30], and uncapped-SnO_2 quantum dots [31] etc.,

Indeed, multi-component condensations (MCCs) offer an attractive synthesis strategy in organic chemistry. They allow for the rapid and efficient generation of products in a single step, making them particularly useful in the synthesis of complex molecules. The key advantage of MCCs lies in the ability to achieve structural diversity by simply varying the reacting components, which makes them versatile and adaptable to different synthetic needs. The use of solid acid catalysts has indeed gained greater importance in organic synthesis, including multi-component condensations. Solid acid catalysts [32, 33] are heterogeneous

catalysts that are typically supported on solid materials, such as zeolites, metal oxides, or resins. They provide several advantages over traditional homogeneous acid catalysts as reusability, environmental friendliness, improved product selectivity, and tolerance to water and impurities.

There are different examples of commercially available drugs which consist imidazole ring (Fig. 1) such as Ornidazole (Antiprotozoal), Metronidazole (antibacterial), Satranidazole (Anti-amoebic) and Losartan (hypertension) [34]. Recently, interest in imidazole-containing structures from their widespread occurrence in molecules exhibit biological activities such as antimicrobial [35], antiviral [36], antioxidant [37], antitumor [38], oxidative stress [39],dual inhibitor of HSP90 and Topo-II in cancer therapy [40], SARS-CoV-2 [41, 42], inhibitor of Covid-19 [43], receptor for Alzheimer [44]and various therapeutic and biological applications[45].Imidazoles and their derivatives exhibit not only biological activity but also exhibit various engineering applications [46–49].

Most of the synthetic methods under different catalysts have suffered from disadvantages such as metal based catalysts, high temperature, toxic solvents, low efficiency, low purity, high reaction time. Considering the weaknesses mentioned above, in this regard, we attempted to synthesize a new and efficient imidazoles using Tetra butyl ammonium Peroxy disulfate (TBAPDS) as a catalyst. To the best of my knowledge, no reports are available on the use of TBAPDS as a catalyst for the synthesis of 2,4,5-trisubstituted Imidazoles and 2,3,4,5-tetrasubstituted imidazoles.

Results and discussion

Recently, *n*-tetrabutylammonium peroxydisulfate [$(n\text{-}Bu_4N)_2S_2O_8$] [50] has been one of the important oxidizing reagents that has been used as a versatile radical oxidant, and also involved acid induced processes to accomplish important transformations in synthetic organic chemistry. This reagent is readily soluble in most organic solvents, such as acetonitrile, dichloromethane, acetone and methanol.

Initially, the investigation was begun with benzil (dibenzoyl or diphenyl ethanedione) (**1**), aldehyde (**2**) and NH_4OAc (**3**) as a model substrates (1:1:2) in the presence of potassium persulphate in EtOH to produce 2,4,5-triaryl-1H-imidazoles. Consequently, the attempt was successful and the expected product was formed from the starting materials in good yield (74%) (Table 1, entry1). Next, we evaluated the effect of solvent by screening a variety of polar, nonpolar and protic solvents like methanol (71%), acetonitrile (58%) Table 1 (entry 2, 3), but less yield was

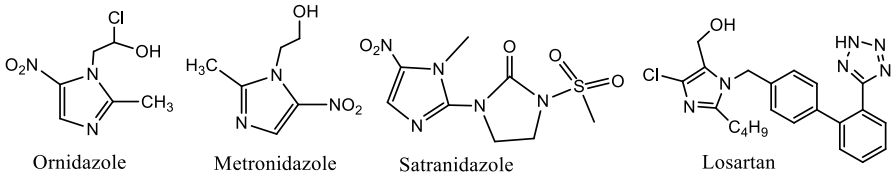


Fig. 1 Imidazole based standard drugs

Table 1 Optimization of the reaction conditions for the synthesis of substituted Imidazoles

Entry	Catalyst (mol %)	Amine source	Solvent	Yield (%) [a]
1	$K_2S_2O_8$(20)	NH_4OAc	*EtOH*	74
2	$K_2S_2O_8$(50)	NH_4OAc	*Me OH*	71
3	$K_2S_2O_8$(20)	NH_4OAc	CH_3CN	58
4	$K_2S_2O_8$ + TBAB	NH_4OAc	CH_3CN	54
5	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	CH_3OH	71
6	**$(Bu_4N)_2S_2O_8$(20)**	**NH_4OAc**	**CH_3CN**	**96**
7	$(Bu_4N)_2S_2O_8$(20)	NH_4Cl	CH_3CN	–
8	$(Bu_4N)_2S_2O_8$(20)	$(NH_4)_2SO_4$	CH_3CN	Trace
9	$(Bu_4N)_2S_2O_8$(20)	$(NH_4)_2CO_3$	CH_3CN	Trace
10	$(Bu_4N)_2S_2O_8$(20)	Aqu.NH_3	CH_3CN	35
11	$(Bu_4N)_2S_2O_8$(10)	NH_4OAc	CH_3CN	84
12	$(Bu_4N)_2S_2O_8$(50)	NH_4OAc	CH_3CN	92
13	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	water	–
14	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	DCM	34
15	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	Toluene	38
16	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	–	Trace
17[b]	$(Bu_4N)_2S_2O_8$(20)	NH_4OAc	CH_3CN	Trace

