

Natural phosphate supported vanadium as a recyclable heterogeneous catalyst for reductive amination of carbonyls

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Abstract— A new interesting application of natural phosphate (NP) as heterogeneous catalyst for reductive amination of carbonyls is reported. The modification of NP by vanadium leads to a new catalyst V/NP with a high catalytic activity in this type of transformation. The reaction was performed with a small catalytic amount of catalyst and the envisioned amines were obtained with a high yield at room temperature. The scope and limitations of the catalyst were evaluated, and the results are discussed.

Index Terms— Natural phosphate; vanadium; reductive amination; carbonyl; heterogeneous catalysis.

1. INTRODUCTION

Nitrogen containing molecules have raised considerable attention in organic synthesis, with their great technical interest, they have a wide range of possible applications such as solvents, dyes, intermediates for pharmaceuticals [1], agrochemical, biotechnology and other use in the industrial chemistry[2]. In view of their considerable potential, several methods have been developed and one of the most common methods used to prepare this type of molecules is the direct reductive amination of carbonyls with amines in the presence of a reducing agent.

In this context, a variety of catalysts has been reported previously in the literature such as : H_2 -Pd/C [3], AuNPore [4], HMMS-NH₂-Pd [5], Ru(H)TsDPEN [6], NaH₂PO₄·H₂O/NaBH₄ [7], ChCl/Urea [8], TMSOAc/ZnCl₂-NaBH(OAc)₃ [9], H₂-Fe@Pd/C [10], H-mZSM-5 and Ni/H-mZSM-5 [11], oxo-rhenium complexes-PhSiH₃ [12], Hantzschester [13], Ni(OAc)₂-PCy₃-hydrosilylation [14], PdMPA/SiO₂ [15], dihydropyridine [16], Li-arene [17], Zn(OTf)₂-PMHS [18], PdOeFe₃O₄- PMHS [19], S-Benzyl isothiuronium chloride [20], silicachloride-NaBH₄ [21], Ga(OTf)₃-triethylsilane [22], Ti(OⁱPr)₄-HCl-NH₃BH₃ [23], ZBHNMP [24], Na(CN)BH₃ and Si-CBH [25], NaBH₄-silica phosphoric acid [26], 5-ethyl-2-methylpyridine borane [27].

Despite the efficiency of the majority reported catalysts, all of them suffer from some limitations: use of hazardous solvents, and stoichiometric metal hydride, the catalysts are non-recoverable and very expensive, or possess important drawbacks such as the cyanoborohydride reagents which can generate poisonous cyanide by-product.

Consequently, attention is given to the development of non-toxic, economical, green and easily recyclable heterogeneous catalysts. For several years, our group has been developing new recyclable heterogeneous systems by using natural phosphate alone or conveniently modified as catalyst for several transformations like hydration of aromatic nitriles [28], Suzuki-Miyaura Reaction [29], as well as reforming of methane [30] and hydrogenation of crotonaldehyde[31]. In this work, we decided to develop a facile and efficient methodology for direct reductive amination of carbonyls, using natural phosphate-supported vanadium (V/NP) and NaBH₄ at room temperature.

2. EXPERIMENTAL SECTION

The products were purified on silica-gel column (Merck; 230–400 mesh) and analyses on a Shimadzu GC 2010 Plus Gas Chromatograph. ¹H and ¹³C NMR spectra were measured on Jeol spectrometer operating at 300 MHz for proton, 75 MHz for carbon using CDCl₃ as the solvent. All other reagents and solvents were obtained from Sigma Aldrich.

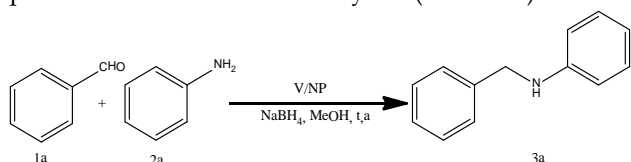
2.1. PREPARATION OF THE CATALYST V/NP

The natural phosphate used in this work was prepared as described in previous literature [32]. The V/NP catalyst was also prepared and characterized according to the procedures described in the earlier paper [33], using 10 g of NP with NH₄VO₃ (1 mmol) in 10 mL in aqueous oxalic acid solution 0.1 M. The mixture was stirred at room temperature for 30 min, the resulting was evaporated to dryness, dried under vacuum and calcined at 800°C for 2 h.

2.2. GENERAL PROCEDURE FOR REDUCTIVE AMINATION OF CARBONYLS.

In a round bottom flask (10 mL), aldehyde 1a (1mmol), amine 2a (1 mmol) and V-NP (50 mg) were successively added in methanol solution (2 mL), stirred for 5 min, then NaBH₄ (1 mmol) was added. The mixture was stirred at room temperature for 60 min and the progress of reaction monitored by thin layer chromatography (TLC).

