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AN UNEXPECTED REACTIVITY OF SIMPLE HETEROGENEOUS MIXTURE OF γ-ALUMINA AND POTASSIUM FLUORIDE : 1-HYDROXYALKANE PHOSPHONIC ESTERS SYNTHESIS FROM NON-ACTIVATED KETONES IN "DRY MEDIA".

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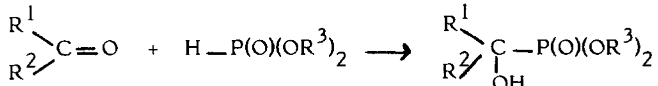
Summary - 1-Hydroxyalkane phosphonic esters are readily obtained from non-activated ketones and dialkylphosphites by adsorbing them together on a heterogeneous γ-alumina-potassium fluoride mixture.

We reported in previous papers[1-2], 1-hydroxyalkane phosphonic ester preparation using potassium or caesium fluoride on chromatographic alumina. This method was very efficient for aldehydes which gave quantitative yields, but only activated ketones reacted easily. Recent results obtained in this field [3] prompt us to report our work.

We describe now that the simple heterogeneous mixture of finely powdered γ-alumina and potassium fluoride can promote the condensation of non-activated ketones **1** (dialkyl, arylalkyl, cyclic and diaryl) with dialkylphosphites **2** at room temperature : the final product **3** is obtained in good to quantitative yield (see table). Nevertheless, benzophenone is less reactive.



1 **2** **3**

For the same reaction time, we observed that a 1:1 weight ratio of fluoride to γ-alumina was optimal. A different ratio lowered the reaction rate. It is not necessary to use expensive chromatographic alumina. The well known supported potassium fluoride/alumina for anionic activation [4-6] was also efficient, its reactivity being comparable to the simple mixture of solids at room temperature and without solvent. Our heterogeneous catalyst was very easy to prepare and offered a remarkable efficiency for the addition of non-activated ketones with dialkylphosphites. Its catalytic action was very selective for non-activated ketones : in the case of α-chlorinated ketones, cyclisation to epoxyphosphonates was observed. In the case of aldehydes, the yield of isolated product is lowered by difficulties of desorption from the solid catalyst.

A typical procedure is as follows : commercial potassium fluoride (2.5 g) (no dehydration is necessary) was mixed with γ-alumina (2.5 g) (Merck, n° 1095) finely powdered before use. The heterogeneous catalyst was added slowly by small portions to the equimolar mixture of ketone **1** (10 mmol) and dialkylphosphite **2** (10 mmol), without organic solvent, at room temperature. After the appropriate time (see table), the mixture was eluted with dichloromethane (2 x 25 ml). The organic phase was evaporated under reduced pressure and the 1-hydroxyalkanephosphonic ester **3** was easily obtained. The purity of the crude product was controlled by T.L.C. on silica gel (eluent : ether/petroleum ether 60°-80°, 1:1).

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Table

R^1	R^2	R^3	Reaction time	Yield of **3** %^{a}	mp or bp/Torr ^{d} (°C)
CH_3	CH_3	CH_3	30 mn	85 ^{b}	72
CH_3	CH_3	C_2H_5	15 mn	95 ^{b}	120/0.03
CH_3	C_2H_5	CH_3	1 h	75 ^{b}	80/0.03
C_6H_5	CH_3	C_2H_5	1 h	73	77
C_6H_5	C_6H_5	C_2H_5	3 h	50	164
C_6H_5	C_6H_5	CH_3	6 h	57	171
$-(CH_2)_5-$		C_2H_5	15 mn	95	81
CH_3	CH_3	$(CH_3)_2CH$	1 h	$90^{b,c}$	59 or 70/0.025
CH_3	C_2H_5	$(CH_3)_2CH$	1 h	$83^{b,c}$	100/0.025
C_6H_5	C_2H_5	CH_3	3 h	68	126
CH_3	CH_3	$CH_3(CH_2)_3$	1 h	$75^{b,c}$	110/0.025
C_6H_5	C_6H_5	$C_6H_5-CH_2$	24 h	50	154
CH_3	CH_3	$C_6H_5-CH_2$	1 h	50	81

^{a} Yield of crude, isolated product having correct mp, IR, ^{1}H NMR spectra before further purification ; ^{b} 100 % estimated by ^{1}H NMR ; ^{c} supported potassium fluoride alumina is used ; ^{d} bulb to bulb short-path distillation.

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