Reaction conditions:benzil (**1a**, 10 mmol), aldehyde (**2a**, 10 mmol), *N* source (3**a**, 20 mmol),20 mol% $(Bu_4N)_2S_2O_8$ at 75 °C for 3 h. [a]represent reaction conditions where as [b]represent yields of unoptimized products

reported when compared to methanol. Further, we examined different catalytic systems because potassium per sulfate inorganic salt is soluble in water and hence less yields were observed in acetonitrile solvent. To improve the profile of the reaction, we carried out the reaction with $K_2S_2O_8$ + TBAB (*n*-tetra butyl ammonium bromide) mixture reagent (Table 1, entry 4), but lower yield (54%) was formed here too. As a result, we moved to another reagent, tetrabutylammonium peroxydisulfate in methanol solvent (Table 1, entry 5) reaction proceeded well and the yield 71%. Furthermore, we changed the solvent system from protic to aprotic with the organic solvent acetonitrile (Table 1, entry 6) where we observed excellent yield (96%). After that, we focused on different *N* (amine) sources in which there was no reaction with ammonium chloride (Table 1, entry 7), a trace amount of product was observed with ammonium carbonate (Table 1, entry 8) and ammonium sulfate (Table 1, entry 9), and with aq.ammonia (Table 1, entry 10) lower yield (35%) was observed.

In further investigation, we have carried out the standard reaction at different mole ratios of catalytic systems, initially, 10 mol% of catalyst gave 84% of yield, 50 mol% of catalyst gave 92% yield where as 20 mol% catalyst gave 96% of yield. So there was no significant difference in the yields 20 and 50 mol%, therefore we decided to use 20 mol% of the catalyst is the best one for this reaction. And also, we studied different solvent systems, there was no product formation in water medium (Table 1, entry 13), less yield of product was formed (34%) with 1,2-dichloromethane (DCM) solvent (Table 1, entry 14), and with toluene (38%) yield was obtained

(Table 1, entry 15). Therefore, the optimum conditions for the formation of substituted imidazoles with different catalysts and different amine (nitrogen) sources in various solvent systems, as starting materials, are taken as benzil **1a** (1.0 eq, 10 mmol)**,** aromatic aldehyde **2a** (1.0 eq, 10 mmol), NH_4OAc **3a** (2.0 eq, 20 mmol), with 20 mol% $(Bu_4N)_2S_2O_8$ at 60–65 °C for about 2–3 h. For the preparation of tri substituted imidazole, the molar ratio of benzil, aldehyde, and NH_4OAc was 1:1:2, whereas for the preparation of tetra substituted imidazole, equal molar ratio of all substrates (benzil, aldehydes, aniline, and NH_4OAc) was used.

To demonstrate the versatility of this protocol, further, we investigated the scope of this reaction under the optimized conditions and the results are presented in Table 2. Similarly, a variety of substituted aldehydes possessing electron-donating, electron-withdrawing functional groups, and aliphatic aldehydes reacted with benzil to afford the corresponding tri substituted imidazole 4a–4n in 77–96% yield without any side products. The products were formed in good to excellent yields and with various functional groups such as hydroxyl, alkoxy, halogen, and nitro groups, with the amine group also a good yield was obtained (Scheme 1, Table 3).

The reusability of the catalytic system was explored. The catalyst was separated by simple filtration and washed with ethyl acetate after the reaction was completed, and it was reused for two consecutive cycles within the same time frame, with a slight decrease in catalytic activity (4%) (Table 4, entry 3) (Scheme 2).

