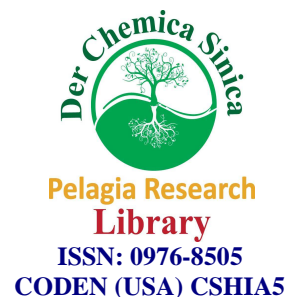




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Synthesis of 2,4,5-triaryl-1H-imidazoles using anhydrous Pb(OAc)₂ as a catalyst in C₂H₅OH

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ABSTRACT

A simple and versatile synthesis of 2,4,5-Triaryl-1H-imidazole derivatives is achieved by pathway of Multicomponent reaction involving cyclocondensation of 1,2-dicarbonyl compound, aromatic aldehyde and ammonium acetate as a source of ammonia in presence of anhydrous Lead acetate as a catalyst in ethyl alcohol. The remarkable features of this synthetic pathway are simple workup, short reaction time, high yields and use of anhydrous Pb(OAc)₂ as an effective catalyst.

Keywords: 2, 4, 5-Triaryl-1H-imidazole, Multicomponent reaction, anhydrous lead acetate, high yields, effective catalyst.

INTRODUCTION

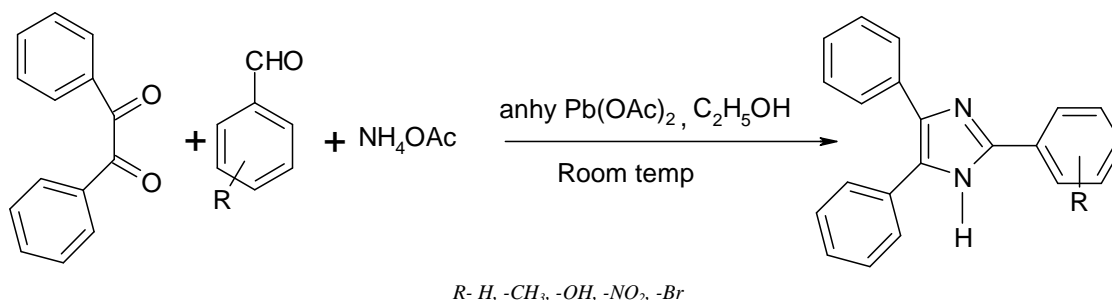
Multicomponent reactions (MCRs) have emerged as an important tool to synthesise complex and bioactive organic compounds by using simple and easily available materials.^[1,2,3] Further, MCRs are known to show high atom economy and selectivity during reaction.^[4,5]

The survey of related literature shows that organic compounds containing imidazole nucleus into their structure shows a wide range of biological activities. The derivatives of imidazole act as inhibitors of P38 MAP kinase^[6] and B-Raf kinase.^[7] They also act as herbicides,^[8] pesticides,^[9] glucagon receptors^[10] as well as anti-inflammatory,^[11] antitumor,^[12] and antithrombotic^[13] agents. Thus, substituted imidazoles including 2,4,5-Triaryl-1H-imidazoles constitutes a class of biologically active and hence commercially important heterocyclic compounds.

A number of methods for the synthesis of 2,4,5-Triaryl-1H-imidazoles have been formulated which involves use of sulfuric acid immobilized on silica Gel,^[14] KH₂PO₄,^[15] microwave irradiation(solvent and catalyst free),^[16] ionic liquid,^[17] ceric ammonium nitrate (CAN),^[18] oxalic acid,^[19] Eu(OTf)₃,^[20] [Hmim]HSO₄,^[21] ZrCl₄,^[22] Yb(OTf)₃,^[23] NiCl₂.6H₂O,^[24] sodium bisulfate,^[25] iodine,^[26] nano crystalline magnesium oxide,^[27] silica sulfuric acid,^[28] acetic acid,^[29] L-proline,^[30] PEG-400,^[31] Cu(TFA)₂,^[32] tetrabutyl ammonium bromide(TBAB),^[33] (NH₄)₆Mo₇O₂₄.4H₂O,^[34] InCl₃.6H₂O,^[35] Zr(acac)₄,^[36] anhydrous FePO₄,^[37] and uranyl nitrate supported on acidic alumina.^[38]

These reported methodologies suffers from one or other drawback such as harsh reaction condition, difficult work up procedure, long reaction time, poor yields, use of expensive and hazardous catalyst. In this regard, we would like

to report a method for the synthesis 2,4,5-Triaryl-1H-imidazoles which is simple, mild, involving use of cost effective and efficient catalyst. Also, it gives high yields of corresponding products.



Scheme1

MATERIALS AND METHODS

The reaction was monitored by TLC using 0.25 mm E-Merck silica gel plates, which were visualized in Iodine Chamber. Melting points were taken in open capillaries. ¹H NMR in d₆ on 300 MHz using TMS as an internal standard. Mass Spectra was recorded on Shimadzu GC-MS-QP-2010 model using Direct Injection Probe technique.

