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Natural Phosphate Doped with Potassium Fluoride: Efficient Catalyst for the Construction of a Carbon−Carbon Bond

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Abstract:

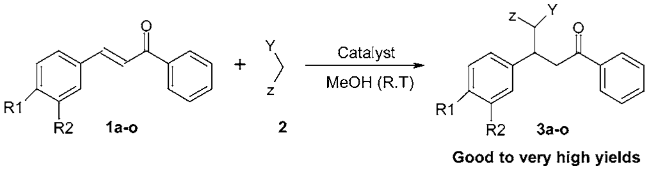
Natural phosphate-doped catalyst was found to be an efficient, environmentally attractive, and selective solid base catalyst for 1,4-Michael addition. The products of undesirable side reactions resulting from 1,2-adddition, polymerization, and bis-addition are not observed. The workup procedure is simplified by simple filtration with the use of natural phosphate alone or doped with potassium fluoride. Potassium fluoride-doped natural phosphate is used as catalyst for a facile synthesis of 4*H*-chromene under heterogeneous conditions.

Introduction

Several very mild and highly selective organic transformations have been achieved on the surface of natural phosphate (NP). For example, Knoevenagel condensation,[1] dipolar addition,[2] Friedel-Craft alkylation,[3] Claisen−Schmidt condensation,[4] and other reactions[5] have been reported. The use of natural phosphate in the heterogeneous catalysis represents a very interesting choice in the sense of the green chemistry. As a matter of fact, NP is insoluble in organic solvents and in water; it is cheaper and more economical, reuseable, and hence, harmless to the environment. For those reasons, heterogeneous catalysis by way of natural phosphate can be considered as a new attempt to develop the notion of "clean chemistry".

The Michael addition has attracted enormous attention as one of the most important carbon−carbon or carbon−sulfur reactions in organic synthesis. Various solid catalysts have been found useful in heterogeneous media, including zeolite,[6] Mg−Al hydrotalcite,[7] aluminium oxide,[8] montmorillonite/$NiBr_2$,[9] synthetic phosphate $Na_2CaP_2O_7$,[10] fluoroapapatite,[11] hydroxyapatite,[12] and other catalysts with more or less success.[13−17]

Scheme 1. **Formation of carbon−carbon bond in the presence of NP or KF/NP catalysts**



We previously reported that NP alone is capable of catalyzing the construction of sulfur−carbon bonds.[18] We have also shown that doping with potassium fluoride increases the activity of natural phosphate.[18]

In this contribution we report a mild and convenient method for the heterogeneous catalysis of the construction of a carbon−carbon bond using NP alone or doped with potassium fluoride (Scheme 1).

Preparation of the Catalyst and Structural Characteristics

Natural phosphate was obtained in the Khouribga region (Morocco).[19] The utilization of NP requires initial treatments such as crushing and washing. To be used appropriately in heterogeneous synthesis, the NP is treated as follows, according to techniques of attrition, sifting, calcinations, and

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(19) Natural phosphate (NP) was obtained from the Khouribga region (Morocco). It is readily available (raw or treated) from CERPHOS 37, Bd My Ismail, Casablanca, Morocco.

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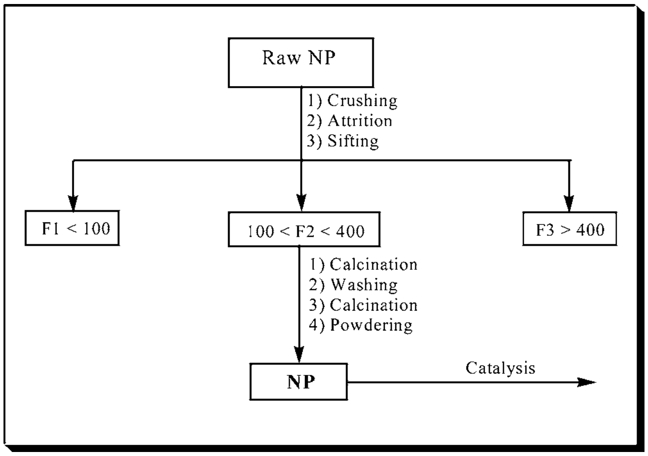