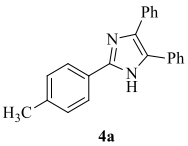
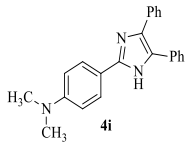
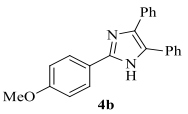
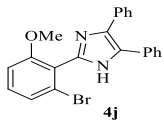
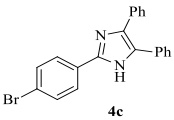
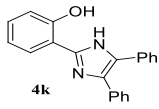
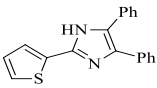
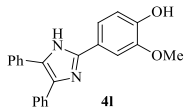
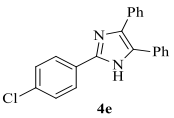
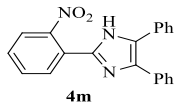
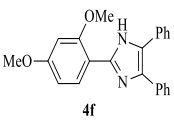
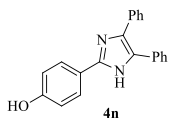
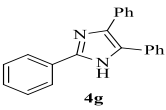
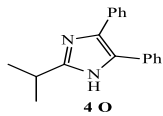
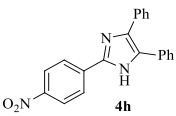
One of the product 2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole was formed by the reaction of *p*-anisaldehyde coupled with benzil and ammonium acetate in the presence of bis (tetrabutylammonium) peroxydisulfate under acetonitrile solvent and reflux conditions. Product was isolated from reaction mixture as white solid and submitted to ^{1}H NMR spectroscopy in that spectra, protons were present in that at chemical shift value of δ 7.89–7.79 (m, 2H) ppm, two aromatic protons indicates those are present meta position to the methoxy group result from aldehyde, at chemical shift value of 7.54 (d, $J = 13.4$ Hz, 4H) and 7.40–7.27 (m, 6H). All these aromatic protons responsible for benzil and resonate at a chemical shift value of δ 7.03–6.92 (m, 2H) ppm. These two aromatic protons indicate that they are present ortho position to methoxy group results from aldehyde and another singlet peak at δ 3.86 ppm (s, 3H, Ar-OCH_3) due to the presence of methoxy protons. In^{13}C-NMR at δ160.2 ppm peak appeared, which is responsible for aromatic carbon attached to the methoxy group (OCH_3) and at δ 55.4 ppm indicates methoxy carbon (OCH_3). This compound was also confirmed by the ESI Mass $[M+H]^+$ peak observed at m/z 327. Finally, confirmation and purity have been studied by using HRMS $[M+H]^+$ calcd: For $C_{22}H_{19}N_2O$ 327.1505, found: 327.1500.

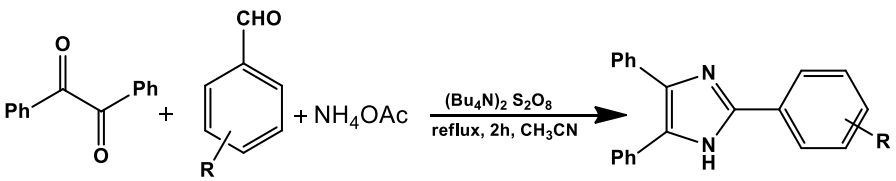
Mechanism

The plausible mechanism for the synthesis tri and tetra substituted imidazole using bis (tetrabutylammonium) peroxydisulfate as a catalyst was summarized in Scheme (Scheme 3 and 4).

We, suggest that initially, the catalyst protonates the carbonyl group of aromatic aldehyde (1) with ammonia produced from ammonium acetate, generating

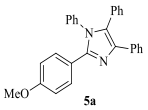
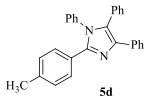
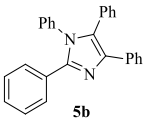
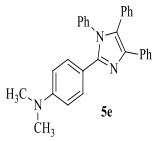
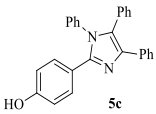
Table 2 Bis(tetrabutylammonium) peroxydisulfate catalyzed synthesis of 2,4,5-triaryl imidazoles (4a–4o)

Entry	Product	Time (min)	Yield (%)	Entry	Product	Time (min)	Yield (%)
1	 **4a**	122	92	9	 **4i**	132	84
2	 **4b**	128	90	10	 **4j**	129	88
3	 **4c**	125	88	11	 **4k**	131	79
4	 **4d**	130	85	12	 **4l**	127	80
5	 **4e**	128	86	13	 **4m**	132	77
6	 **4f**	134	90	14	 **4n**	125	81
7	 **4g**	120	96	15	 **4 O**	115	86
8	 **4h**	126	79				



Scheme 1 Synthesis of 2,4,5 triaryl imidazoles (4a–4o)

Table 3 bis(tetrabutylammonium) peroxydisulfate catalyzed synthesis of 1,2,4,5-tetra aryl imidazoles (5a–5e)

