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Communication

Multifunctional Catalysis of Heteropoly Acid: One-Pot Synthesis of Quinolines from Nitroarene and Various Aldehydes in the Presence of Hydrazine

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12-Molybdophosphoric acid catalyzed transfer hydrogenation of nitroarene by hydrazine in a homogeneous phase. This catalytic system was applicable to one-pot quinolines synthesis in the presence of various aldehydes in water. This method provides a new and efficient protocol in terms of mild reaction conditions, clean reaction profiles, small quantity of catalyst, and simple work-up procedure.

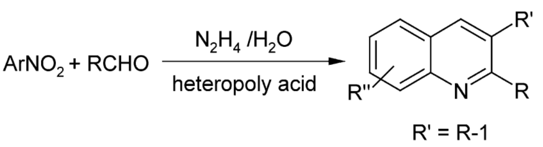
Keywords: Aldeydes; Hydrazine; Quinoline derivatives; Transfer hydrogenation; 12-Molybdophosphoric acid; Nitroarene.

The synthesis of the a quinoline ring has been the subject of continued interest as several derivatives of this heterocyclic unit, which have been found to possess useful biological activities such as bactericidal,[1] antimalarial,[2] and antiinflammatory,[3] etc. Various reactions such as the Skraup, Dobner-von Miller, Conrad-Limpach, Friedlaender and Pfitzinger synthesis are the common-used routes for the formation of quinolines. In contrast to the conventional synthesis, which frequently require harsh and cumbersome acidic reaction conditions, the formation of quinoline skeletons has been attempted by a remarkable catalytic action of transition metal catalysts such as palladium,[4] rhodium,[5] ruthenium,[6] and iron.[7] However, many of these procedures are not showed a fully satisfactory with a regard to the operational simplicity, the cost of the reagent and the isolated yield. Thus, the drive is continuing to find a better and improved methodology.

Development of methods using heteropoly acids (HPAs) as catalysts for fine organic synthetic processes a relevant to fine chemicals, such as flavors, pharmaceuticals, and food industries,[8] that have been under attention in the last decade. Heteropoly acids are the more active catalysts than conventional inorganic and organic acids for various reactions in solution.[9] They were used in industrial catalysts for several liquid-phase reactions,[10–13] such as alcohol dehydration,[14] alkylation,[15] or esterification[16] reactions.

Continuing our research into the development of new synthetic methodologies and the utilization of heteropoly acids,[17-20] we studied the behavior of nitroarene and various aldehydes in the presence of hydrazine against heteropoly acids, and herein reported a new one-pot synthesis of quinolines (Scheme I).

Scheme I



The toxic and the volatile nature of many organic solvents, particularly chlorinated hydrocarbons and benzene, which are widely used in organic synthetic procedures, have posed a serious threat to the environment. There have been considerable researches recently into replacing the use of these volatile organic solvents with clean ones as a reaction media.[21] Performing organic reactions in aqueous media has attracted much attention, because water would be considered safe, non-toxic, environmentally friendly, and cheap if compared to organic solvents.[22] Moreover,

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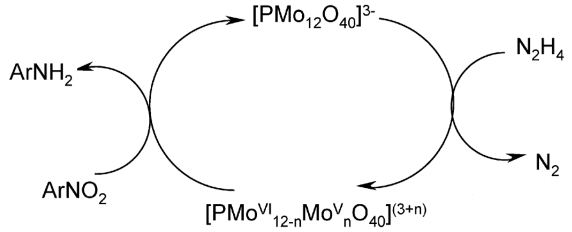
when a water soluble catalyst is used, the insoluble products can be separated by a simple filtration and the catalyst system can be recycled. Therefore, the development of a catalyst system that is not only stable toward water but also completely soluble in this solvent seems highly desirable.

Hydrated HPA which usually contains 11-28 water molecules per Keggin unit at ambient temperature, is moderately soluble in polar organic solvents, such as alcohol, ether, ketone, carboxylic acid and ester, whereas anhydrous HPA is scarcely soluble therein. It is therefore preferable to use a hydrated HPA for examining its homogeneous acid catalysis in organic media.