EXPERIMENTAL

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

A reaction mixture of benzil (1mmol), benzaldehyde (1mmol) and ammonium acetate (2mmol) was prepared by using C₂H₅OH as a solvent. In this catalytic amount of anhydrous Pb(OAc)₂ (0.1mmol) was added and reaction mixture was stirred magnetically. The progress of reaction was monitored by TLC. After the completion of reaction as indicated by TLC, reaction mixture was poured in water and solid was filtered. The obtained product was washed with water and further purified by recrystallization from hot ethanol. All the derivatives were characterized by IR and ¹HNMR.

Spectral analysis of selected 2, 4, 5-Triaryl-1H-imidazoles

Entry 2b. 2-p-tolyl-4, 5-diphenyl-1H-imidazole

¹HNMR (400 MHz, DMSO): δ = 2.33(s,3H), 7.19 (t,1H,J=7.3 Hz), 7.33 (t,4H,J=7.3Hz), 7.36 (t,1H, J=7.2Hz), 7.46 (t, 2H, J=7.3Hz), 7.50 (d, 2H, J=7.1Hz), 7.58 (d, 2H, J=7.7Hz), 8.00 (d,2H, J=8.1 Hz), 12.45 (br,1H) ppm
IR (KBr, cm⁻¹) = 3419,3029,1594,1500,1450,1126,1069,971,824,763,670.

Entry 8b. 2-(4-bromophenyl)-4,5-diphenyl-1H-imidazole

¹HNMR (400 MHz, DMSO): δ = 7.21 (t,1H,J=7.3Hz), 7.34 (t,2H,J=7.2Hz), 7.41(t,1H,J=7.9Hz), 7.42(t,2h,j=7.3Hz), 7.49-7.56 (m,6H), 8.10 (d,2H,J=7.1Hz), 12.83 (br,1H) ppm
IR (KBr, cm⁻¹) = 3442,3029,1600,1520,1490,1450,1430,1130,1070,827,690.

RESULTS AND DISCUSSION

The optimum condition for the synthesis of 2,4,5-Triaryl-1H-imidazole derivatives was established by considering a reaction between benzil, benzaldehyde and ammonium acetate as model reaction. It was performed in the presence of anhydrous Pb(OAc)₂ in C₂H₅OH as a catalyst

A proper solvent for the reaction was selected by investigating the effect of different solvents on reaction time and yield of product for model reaction. We observed that the reaction time was long and yield of the corresponding product was low when the reaction was performed in solvents of low polarity (Table 1, Entries 1 and 2). Even in CH₃CN the reaction time and yield were not satisfactory (Table 1, Entry 3). The reaction gave maximum yield of product in short time period when it was performed in polar solvent such as C₂H₅OH (Table1, Entry-4)

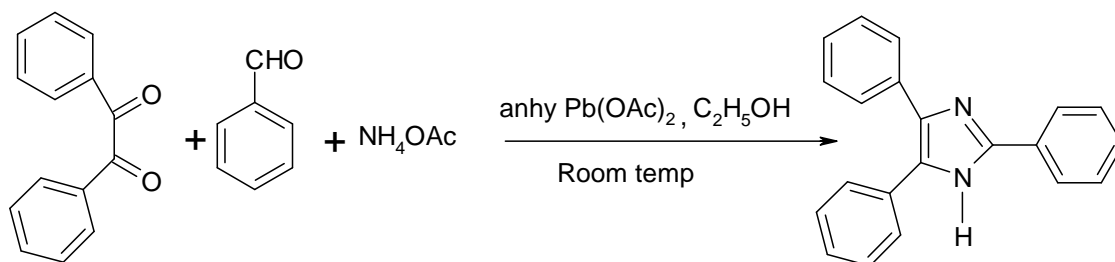


Table 1. Investigation of solvent effect for the synthesis of 2,4,5-Triaryl-1H-imidazole

Entry	Catalyst	Solvent	Time (min.)	Yield ^a (%)
1	anhydrous Pb(OAc) ₂	CHCl ₃	65	52
2	anhydrous Pb(OAc) ₂	CH ₂ Cl ₂	50	58
3	anhydrous Pb(OAc) ₂	CH ₃ CN	45	62
4	anhydrous Pb(OAc) ₂	C ₂ H ₅ OH	30	88

^aIsolated Yields

On the basis of results as shown in Table 1, C₂H₅OH was selected as the most appropriated solvent for **Scheme 1**.

The efficiency of anhydrous Pb(OAc)₂ as a catalyst was determined with respect to its amount to be loaded in reaction mixture. There was no improvement in yield with increment in loading amount of catalyst from 0.01 mmol to 0.05 mmol. A satisfactory yield in short reaction time was obtained with 0.1 mmol of catalyst. There was no appreciable improvement in yield even if loading amount was increased to 0.2 mmol.

