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A mild convenient ultrasound assisted synthesis of 2-aryl benzoxazoles catalyzed by KCN/MWCNT as an efficient heterogeneous nanocatalyst

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ABSTRACT

In this research, it was presented a simple and efficient method for one-pot synthesis of 2-arylbenzoxazoles which were directly synthesized from *o*-aminophenol and aromatic or heteroaromatic aldehydes catalyzed by MWCNTs supported KCN in DMF media under ultrasound irradiation. MWCNTs supported KCN was prepared under ultrasound irradiation and was characterized by XRD and FT-IR techniques. The catalyst was used as a convenient, eco-friendly, easy available and highly efficient heterogeneous nanocatalyst which combined with ultrasound irradiation for synthesis of benzoxazole derivatives such as; 2-(2-hydroxyphenyl)-1, 3-benzoxazole (**2**, 96%), 2-(4-chlorophenyl)-1,3-benzoxazole (**5**, 94%) and 2-(2-thiophen-2-yl)-1,3-benzoxazole (**12**, 92%). Aldehydes having either electron-donating or withdrawing groups were used to afford 2-arylbenzoxazoles as target products in short reaction times with excellent yields and high purities. Also, this procedure has advantages such as; simplicity of the workup, reusability of catalyst, low cost and mild conditions. The structure of the obtained products was characterized by nuclear magnetic resonance (NMR) and infrared (IR) spectral data.

1. Introduction

Benzoxazoles and their derivatives have gained considerable attention because they possess several chemotherapeutic activities and biological activities [1,2]. Recent pharmaceutical applications of benzoxazole derivatives are including: anticancer, anti-HIV-1 and antimicrobial [2], antifungal [3], RSK2 inhibitors [4], antidepressants [5], Human GST P1-1 inhibitors [6], COX inhibitors [7], antitumor and antibiotic [8]. There are few methods for the synthesis of benzoxazole rings. One of the most common routs for the synthesis of benzoxazoles involves the reaction between 2-aminophenol and carboxylic acid with a strong acid [9,10] and the other methods is oxidative cyclization of 2-aminophenols and aldehydes using different oxidant agents such as; $PhI(OAc)_2$ [11], Cu nanoparticle [12], *o*-iodoxybenzoic acid (IBX) [13], PCC [14], $Bi(OTf)_3$ [15], heteropolyacid [16], Ru-catalyzed hydroamination of diynes [17]. Most of these reactions suffer drawbacks such as; lengthy procedures that needs excess reagents, harsh reaction conditions, toxic transition metal and difficulty in the preparation of catalyst. Recently nano catalysts have been used for synthesis of oxazole rings because of the number of available active sites which in turn increases the catalytic activity [12,18].

Carbon nanotubes (CNTs) possess some physical and chemical properties such as high surface areas, mechanical stability, structural integrity, resistance in acidic/basic conditions and controllable dimensional characteristics [19,20]. Also the proper pore sizes of them lead to diffusion, reaction and desorption of chemical species [21]. These properties of CNTs beside their lightness make them worthwhile as heterogeneous catalyst supports.

Ultrasound has been used as an important technique for the synthesis of various products in recent decades [22–32]. Ultrasound has some notable features which make it more convenient than traditional methods. Some of the features are: formation of purer products, higher yields and selectivity, easier manipulation, milder conditions, shorter reaction time, and easier work-up. Also it leads to high efficiency, low waste, low energy, and temperatures requirements [33,34].

In continuation of our previous works on the synthesis of heterocyclic compounds by ultrasonic irradiation [35–37], herein, we wish to report a convenient and mild method for synthesis of 2-aryl substituted benzoxazoles using KCN/multi walled carbon nanotube as a heterogeneous catalyst under ultrasound irradiation in DMF solution.

2. Experimental

2.1. Materials

All of the materials such as; aldehydes (95–99%), *o*-aminophenol (99%), DMF (99%), methanol (99%), and potassium cyanide (96%) were of commercial reagent grade purchased from the Merck Chemical

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Company. The aromatic aldehydes and *o*-aminophenol were further purified by standard procedures and the purity determined by thin layer chromatography (TLC).

