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Research Article

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A New Method for Synthesis of 2, 4, 5-Triaryl-1H-Imidazoles by Using L-Proline-NO_3 (Ionic Liquid) as catalyst

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Abstract: The L-Proline nitrate is a homogeneous, green catalyst. Excellent catalytic properties Activity for synthesizing 2, 4, 5-triaryl substituted imidazole using a mixture of aromatic aldehyde, benzyl or benzoin, and ammonium acetate in ethyl alcohol as a solvent.

Keywords: L-Proline nitrate, Aromatic aldehyde, Benzil or benzoin, Ammonium acetate, Ethyl alcohol, 2, 4, 5-Triaryl substituted imidazole.

INTRODUCTION

Imidazole is a Planner 5-membered heterocyclic ring containing 3 carbon atoms and 2 nitrogen atoms, with N in the 1st and 3rd positions of the ring. The imidazole ring is part of several important natural products such as purines, histamines, histidines and nucleic acids. As a polar and ionizable aromatic compound, it is used as a drug to improve the pharmacokinetic properties of lead molecules and therefore to optimize the proposed solubility and bioavailability parameters of poorly soluble lead molecules. Imidazole derivatives have occupy a unique position in the field of medicinal chemistry. A reaction that combines two or more ingredients in one process to

produce a product that is part of all the ingredients [1]. 2,4,5 Triphenylimidazoles have a wide range of biological activities and their use in synthetic chemistry.

The imidazole ring system is one of the most important substructures found in many natural products and pharmacologically active compounds, so it is a fungicide, herbicide, plant growth regulator, and some kinase inhibitors. It can be used as an antibacterial agent [2,3], Glucagon receptors [4] and antitumors [5]. In recent years, substituted imidazoles have been widely used in ionic liquids [6] and are undergoing a new "green chemistry"approach. They are used as photosensitive compounds in photography [7].

Due to its great importance, many synthetic strategies have been developed, including hetero cope rearrangements[8]and the four-component condensation of aryl glyoxal, primary amines, carboxylic acids, and isocyanides on royal resins [9]. .

These have been reported in the literature on the synthesis of 2, 4, 5-trisubstituted imidazoles induced by zeolite HY [10], ionic liquids [11], itterbium triflate [12], silica-sulfuric acid [13]: Is part of the method. , $InCl_3$ was catalyzed. $3H_2O$ [14], L proline [15], DABCO [16], $SbCl_3$ [17], Rochelle salt [18].

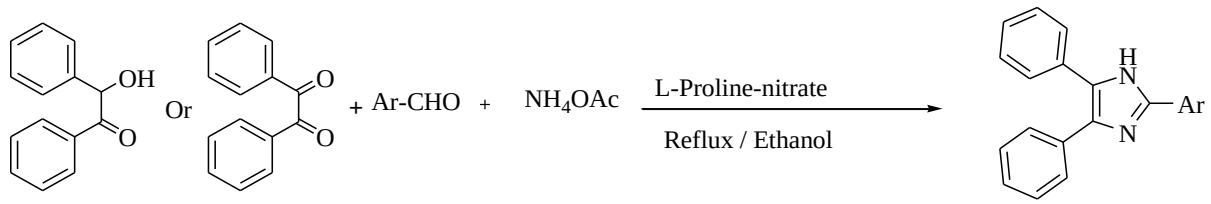
However, most of the reported methods have certain restrictions, such as expensive catalysts, solvent, toxicity, restrictions on large scale application important product separation processes, difficulty in recovering high boiling solvent, excessive amounts of catalysts. Therefore, it would be highly desirable to develop a simple and efficient method for synthesizing 2,4,5-triaryl-1H-imidazole derivatives.

Proline is a proteinogenic amino acid, but it does not contain the amino group -NH, but it is a secondary amine. Secondary amine nitrogen exists in the form of NH2 + protonated under biological conditions, and the carboxyl group exists in the form of deprotonated -COO-. The "side chain" of the alpha carbon connects to nitrogen to form a pyrrolidine loop and is classified as an aliphatic amino acid. It is not essential for humans. That is, the body can synthesize it from the non-essential amino acid glutamic acid.

