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Natural phosphate doped with potassium fluoride and modified with sodium nitrate: efficient catalysts for the Knoevenagel condensation

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Abstract—A high yield synthesis of activated alkenes is described using the inexpensive natural phosphate alone, doped with potassium fluoride or modified by sodium nitrate. The Knoevenagel condensation was carried out in mild conditions at room temperature in methanol. The catalytic activity of these phosphates are compared. © 2002 Elsevier Science Ltd. All rights reserved.

Catalysis of organic reactions by natural inorganic solids is an important new dimension in preparative organic chemistry. The applications of inorganic solids such as natural calcium phosphate (NP)[1] as efficient catalyst of inorganic transformations have been exploited recently for several reactions.[2,3] The NP has several advantages, as it is inexpensive, environmentally friendly, non-toxic, recoverable, reusable and also a mild catalyst.

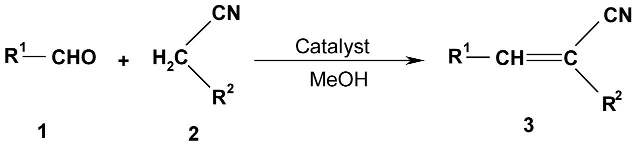
The Knoevenagel reaction is one of the most important C–C bond forming reactions available, because the alkenes synthesized are very useful intermediates in organic synthesis. In recent years, the Knoevenagel reaction has been carried out in heterogeneous media in the presence of several solids.[4] Recently, we have shown that NP and synthetic phosphates are excellent catalysts of this reaction.[2,5]

Potassium fluoride supported on NP has been used to promote several reactions.[3] Recently, we have reported that sodium nitrate modified NP can promote efficiently the Claisen–Schmidt condensation[6] and the epoxidation of electron-deficient alkenes.[7]

We report here the utilization of NP alone, doped by KF and modified by $NaNO_3$ as heterogeneous catalysts for the Knoevenagel condensation between an aldehyde **1** and an activated methylene **2** at room temperature in methanol (Scheme 1).

Natural phosphate comes from an extracted ore in the region of Khouribga (Morocco). The fraction of 100–400 μm grain size has been washed with water, calcined at 900°C for 2 h, washed again, calcined at 900°C for 0.5 h and ground (63–125 μm). The structure of NP is similar to that of fluorapatite ($Ca_{10}(PO_4)_6F_2$), as shown by X-ray diffraction pattern and chemical analysis.[3f]

The KF/NP was prepared by evaporating to dryness a solution of potassium fluoride (1 g) in water in the presence of NP (8 g). On the other hand, the impregnation of the NP with a solution of sodium nitrate ($NaNO_3/NP = 1/2$ w/w) followed by calcination gives the modified natural phosphate $NaNO_3/NP$. The general procedure of preparation and characterization of this catalyst were described in our previous work.[6,7] In a typical procedure, the aldehyde **1** (1.5 mmol) and the active methylene compound **2** (1.5 mmol) in methanol (1 mL) were stirred with phosphate catalyst (NP, KF/NP or $NaNO_3/NP$) (0.1 g) at room temperature for the specified time (Table 1). Workup included extraction



Scheme 1.

Keywords: natural phosphate; potassium fluoride; sodium nitrate; heterogeneous catalysis; Knoevenagel condensation.

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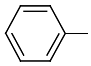
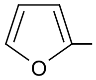
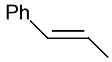
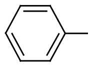
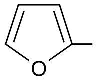
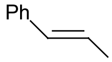
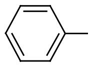
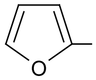
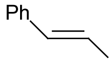
with CH_2Cl_2, filtration and evaporation. Products were subsequently purified by distillation under vacuum or recrystallization and identified by ^1H NMR and IR spectroscopy.

The results for a variety of alkenes prepared by the Knoevenagel condensation catalyzed by NP, KF/NP and $NaNO_3$/NP are summarized in Table 1. It shown that NP used in methanol can promote the Knoeve-

Table 1. Synthesis of alkenes **3** by the Knoevenagel reaction using NP, KF/NP and $NaNO_3$/NP

Product			Yield/% (time/min)[a]		
Alkene	R^1	R^2	NP	KF/NP	$NaNO_3$/NP
3a		—CN	81 (15) 98 (30)	82 (3) 90 (10)	96 (1)
3b		"	88 (3)	91 (3)	98 (3)
3c		"	88 (1)	98 (1)	98 (1)
3d		$—CO_2Me$	58 (30) 89 (60)	57 (5) 86 (30) 96 (60)	80 (5) 96 (30)
3e		"	75 (1) 86 (5)	98 (1)	98 (1)
3f		"	72 (5) 84 (10)	80 (3)	85 (1)
3g		$—CO_2Et$	21 (60)	60 (30) 68 (60)	81 (15) 94 (60)
3h		"	84 (30)	93 (1)	96 (1)
3i		"	80 (30)	90 (10)	98 (10)

[a] Yields in pure products isolated by distillation under vacuum, recrystallized with CCl_4 and identified by ^1H-NMR and IR spectroscopy.

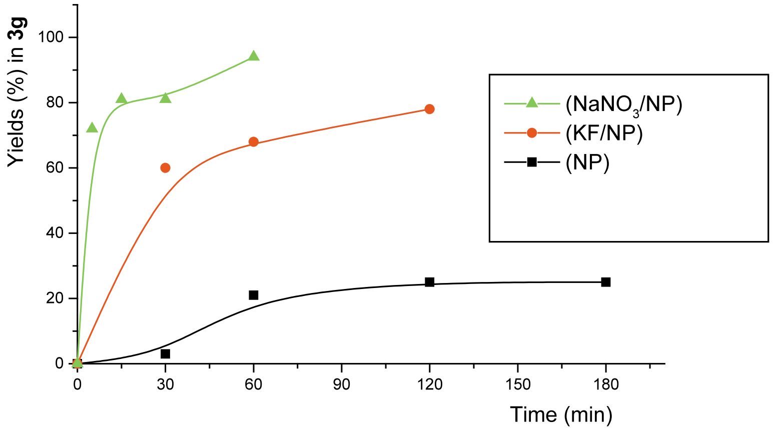


Figure 1. Comparison of the catalytic activity of NP, KF/NP and $NaNO_3$/NP in the synthesis of alkene **3g**.

nagel condensation with good yields. In the case of **3d** and **3g**, the reaction rate is much slower and requires a comparatively longer time for completion. However, under the same conditions used for NP, the catalysts KF/NP and $NaNO_3$/NP are more reactive, the best being $NaNO_3$/NP (Fig. 1).

In summary, we have reported an efficient and convenient route to the synthesis of the activated alkenes by a Knoevenagel condensation. NP doped by potassium fluoride or modified by sodium nitrate enhance the yields obtained and reduce considerably the longer reaction times. The yields are very high in a few minutes.

Acknowledgements

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