2.2. Apparatus

IR spectra were recorded as KBr pellets on a Perkin-Elmer 781 spectrophotometer or an Impact 400 Nicolet FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ solvent on a Bruker DRX-400 spectrometer with tetramethylsilane as internal reference. Melting points were obtained with a Yanagimoto micro melting point apparatus are uncorrected. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company). A BANDELIN ultrasonic HD 3200 with probe model KE 76, with the diameter of 6 mm, was used to produce ultrasonic irradiation and homogenizing the reaction mixture. Piezoelectric crystal of this kind of probe normally works in the range of 700 kHz, but by using some proper clamps, the output frequency of piezoelectric crystal have controlled and reduced to 20 kHz. Therefore, the induced frequency of probe to the reaction mixture is equal to 20 kHz. By changing the power of tip the cavitations rate is displaced so that the tip frequency under various amounts of power is constant. A thermal method was used for the calibration of ultrasonic power. Bruker, S4. Nanostructures were characterized using a Holland Philips Xpert X-ray powder diffraction (XRD) diffractometer (Cu Kα radiation, $k = 0.154056$ nm), at a scanning speed of 2°/min from 10° to 100° (2θ).

2.3. The power measurement by calorimetric method

We assessed the cavitational energy applied by ultrasonication calorimetrically with water. The piezoelectric transducer was connected to the frequency generator, HD-3200 (with frequency; 20 kHz). The probe (KE-76) was dipped in a jacketed cylindrical vessel. For calorimetric measurement, the jacket was empty and connected to vacuum to minimize heat losses. In this method, by measuring the rate of temperature increase due to the conversion of ultrasound energy into heat and calculating $P_{acoustic}$ according to: $P = mc\Delta T/t$, where m is the mass of water (g), c is the specific heat capacity of water (4.18 J/g/k), ΔT is the difference in temperature (K) and t is the sonication time (s).

2.4. Preparation of multiwalled carbon nanotube supported potassium cyanide

A mixture of KCN (20 mg, 0.30 mmol) and MWCNTs (80 mg) was taken in methanol (20 ml) as solvent. Then, the reaction mixture was stirred at room temperature for 2 h. After this time, it was irradiated under ultrasound condition with the power 45 W for 30 min. Then, the prepared catalyst was isolated by vacuum filtration and washed with 1:1 water:methanol mixture. The catalyst was characterized and confirmed by IR and XRD techniques.

2.5. Typical procedure for the synthesis of 2-substituted benzoxazoles

A mixture of *o*-aminophenol (1.1 mmol), substituted benzaldehydes (2.2 mmol) and KCN/MWCN (0.01 g) was added to DMF (4 ml) as solvent and the reaction mixture was irradiated in ultrasonic apparatus with the power 60 W at 55% amplitude and at frequency of 20 kHz for range 12–650 s. The progress of the reaction was monitored using thin-layer chromatography (petroleum ether:ethyl acetate, 6:2). After completion of the reaction, 10 ml ethyl acetate was added and the reaction mixture was filtered to separate out the catalyst. The catalyst residue was washed with chloroform and dried for reuse. Then, the organic layer was washed with water (5 ml). The organic solvent and other residues were stripped in a vacuum evaporator. The product was purified by recrystallization in a boiling mixture of ethanol/water (1:1) to give pure product. The obtained pure benzoxazoles were characterized by spectroscopic data and melting points and identified by comparison of their physical and spectral data with those of authentic samples.

2-Phenyl-1,3-benzoxazole: Light brown solid; m.p. = 98–100 °C (m.p. = 102–103 °C [38]); IR (KBr)/ν (cm^{-1}) 1615 (C=N), 1551, 1448 (C=C, Ar), 1242 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.29–8.26 (2H, m, phenyl), 7.80–7.78 (1H, m, fused phenylene), 7.62–7.59 (1H, m, phenyl), 7.56–7.54 (3H, m, phenyl), 7.38–7.36 (2H, m, fused phenylene).

2-(2-Hydroxyphenyl)-1,3-benzoxazole: White solid; m.p. = 123–124 °C (m.p. = 125–126 °C [39]); IR (KBr)/ν (cm^{-1}) 3143 (OH), 1630 (C=N), 1544, 1485 (C=C, Ar), 1248 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 11.50 (1H, s, OH), 8.04 (1H, dd, J = 7.6, 1.4 Hz, phenyl), 7.75 (1H, m, fused phenylene), 7.63 (1H, m, fused phenylene), 7.47–7.40 (3H, m, fused phenylene, phenyl), 7.14–7.12 (1H, m, phenyl), 7.04–7.00 (1H, m, phenyl); ^{13}C NMR ($CDCl_3$, 100 MHz)/δ (ppm) 162.90 (C-oxazole), 158.70 (C-phenyl), 149.13 (C-fused phenylene), 140.00 (C-fused phenylene), 133.56 (C-phenyl), 127.10 (C-phenyl), 125.30 (C-fused phenylene), 125.00 (C-fused phenylene), 119.56 (C-phenyl), 119.25 (C-fused phenylene), 117.40 (C-phenyl), 110.66 (C-fused phenylene).