Proline is naturally present in many foods, and Richard Willstätter first isolated proline in 1900. They obtained the amino acid during the study of N-methyl proline and reacted the sodium salt of diethyl malonate with 1, 3-dibromopropane to synthesize proline. Next, Emil Fischer isolated proline from the degradation products of casein and the γ-phthalimide propylmalonic acid ester and announced the synthesis of proline from the phthalimide propylmalonic acid ester. The name proline comes from one of its constituents, pyrrolidine. Proline is the only proteinogenic amino acid that is a secondary amine because the nitrogen atom is attached to both the alpha carbon and the chain of three carbons, which together form a five-membered ring. Given this activity of L-proline Nitrate, we have described an efficient method of using L-proline Nitrate as an efficient catalyst for the synthesis of 2, 4,5triaryl1HImidazoles.

2. RESULTS AND DISCUSSION

We are continuing research to develop new synthetic methods. Here, we report an efficient synthetic method for synthesizing 2, 4, 5-triarylimidazole from benzyl / benzoin, aldehyde, and ammonium acetate in the presence of L-proline nitrate (Scheme 1 representative). A standard model reaction for investigating the reaction of 4-chlorobenzaldehyde (2a) as an aldehyde, compound 1benzyl and ammonium acetate (3) in the presence of L-proline nitrate in ethanol, and optimizing the reaction conditions. I considered it.



1 **2(a-l)** **3** **4(a-l)**

To determine the effect of the solvent on the model response, the solvent was tested and the results obtained are shown in Table 1. At reflux temperature, various solvents such as acetonitrile, chloroform, dioxane, methyl alcohol, water, water: ethyl alcohol (1: 1), ethyl alcohol were screened.

Table1: Solvent screening for the synthesis of 4g[a]

Sr No.	Solvent	Time (hr)	Yield [b]
1	Acetonitrile,	6	30
2	Dioxane,	6	21
3	Chloroform	6	28
4	Methyl alcohol	6	80
5	Water	6	24
6	Water: ethyl alcohol (1:1)	6	60
7	Ethyl alcohol	6	90

[a] Reaction conditions: 1 (1 mmol), 2a (1 mmol), 3 (2 mmol), L-Proline nitrate at reflux temperature. [b]Isolated yields.

The Model reactions at 2.5, 5, 7.5, 10, 12.5 mol % L-Proline-NO_3 in ethyl alcohol at reflux temperature were investigated to determine the exact catalyst concentration. The products were obtained in 24, 50, 80, 90 and 92%, with respective yield. This shows that the reaction can be accelerated with only 10 mol % of L-Proline-NO_3 **(Table2).**

Table 2: Effect on catalyst concentration[a]

Entry	Concentration of catalyst in Mole (%)	Time (hr)	Yield [b]
1	2.5	8	24
2	5	8	50
3	7.5	8	80
4	10	5	90
5	12.5	5	92

[a]Reaction conditions: 1 (1 mmol), 2a (1 mmol), 3 (2 mmol) and L-Proline nitrate at reflux temperature. [b]Isolated yields.

Using optimized conditions, we extended our study to a wide range of arylaldehydes, including either EW or ED substituents, and investigated the scope of this method **(Table 3).** However, the electronic properties of the aryl substituents in the aldehyde did not have a strong effect on yield. As described above, the electron-withdrawing substituted aromatic aldehyde and the aromatic aldehyde having an electron donating group on the aromatic ring were converted cleanly under the

reaction conditions, and the corresponding product was produced in a good yield. The reaction is equally good with heteroaromatic aldehydes, with good product yields **(Table 3)** compound 4,b,g,I& k.

Table 3: Synthesis of 2, 4, 5, triaryl-substituted imidazole catalyzed by L-proline nitrate.