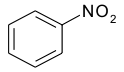
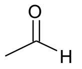
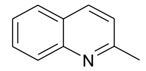
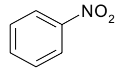
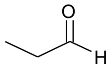
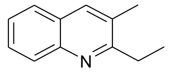
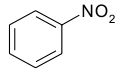
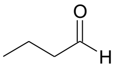
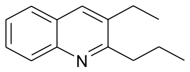
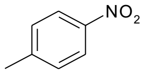
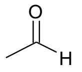
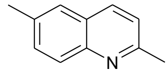
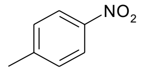
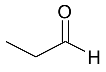
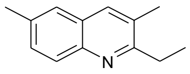
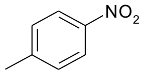
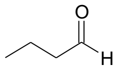
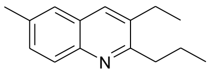
According to the previous works,[23] 12-Molybdophosphoric acid catalyzed transfers hydrogenation of nitroarene by hydrazine in a homogeneous phase. While the hydrazine reduces the catalyst to form the active species, nitroarene reoxidizes Mo(V) to Mo(VI). The catalytic cycle is shown in Scheme II. Protic solvents, such as water, enhance the reduction reaction since they take part in the ionic reaction stabilizing the lower oxidation state. This catalyst system was applicable to the quinolines synthesis.

Scheme II



Quinoline syntheses using various aldehydes in the presence of the heteropoly acid catalyst are summarized in Table 1. A variety of aldehydes reacted smoothly with nitroarene; in the presence of hydrazine and catalytic amount of heteropoly acid to give the corresponding quinolines in high yields.

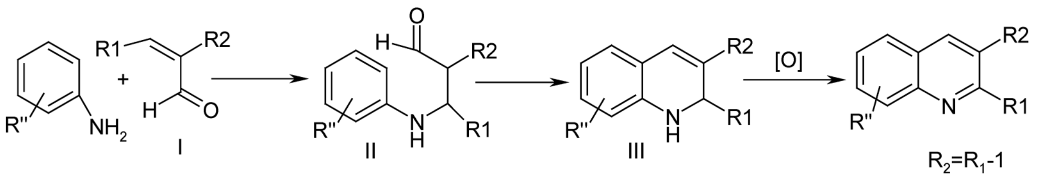
Table 1. Aldehydes, nitroarene and quinoline derivatives

Entry	Nitroarenes	Aldehydes	Quinoline Derivatives	Yield (%)
1				98
2				97
3				98
4				96
5				97
6				95

A Reaction only gave 2-substituted quinolines from the reaction with acetaldehyde. One plausible explanation for this regioselectivity is presumably, this process involves an aldol condensation between aldehydes in presence of heteropoly acid as an efficient acid catalyst and then Michael addition of aniline to the vinyl ketone followed by subsequent cyclization and aromatization under the catalysis of HPA as delineated in (Scheme III).

To better understand the regiochemistry in this quinoline synthetic method, we thought it was important to confirm that α,β-unsaturated carbonyl compound (I) and (II) were indeed involved as an intermediate. For this purpose, we screened various reaction conditions to obtain α,β-unsaturated carbonyl compounds (I) and (II) by increasing the concentration of reactants and shortening the reaction time. In one case, for example, a mixture of acetaldehyde, nitrobenzene ,and hydrazine in 15 mL of water was stirred in the presence of heteropoly acid for 30 min to give corresponding α,β-unsaturated carbonyl compound (I), (II) and quinoline. α,β-unsaturated carbonyl compound (I) and (II) were isolated and structurally characterized and were converted to the corresponding quinoline by cyclization and oxidation (heteropoly acid was tentatively proposed to be the ox-

Scheme III



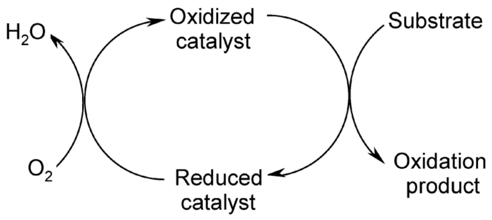
idant).