After completion, water (10 mL) was added and the reaction mixture was extracted with CH₂Cl₂ (2 × 20 mL). The combined organic layers was dried over anhydrous MgSO₄ and evaporated. The crude product was purified by silica gel column chromatography using hexane-EtOAc (9:1) to afford the pure amine 3a in 87% isolated yield (Scheme 1).



Scheme 1. Synthesis of N-benzylaniline catalyzed by V/NP

2.3. RESULTS AND DISCUSSION:

Catalyst characterization

In previously work [33], we have described the characterization of V/NP catalyst using various analytical methods. The following are the main findings of these analyzes. The XRD diffractogram of V/NP was similar to that of naturel phosphate alone and the peaks were identical to those of hexagonal systems P/63/m group space, indicating that vanadium loading did not affect the apatite structure of NP. Any new phase has been detected and no peaks corresponding to the vanadium were observed, probably because of their low content. However, the presence of V₂O₅ is observed by IR spectroscopy which shows an intense band around 870 cm⁻¹ attributed to the antisymmetric elongation vibration mode of V-O-V groups. The specific area of V/NP was calculated by using BET analyses and the average value obtained is the order 7.18 m², that remains very low compared to silica or alumina but it is very interesting compared to those of NP alone (1.43 m²). The morphology of the surface of the V/NP was observed using scanning electronic microscopy (SEM). The images obtained revealed the presence of small, irregular and heterogeneous particles, forming agglomerates of different sizes (10-100 μm) which is similar to the reported literature [33].

To explore the possibility of the reaction and the potential activity of the catalysts (NH₄VO₃, NP and V/NP) in the reductive amination of carbonyl, we initially investigated the model reaction of benzaldehyde reacted with aniline in the presence of NaBH₄ as a reducing agent (Table 1). Only a trace of product was observed by using the ammonium vanadate despite increasing the catalyst amount and reaction time (Entry 1). In the presence of NP alone as catalyst (Entry 2), the N-benzylaniline was formed with 50% which suggest that naturel phosphate was active in this transformation. The use of V/NP (Entry 3) displayed a high activity for reductive amination of carbonyl and the synergetic effects between the vanadium and naturel phosphate was shown by giving the

desired product in good yields (87%). In view of these

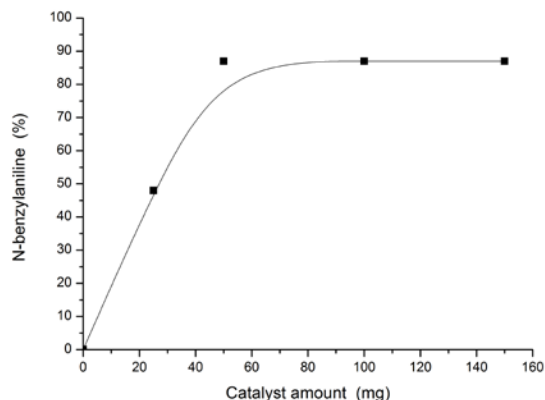


Fig. 1. The V/NP catalyst amount effect in the reductive amination of benzaldehyde.

promising results, we optimized several reaction conditions, including the catalyst loadings, solvent and reaction time.

To evaluate the catalyst effect, we studied the same reaction model of benzaldehyde with aniline in the presence of NaBH₄ at room temperature for 60 min, using different amount of V/NP ranging from 0,25 mg to 200 mg. As observed during the two first tests, increasing the catalyst loading results in an important gradual increase of the desired product yield. The use of 50 mg of V/NP was sufficient and furnished the desired N-benzylaniline in very good yield (87%, Fig. 1) whereas increasing the amount of catalyst up to 100 mg does not affect the yield which remains stable even with 200 mg of V/NP. This result proved that 50 mg of V/NP is the optimal amounts able to catalyze this reaction.

To assess whether the nature of used solvent affect the yield of the transformation, different solvents were tested in the reaction model of the reductive amination of aniline to find the appropriate solvent.

Table 2 summarized the results of the solvent effect. As

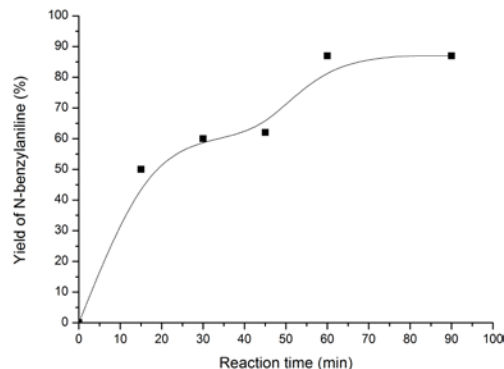


Fig. 2. The reaction time effect in the reductive amination of benzaldehyde.

observed the reaction failed when using water, acetonitrile

TABLE 2
SOLVENT EFFECT IN THE REDUCTIVE AMINATION OF
BENZALDEHYDE WITH ANILINE.