Entry	Ar-	Time (h)		Yield (%)		M.P °C	
		Benzil	Benzoin	Benzil	Benzoin	Found	Literature
4a	C_6H_5	5	6	92	90	274	272-273 [18]
4b	4-OHC_6H_4	6	7	94	92	270	269-270 [19]
4c	3-OCH_3,4-OHC_6H_4	5	6.5	90	88	255	255-256 [19]
4d	4-$OCH_3C_6H_4$	4.3	7.5	82	80	226	227-228 [18]
4e	4-$NO_2C_6H_4$	6.3	8.0	90	86	232	231-232 [19]
4f	4-$CH_3C_6H_4$	5.3	6.2	92	87	228	226-227 [18]
4g	4-ClC_6H_4	5	6.5	94	90	270	270-271 [19]
4h	4$(CH_3)_2NC_6H_4$	4.3	5.3	92	89	259	260-261 [18]
4i	4-FC_6H_4	4.0	6.0	94	92	191	189-190 [19]
4j	2-ClC_6H_4	4.5	6.5	92	89	194	194-195 [15]
4k	C_4H_3O	5	6.0	94	91	200	198-200 [19]
4l	C_4H_3S	6.5	8.5	92	90	261	259-260 [19]

MATERIAL AND METHODS

All The chemicals used in this method were obtained from Merck without Purification. Melting points had been determined in an open capillary tube and are uncorrected. The development of the reactions were monitored by TLC. ^{1}H NMR spectra were recorded on a 400 MHz BRUKER spectrometer in DMSO as a solvent at Solapur University.

General Procedure for the synthesis of 2, 4, 5-triarylimidazoles (4a-l): Benzil or benzoin (1 mmol), aldehyde (1 mmol), ammonium acetate (2 mmol), and L-Proline-NO_3 in ethyl alcohol (15 ml) stirred and refluxed at temperature for 4 to 9 h. The development of the reaction was monitored by TLC. After reaction completion, recrystallized from ethyl alcohol to get the Pure product 4(a- l).

Spectral data for all synthetic compounds
2,4,5-triphenyl-1*H*-imidazole (4a): IR (KBr, cm^{-1}):3052, 1472, 1452, 1120, 698. ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 12.40 (brs, 1H, NH), 7.31–8.14(m, 15H, Ar-H). EIMS (m/z, %): 297 (M+1). Elemental analysis.,$C_{21}H_{16}N_2$: C, 85.11; H, 5.44; N, 9.45. Found: C, 85.02; H, 5.42; N, 9.42.
4-(4,5-diphenyl-1*H*-imidazol-2-yl) phenol (4b): IR (KBr, cm-1): 3265, 3038,1689, 1602, 1491, 689. ^{1}H NMR (400 MHz, DMSO-d6, δ ppm): 12.37 (s, 1H, NH), 9.62 (s, 1H, OH), 7.87 (d, 2H, J = 8.4 Hz, Ar-H), 7.55 (d, 2H, J = 7.6 Hz, Ar-H), 7.66 (m, 10H, Ph), EIMS (m/z, %): 313 (M^{+1}) Elemental analysis. $C_{21}H_{16}N_2O$: C, 80.75; H, 5.16; N, 8.97. Found: C, 80.61; H,5.17; N, 8.19.

2-(4-methoxyphenyl)-4,5-diphenyl-1*H*-imidazole(4d): IR (KBr, cm^{-1}): 3028, 1619, 1492, 1254, 1030, 693. ^{1}H-NMR (400 MHz, DMSO-d_6, δ ppm): 12.50 (brs, 1H, NH), 7.91 (d, 2H, J =8.8 Hz, Ar), 7.31-7.82 (m, 10H, Ph), 3.70 (s, 3H, CH_3). EIMS (m/z, %): 327 (M^{+1}). Elemental analysis. $C_{22}H_{18}N_2O$: C, 80.96; H, 5.56; N, 8.58. Found: C,80.89; H,5.39; N, 8.42.

2-(4-Nitrophenyl)-4,5-diphenyl-1*H*-imidazole (4e): FTIR (KBr, cm-1): 3395, 1580, 1562, 1335 cm-1 ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 11.91 (brs N-H), 7.16-7.82 (m, 10H, Ph), 7.91-8.35 (d, 2H, J =10 Hz, Ar) 7.62-8.10 (d, 2H, J= 10Hz, Ar), EIMS (m/z, %): 342 (M^{+1}). Elemental analysis. $C_{21}H_{15}N_2O$: C,73.89; H,4.43; N, 12.31. Found: C, 73.19; H,4.21; N, 12.01.

