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Technical Note

Ultrasound-activated Knoevenagel condensation of malononitrile with carbonylic compounds catalysed by alkaline-doped saponites

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Abstract: α,β-Unsaturated nitriles have been synthesized by Knoevenagel condensation of a carbonylic compound with malononitrile, assisted by sonochemical irradiation. Two alkaline-promoted clays (Li^+- and Cs^+-exchanged saponites) have been employed as catalysts. The influence of the carbonylic compound (benzaldehyde or cyclohexanone) and the use of a solvent on the catalytic activity have been studied. Remarkable increase in the conversion values has been found when the reaction is activated by ultrasound, as compared with the thermal activation. In this green, solvent-free procedure, α,β-unsaturated nitriles have been produced in very high yields (97%) when the Cs^+-saponite is used as catalyst.

Keywords: alkaline clay minerals; basicity; ultrasound activation; α,β-unsaturated nitriles; Knoevenagel condensation

INTRODUCTION

Knoevenagel condensation, a versatile reaction for the formation of carbon-carbon bonds, has numerous applications in the synthesis of α,β-unsaturated nitriles and α,β-unsaturated esters (Scheme 1), which are important intermediates or end products in the fine chemical industry, such as prepolymers[1] or antihypertensives and calcium antagonists.[2] Many solid base catalysts have been used to obtain the corresponding Knoevenagel products.[3–6]

The application of new catalytic methods in the fine and specialty chemicals industry has increased in recent years in order to minimize both production cost and waste generation.[7,8] Ultrasonic energy promotes some chemical reactions and is nowadays presented as an alternative tool to prepare fine chemicals under mild conditions.[9,10] The sonochemical effect results from the interaction between a suitable field of acoustic waves and a reacting chemical system, interaction being given by the intermediate phenomena of acoustic cavitation. Three important factors must be considered: the chemical system, the acoustic field, and the bubble field. The chemical effects of ultrasound are attributed to the collapse of the cavitation bubbles, which upon implosion contain the reactant mixture under high temperatures and pressures. These phenomena are especially useful when the catalyst is a solid material. When a chemical reaction occurs in the presence of both a solid catalyst and ultrasonic irradiation, the activity usually increases.[11]

In this contribution, the catalytic behaviour of saponite doped with alkaline cations in the synthesis of α,β-unsaturated nitriles is studied, using ultrasonic irradiation to activate the reactions. These compounds are formed by the condensation of a carbonylic compound (aldehyde or ketone) with the acidic hydrogens close to nitrile or ester groups (Scheme 1), catalyzed by alkaline solids able to abstract such acidic hydrogen atoms. Some variables that influence the

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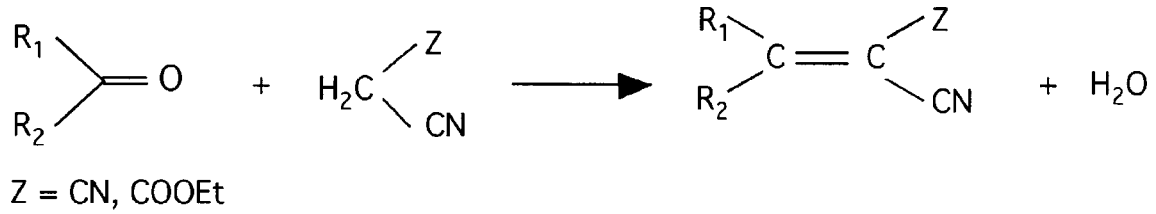


Scheme 1. Base-catalyzed Knoevenagel aldol-type reaction.

reactions are investigated, namely: (i) the alkaline cation doping the clay (Li^+ or Cs^+), (ii) the carbonylic compound involved in the reaction (aldehyde or ketone), (iii) the activation of the reaction by ultrasonic irradiation or by 'classical' thermal activation, and (iv) the development of the reaction with or without solvent.

EXPERIMENTAL

Preparation and characterization of the catalysts

The starting material used in this work is a natural saponite from Yunclillos deposit (province of Toledo, Spain), supplied by Tolsa, SA. The $\leq 2\,\mu m$ fraction of the clay was obtained by careful aqueous decantation of the raw material. The chemical weight percent composition of this clay is: SiO_2: 49.45; Al_2O_3: 4.72; Fe_2O_3: 1.29; MgO: 24.34; TiO_2: 0.20; MnO: 0.03; CaO: 0.78; Na_2O: 0.07; K_2O: 0.44; and loss on ignition: 18.31 wt%. X-ray diffraction shows that this fraction contains very small amounts of sepiolite and quartz as the only mineral impurities. Considering these impurities, the structural formula of the saponite, on the basis of 22 oxygen atoms, was found to be: $(Si_{7.42}Al_{0.58})(Mg_{5.16}Fe_{0.14}Al_{0.26}Mn_{0.004}Ti_{0.02})O_{20}(OH)_4$ [$Mg_{0.24}Ca_{0.124}Na_{0.020}K_{0.084}$]. The cation exchange capacity (CEC) of this solid was 115 meq/100 g of dry clay, and the BET specific surface area was $161\,m^2\,g^{-1}$.