Entry	Solvent	Isolated Yield ^a (%)
1	Hexane	No product
2	CH ₃ CN	No product
3	H ₂ O	No product
4	EtOH	38 ^b
5	MeOH	87 ^b

^a Reaction condition: aniline (1 mmol), benzaldehyde (1 mmol), NaBH₄ (1 mmol), solvent (2 mL) in the presence of the catalyst at room temperature for 60 min.

^b Isolated yield.

and hexane as solvents and no product was detected (Entries 1-3). Under similar condition, the use of ethanol was less tolerated and the product was isolated in moderate yield (38%, entry 4). In conclusion, the last assay (Entry 5) proved that methanol was the best solvent for this reaction affording the desired product in 87%.

Herein, we investigated the influence of reaction time in this transformation. It was found that the formation of amine is gradually increased with time and 60 min was sufficient to give the product in good yield (Fig. 2). Increasing the reaction time up to 90 min does not affect the yield, which remains unchanged.

Therefore, the final optimized reaction parameters were 50 mg of V/NP catalyst, methanol as the solvent and 60 min for reaction time at room temperature.

In order to study the limitations and the general application of the V/NP in the reductive amination of carbonyls, different derivatives of aldehyde were explored in the synthesis of various substituted amines.

The results reported in Table 3, shows that all aromatic aldehydes were efficiently converted to the corresponding amines in good to excellent yields and the presence of electron donating or withdrawing groups were tolerated. Benzaldehyde was converted to the corresponding product in very good yield (87%, Entry 1) also the 4-Chlorobenzaldehyde gave desired amine in good yield (78%, Entry 2). Whereas attempts with aromatic aldehyde with electron withdrawing group led to desired product in moderate yield (49%, Entry 3). In the case of alkyl aldehyde, the reductive amination of acetaldehyde was successfully achieved in excellent yield (96%, Entry 4). Finally, very interesting results were observed in both aniline and morpholine reacted with sterically hindered 2-hydroxybenzaldehyde to produce their corresponding amines in good yield (Entry 5 and 6).

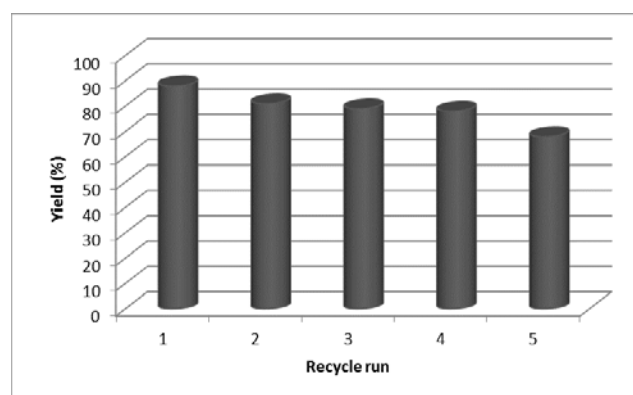
TABLE 3
REDUCTION AMINATION OF VARIOUS ALDEHYDES USING V/NP AS
CATALYST.

Entry	Aldehyde	Amine	Product ^a	Yield ^b (%)
1				87
2				78
3				49
4				96 ^c
5				80 ^c
6				88

^a Reaction condition: aniline (1 mmol), benzaldehyde (1 mmol), NaBH₄ (1 mmol), MeOH (2 mL), V/NP (50 mg).

^b Isolated yield.

^c Time 90 min.



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3. RECYCLABILITY

The most important factor of any catalyst system is the recyclability and the ability to reuse the catalyst several times to make the process ecofriendly.

The recyclability of the catalyst V/NP was investigated by using the model reaction of benzaldehyde with aniline under optimal conditions. After completion of each reaction cycle, the catalyst was recovered recuperated by simple filtration, washed with distilled water and ethanol for three times. Dried in an oven at 150 °C then reused again in other cycle of the reaction. The study proved that the catalyst could be reused five times with a slight decrease of its catalytic activity (Fig. 3).

4. CONCLUSION

In summary, we have developed an efficient and simple catalyst system for the direct reductive amination of carbonyls taking advantage of a synergetic effect of natural phosphate with vanadium. The good activity of this heterogenous catalyst in the reductive amination of various aldehydes at mild reaction conditions, low cost and availability of NP and also the reusability of the catalyst for several times makes this protocol ecofriendly. Further studies are underway in our laboratory to develop this system and their applications in other reactions.

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