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Environmental-friendly synthesis of oxazolines, imidazolines and thiazolines catalyzed by tungstophosphoric acid

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Abstract

A convenient and green method for the synthesis of aromatic 2-oxazolines, 2-imidazolines and 2-thiazolines using tungstophosphoric acid (TPA), a commercially available, stable and reusable catalyst, from the reaction of aromatic nitriles and 2-aminoalcohols, ethylenediamine or 2-aminoethanethiol under solvent-free conditions is reported. It is noteworthy that this procedure could be used for selective synthesis of mono- and bis-oxazolines and imidazolines from dicyanobenzene. In three cases the catalyst could be reused several times without significant loss of its catalytic activity.

Keywords: Oxazoline; Imidazoline; Thiazoline; Nitrile; Tungstophosphoric acid

1. Introduction

2-Oxazolines, 2-imidazolines and 2-thiazolines are very important moieties due to their extensive applications in chemistry, biochemistry and pharmacology [1–4]. These heterocycles are found in the structures of many biologically active natural products [5]. They also exhibit several pharmaceutical activities such as antidiabetic [6], antihypertensive [7], antidepressive [8], anticancer [9], anti HIV-1 [10], antitumor [11] and antialzheimer [12] activities. They are also known as important intermediates in organic transformations [13]. Optically active mono- and bis-derivatives of these heterocycles have been widely used as both auxiliary and ligand in asymmetric synthesis [14].

Several publications have been described for the preparation of 2-substituted oxazolines, imidazolines and thiazolines from different precursors such as carboxylic acids [15], esters [16], nitriles [17–19], amides [20], aziridines [21] and aldehydes [22]. Various reaction conditions and a variety of homogeneous and heterogeneous catalysts have been applied for this purpose. Although these methods are valuable, most of them involve one or more disadvantages including harsh reaction conditions, long reaction times, low yields of products, the use of stoichiometric amounts of catalysts, the use of excess amounts of reagents and relatively expensive reagents and/or toxic solvents. So, the development of an efficient, simple and environmentally benign catalytic procedure for the synthesis of these heterocycles is still in high demand.

In recent years, the use of polyoxometalates as homogeneous and heterogeneous catalysts has attracted especial attention in organic synthesis due to economical and environmental considerations [23]. Heteropoly acids with Keggin structure are the most important class of polyoxometalates, which have unique physical properties. They have been widely used as solid acid catalysts because of their easy handling, easy work-up, thermal stability, nontoxicity and stability toward air and moisture. Among them tungstophosphoric acid (TPA) is the most reactive one that received more attention than the other heteropoly

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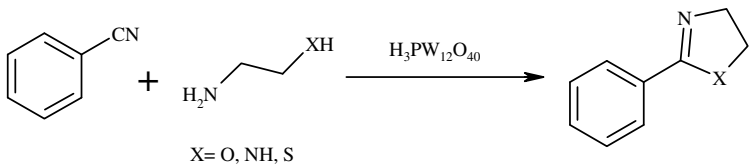

Scheme 1.

acids [24,25]. In the present paper, we wish to report the use of this environmental-friendly catalyst in the synthesis of 2-substituted oxazolines, imidazolines and thiazolines (Scheme 1).

2. Experimental

All materials were commercial reagent grade and were prepared from Merck or Fluka. ^{1}H NMR spectra were recorded on a Bruker-Arance AQS 300 MHz. IR spectra were run on a Philips PU9716 spectrophotometer. All melting points were obtained by Stuart Scientific apparatus. TLC monitored all reactions and all yields refer to isolated products.

2.1. General procedure for the conversion of nitriles to 2-oxazolines

A mixture of aromatic nitriles (1 mmol), 2-aminoalcohols (4 mmol per each nitrile group) and $H_3PW_{12}O_{40}$ (1 mol%) was placed in a round bottom flask and heated for appropriate time (Table 2) at 100 °C. After completion of the reaction, as indicated by TLC, the mixture was cooled to room temperature and diluted with CH_2Cl_2 (10 ml), and was filtered. The solid material was washed with CH_2Cl_2 (10 ml). The solvent was evaporated and the residue was purified by recrystalization in *n*-hexane or by column chromatography. IR, m.p. and ^{1}H NMR spectral data confirmed the identities of the products.

