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ZINC ACETATE CATALYZED AN EFFICIENT SYNTHESIS OF 2,4,5-TRIPHENYL-1*H*-IMIDAZOLE DERIVATIVES UNDER SOLVENT-FREE CONDITION

V. P. Sondankar[a*], N. R. Rathod[a] and S. R. Bhusare[b]

[a]*Department of Chemistry, Phulsing Naik College, Pusad-445 216, MS, India*
[b]*Department of Chemistry, Dnyanopasak College, Parbhani-431 401, MS, India*
**Corresponding Author E-mail: vpsondankar@rediffmail.com*

Abstract

An efficient and rapid synthesis of 2,4,5-triphenyl-1*H*-imidazole derivatives under solvent- free condition has been carried out by the condensation of benzil, arylaldehyde and ammonium acetate at 110 °C using zinc acetate as a catalyst. The short reaction time, good yield, easy workup and solvent-free condition are the main features of the present method.

Keywords: Benzil, arylaldehyde, ammonium acetate, zinc acetate, solvent-free.

Introduction

In modern organic synthesis multi component reactions (MCRs) involving one pot has attracted much interest due to their high atom economy and high selectivity[i-ii]. Further these reactions have been emerged as powerful tool for synthesis of complex drug molecules from simple and readily available starting materials. Many organic solvents particularly the toxic chlorinated hydrocarbons widely used for organic reactions have given a serious threat to the environment[iii]. Therefore the design of solvent free reactions has been emerged as an important technique in the green synthetic organic chemistry[iv-v]. Conventional heating reactions are attractive due to their simplicity and cheapness. Triphenyl-1H- imidazole derivatives are mainly used as photosensitive compounds in photography[vi-viii], electroluminescent materials[ix-x] and optical materials[xi-xii].The imidazole ring system is found in many natural products and pharmacologically active compounds. Imidazoles are generally used in pharmaceutical industry as they have unique physical and biological properties to play an important role in biochemical processes[xiii-xvi]. They are inhibitors of p38 kinase (SB203580)[xvii] and cyclooxygenase-2 (COX-2)[xviii],fungicides[xix] , herbicides, anti-inflammatory agents, anti-thrombiotic agents, plant growth regulators[xx-xxii].

Several methods have been reported in the literature for the synthesis of substituted triphenyl-1H-imidazoles. Some of them are hetero-Cope rearrrangement[xxiii], three component cyclocondensation of 1,2-diketone, α-hydroxyketone or α-keto monoxime with an aldehyde and ammonium acetate using ZnO[xxiv] or $(NH_4)_6Mo_7O_{24}.4H_2O$[xxv], four component condensation of arylglyoxals,primary amines,carboxylic acids and isocyanides on Wang resin[xxvi], reaction of N-(2-oxo)-amides with ammoniumtrifluoroacetate[xxvii]. In addition they have been prepared by the addition of substituted alcohol to a thiomide and subsequent oxidation with PDC[xxviii], reaction of aryl nitriles and α,α-dithioarylnitromethanes[xxix] or by

multistep syntheses[xxx]. Recent methods involve the use of microwave irradiation[xxxi] or ionic liquids[xxxii]. Despite their potential utility, most of these methods have drawbacks of their own.

To further discover the new synthetic applications of 2, 4, 5-triphenyl-1H-imidazole derivatives as scaffolds, herein we report a simple and time saving synthesis of 2,4,5-triphenyl-1H-imidazole derivatives by conventional heating with the use of zinc acetate as catalyst.

Result and discussion

Generally the synthesis of triphenyl-1H-imidazole derivatives is carried out in polar organic solvents like methanol, ethanol, acetic acid, etc. which leads to complex isolation and recovery process. Further these processes generate waste containing catalyst which needs to be treated and disposed off. Hence solvent free reactions are preferred in the green synthesis.

