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Catalytic properties of alkali metal-modified oxide supports for the Knoevenagel condensation: Kinetic aspects

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ABSTRACT

The characterization of the alkali-modified metal oxides surface basicity by condensation of benzaldehyde with some methylenic compounds (ethyl cyanoacetate, ethyl acetoacetate and diethyl malonate) as test reaction were studied with a series of lithium, sodium, potassium, rubidium and cesium impregnated simple oxide matrices (SiO_2, Al_2O_3, $Nb_2O_5{\cdot}nH_2O$ and Nb_2O_5). The condensation of benzaldehyde and other substituted benzaldehydes with ethyl acetoacetate using these catalysts and in absence of any solvent, is also proposed as a "green method" in the preparation of pharmaceuticals in the line of calcium channel blockers and antihypertensives. The role of the support nature in the Knoevenagel condensation activity is considered.

1. Introduction

In the production of Fine Chemicals, the development of environmentally friendly solid catalysts has known a recent growing interest. Base catalysed processes such as aldolisation, alkylation, Knoevenagel condensation and Michael addition are commonly used for the manufacture of these chemicals. A better preservation of environment would require the substitution of liquid bases and organometallics by solid catalysts. Indeed solid catalysts have many advantages from the technical point of view: they present fewer disposal problems, while allowing easier separation and recovery of the products, catalysts and solvent if any. They are non-corrosive, and offer environmentally benign and more economical pathways for the synthesis of fine chemicals.

In the literature, several solid catalysts with basic properties have been proposed. There are catalysts mainly based on alkali metals supported on matrix having high surface area such as zeolites, mesoporous molecular sieves [1], oxides, mixed oxides and doped oxides [2,3]. Most of the papers are devoted to cesium oxide supported on metal oxides, or zeolites, or mesoporous matrices. However, there are few studies of these supports modified with all alkali metal elements.

Different reactions have been studied on solid bases. In particular, the kinetic study of Knoevenagel condensation has been used to measure the total amount of basic sites and the basic strength distribution in solid catalysts. This reaction can also be used to form C–C bonds through the reaction of a carbonyl with an active methylenic group [4]. It is widely used in the synthesis of important intermediates or end-products for perfumes [5], pharmaceuticals [6], calcium antagonists [7], and polymers [8].

In the present work, we have used the Knoevenagel condensation as probe reaction to study the basicity and reactivity of a series of alkali-modified metal oxides, which have been prepared by impregnation with alkali metal acetates. We have chosen three types of oxides (SiO_2, Al_2O_3, hydrated and dehydrated Nb_2O_5), which present various acidities and therefore give rise to the different strength of interaction with alkali metals. The acidic–basic properties of these materials were previously tested in the cyclisation of acetonylacetone, decomposition of isopropanol and hydrosulphurisation reaction [9]. The modification of niobia supports (hydrated and dehydrated) with alkali metal species creates acid–base catalysts highly selective in the methanethiol production, whereas the impregnation of silica and alumina with these species leads to the generation of basicity [9].

We have also employed the Knoevenagel condensation to prepare compounds of the type A, which are intermediates in the preparation of some dihydropyridines of type B (Scheme 1). Dihydropyridines chemistry is of interest not only from point of view of fundamental research on heterocyclic compounds [10], but especially because of expanding practical applications of

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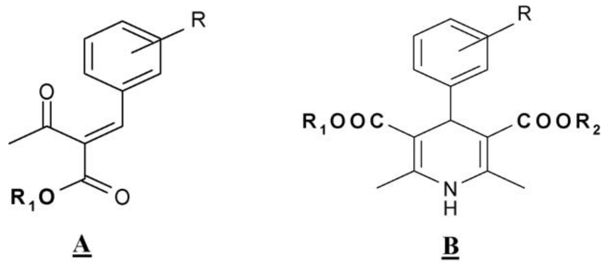

Scheme 1. Structure of the intermediate for the synthesis of 1,4-dihydropyridines (compound of type A), and general structure of 4-aryl-1,4-dihydropyridine derivatives (compound of type B).

1,4-dihydropyridine derivatives as pharmaceuticals in the line of calcium channel blockers [11,12].

2. Experimental

2.1. Catalysts preparation

Acetates of alkaline metals (Li, Na, K, Rb or Cs) were deposited onto SiO_2 (Ventron, 365 m^2/g), Al_2O_3 (Sasol, 190 m^2/g) and $Nb_2O_5 \cdot nH_2O$ (CBMM, Brazil, 30 m^2/g) by the incipient wetness impregnation method to prepare three series of catalysts. The outgassed SiO_2, Al_2O_3 and $Nb_2O_5 \cdot nH_2O$ (373 K, 2 h in the oven) were filled in with the appropriate amount of an aqueous solution of acetate (CH_3COOLi, CH_3COONa, CH_3COOK, CH_3COORb or CH_3COOCs, Aldrich, a volume of the solution ideally equal to the pore volume of the support) and located in an evaporator flask, where the catalyst was rotated and heated at 373 K for 1 h. The impregnated powder was dried at 373 K for 18 h and then calcined at 773 K for 10 h in an oven. In such a case we obtained three series of catalysts; X/SiO_2, X/Al_2O_3 and $X/Nb_2O_5 \cdot nH_2O$ (X = Li, Na, K, Rb, or Cs, respectively).