Entry	Product	Time (min)	Yield (%)[b]	Entry	Product	Time (min)	Yield (%)[c]
1	 **5a**	184	90	4	 **5d**	187	88
2	 **5b**	180	89	5	 **5e**	192	87
3	 **5c**	186	85				

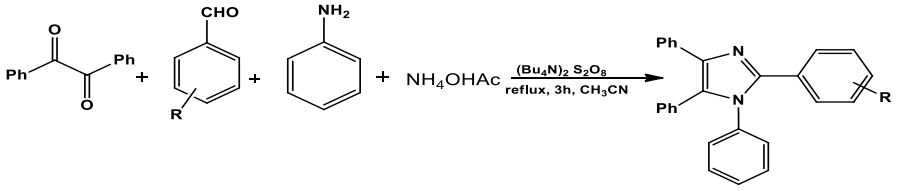
[a]Reaction conditions:benzil (**1a**, 10 mmol), aldehyde (**2a**, 10 mmol), aniline (**3a**, 10 mmol), *N* source (**4a**, 20 mmol), 20 mol% $(Bu_4N)_2S_2O_8$ at 65 °C for ~ 3 h

[b]Isolated and unoptimized yields

[c]Reaction at R. T

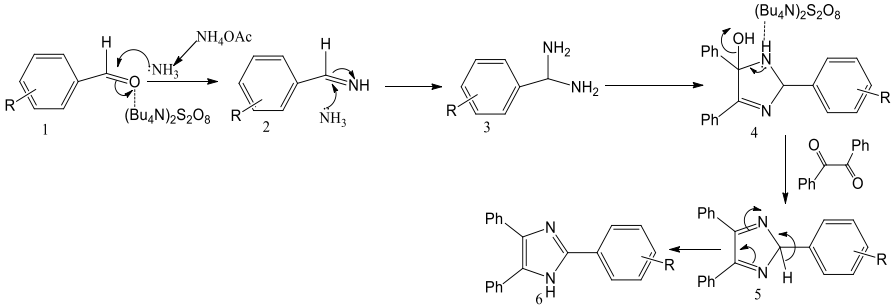
Table 4 Recyclability studies of the catalyst $[(n\text{-}Bu_4N)_2S_2O_8]$

S. no	Cycle no	Yield (%)
1	1	85
2	2	84
3	3	80

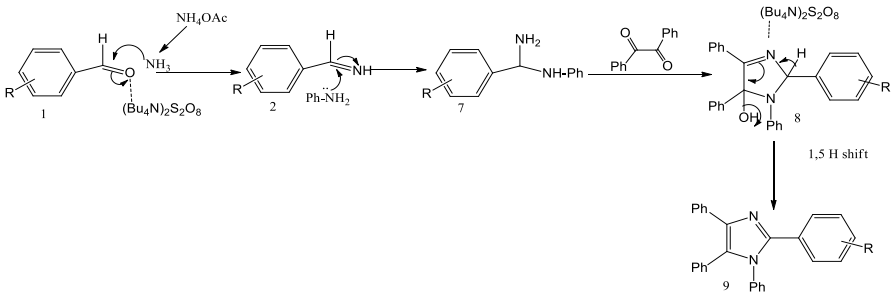


Scheme 2 Synthesis of 2,3,4,5-tetrasubstituted imidazoles

intermediate (2). The intermediate (2) gets converted into diamine (3) [51] by reacting with another ammonia molecule. The Nucleophilic reaction of compound (3) with protonated benzil creates intermediate (4) [52]. After that, intermediate (4) gets converted into (5) [53] by loss of water in the presence of catalyst, which further undergoes intermolecular hydrogen shift (1,5 shift) to afford the corresponding imidazoles (6). Tetra substituted imidazoles (9) were also synthesized in the same



Scheme 3 Plausible mechanism for the synthesis of tri aryl imidazoles



Scheme 4 Plausible mechanism for the synthesis of tetra aryl Imidazoles

methodologies by changing the amine source. Here; instead of ammonium acetate, aromatic amine is employed.

Experimental section

General procedure for the synthesis of bis (tetrabutylammonium) peroxy disulfate

Bis (tetrabutylammonium) peroxydisulfate is commercially available, but it can easily be prepared by simple extraction of tetrabutylammonium hydrogen sulfate (10.6 g, 32.0 mmol) and potassium per sulfate (4.35 g, 16.0 mmol) were dissolved in 70 mL of distilled Water and the solution was stirred for 30 min at room temperature. The solution was extracted with dichloro methane (3 × 10 mL), and the combined organic layers were washed with distilled water (2 × 15 mL), dried over anhydrous Na_2SO_4, and filtered. Evaporation of the organic solvent through vacuo and subsequent drying under high vacuum gave the desired product as a white solid in 95% yield. M.p118–120 °C.

