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Recyclable Pd(II)complex catalyzed oxidative sp^2 C–H bond acylation of 2-aryl pyridines with toluene derivatives

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ABSTRACT

A recyclable polymer–anchored Pd(II) complex **C** was synthesized and characterized using different spectroscopic techniques. In addition the catalytic efficiency of the Pd (II) complex **C** was evaluated for *ortho*-acylation of 2-aryl pyridines with toluene derivatives to form aryl ketones via cross dehydrogenative coupling. In this catalytic process toluene acts as an effective coupling partner upon sp^3 C–H bond oxidation for sp^2 C–H bond acylation of 2-aryl pyridines in the presence of Pd(II)/TBHP system on water. Furthermore, the catalyst **C** was highly stable and could be easily recovered and reused for four cycles with no significant decrease in its activity and selectivity.

1. Introduction

The direct aromatic C–H bond functionalization is one of the most challenging and reliable strategy to construct C–C and C–heteroatom bonds [1]. Among the various C–H activation techniques, the directing group assisted C–H bond activation and dehydrogenative cross-coupling are most facile methods that has gained considerable attention over traditional cross-coupling methods [2]. Benzophenones constitute prominent structural motifs of top 200 most-sold pharmaceuticals that exhibit broad spectrum of biological activities including cholesterol regulation(-Tricor), anti-inflammatory effects (Sector), and selective estrogen receptor modulation (Evista) [3]. Several methods for the introduction of a carbonyl moiety have been developed, including the traditional Friedel–Crafts acylation, the coupling of aryl compounds with aliphatic olefins and carbon monoxide in presence of Ru has been generally employed [4]. These methods however showed poor selectivity and formation of waste materials due to the use of excess Lewis acids. Further the use of expensive ruthenium catalyst, handling of carbon monoxide and generation of high reaction temperature suggests that new sustainable methods are highly desirable.

In order to solve the selectivity issue, direct transformations such as arylation, olefination, halogenation, and amination with the assistance of conventional directing groups like pyridines, amides, esters, imines, ketones, oxazolines, and nitriles have been reported [5]. In contrast carbonylative C–H bond functionalizations (acylation) have been investigated to a lesser extent. Transition metal catalyzed C–H activation of arenes has been achieved mostly by employing palladium, ruthenium, rhodium, copper and Iron catalysts [6]. To the best of our knowledge aldehydes, alcohols, α-oxocarboxylic acids, arylmethyl amines, carboxylic acids, diketones, benzylic ethers and CO with PhI as acyl sources for transition-metal-catalyzed carbonylative coupling reactions of directed group assisted arene C–H bonds have been described [7]. Among them, the catalytic cycle between Pd(II) and Pd(IV) is one of the major pathways [8], in which a number of oxidants such as $K_2S_2O_8$, TBHP, BQ, DDQ, PIDA have been widely employed. Organic reactions conceded 'On-water' have become one of the most intriguing area of research in green chemistry as it is universal medium for all chemical reactions of life [9]. The pioneering work for rate

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enhancements “on water” was first demonstrated by Breslow and Sharpless inspired the intense research “on water” catalysis [10]. Design and development of efficient catalytic processes with energy minimization, replacement of toxic catalysts and hazardous solvents with relatively benign solvents such as water, catalyst-free synthesis, and high atom economy are some of the most essential components of an ideal green synthesis [11].

Despite great achievements in green catalysis, most of the organic transformations are incompatible with water since most of the organic compounds do not dissolve in water while solubility is generally considered a prerequisite for reactivity. This tends to be an important challenge and emerging as an attractive area of research for organic chemists.

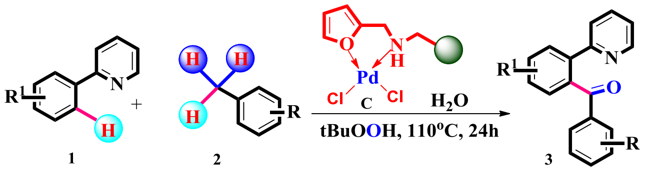
Polystyrene is one of the most commonly employed reliable polymeric support due to its low cost, ready availability and chemical inertness in recent years. A variety of polymer-supported metal catalysts for the C–C coupling reactions were reported [12].

In terms of green and environmental perspective cross dehydrogenative coupling, commercially available alkyl benzenes as acylating agents is considered as ideal, eco-economical protocol. Carbon-carbon bond formation via C–H activation in water is another potential clean process that can have both high atom efficiency and easy recycling of the catalyst.

Recently, palladium-catalyzed oxidative *ortho*-acylation of inactive C(sp2)–H bonds via C–H, C–C, and C–O bond cleavage of toluenes was reported for the synthesis of aromatic ketones [13].