However, in our previous report, Keggin-type heteropoly acid is a highly efficient solid acid catalyst for oxidative cleavage of C=N bond, and it is also a convenient and efficient method for the regeneration of carbonyl compounds from semicarbazones, hydrazones, and oximes, using Keggin-type heteropoly acid as a green, reusable and superior catalyst.[24] A process involving the intermediacy of Schiff's base can be ruled out.

In order to confirm the utility of HPA as effective catalysts, this reaction was repeated in the absence of the HPA. The results show that in the absence of the HPA transfer hydrogenation reaction did not proceed and only small amount of hydrazone was produced.

A Selective oxidation with mixed oxides and oxide-like catalysts such as heteropoly acids involves the activation of C-H or C-C bonds as well as of the oxidant on the catalyst surface and frequently occurs by a Mars-van Krevelen redox mechanism,[25] which may be represented by (Scheme IV). The catalyst oxidized the substrate and then, in a separate step, is reoxidised by O_2.

Scheme IV



Catalyst was also found to be reusable, although gradual decline of activity was observed. Heteropoly acid maintained their Keggin structure in the course of the reactions, which were conformed by examining their IR spectra. Previous studies indicated the reoxidation of the catalyst without losing the Keggin structure.[23] Better results were obtained when, after the first run, the product filtered off, the solvent was evaporated and the remained catalyst was washed with CH_2Cl_2, and reused. Apparently, the treatment with CH_2Cl_2 removed tars more efficiently from the catalyst surface. Such procedure applied for synthesis of 2-methyl-quinoline (Table 1, entry 1), and in second run the product was obtained in 80% yield.

Many protocols for the Skraup-Doebner-Von Miller quinoline synthesis, have been developed because of the importance of quinolines as pharmaceuticals, ligands, and functional materials.[26]

Heteropoly compounds have several advantages as catalysts, the most important being their multifunctionality and structural mobility. On the one hand, they have a very strong Bronsted acidity; on the other hand, they are efficient oxidants, exhibiting fast reversible multielectron redox transformations under mild conditions.

In summary, we describe a convenient and efficient protocol for the synthesis of quinolines using heteropoly acid as a green recyclable and bifunctional (acid and redox) catalyst. The simple experiment procedure combined with the ease of recovery and reuses of this catalyst to make this procedure quite simple, more convenient and environmentally benign.

EXPERIMENTAL

Melting points were measured by using the capillary tube method with an electrothermal 9200 apparatus; IR spectra were recorded from KBr disk on the FT-IR Bruker Tensor 27. GC spectra were carried out on a Network GC System-Agilent 5973 spectrometer. GC/mass analysis using Agilent 6890 GC system Hp-5 capillary 30 m × 530 μm × 1.5 μm nominal. ^{13}C NMR ^{1}H NMR spectra were recorded on a Bruker AQS 300 MHz Avance Spectrometer in DMSO. d_6 (Chemical Shifts are given as δ in ppm). The reaction course and purity of the final products were followed by TLC on silica gel. Commercial reagents and solvents were purchased from standard chemical supplier.

Typical procedure

About 0.03 mmol Keggin-type heteropoly acid, nitroarene (1 mmol), aldehyde (1 mmol), and 15 mL of water (solvent) were taken in a round bottom flask. Then, (1.5 mmol) hydrazine hydrate (80%) was added slowly to the stirred contents over a period of 30 min, the flask was maintained at 40-50 °C for 2 h. After the completion of reaction (monitored by thin layer chromatography (TLC)), the product was separated from the reaction mixture by extracting it with dichloromethane, purified by column chromatography, and analyzed by Mass, ^{13}C NMR, ^{1}H NMR and FT-IR spectra.

All compounds were known and their physical and spectroscopic data were compared with those of authentic samples and found to be identical.[27,28,29]

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