2.2. General procedure for the conversion of nitriles to 2-imidazolines

To a mixture of aromatic nitriles (1 mmol) and ethylenediamine (4 mmol per each nitrile group) was added $H_3PW_{12}O_{40}$ (1 mol%) and heated for appropriate time (Table 3) at 110 °C. After completion of the reaction (monitored by TLC), the mixture was cooled to room temperature and diluted with CH_2Cl_2 (10 ml), and was filtered. The catalyst was washed with CH_2Cl_2 (10 ml). The solvent was evaporated and the residue was purified by recrystalization or by column chromatography. The products were identified by IR, m.p. and ^{1}H NMR spectral data.

2.3. General procedure for the conversion of nitriles to 2-thiazolines

Aromatic nitriles (1 mmol), 2-aminoethanethiol (1.1 mmol per each nitrile group) and $H_3PW_{12}O_{40}$ (0.5 mol%) were mixed and heated for appropriate time (Table 4) at 110 °C. At the end of reaction, as indicated by TLC, the mixture was cooled to room temperature and diluted with CH_2Cl_2 (10 ml), and was filtered. The solid material was washed with CH_2Cl_2 (10 ml). Evaporation of the solvent and purification of crude product by recrystalization in *n*-hexane or by column chromatography gave the desired thiazoline. The products identity was confirmed by IR, m.p. and ^{1}H NMR spectral data.

2.4. Catalyst recovery and reuse

To a mixture of benzonitriles (2 mmol), 2-aminoalcohols (8 mmol) in a round bottom flask was added $H_3PW_{12}O_{40}$ (2 mol%) and heated for 3.5 h at 100 °C. The reaction progress was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and diluted with CH_2Cl_2 (10 ml), and was filtered. The catalyst was washed with CH_2Cl_2 (10 ml), dried at 110 °C, and then reused in the next run. The solvent was evaporated and the residue was purified by recrystalization in *n*-hexane or by column chromatography.

The above mentioned reaction was repeated and the filtrates were collected for determining the catalyst leaching after each run. The amount of catalyst leached was determined by ICP.

Spectroscopic data: *3-(4′,5′-Dihydro-1H-imidazol-2′-yl)-benzonitrile* (Table 3, entry 10): m.p.: 133–134 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.81 (s, 4H, $2CH_2$), 4.2 (brs, 1H, NH), 7.51 (t, J = 7.8 Hz, 1H, ArH), 7.71 (d, J = 7.7 Hz, 1H, ArH), 8.01 (d, J = 7.9 Hz, 1H, ArH), 8.05 (s, 1H, ArH). MS; *m/z* = 171 (M^+, 8.89%), 169 (44.05%), 142 (76.19%), 128 (100%).

2-(4′-Pyridyl)-4,5-dihydro-1,3-thiazole (Table 4, entry 2): m.p.: 74–76 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.48 (t, J = 8.5 Hz, 2H, CH_2–S), 4.51 (t, J = 8.5 Hz, 2H, CH_2–N), 7.68 (dd, J = 1.5 & 4.5 Hz, 2H, ArH), 8.71 (dd, J = 1.5 & 4.5 Hz, 2H, ArH). MS; *m/z* = 164 (M^+, 93.15%), 162 (4.67%), 136 (17.12%).

2-(3′-Chlorophenyl)-4,5-dihydro-1,3-thiazole (Table 4, entry 6): m.p.: 54–56 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.45 (t, J = 8.4 Hz, 2H, CH_2–S), 4.48 (t, J = 8.4 Hz, 2H, CH_2–N), 7.36 (t, J = 7.8 Hz, 1H, ArH), 7.45 (d, J = 8.1 Hz, 1H, ArH), 7.71 (d, J = 7.6 Hz, 1H, ArH), 7.86 (s, 1H, ArH).

2-(3′-Nitrophenyl)-4,5-dihydro-1,3-thiazole (Table 4, entry 10): m.p.: 135–137 °C, ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.53 (t, J = 8.4 Hz, 2H, CH_2–S), 4.53 (t, J = 8.4 Hz, 2H, CH_2–N), 7.63 (t, J = 8.0 Hz, 1H, ArH), 8.19 (d,