2-(3-Hydroxy-phenyl)-1,3-benzoxazole: White solid; m.p. = 172–174°C; IR (KBr)/ν (cm^{-1}) 3428 (OH), 1600 (C=N), 1550, 1452 (C=C, Ar), 1241 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.91 (1H, s, OH), 7.75–7.73 (3H, m, fused phenylene, phenyl), 7.70 (1H, m, fused phenylene), 7.42–7.41 (3H, m, fused phenylene, phenyl), 7.00 (1H, m, phenyl). ^{13}C NMR (DMSO, 100 MHz)/δ (ppm): 162.8 (C-oxazole), 158.4 (C-phenyl), 150.6 (C-fused phenylene), 141.9 (C-fused phenylene), 131.0 (C-phenyl), 128.0 (C-phenyl), 125.9 (C-fused phenylene), 125.3 (C-fused phenylene), 120.3 (C-phenyl), 119.6 (C-fused phenylene), 118.5 (C-phenyl), 114.1 (C-phenyl), 111.4 (C-fused phenylene).

2-(2-Chlorophenyl)-1,3-benzoxazole: Light yellow solid; m.p. = 63–65 °C (m.p. = 61–64 °C [14]); IR (KBr)/ν (cm^{-1}) 1606 (C=N), 1537, 1452 (C=C, Ar), 1244 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.17 (1H, dd, J = 7.20, 1.6 Hz, phenyl), 7.88–7.86 (1H, m, fused phenylene), 7.65–7.63 (1H, m, fused phenylene), 7.60–7.58 (1H, m, phenyl), 7.49–7.38 (4H, m, fused phenylene, phenyl).

2-(4-Chlorophenyl)-1,3-benzoxazole: Light brown solid; m.p. = 149–151 °C (m.p. = 153–154 °C [38]); IR (KBr)/ν (cm^{-1}) 1614 (C=N), 1482, 1550 (C=C, Ar), 1243 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.2–8.19 (2H, m, phenyl), 7.79–7.77 (1H, m, fused phenylene), 7.61–7.58 (1H, m, fused phenylene), 7.53–7.51 (2H, m, phenyl), 7.39–7.37 (2H, m, fused phenylene).

2-(2,4-Dichlorophenyl)-1,3-benzoxazole: Light brown solid; m.p. = 120–123°C (m.p. = 118–119 °C [40]); IR (KBr)/ν (cm^{-1}) 1662 (C=N), 1588, 1466 (C=C, Ar), 1241 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.13 (1H, d, J = 8.40 Hz, phenyl), 7.86–7.84 (1H, m, fused phenylene), 7.64–7.60 (2H, m, fused phenylene), 7.43–7.40 (3H, m, fused phenylene, phenyl); ^{13}C NMR ($CDCl_3$, 100 MHz)/δ (ppm): 160.07 (C-oxazole), 150.51 (C-fused phenylene), 141.58 (C-fused phenylene), 137.54 (C-phenyl), 134.24 (C- phenyl), 132.51 (C-phenyl), 131.30 (C-phenyl), 127.43 (C-phenyl), 125.81 (C-phenyl), 124.82 (C-fused phenylene), 124.71 (C-fused phenylene), 120.56 (C-fused phenylene), 110.77 (C-fused phenylene).

2-(3-Methoxyphenyl)-1,3-benzoxazole: Light yellow solid; m.p. = 72–74 °C (m.p. = 71.3–73.8 °C [41]); IR (KBr)/ν (cm^{-1}) 1642 (C=N), 1541, 1453 (C=C, Ar), 1278 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ (ppm): 8.11 (1H, m, phenyl), 7.47 (1H, m, fused phenylene), 7.44–7.42 (2H, m, fused phenylene), 7.26 (1H, m, fused phenylene), 7.18–7.14 (1H, m, phenyl), 7.09–7.07 (1H, m, phenyl), 6.95–6.91 (1H, m, phenyl), 3.89 (3H, s, Me).

2-(4-Methoxyphenyl)-1,3-benzoxazole: Light yellow solid; m.p. = 100–101°C (m.p. = 103–105 °C [38]); IR (KBr)/ν (cm^{-1}) 1613 (C=N), 1501, 1452 (C=C, Ar), 1249 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/δ

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