Figure 1. **Preparation of natural phosphate (NP).**

washing (Figure 1). The fraction of particle size 100−400 μm, rich in phosphates, was isolated, washed with water, calcined at 1173 K for 2 h, and sieved. The samples were reactivated at 773 K prior to use as catalysts.[20]

NP and KF/NP were characterized by using X-ray diffraction pattern (XRD), BET, scanning electron microscopy (SEM), chemical composition, and IR spectra. The structure of the NP is similar to that of fluoroapatite, as shown by the X-ray diffraction pattern. This solid presented a very low surface area (BET) at ca. 1 $m^2\ g^{-1}$. The chemical composition was determined as: P_2O_5 (34.24%), CaO (54.12%), F^- (3.37%), SiO_2 (2.42%), SO_3 (2.21%), CO_2 (1.13%), Na_2O (0.92%), MgO (0.68%), Al_2O_3 (0.46%), Fe_2O_3 (0.36%), K_2O (0.04%), and several metals (Zn, Cu, Cd, V, U, Cr) in the range of ppm.

The KF/NP catalysts were prepared by addition of NP to a solution of KF in water. Ratios of KF:NP were varied on a mass basis from 1:2 to 1:16. Evaporation of water gave the catalysts, designated by the codes KF/NP-r where $r = 2-16$, and represents the mass ratio of KF/NP. The catalysts were all gray powders, the colour of NP itself.

The analysis of the material is illustrated by KF/NP-8, the most active of the catalysts. The IR data shows the presence of some additional H-bonded water at 3250 cm^{-1} and 1636−1675 cm^{-1} for the supported solid. On the other hand, the X-ray diffraction of KF/NP gives a diffraction pattern almost identical to that of NP itself. Peak positions and intensities are essentially unaltered. We showed previously[18] that supporting KF on NP causes the formation of a more open structure which incorporates KF in such a way that crystalline KF is not formed in significant quantities. However, it appears that the basic structure of NP is not destroyed, indicating a less profound interaction of KF with NP than is the case with alumina.[21] The morphology of the surface of the solid was observed in scanning electron micrograph (SEM) images of KF/NP in comparison with those of NP. It clearly appears that some modifications have taken place at the surface of the catalyst.

Table 1. **Influence of mass ratio KF:NP on conversion**

	conversion of **1a** and methylcyanoacetate (%)			
time/min	KF/NP-2	KF/NP-4	KF/NP-8	KF/NP-16
5	60	66	56	44
10	61	76	89	87
15	75	65	94	89

The surface area and pore volume of the NP were increased by doping with KF. Thus, the results obtained are 8.9 $m^2\ g^{-1}$ and 0.128 $cm^3\ g^{-1}$ for KF/NP and 1 $m^2\ g^{-1}$ and 0.005 $cm^3\ g^{-1}$ for NP. These results are in contradiction to that reported for typically supporting metal salts on solids.[22]

Results and Discussion

Methylcyanoacetate and chalcone ($R_1 = R_2 = H$, Scheme 1) were chosen as model substrates to determine suitable reaction conditions. The best weight ratio of KF/NP is 1/8 (Table 1). We proceeded to study the solvent effect in the synthesis of product **3b** using the KF/NP catalyst.

In the cases of hexane and dichloromethane, no product was observed. The use of *n*-butanol, 2-propanol, ethanol, and methanol gave after 15 min of reaction, 48, 60, 80, and 94% yield of **3b**, respectively. It can be concluded that methanol is the best solvent for this reaction. A similar effect of solvent has been observed in the use of the natural phosphate catalyst.[18] In the absence of the solvent, only a 55% yield is obtained. This behaviour indicates that some solvent is needed to facilitate the contact between the reagents and active site.

The study of the influence of the volume of the solvent showed that with 0.5−2 mL of methanol the best yield was obtained. An increase in the volume up to 3 mL slightly decreases the reaction yield (75%), and this drops further to 65% when a volume of 10 mL is used. The large volume of the solvent reduces the concentration which explains the decrease of the yields.

