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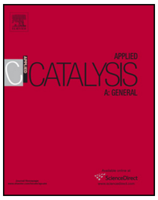

K_3PO_4-catalyzed carbonylation of amines to formamides

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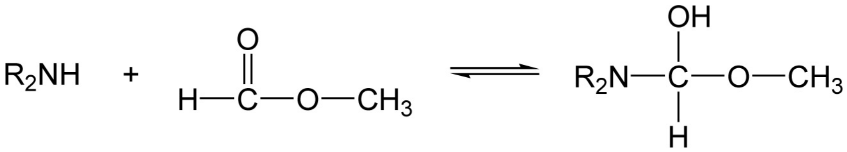
ABSTRACT

Synthesis of formamides from the catalytic carbonylation of amines with CO is of great interest due to their wide applications of formamides as synthetic intermediates and aprotic polar solvents. Up to now, the most commonly used catalysts are either expensive noble metal compounds or difficult-to-handle alkali metal alkoxides. We have found that a solid base, K_3PO_4 is a highly active and selective catalyst for the carbonylation of primary and cyclic secondary amines, producing corresponding formaldehydes in yields up to 99% at relatively mild conditions. Spectroscopic and quantum mechanical calculation results indicate that such high activity of K_3PO_4 is closely related to the strong hydrogen bonding ability of PO_4^{3-} with the amino group of an amine, thereby enhancing the nucleophilicity of the amino group enough to interact with a neutral molecule, CO and mediating proton transfer from the amino group to the carbonyl group. Characterization of spent catalyst by FT-IR and XRD implies that small portion of K_3PO_4 is converted into less active K_2HPO_4 during the carbonylation reaction.

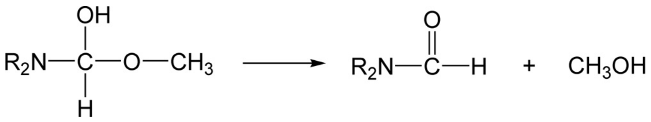
1. Introduction

Formamides are unique solvents that can dissolve wide variety chemicals including inorganic salts, polymers, natural products, and dyes because of their high dielectric constant and electron-donor characteristics [1,2]. They are also being widely used as aprotic solvents for chemical reactions and as intermediates in various organic syntheses. For instance, *N*,*N*-dimethylformamide (DMF) is one of the few solvents suitable for dissolving polyacrylonitrile. Formamides also find applications as extracting agents in several extraction processes such as the selective separations of acetylenes from olefins, butadiene from C_4 raffinates, SO_2 from CO_2-containing gases, and aromatics from hydrocarbon mixtures [3–7].

Formamides can be prepared by reacting methylformate, prepared separately from CO and methanol, with ammonia, primary amines or secondary amines as shown in Eqs. (1) and (2). The most striking feature of this process is that the reactions can be conducted in the absence of a catalyst and thus any additional process to remove catalyst is not required. One drawback is that the economic efficiency of the process is heavily dependent on the price of methylformate [8,9].



$$R_2NH + H-\overset{\overset{\Large O}{\|}}{C}-O-CH_3 \rightleftharpoons R_2N-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-O-CH_3 \qquad (1)$$



$$R_2N-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-O-CH_3 \longrightarrow R_2N-\overset{\overset{O}{\|}}{C}-H + CH_3OH \qquad (2)$$

Catalytic *N*-formylation of amines by various formylating agents such as formic acid, paraformaldehyde has also been reported. A number of catalytic systems have been developed and as a result, significant advance has been made [10–14]. Nonetheless, the *N*-

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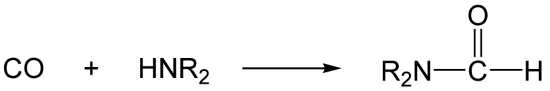
formylation process needs to be further improved in terms of material costs and catalyst recovery for practical application.

Industrially, formamides are being manufactured from the direct carbonylation reactions of amines by CO in alcohol solvents in the presence of an alkali metal alkoxide such as $NaOCH_3$ and $KOCH_3$ as shown in Eq. (3). The direct synthesis using alkali metal alkoxides is proven to be highly effective for manufacturing formamides in high yields, but the handling of water-sensitive alkali metal alkoxides requires extreme care because they are easily converted to inactive alkali metal hydroxides and/or alkali metal formates by the reaction with water [15,16].



$$CO + HNR_2 \longrightarrow R_2N{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}H \qquad (3)$$

As alternatives to alkali metal alkoxides, group 4–10 organometallic compounds have been employed as catalysts for the carbonylation reactions of amines [17–22]. However, most of transition metal complexes were found to exhibit high activities only at elevated temperatures and pressures even with precious metal compounds [23–29]. Recently, oxidative carbonylation of amines has been developed to prepare formamides at mild conditions without using transition metal complexes [30]. This is an elegant process in that the carbonylation is catalyzed by inexpensive bases such as K_2CO_3 and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) at relatively low temperatures of 90 °C, but the additional use of $NaIO_4$ as an oxidant and NaI as a promoter could be a drawback of this process. As a means of avoiding the use of toxic carbon monoxide, the reductive functionalization of CO_2 with amines to formamides has been intensively investigated, and as a result, highly active catalysts based on Ru and Fe have been developed [31–34]. Although the advance has been significant, the performance of catalysts needs to be further improved to compete with that of the conventional alkali metal alkoxide catalysts.