General procedure for the synthesis of 2,4,5-triarylimidazoles (4a–4o)

To the stirred solution of acetonitrile (10 mL), substituted aldehydes (10 mmol) and bis(tetra butyl ammonium) peroxydisulfate (0.034 g, 20 mol%) were added and stirred for 10 min. To this ammonium acetate (0.76 g, 10 mmol) followed by 1,2-diketone (2.1 g, 10 mmol) was added, after which the reaction mixture was heated at 60–65 °C until completion of the reaction as indicated by TLC.The reaction mixture was cooled to the room temperature and the solvent was removed by rotary evaporator. Reaction progress was monitored by TLC. After completion of the reaction, the product was filtered. The residue was washed with ethyl acetate. The ethyl acetate was evaporated under vacuum and the obtained solid was purified by recrystallization process in ethyl acetate and *n*-hexane.

4,5-diphenyl-2-(p-tolyl)-1H-imidazole (4a)

M.P: 229–231 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.77 (d, $J = 8.1$ Hz, 2H, Ar–H), 7.52 (d, $J = 7.2$ Hz, 4H, Ar–H), 7.36–7.18 (m, 8H, Ar–H), 2.38 (s, 3H, Ar–CH_3).^{13}C NMR (125 MHz, $CDCl_3$)δ 146.2, 138.7, 132.8, 129.5, 128.4, 127.7, 127.0, 125.2, 21.3 IR (υ, neat)3021, 2961, 2925, 1677, 1582, 1216, 771 cm^{-1}MS (ESI) *m/z*311 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{22}H_{19}N_2$ 311.1543, found: 311.1553.

2(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (4b)

M.P: 227–228 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.89–7.79 (m, 2H, Ar–H), 7.54 (d, $J = 13.4$ Hz, 4H, Ar–H), 7.40–7.27 (m, 6H, Ar–H), 7.03–6.92 (m, 2H, Ar–H), 3.86 (s, 3H, Ar–H–OCH_3).δ 160.2, 146.0, 132.4, 128.6, 127.8, 127.4, 126.8, 122.5, 114.3, 55.4.3057, 2924, 2801, 1611, 1492, 1249, 1219, 771. cm^{-1}MS (ESI) *m/z*327 $[M+H]^+$calcd: For $C_{22}H_{19}N_2O$ 327.1505, found: 327.1500.

2-(4-bromophenyl)-4,5-diphenyl-1H-imidazole (4c)

M.P:265–266 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.89 (d, $J = 8.5$ Hz, 2H, Ar–H), 7.41 (t, $J = 7.2$ Hz, 6H, Ar–H), 7.2–7.08 (m, 6H, Ar–H).^{13}C NMR (125 MHz, $CDCl_3$)δ 144.8, 131.1, 129.2, 127.9, 127.7, 126.7, 121.5. IR (υ, neat) 3061, 2920, 2851, 1484, 1463, 1219, 970, 771 cm^{-1},MS (ESI) *m/z*375 $[M+H]^+$,HRMS (ESI) $[M+H]^+$ calcd: For $C_{21}H_{16}N_2Br$ 375.0491, Found: 375.0513.

4,5-diphenyl-2-(thiophen-2-yl)-1H-imidazole (4d)

M.P:255–257 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.52 (d, $J = 8.7$ Hz, 4H, Ar–H), 7.46–7.43 (m, 1H, Ar–H), 7.36–7.27 (m, 7H, Ar–H), 7.09 (dd, $J = 5.0$, 3.7 Hz, 1H, Ar–H).^{13}C NMR (125 MHz, $CDCl_3$)δ δ 141.6, 133.7, 127.7, 127.5, 127.0, 126.5, 124.8, 123.7 IR (υ, neat)2955, 2920, 2851, 1710, 1645, 1490, 1219, 772 cm^{-1}MS (ESI) *m/z*303 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{19}H_{15}N_2S$ 303.0964, Found:303.0958.

3(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (4e)

M.P: 259–260 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.89–7.84 (m, 2H, Ar–H), 7.54 (d, $J = 7.9$ Hz, 4H, Ar–H), 7.45–7.40 (m, 2H, Ar–H), 7.38–7.29 (m, 6H, Ar–H)..^{13}C NMR (125 MHz,$CDCl_3$)δ 148.5, 148.1, 147.2, 147.1, 146.0 IR (υ, neat)2922, 2850, 1484, 1433, 1219, 772 cm^{-1}MS (ESI) *m/z*331 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{21}H_{16}ClN_2$ 331.1007, Found: 331.1003.