In general the use of NP alone as a heterogeneous catalyst in the Michael addition has allowed the isolation of the 1,4-addition product with moderate to good yields (Table 1). The reaction is relatively slow.

Solid catalysts become particularly interesting when they can be regenerated. Indeed, in our case, NP was recovered quantitatively by simple filtration and regenerated by calcination at 700 °C during 15 min. The recovered catalyst was reused several times without loss of activity, even after the seventh cycle product **3b** was obtained with the same yield.

Under the best conditions, the use of NP doped by KF remarkably increases the catalytic activity and decreases the reaction time in the Michael addition (Table 2). In all cases the use of KF/NP as heterogeneous catalyst in the Michael addition allowed the isolation of products **3** rapidly and with excellent yields (91−96%; Table 2), except in the case where the nucleophile is nitromethane.

In the presence of 0.01 g of KF alone (the present quantity in the KF/NP, 1/8 catalyst) no 1,4-addition product was

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Table 2. **Synthesis of products 3 by Michael addition using NP and KF/NP**

						NP		KF/NP	
entry	products	R_1	R_2	Y	Z	yield (%)	time[a] (min)	yield (%)	time[a] (min)
1	**3a**	H	H	CN	CN	95	30	96	10
2	**3b**	H	H	CO_2Me	CN	95	60	94	15
3	**3c**	H	H	H	NO_2	25	360	60	360
						90	180[b]	91	30[b]
4	**3d**	Cl	H	CN	CN	56	40	96	20
5	**3e**	Cl	H	CO_2Me	CN	46	60	95	45
6	**3f**	Cl	H	H	NO_2	50	180[b]	92	45[b]
7	**3g**	Me	H	CN	CN	94	150	96	30
8	**3h**	me	H	Co_2Me	CN	75	240	96	60
9	**3i**	Me	H	H	NO_2	90	180[b]	92	45[b]
10	**3j**	OMe	H	CN	CN	79	120	96	40
11	**3k**	OMe	H	Co_2Me	CN	83	240	96	90
12	**3l**	OMe	H	H	NO_2	60	180[b]	90	60[b]
13	**3m**	H	NO_2	CN	CN	63	60	94	40
14	**3n**	H	NO_2	CO_2Me	CN	60	60	91	80
15	**3o**	H	NO_2	H	NO_2	42	180[b]	91	60[b]

[a] Yields in pure products isolated by chromatography, recrystallized with *n*-hexane/ethyl acetate and identified by ^1H and ^{13}C NMR and IR spectrometry. [b] The reaction mixture was stirred at 65 °C, traces of polymerization products were observed.

observed under the reaction conditions, and only the starting material was isolated. No by-products resulting from the undesirable 1,2-adddition and/or bis-addition side reactions (usually observed under classical conditions in some cases) were observed. However, reaction of nitromethane with various Michael acceptors gives traces of polymerization products (no isolated).

For the catalytic activity of KF/NP in this Michael addition we speculate that the reaction occurs at the surface rather than inside the tunnels of the catalyst. The dimensions of the pore in our catalyst (KF/NP) are not large enough compared to those of zeolites.[23] Thus, we estimate that the surface of KF/NP presents certainly multicatalytic active sites. The basic sites abstract the proton from activated methylene, and the acidic sites[24] probably induced the polarization of the C═O bond for the Michael addition. Consequently, the C−C bond formation is accelerated, and the final product is obtained after protonation of the resulting enolate.

The results obtained in this reaction with KF/NP as catalyst were compared to those using other catalysts. Thus, the activity of KF/NP was higher than NP, KF,[25] Al_2O_3,[26] KF/Al_2O_3,[13] and Al−hydrotalcite[27] and slightly lower than Mg−Al−*O-tert*-Bu-hydrotalcite[27] (Table 3).

Reaction of salicylaldehyde **4** and malononitrile was investigated to establish conditions for the preparation of 4*H*-chromene **7**.[28] The reaction of salicylaldehyde with an excess of active methylene compound gave product **7** in excellent yield.