Table 2. Investigation of catalytic effect of anhydr.Pb(OAc)₂ on synthesis of 2, 4, 5-Triaryl-1H-imidazoles

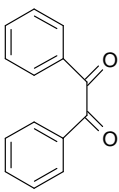
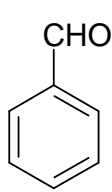
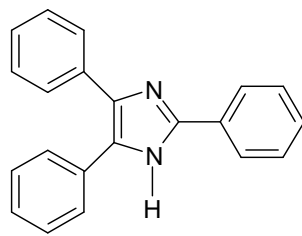
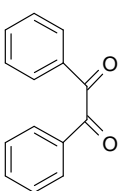
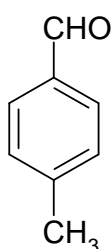
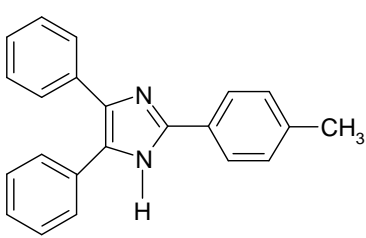
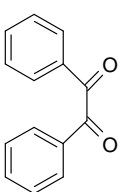
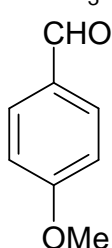
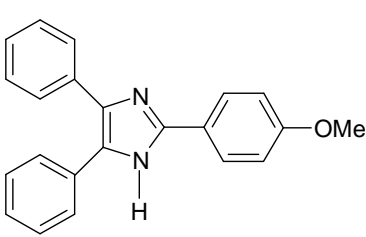
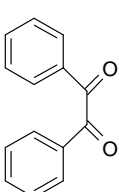
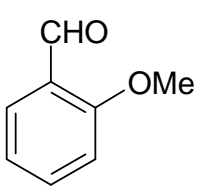
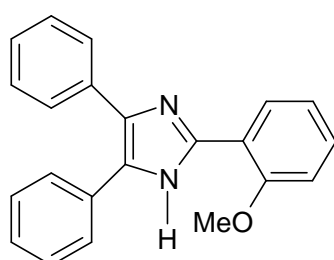
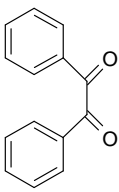
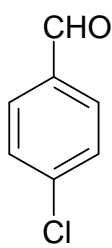
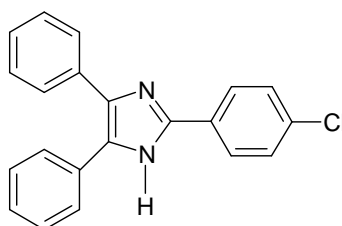
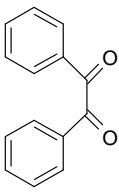
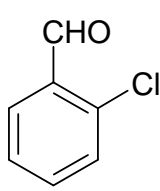
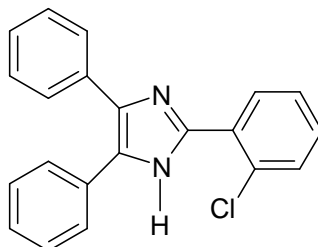
Entry	anhydrous Pb(OAc) ₂ (mmol)	Time (min.)	Yield ^b (%)
1	0.01	45	52
2	0.05	40	58
3	0.1	30	88
4	0.2	29	88

^bIsolated yields

Thus, the most appropriate loading amount for anhydrous Pb(OAc)₂ as a catalyst was found to be 0.1 mmol as per results summarized in Table 2.

Thus, 0.1 mmol anhydrous Pb(OAc)₂ as catalyst and C₂H₅OH as solvent was selected as the most appropriate reaction condition to synthesize 2,4,5-Triaryl-1H-imidazoles. The scope of **Scheme 1** was further investigated by reacting benzil with different aromatic aldehydes and ammonium acetate under appropriate condition thus established.

Table 3. Synthesis of 2,4,5-Triaryl-1H-imidazoles using anhydrous $\text{Pb}(\text{OAc})_2$ in $\text{C}_2\text{H}_5\text{OH}$ as catalyst

Entry	Benzil ^a	Aldehyde	Product ^b	Time (min.)	Yield ^c (%)
1				30	88
2				35	86
3				40	85
4				45	85
5				45	84
6				45	82

7				50	82
8				52	80
9				25	92
10				25	90

^aThe substrate was treated with aldehyde (1mmol) and ammonium acetate (2mmol) in presence of anhydrous $Pb(OAc)_2$ in C_2H_5OH as a catalyst.

^bAll products were identified by their IR and 1H NMR spectra.

^cIsolated Yields.

The above results have shown that all the three components reacted smoothly in **Scheme 1**, in presence of anhydrous $Pb(OAc)_2$ in C_2H_5OH as a catalyst and gave moderate to good yields of corresponding products (Table 3). Thus, anhydrous $Pb(OAc)_2$, a Lewis acid was proved to be an efficient catalyst to give desired products under mild conditions. Moreover, various aromatic aldehydes containing either electron donating or electron withdrawing substituents at different position worked well under present reaction condition (Table 3). This proved the wide scope and generality of the present protocol.

CONCLUSION

Thus, anhydrous $Pb(OAc)_2$ in C_2H_5OH is found to be an excellent catalyst for the three component, one pot synthesis of 2, 4, 5-Triaryl-1H-imidazoles. The catalyst and solvent are inexpensive, readily available and easy to handle materials. Different aromatic aldehydes react smoothly under present reaction condition giving satisfactory yields of the corresponding 2, 4, 5-Triaryl-1H-imidazole derivatives in short time period.

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