2(2,4-dimethoxyphenyl)-4,5-diphenyl-1H-imidazole (4f)

M.P:230–231 ºC, ^{1}HNMR (500 MHz, $CDCl_3$) δ 8.38 (d, $J = 8.7$ Hz, 1H, Ar–H), 7.69–7.49 (m, 4H, Ar–H), 7.46–7.15 (m, 6H, Ar–H), 6.65 (dd, $J = 8.7$, 2.3 Hz, 1H, Ar–H), 6.56 (d, $J = 2.2$ Hz, 1H, Ar–H), 3.99 (s, 3H, Ar–OCH_3), 3.85 (s, 3H, Ar–OCH_3).^{13}C NMR (125 MHz, $CDCl_3$)δδ 161.1, 156.9, 144.2, 133.3, 129.7, 128.6, 127.8, 127.1, 111.4, 105.8, 98.8, 55.9, 55.5.IR (υ, neat)3434, 2924, 2852, 1611, 1584, 1462,12.7,1160, 1027, 747.cm^{-1}MS(ESI) *m/z*357 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{23}H_{21}O_2N_2$ 357.1597, Found: 357.1614.

2,4,5-triphenyl-1H-imidazole (4g)

M.P: 272–272 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.92 (d, $J = 7.0$ Hz, 2H, Ar–H), 7.57 (d, $J = 6.9$ Hz, 4H, Ar–H), 7.52–7.28 (m, 9H, Ar–H). (m, 6H, Ar–H).^{13}C NMR (125 MHz, $CDCl_3$) δ 129.8, 128.9, 128.6, 127.8, 127.5, 125.2 IR (υ, neat)3031, 2917, 2311, 1458, 1219, 771 cm^{-1}MS (ESI) *m/z*297 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{21}H_{17}N_2$ 297.1386, Found: 297.1404.

3(4-nitrophenyl)-4,5-diphenyl-1H-imidazole (4h)

M.P:240–242 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 8.29 (d, $J = 8.9$ Hz, 1H, Ar–H), 8.08 (d, $J = 9.0$ Hz, 1H, Ar–H), 7.56 (d, $J = 6.3$ Hz, 1H, Ar–H), 7.41–7.30 (m, 1H, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$)δ 146.4, 143.6, 136.2, 128.0, 125.4, 123.6. IR (υ, neat)3432, 2987, 2927, 2252, 1516, 1339, 1051, 1006, 743 cm^{-1}MS (ESI) *m/z*342 $[M+H]^+$

4(4,5-diphenyl-1H-imidazol-2-yl)-N,N-dimethyl aniline (4i)

M.P: 258–259 °C,^{1}HNMR (500 MHz, $CDCl_3$) δ 7.81 (d, $J = 7.5$ Hz, 2H, Ar–H), 7.54 (d, $J = 6.3$ Hz, 4H, Ar–H), 7.38–7.28 (m, 6H, Ar–H), 6.72 (d, $J = 8.6$ Hz, 2H, Ar–H), 3.11–2.91 (m, 6H, Ar–H) ^{13}C NMR (125 MHz, $CDCl_3$)δ 171.1, 150.7, 146.7, 132.4, 131.4, 129.7, 128.4, 127.8, 127.2, 126.6, 121.9, 112.0, 40.2. IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746 cm^{-1}MS (ESI) *m/z*340 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{23}H_{21}N_3$ 340.1814, Found: 340.1826.

2-(2-bromo-6-methoxyphenyl)-4,5-diphenyl-1H-imidazole (4j)

M.P:186–187 °C,^{1}HNMR (500 MHz, $CDCl_3$) δ 8.61 (d, $J = 2.6$ Hz, 1H, Ar–H), 7.74–7.48 (m, 4H, Ar–H), 7.47–7.27 (m, 7H, Ar–H), 6.89 (dd, $J = 8.9$, 2.3 Hz, 1H, Ar–H), 4.02 (s, 3H, $–OCH_3$). ^{13}C NMR (125 MHz, $CDCl_3$)δ 154.6, 142.5, 138.2, 137.2, 135.8, 131.8, 130.8, 128.6, 127.7, 119.9, 114.3, 112.9, 56.2. IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746 cm^{-1}MS (ESI) *m/z*405 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{22}H_{18}ON_2Br$ 405.0597, Found: 405.0616.$cm^{-1.}$