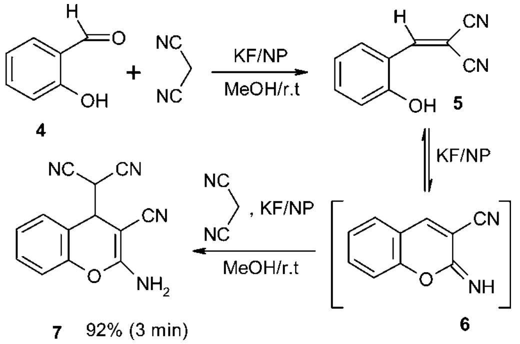
The reaction probably proceeds, in the first step, by a Knoevenagel condensation to give benzylidene derivative **5** and then imino coumarin **6**. The intermediate **5** has been identified by ^1H and ^{13}C NMR spectra along with 4*H*-chromene **7**, when one equivalent of malononitrile is allowed to react with salicylaldehyde **4**. The intermediate **6** is converted by Michael addition with the excess of malononitrile present in the reaction mixture to the 4*H*-chromene **7** (Scheme 2).

Table 3. **Comparison of KF/NP with several heterogeneous catalysts in the synthesis of products 3a and 3c by Michael addition**

	yields (time) [(%) (min)]	
solid catalyst	**3a**	**3c**
KF/NP	96 (10)[b]	91 (30)[a]
NP	95 (30)[b]	90 (180)[a]
KF[25]	−	94 (90)[c,d]
Al_2O_3[26]	40 (3)[e]	−
KF/Al_2O_3[13]	−	95 (1200)[b,d]
Mg−Al−hydrotalcite[27]	88 (120)[b]	−
Mg−Al−*O-tert*-Bu-hydrotalcite[27]	−	93 (10)[b]

[a] Reaction carried out at 65 °C. [b] Reaction carried out at room temperature. [c] Reaction carried out at 81 °C. [d] Using 3 g of catalyst per 5 mmol of substrate. [e] Reaction carried out at 100 °C.

Scheme 2. **Preparation of 4*H*-chromene 7 in the presence of KF/NP catalyst**



Conclusions

Thus, a critical requirement of selective 1,4-addition without any side reaction, condensation, dimerization, or rearrangements in Michael reaction is made possible with the NP and NP doped with KF. These catalysts bring advantages such as high catalytic activity and selectivity under very mild liquid-phase conditions, easy separation of the catalyst, use simple filtration, possible recycling of the catalyst, use of nontoxic and inexpensive catalysts, and especially, elimination of salts and by-product pollutants. Potassium fluoride-doped natural phosphate is used as the catalyst for a facile synthesis of 4*H*-chromene under heterogeneous conditions. This solid base catalyst becomes then a practical alternative to soluble bases.

Experimental Section

^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Bruker DRX-400 spectrometer in $CDCl_3$, using $CDCl_3$ as internal standard. The chemical shifts (δ) are expressed in ppm relative to $CDCl_3$ and coupling constant (J) in hertz. IR spectra were obtained on a FTIR (ATI Mattson-Genesis Series) and reported in wavenumbers

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(cm^{-1}). Surface area and pore size analysis were carried out at 77 K on a Micromeritics ASAP2010 instrument using nitrogen as adsorbent. X-ray diffraction patterns of the catalysts were obtained on a Philips 1710 diffractometer using Cu Kα radiation, and SEM images were taken on a Hitachi S-2400 microscope. Melting points were determined with a “Thomas-Hoover” melting (capillary method) apparatus and are uncorrected. Flash column chromatography was performed using Merck silica gel 60 (230−400 mesh ASTM).

Typical Experimental Procedure. To a flask containing an equimolar mixture (1 mmol) of active methylene compound **2** and chalcone derivatives **1** in methanol (1 mL) was added 0.1 g of phosphate catalyst (NP or KF/NP), and the mixture was stirred at room temperature or 65 °C until completion of the reaction, as monitored by thin-layer chromatography (TLC). The reaction mixture was filtered and the catalyst washed with dichloromethane. After concentration of the filtrate under reduced pressure the residue was subjected to chromatography or recrystallization (*n*-hexane/ethyl acetate), leading to the Michael adduct as a solid. The product structure was analysed by ^{1}H and ^{13}C NMR and IR spectrometry.

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