In our study we have chosen zinc acetate catalyst to prepare 2,4,5-triphenyl-1H-imidazole by using benzyl, benzaldehyde and ammonium acetate after trying other catalysts . The samples were heated conventionally in an oil bath between 105 °C to 120 °C. The corresponding results are summarized in table 1. It was found that the reaction time for different aromatic aldehydes differ in the range of temperature cited above. Increase in temperature above this range does not increase the productivity of the reaction to remarkable extent. A 5 mole % concentration of catalyst was found to give best yields of the products. Throughout our study we have maintained the same concentration of catalyst.

After optimizing the reaction conditions we synthesized various trisubstituted-1H-imidazoles using differently substituted aromatic aldehydes under classical heating conditions (Table 2). We found that there is no remarkable effect of electron releasing or electron withdrawing substituted aryl ring of aldehyde on the yield of products. However the presence of electron releasing substituent on aryl ring of aldehyde, elevation in temperature and prolonging in reaction time lead to an increase in product yield. In conclusion we have developed simple, efficient and environmentally benign method for synthesis of 2,4,5-triphenyl-1H-imidazole derivatives using zinc acetate as catalyst.

Table 1: Optimization of reaction condition for synthesis of 2,4,5-triphenyl-1H-imidazole derivatives under classical heating conditions [Benzil (1 mmol),benzaldehyde (1 mmol) and ammonium acetate (2 mmol)]

Entry	Zn $(CH_3COO)_2$(mole%)	Temp. (°C)	Time (min)	Yield (%)
1	3	105	15	68
2	3	115	20	70
3	3	125	25	73
4	5	105	15	78
5	5	115	20	89
6	5	125	25	83
7	7	105	15	76
8	7	115	20	79
9	7	125	25	81

Table 2:- Synthesis of 2,4,5-triphenyl-1H-imidazole derivatives using 5 mole % $Zn(CH_3COO)_2$ under classical heating conditions at 115 °C

Product	R	Time (min)	Yield (%)	m.p. (°C)
a	H	20	89	271-274
b	2-Cl	23	81	189-192
c	4-Cl	23	83	257-259
d	2- Br	25	86	264-267
e	3-NO_2	25	76	268-270
f	2-OH	20	86	202-205
g	4-OH	20	78	266-269
h	4-OCH_3	20	82	229-233
i	4- $(CH_3)_2NH$	20	85	255-257

Conclusion

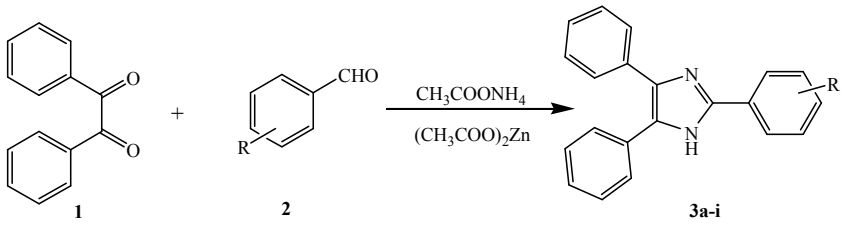
In conclusion we have developed simple, efficient and environmentally benign method for the synthesis of 2,4,5-triphenyl-1*H*-imidazole derivatives using zinc acetate as a catalyst. The advantages of the present method include high yields of products, simple experimental procedure, and low toxicity of reagents. Both analytical and spectroscopic data of synthesized compounds are in full accord with the proposed structures of the products.

Experimental

All solvents were used as commercial anhydrous grade without further purification. High purity chemicals of commercial grade were purchased from E. Merck Company. These were used directly without further purification. Melting points were determined by simple capillary method using Thile's tube and were uncorrected. Merck aluminum sheets 20 × 20 cm coated with silica gel 60 F 254 were used for thin layer chromatography to monitor progress of reaction. Column chromatography was carried out with silica gel (80–120 mesh) as the adsorbent, eluting with petroleum ether/ethyl acetate (9:1). Melting points were determined in open capillary tube and are uncorrected. Infrared (IR) spectra were scanned using SHIMADZU IR spectrophotometer by KBr pallet technique. ^{1}H NMR (400 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ as solvent and TMS as international standard on a BRUKER ADVANCE II spectrometer. Mass spectra were taken on a Q-Star pulsar LC-MS instrument. The reaction mixture was conventionally heated on oil bath using air condenser (to avoid suffocation if any). Yields reported are the yields of isolated crude products.