2(4,5-diphenyl-1H-imidazol-2-yl)phenol (4k)

M.P:204–205 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 12.3 (brs, 1H, Ar–H), 8.02–7.84 (m, 3H, Ar–H), 7.65–7.36 (m, 7H, Ar–H), 7.29–7.15 (m, 4H, Ar–H), 4.38 (brs, 1H, –OH). ^{13}C NMR (125 MHz, $CDCl_3$)δ δ 147.8, 141.4, 134.6, 132.1, 131.2, 129.5, 128.7, 128.0, 127.7, 125.2. 124.1. IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746 cm^{-1}MS (ESI) *m/z*313 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For$C_{21}H_{17}ON_2$ 313.1335, Found: 313.1352.

2-(2-nitrophenyl)-4,5-diphenyl-1H-imidazole (4m)

M.P:232–234 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 8.01–7.95 (m, 2H, Ar–H), 7.81–7.77 (m, 1H, Ar–H), 7.67 (ddd, $J = 8.7$, 2.5, 1.3 Hz, 1H, Ar–H), 7.61–7.48 (m, 6H, Ar–H), 7.39–7.28 (m, 4H, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$)δ 134.8, 132.9, 132.0, 129.8, 129.0, 128.6, 128.5, 127.8, 127.6, 126.7. IR (υ, neat)3419, 3029, 2921, 2852, 1668, 1645, 1530, 1452, 1347, 1025, 696 cm^{-1}MS (ESI) *m/z*342 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{21}H_{16}O_2N_3$ 342.1237, Found: 342.1254.

4-(4,5-diphenyl-1H-imidazol-2-yl)phenol (4n)

M.P:242–243 °C, ^{1}HNMR (500 MHz, $CDCl_3$)δ δ 7.76 (d, $J = 8.6$ Hz, 2H, Ar–H), 7.40 (d, $J = 6.8$ Hz, 4H, Ar–H), 7.23 –7.05 (m, 6H, Ar–H), 6.76 (t, $J = 11.1$ Hz, 2H, Ar–H), 6.05 (brs, 1H, Ar–OH) ^{13}C NMR (125 MHz, $CDCl_3$)δ δ 147.8, 141.4, 134.6, 132.1, 129.5, 128.7, 128.2, 128.0, 127.6, 127.7, 124.0.IR(υ,neat)3417, 2922, 2853, 2254, 1659, 1457, 1023, 770 cm^{-1}MS (ESI) *m/z*313 $[M+H]^+$ HRMS (ESI) $[M+H]^+$ calcd: For $C_{21}H_{17}ON_2$ 313.1335, Found: 313.1351.

3(4-methoxyphenyl)-1,4,5-triphenyl-1H-imidazole (5a)

M.P: 173–174 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ δ 7.64–7.55 (m, 2H, Ar–H), 7.40–7.31 (m, 2H, Ar–H), 7.30–7.15 (m, 9H, Ar–H), 7.13–7.09 (m, 2H, Ar–H), 7.06–6.99 (m, 2H, Ar–H), 6.80–6.72 (m, 2H, Ar–H), 3.77 (s, 3H, $Ar–OCH_3$). ^{13}C NMR (125 MHz, $CDCl_3$)δ δ 159.5, 146.8, 137.9, 137.2, 134.4, 131.0, 130.7, 130.4, 130.2, 129.0, 128.4, 128.2, 128.0, 127.8, 127.3, 126.4, 123.0, 113.5, 55.1. IR (υ, neat)2955, 2920, 2851, 1710, 1645, 1490, 1219, 772 cm^{-1}MS (ESI) *m/z* 403 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{28}H_{23}ON_2$ 403.1804, found 403.1822.

1,2,4,5-tetraphenyl-1H-imidazole (5b)

M.P:220–221 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.63–7.57 (m, 2H, Ar–H), 7.46–7.39 (m, 2H, Ar–H), 7.31 –7.17 (m,12H, Ar–H), 7.15–7.09 (m, 2H, Ar–H), 7.07–7.01 (m, 2H, Ar–H). ^{13}C NMR (125 MHz, $CDCl_3$)δ 131.1, 129.0, 128.9, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.3, 126.5 IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746. cm^{-1}MS (ESI) *m/z* 373 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{27}H_{21}N_2$ 373.16993, found 373.1718.