The fourth series of catalysts (X/Nb_2O_5, X = Li, Na, K, Rb, or Cs, respectively) was prepared using $Nb_2O_5 \cdot nH_2O$ as a support but after a different pre-treatment. $Nb_2O_5 \cdot nH_2O$ was dried at 373 K for 5 h and then calcined at 773 K for 10 h in the oven and in the presence of an airflow during 6 h. The calcined support, denoted as Nb_2O_5, was filled in with the appropriate amount of an aqueous solution of the alkaline acetates and located in an evaporator flask, where the catalyst was rotated and heated at 373 K for 1 h. The impregnated powder was dried at 373 K for 18 h and then calcined again at 773 K for 10 h in the oven.

The amount of alkali metal acetate used for the impregnation was calculated for the loading of metal equal to 0.5 mmol/g of the support.

2.2. Characterization of the materials

The texture of the catalysts was characterised using XRD, N_2 adsorption/desorption and infrared spectroscopy in the skeleton vibration region and is reported in [9].

2.3. Reaction procedure: Knoevenagel condensation

An equimolar solution of the two reactants, without any solvent, was kept in a batch reactor in a silicone bath under magnetic stirring, while heating up to the reaction temperature (413–433 K). Then, depending on the active methylenic compound employed, 1%, 2% or 10% of catalyst were added and the reaction time started. Samples were taken periodically, and the evolution of the reaction was followed by GC–MS.

3. Results and discussion

3.1. Characterization

The data calculated from the nitrogen adsorption at 77 K were reported in [9]. In general, the BET surface area of silica and dehydrated niobia significantly decreases after the impregnation with alkali metal acetates followed by the calcination. This is accompanied by the increase of average mesopore diameter and, for silica support, also by a significant growth in mesopore volume. It is not the case of alumina-based materials for which all textural parameters slightly depend on the impregnation procedure an hydrated niobia for which the surface area changes depending on the formation of the new phase via the chemical reaction between the support an alkali medium.

From the XRD and IR studies we have concluded previously [9] that the lack or very weak chemical interaction of the support with the impregnating medium, as in the case of silica, leads to the loading of alkali metal oxides on the support surface an easy migration resulting in the agglomeration of oxide species [9]. Moreover, this loading most probably builds additional porosity, which results in the increase of average mesopore volume and diameter. In the case of the interaction of metal oxide with alumina surface protects the agglomeration of alkali metal species and gives rise to a better dispersion. This provokes the remaining of textural parameters of alumina, almost untouched after impregnation with alkali metal acetates. The chemical reaction between alkali metal salt and hydrated niobia changes the textural parameters of the final materials according to the formation of new mixed phases [9].

3.2. Kinetics and mechanism of the Knoevenagel condensation

The condensation between benzaldehyde and the three active methylenic compounds (ethyl cyanoacetate, $pK_a = 9$; ethyl acetoacetate, $pK_a = 10.7$ and diethyl malonate, $pK_a = 13.3$) were carried out with Li, Na, K, Rb and Cs impregnated simple oxide samples, and with the pristine supports (particle size within 0.074 and 0.140 mm) at 413 K.

The conversion values of benzaldehyde in the Knoevenagel condensation with ethyl cyanoacetate ($pK_a = 9$) using metal oxides modified with alkali metals are shown in Fig. 1(A–D). As it has been found, the selectivity to the Knoevenagel product is 100% so conversions are also the yields of product. Incorporation of the alkali cations significantly increases the activity for alumina and silica supports but decreases the activity of hydrated and dehydrated niobia supports. The order of activity found for the unmodified supports was the following: $Nb_2O_5 \cdot nH_2O > Nb_2O_5 > Al_2O_3 > SiO_2$.

Benzaldehyde has also been condensed with ethyl acetoacetate ($pK_a = 10.7$). The results at 413 K and 300 min time of the reaction are given in Table 1 and the trend followed by the catalysts it is showed in Fig. 2. The activity orders are

Series X/SiO_2: $K > Rb \approx Na > Cs > Li$
Series X/Al_2O_3: $K > Cs > Rb \approx Na \approx Li$
Series $X/Nb_2O_5 \cdot nH_2O$: $Rb > K > Na > Li > Cs$
Series X/Nb_2O_5: $Rb > K > Na > Cs > Li$

These results indicate that the studied catalysts possess basic sites capable of abstracting protons of $pK_a \leq 10.7$. However, other reaction products are formed, in addition to the Knoevenagel condensation product. Thus, one mole of this last product can condense again with another mole of ethyl acetoacetate to give different products and also the ethyl acetoacetate can suffer