Typical Procedure for Preparation of 2,4,5-Triphenyl-1H-imidazole derivatives

A mixture of benzil (1 mmol), arylaldehyde (1 mmol), ammonium acetate (2 mmol) and zinc acetate (5 mole %) were placed in a 50 ml conical flask and mixed thoroughly. The mixture was heated to 110 °C in an oil bath for 20 minutes using air condenser. After completion of the reaction, as indicated by thin layer chromatography (petroleum ether/ethyl acetate, 8:2), the products were cooled to room temperature. A small amount of cold water (7-10ml) was poured into the flask slowly. After 10 minutes, the resulting precipitate was filtrated, dried and then crystallized from ethyl alcohol.



1 2 3a-i

3a: R=H **3b: R=2-Cl** **3c: R=4-Cl**
3d: R=2-Br **3e: R=3-NO_2** **3f: R=2-OH**
3g: R=4-OH **3h: R=4-OCH_3** **3i: R=4-$(CH_3)_2NH$**

Scheme1: Zinc acetate catalyzed synthesis of 2,4,5-trisubstituted imidazoles.

2,4,5-triphenyl-1H-imidazole (3a): Solid; yield 89%; m.p. 271-274^{0}C; reaction time 20 minute; IR (KBr): 3445, 2987, 2468, 1635, 1493, 1212 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): ð12.65 (s, 1H), 7.22 - 8.10 (m, 15H); ^{13}C NMR (75 MHz, DMSO): ð145.3, 137.6, 131.4 129.8, 128.9, 127.2, 124.2; EIMS: *m/z* = 296; Anal. Calcd. for $C_{21}H_{16}N_2$: C, 85.11; H,5.44; N, 9.45. Found: C, 85.11; H, 5.36; N, 9.32.

2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (3c): Solid; yield 83%; m.p. 257-259 ^{0}C; reaction time 23 minute; IR (KBr): 3448, 3052,1638,1492,1322 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): ð12.74 (s, 1H), 8.14 (d, 2H) 7.21 - 7.52 (m, 12H); ^{13}C NMR (75 MHz, DMSO): ð 146.4, 130.2, 129.7 128.6, 127.7, 126.8, 125.2, 116.1; EIMS: *m/z* = 340; Anal. Calcd. for $C_{21}H_{15}N_2Cl$: C, 76.24; H,4.57; N, 8.47. Found: C, 76.18; H, 4.43; N, 8.42.

2-(3-nitrophenyl)-4,5-diphenyl-1H-imidazole (3e): Solid; yield 76%; m.p. 268-270^{0}C; reaction time 25 minute; IR (KBr): 3450, 3072,1612,1518,1338 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): ð13.14 (s, 1H), 8.91 (s, 1H), 8.51(d,1H), 8.26 (d,1H), 7.80 (d,1H), 7.32 - 7.55 (m, 10H); ^{13}C NMR (75 MHz, DMSO): ð148.2, 143.2 131.6, 129.9 128.6, 127.3, 122.8, 119.2; EIMS: *m/z* = 350; Anal. Calcd. for $C_{21}H_{15}N_3O_2$: C, 73.89; H, 4.43; N, 12.31. Found: C, 73.78; H, 4.35; N, 12.38.

2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole (3h): Solid; yield 82%; m.p. 229-233 ^{0}C; reaction time 20 minute; IR (KBr): 3430, 3027, 2958, 1612, 1500,1243 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): ð12.46 (s, 1H), 8.1 (d, 2H), 7.32 - 7.55 (m, 10H); 7.1(d, 2H), 3.86 (s,3H); ^{13}C NMR (75 MHz, DMSO): ð159.2, 145.4, 128.6, 127.6, 126.8, 122.8, 114.2, 55.1; EIMS: *m/z* = 326; Anal. Calcd. for $C_{22}H_{18}N_2O$: C, 80.96; H,5.56; N, 8.58. Found: C, 81.07.78; H, 5.43; N, 8.63.

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