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A natural phosphate and doped-catalyzed Michael addition of mercaptans to α,β-unsaturated carbonyl compounds

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Abstract—The natural phosphate and doped by potassium fluoride catalyzed Michael addition of mercaptans to chalone derivatives with high yields in few minutes and under mild reaction conditions. Products of undesirable side reactions resulting from 1,2-addition, polymerisation and bis-addition are not observed. The work-up procedure is simplified by simple filtration with the use of natural phosphate alone or doped with potassium fluoride. © 2002 Elsevier Science Ltd. All rights reserved.

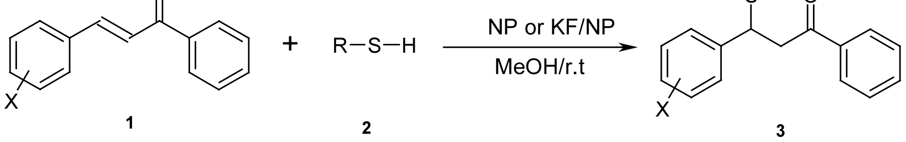
The Michael addition of mercaptans to α,β-unsaturated carbonyl compounds is important reaction in organic synthesis.[1]

The heterogeneous catalysis of the Michael addition was carried out in the presence of Al_2O_3,[2] Al_2O_3/KF,[3] $Al_2O_3/ZnCl_2$,[4] various fluorides,[5] montmorillonite/$NiBr_2$,[6] SiO_2,[7] functionalised silica,[8] Mg-Al hydrotalcite,[9] zeolite.[10] More recently, it has been shown that natural phosphate,[11] natural phosphate doped with mineral salt[12] and synthetic phosphate[13] have catalytic application in organic synthesis.

In continuation of our ongoing program to develop a heterogeneous catalysis, we describe in this paper, the use of natural phosphate and doped with KF as an inorganic support of the Michael addition between chalcone derivatives **1** and mercaptans **2**, at room temperature, with a solvent (Scheme 1).

Natural phosphate (NP)[14] 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). NP is identified by X-ray diffraction, IR spectroscopy and chemical analysis. Surface area of calcined NP was determined by the BET method from the adsorption–desorption isotherm of nitrogen at its liquid temperature, using conventional volumetric apparatus (1 m^2 g^{-1}).

The preparation of the KF/NP material involves a simple evaporation of potassium fluoride solution in the presence of NP. Such a process has been used for the production of KF/Al_2O_3,[15] as well as KF/ZnO and $KF/AlPO_4$.[16] The latter two are useful catalysts for the Michael reaction[16] and low temperature butene isomerisation,[17] respectively. While their structures have not been thoroughly investigated, Zhu and Xu indicate that there is an interaction of KF with the $AlPO_4$ support.[17] KF/Al_2O_3 is most thoroughly studied and it is well established that the structure is a complex mixture of various tetra- and hexa-fluoroaluminates, as a result of extensive reaction between the components.[15]



Scheme 1.

Keywords: natural phosphate; potassium fluoride; heterogeneous catalysis; Michael addition; recyclable catalyst.

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We showed in our previous works[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 the NP is not destroyed, indicating a less profound interaction of KF with NP than is the case with alumina. The surface area of calcined KF/NP is 8.9 m^2 g^{-1}.

Thiophenol and chalcone (X = H, Scheme 1) were chosen as model substrates to determine suitable reaction conditions.

In the presence of NP various solvents were tested. Thus, after 15 min of reaction the yields obtained of product **3a** are 95 and 91 in the presence of methanol and ethanol, respectively. In the cases of butanol, isopropanol, dimethylformamide, tetrahydrofurane, dioxane or hexane no product **3a** was observed under the reaction conditions, only the starting material was isolated.

The NP shows an interesting catalytic activity in Michael addition and yields superior to 86% are obtained in all cases[19] (Table 1). The products of undesirable side reactions resulting from 1,2-addition, polymerisation and bis-addition are not observed. The surface of NP to acidic character[20] probably induced the polarization of the C=O bond for the Michael addition.

The use of NP is particularly interesting since its regenerated by calcinations at 700°C during 15 min, and after five successive recoveries, product **3a** was obtained with same yield.

Under the same conditions,[19] the use of NP doped by KF, remarkably, increases the catalytic activity in the Michael addition. The yields are very high (92–97%) in few minutes (Table 1). For example, for the product **3b**, the yield is 96% (2 min). The best weight ratio of NP/KF is 8/1. In the presence of 0.01 g of KF alone (the present quantity in the KF/NP: 1/8 catalyst) the product of 1,4-addition was obtained with low yield (40%).

Table 1. Synthesis of products **3** by Michael addition using NP and KF/NP

Products	X	R	Yield/% (time/min)[a]	
			NP	KF/NP
3a	H	-Ph	95 (15)	96 (05)
3b	H	-2-NH_2Ph	97 (10)	96 (02)
3c	H	-CH_2-CO_2Et	56 (45)	95 (05)
3d	*m*-NO_2	-Ph	92 (10)	93 (02)
3e	*m*-NO_2	-2-NH_2Ph	94 (10)	92 (02)
3f	*m*-NO_2	-CH_2-CO_2Et	96 (20)	95 (05)
3g	*p*-Cl	-Ph	96 (15)	93 (05)
3h	*p*-Cl	-2-NH_2Ph	96 (10)	97 (02)
3i	*p*-Cl	-CH_2-CO_2Et	86 (20)	97 (05)

[a] Yields in pure products isolated by recrystallization with AcOEt/CH_2Cl_2 and identified by ^1H, ^{13}C NMR and IR spectroscopy.

The best solvents to carry out this addition by NP/KF are methanol, ethanol, butanol and isopropanol. A similar effect of solvent has been observed in the hydration of nitriles[21] and in the preparation of α-hydroxyphosphonates.[22]

In conclusion the selective Michael addition of mercaptans to simple and substituted chalcones was achieved in good yields and few minutes, under mild reaction conditions, in the presence of 0.1 g of natural phosphate alone or doped by KF. The high reactivity and specificity of our catalysts coupled with their ease of use and reduced environmental problems makes them attractive alternatives to homogenous base reagents.

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

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19. The general procedure is as follows: To a flask containing an equimolar mixture (1 mmol) of thiol **2** and chalcone derivative **1** in methanol (1.5 ml), NP or KF/NP (0.1 g) was added and the mixture was stirred at room temperature until completion of the reaction, as monitored by thin layer chromatography (TLC). The catalyst was filtered, washed with dichloromethane and the filtrate was concentrated under reduced pressure. The crude product was purified by recrystallization. The product was analysed by ^{1}H, ^{13}C NMR and IR spectrometry.
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