In view of minimizing the waste/side product formation the use of toxic gaseous carbon monoxide and homogeneous Pd catalyst stands as hindrance for economical and sustainable chemistry for the reported methods. In all the above-mentioned procedures for ortho-acylation reactions, the Pd catalysts used are homogeneous in nature and suffer from several drawbacks, such as they may easily be destroyed during the course of the reaction [14]. So, the catalysts are not easily separable from reaction mixtures and they are non-recyclable. In order to overcome the problems associated with homogeneous catalysts and with the growing demand for sustainable synthesis the direct catalytic C–H functionalization under mild reaction conditions becomes highly essential. More Recently homogeneous conditions were replaced with supported palladium nanoparticles in ortho-directed CDC reactions of alkyl benzenes [15]. The main advantage of the given polymeric complex of palladium (II) **C** over palladium (0) nanoparticles catalyst is mainly in twice less loading and better recyclability.

We mainly focused on developing simple, economical, green pathway for carbonylation reaction/ortho-acylation of 2-phenylpyridine. In view of continuous interest to develop simple recyclable polymer bound metal complexes [16], herein we report a facile synthesis of benzophenone derivatives by Pd-catalyzed acylation of 2-phenyl pyridines by employing toluene derivatives as the simple coupling partners. However, ortho-acylation product was obtained in excellent yields with recyclable, heterogeneous Palladium complex under on-water conditions with toluene as an acylating partner (Scheme 1). This protocol is highly appreciable due to being atom and step economic for the direct conversion of C–H bonds to C–C bonds for aryl ketone synthesis.



Scheme 1. Palladium-catalyzed direct *ortho*-acylation of arenes. DG = directing group.

Herein, we report the synthesis and characterization of a new polymer supported furan-2-ylmethanamine derived palladium(II) complex (PS-FMA–Pd) as an effective and highly reusable catalyst for the synthesis of benzophenone derivatives from toluene derivatives and TBHP as the oxidant under on-water conditions. Thus, the synthesized polymer-anchored Pd(II) catalyst showed efficient catalytic application towards a carbonylation reaction in a green pathway without employing carbon monoxide or base or solvent under phosphine free conditions.

2. Experimental

2.1. Material and instruments

Analytical-grade reagents and freshly distilled solvents were used throughout the experiment. The reagents were supplied by Sigma-Aldrich Chemicals Company, USA and Merck Co. Liquid substrates were redistilled and dried with appropriate molecular sieves. Distillation and purification of the solvents and substrates were done by standard procedures.[16] The starting materials and reagents were purchased from various commercial sources and used without further purification. ACME silica gel (60–120 mesh) was used for column chromatography. Analytical thin-layer chromatography (TLC) was performed on pre-coated TLC plates with silica gel 60-F_{254} plates and visualized by UV-light. ^{1}H NMR and ^{13}C NMR spectra were recorded, using tetramethylsilane (TMS) in the solvent of $CDCl_3$ as the internal standard on a 400, 500 MHz spectrometer (^{1}H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm; ^{13}C NMR: $CDCl_3$ at 77.00 ppm). Chemical shifts (δ) were recorded in ppm with respect to TMS as an internal standard and coupling constants are quoted in Hertz (Hz). Mass spectra were recorded on a mass spectrometer by the electron spray ionization (ESI) and the data acquired in positive ionization mode. HRMS spectra were determined on TOF type mass analyzer. FTIR spectra of the samples were recorded on a Perkin-Elmer FTIR 783 spectrophotometer using KBr pellets. A EXSTAR TG/DTA7200 instrument was used for the thermogravimetric (TGA) analysis. Powder X-ray diffraction patterns of the pure functionalized materials were recorded on a Bruker D-8 Advance diffractometer operated at 40 kV voltage and 40 mA current using a Cu tube ($\lambda = 0.15406$ nm) as the radiation source. TEM analysis was carried out by using a JEOL 2010 TEM operated at 200 kV. The metal content in the catalyst was determined using a Varian AA240 atomic absorption spectrophotometer (AAS).

2.1.1. Synthesis of the catalyst

Preparation of polymer-supported furan-2-ylmethanamine (B) (PS-FMA): A 250 mL round-bottomflask equipped with a magnetic stirrer was charged with CH_3CN (100 mL). To this 1% DVB-crosslinked chloromethylated polystyrene (0.5 g, 2.25 mmol/Cl), furan-2-ylmethanamine A (2.3 mL, 22.5 mmol), and NaI (14.9 mg, 0.1 mmol) were added and the mixture was refluxed for 48 h. The mixture was filtered and the residue was washed sequentially with CH_3CN (3×20 mL), 1:1 CH_3OH–1M aq K_2CO_3 (3×20 mL), 1:1 CH_3OH–H_2O (3×20 mL), and Et_2O (3×10 mL), and then dried in an oven.

2.1.2. Preparation of polystyrene-supported Pd(II) complex (C) (PS-FMA-Pd)

To the polystyrene-supported furan-2-ylmethanamine B (0.5 g), EtOH (100 mL) was added and kept for 30 min. A solution of $Pd(CH_3CN)_2Cl_2$ (0.5 g) in EtOH (10 mL) was then added, and the (1:1) mixture was refluxed for 12 h. The polymer-anchored brown colored metal complex, impregnated with the metal, was filtered, washed thoroughly with EtOH (3×30 mL), and finally dried in