Recently, it has been demonstrated that imidazolium-based ionic liquids with a bicarbonate anion ($[HCO_3]^-$) are highly active for the carbonylation of amines to produce formamides [35]. Nonetheless, much needs to be improved for their practical application, especially in terms of cost and recyclability of ionic liquid catalysts.

In a continuation of our study to search for high performance catalysts for the carbonylation of amines, we have found that a solid base catalyst, K_3PO_4 can be used as a promising alternative to alkali metal alkoxides because it is highly active, cost-effective, and easily recyclable. Herein, we report on the catalytic activities of a series of alkali metal phosphates for the carbonylation of amines. The mechanistic aspects of the carbonylation of amines are also discussed on the basis of experimental and computational results.

2. Experimental

2.1. Materials

All the amines used for the carbonylation reactions were purchased from Aldrich Chemical Co., and used as received. Solvents were reagent grades, and were used after distillation over appropriate drying agents under a nitrogen atmosphere prior to use [36]. Carbon monoxide (>99%) was obtained from Air Liquide Korea Co., Alkali metal phosphates were obtained from Aldrich Chemical Co., and used after calcination at 500 °C for 3 h.

2.2. Instrumentation

Liquid products obtained from the carbonylation reactions were characterized on an Agilent 6890 gas chromatograph (GC) equipped with a FID and a DB-5 capillary column, and on an Agilent 6890-5973 MSD GC-mass spectrometer equipped with a HP-MS capillary column. FT-IR spectroscopic analysis was made on a Nicolet 380 spectrophotometer (Thermo Electron Co.). The X-ray diffraction (XRD) patterns were recorded on a Shimadzu X-ray diffractometer (XRD-6000) using nickel-filtered CuKα radiation with a 2θ angle from 10 to 40°. FT-IR spectra were obtained using a Nicolet FT-IR spectrometer (iS10, USA) equipped with a SMART MIRACLE accessory and a Specac Reaction Cell Top Plate (P/N GS 10507) for in situ analysis.

2.3. Carbonylation reaction

Carbonylation reactions of amines were performed in an alcohol using a 100 mL high pressure reactor equipped with a magnetic stirrer and an electrical heater. The reactor was loaded with appropriate amounts of an amine (50 mmol), CH_3OH (20 mL), a catalyst (0.5 mmol) and toluene (2 g) as an internal standard. The reactor was pressurized with 2.0 MPa of CO and then heated to a specified temperature. The pressure inside the reactor was maintained at 4.0 MPa throughout the reaction using a gas reservoir equipped with a high pressure regulator and a pressure transducer. After the completion of the carbonylation reaction, the reactor was cooled to room temperature and the reaction mixture was analyzed by GC, GC–MS, and NMR. Comparison of fresh and spent catalyst was made by means of FT-IR and XRD.

2.4. Catalyst recycle

The catalyst recycle was conducted with K_3PO_4 at 140 °C and 4.0 MPa of CO for 4 h using cyclohexylamine (CHA, 100 mmol) as a substrate and methanol (20 mL) as a solvent. The molar ratio of CHA/K_3PO_4 was set at 100. After the reaction was completed, the reactor was cooled to room temperature, and the liquid product mixture was separated from the solid catalyst using a porous metal filter, and analyzed by GC. The remaining solid catalyst inside the reactor was used for the next cycle with a fresh charge of CHA and CH_3OH (20 mL).

2.5. Computational calculations

The carbonylation reaction of amine in the presence of K_3PO_4 was theoretically investigated using Gaussian 09 program [37]. For simplicity, methylamine was chosen as the model amine. Geometries were fully optimized without any symmetry constraints using nonlocal method B3LYP, a combination of Becke's three-parameter hybrid exchange functional and correlation functional of Lee, Yang and Parr. The 6-31G* basis set was used for all of the atoms. Harmonic force constants were computed at the optimized geometries to characterize the stationary points as minima by the absence of imaginary frequencies. Preliminary transition state geometries were obtained by the PES scan functionality available in Gaussian and then they were subjected to full TS optimizations using an eigenvector following quadratic synchronous transit (QST) algorithm. For selected transition state geometries, confirmation calculations involving intrinsic reaction path (IRC) calculations and frequency calculations with only one imaginary frequency in the reaction coordinate were performed. For a better modelling in consistent with the experimental results, the bulk solvation effect of methanol was also included in the calculation through the self-consistent reaction field theory (SCRF) based on the polarisable continuum model (PCM).