4-(1,4,5-triphenyl-1H-imidazol-2-yl)phenol (5c)

M.P:282–283 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 7.84–7.61 (m, 1H, Ar–H), 7.58–7.27 (m, 6H, Ar–H), 7.26–6.95 (m, 10H, Ar–H), 6.74–6.49 (m, 2H, Ar–H).. ^{13}C NMR (125 MHz, $CDCl_3$)δ 156.4, 145.7, 136.7, 135.9, 135.7, 133.3, 129.7, 129.3, 128.8, 127.7, 127.2, 127.0, 126.7, 125.7, 125.0, 120.1, 113.8 IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746 cm^{-1}MS (ESI) *m/z* 389 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{27}H_{21}ON_2$ 389.1648, found 389.1666.

1,4,5-triphenyl-2-(p-tolyl)-1H-imidazole (5d)

M.P:190–191 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ7.59 (d, $J=7.3$ Hz, 2H, Ar–H), 7.31 (d, $J=8.1$ Hz, 2H, Ar–H), 7.27–7.16 (m, 9H, Ar–H), 7.14–7.09 (m, 2H, Ar–H), 7.06–7.01 (m, 4H, Ar–H) ^{13}C NMR (125 MHz, $CDCl_3$)δ 147.0, 138.0, 137.1, 134.4, 131.0, 130.7, 130.6, 128.9, 128.4, 128.2, 128.0, 127.8, 127.6, 127.3, 126.4. IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746. cm^{-1}MS (ESI) *m/z* 387 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{28}H_{23}N_2$ 387.1855, found 387.1873.

N,N-dimethyl-4-(1,4,5-triphenyl-1H-imidazol-2-yl)aniline (5e)

M.P:215–216 °C, ^{1}HNMR (500 MHz, $CDCl_3$) δ 8.10 (dd, $J=8.3$, 1.2 Hz, 1H, Ar–H), 7.63–7.54 (m, 2H, Ar–H), 7.45 (t, $J=7.7$ Hz, 1H, Ar–H), 7.35–7.14 (m, 9H, Ar–H), 7.14–7.02 (m, 4H, Ar–H), 6.60–6.52 (m, 2H, Ar–H), 2.91 (s, 6H, NMe_3); ^{13}C NMR (125 MHz, $CDCl_3$)δ 170.6, 150.1, 147.6, 137.5, 137.3, 134.2, 1331, 131.1, 130.6, 130.0, 129.9, 129.9, 129.5, 128.2, 128.1, 128.0, 127.6, 126.4, 117.7, 111.4, 40.1. IR (υ, neat)3060, 3014, 2925, 1664, 1609, 1493, 1214, 746 cm^{-1}MS (ESI) *m/z* 416 $[M+H]^+$HRMS (ESI) $[M+H]^+$ calcd: For $C_{29}H_{26}N_3$ 416.2121, found 416.21302.

Conclusion

In summary, we have demonstrated one pot synthesis of tri and tetra substituted imidazoles using a versatile, efficient and ecofriendly tetra butyl ammonium peroxy disulfate as a metal free catalyst. The current investigation involving different mole ratio of catalysts and different solvents were used. Finally 20% mole ratio of TBAPDS was proven excellent efficiency under acetonitrile as solvent (96%). The

mechanistic studies aided in optimizing reaction conditions. Thus, one pot multicomponent reaction proceeds effectively and quickly with the formation of tri and tetra substituted imidazoles with high-to-excellent yields. The catalyst is recyclable with no significant loss in catalytic efficiency. This catalytic system described here is a good complement to previously reported protocols, due to its low cost, reusability, simple workup procedure, and extensive applicability.

This protocol is generic, highly attractive in terms of clean reaction profile, atom economy, and it will undoubtedly offer value to the growing area of organic synthesis, we are optimistic that, with this approach, we will be able to develop the biologically relevant heterocyclic ring system more efficiently.

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Author's contribution NR: Investigation, Validation, Writing—original draft, Methodology. KG: Conceptualization, Validation, Writing—original draft, Supervision, Writing review &editing. RK: Datacuration, Resources, Validation & review.

Declarations

Conflict of interest We declare no conflict of interest.

Ethical Approval Not applicable.

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Authors and Affiliations

Ramesh Nukala[1] · Kumaraswamy Gullapelli[2] · Ramaiah Konakanchi[3]

✉ Ramesh Nukala
nramesh.reddy73@gmail.com

✉ Kumaraswamy Gullapelli
kumargullapelli001@gmail.com

[1] OSPC Division, Indian Institute of Chemical Technology, Hyderabad 500607, India

[2] Department of Chemistry, Mahatma Gandhi Institute of Technology, Hyderabad 500075, India

[3] Department of Humanities and Sciences (Chemistry), VNR Vignana Jyothi Institute of Engineering and Technology, Hyderabad 500090, India