2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole (4g):IR (KBr, cm-1): 3044, 1620, 1445, 1070, 762, 693. ^{1}H`NMR (400 MHz, DMSO-d_6, δ ppm): 12.68 (brs, 1H, NH), 8.07 (d, 2 H, J = 8.4 Hz, Ar-H),8.34 (d, 2H, J = 8.4 Hz, Ar-H), 7.20–7.52 (m, 10H, Ar-H). ES-MS (m/z): 331 (M + 1). Elemental analysis. $C_{21}H_{15}N_2Cl$: C, 76.24; H, 4.57; N, 8.47. Found: C, 76.10; H, 4.39; N, 8.46.

N, N-Dimethyl-4-(4,5-diphenyl-1*H*-imidazol-2-yl)benzene amine(4h): FTIR (KBr, cm^{-1}): 3442, 1624, 1556. 1H NMR (400 MHz, DMSO-d6, δ, ppm): 12.11 (1H, brs, NH), 7.70 (s 6H,- CH_3), 2.30 (S H, OH), 7.50 (d, 2 H, J = 8.4 Hz, Ar-H), 7.13 (d, 2 H, J = 8.4 Hz, Ar-H) 7.50-7.84 (m, 10 H, Ar-H) ES-MS (m/z): 340 (M^{+1}). $C_{23}H_{21}N_3$: C,81.38; H,6.24; N, 12.38. Found: C, 81.18; H,6.10; N, 12.11.

2-(4-fluorophenyl)-4,5-diphenyl-1*H*-imidazole (4i):
IR (KBr, cm^{-1}): 3021, 1492, 1220, 828, 757, 686. ^{1}H-NMR (400 MHz, DMSO-d6, δ ppm): 12.30 (brs, 1H,NH), 7.18-7.50 (m, 10H, Ph), 7.02 (d, 2H, J =8.4 Hz, Ar), 7.18 (d, 2H, J =8.4 Hz, Ar). EIMS (m/z, %):315 (M+1). Elemental analysis. $C_{21}H_{15}N_2F$: C, 80.24; H, 4.81; N, 8.91,. Found: C,80.01; H,4.19; N, 8.47.

2-(2-chlorophenyl)-4,5-diphenyl-1*H*-imidazole (4j): IR (KBr, cm-1): 3424, 3032, 1620, 1513, 1497. ^{1}HNMR (400 MHz, DMSO-d_6, δ ppm): 12.40 (brs, 1H, NH), 7.20–7.40 (m, 14H, Ar-H). ES-MS (m/z): 331 (M + 1). Elemental analysis., $C_{21}H_{15}N_2Cl$: C, 76.24; H, 4.57; N, 8.47. Found: C, 76.14; H, 4.42; N, 8.41.

2-(Furan-2-yl)-4,5-diphenyl-1*H*-imidazole(4k): FTIR (KBr, cm^{-1}): 3322, 2996, 1668, 1534, 1209 ^{1}H NMR (400 MHz, DMSO-d6, δ, ppm): 12.10 (brs, 1H, NH), 7.60–7.71 (m, 3H, Ar), 7.20–8.10 (m, 10H, Ar). EIMS (m/z, %): 287 (M^{+1}). Elemental analysis. $C_{19}H_{14}N_2O$: C,79.70; H, 4.93; N, 9.78. Found: C, 79.41; H,4.26; N, 9.52.

4,5-Diphenyl-2-(thiophen-2-yl)-1*H*-imidazole (4l): FTIR (KBr, cm^{-1}):3341, 2998, 1684, 1545 ^{1}H NMR (400 MHz, DMSO-d6, δ, ppm):12.10 (brs, 1H, NH), 7.63–7.72 (m, 3H, Ar), 7.10–8.11 (m, 10H, Ar). EIMS (m/z, %): 303 (M^{+1}). Elemental analysis. $C_{19}H_{14}N_2S$: C,75.47; H, 4.67; N, 9.26. Found: C, 75.40; H,4.19; N, 9.01.

CONCLUSIONS

We defined our experiment suggest a new route for promising synthesis of multisubstituted imidazoles under reflux conditions by using L-Proline- nitrate as a Catalyst. The above result describe environmentally benign methods, short reaction time, simple work up and high isolated product yield.

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