Li^+-saponite (Li^+-SA) and Cs^+-saponite (Cs^+-SA) were prepared by a two-step synthetic process. First, homoionic Na^+-saponite was obtained by washing saponite ($\leq 2\,\mu m$ fraction) (30 g) three times with $1\,mol\,dm^{-1}$ NaCl solution ($500\,cm^3$). In the second step, Li^+- and Cs^+-exchanged solids were prepared by treating the sodium clay with solutions of the corresponding chlorides: ie LiCl (1.4 g) or CsCl (2.6 g) were added to a suspension containing Na-saponite (10 g) in water ($500\,cm^3$). These suspensions were stirred for 24 h and then washed with water until no chloride anions were detected.

The composition of the clays was determined by atomic absorption (AA) with a Perkin Elmer 4100 ZL spectrometer. Crystalline structures of the samples were analyzed by X-ray diffraction (XRD) with a Siemens Krystalloflex D500 diffractometer, using filtered CuKα radiation.

Catalytic activity

Thermal-activated reactions

Equimolecular amounts (5 mmol) of the carbonylic compound (benzaldehyde or cyclohexanone) and malononitrile (Scheme 2) were placed in a batch reactor at 308 K, in the absence of any solvent. Then, the catalyst (2 wt%) was added and the reaction time started. The reactions were followed by gas chromatography using a KNK-3000-HRGC KONIK instrument equipped with a 60 m phenylsilicone capillary column and a flame ionization detector. The mass spectra of the products were obtained on a Hewlett-Packard HP 5971 A spectrometer. Previous experiments (modifying the stirring rates, between 1500 and 3000 rpm and the particle size of the clay between <0.074 or $0.140\,mm < d < 0.250\,mm$) led us to confirm that there was no control of the reaction by external nor internal diffusion.

Ultrasound-activated reactions

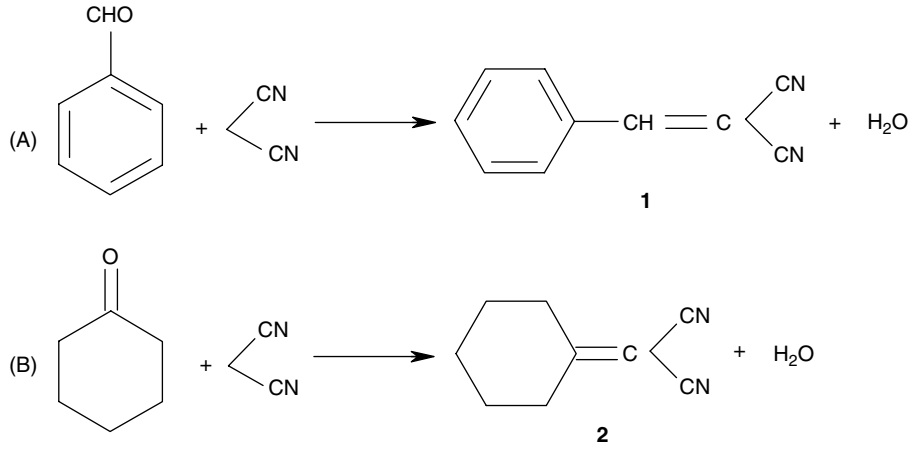
In this case, the reaction was carried out in an ultrasonic cleaning bath (Selecta Ultrasound-H) with a heating system, frequency 40 kHz and power 550 W. Equimolecular amounts (5 mmol) of both reactants (malononitrile and benzaldehyde or malononitrile and cyclohexanone) were mixed in a Pyrex flask without any solvent. The flask was suspended into the ultrasonic bath at 308 K. Then, the catalyst (2 wt%) was added, power was connected and the reaction time started. The reactions were followed by GC as before.

To analyze the influence of carrying out the reaction in a solvent medium, the reactants were dissolved in acetone ($15\,cm^3$) and the reaction was carried out as described above.

RESULTS AND DISCUSSION

Catalyst characterization

Li^+-SA fixes 0.12 wt% of Li^+ (referred to the dehydrated sample), indicating that 0.138 of the exchangeable positions are occupied by this cation in the structural formula given above. Cs^+-SA fixes 0.97 wt% of Cs^+, equivalent to 0.058 positions in the structural formula of the clay. This means that under the above experimental conditions about 16% of the exchangeable positions of the clay were effectively exchanged by Li^+ and only about 7% by Cs^+, the rest of the positions remained occupied by Na^+ cations. Although, in both cases, Li^+ and Cs^+ cations were



Scheme 2. Knoevenagel condensation of malononitrile with carbonylic compounds: (A) benzaldehyde, (B) cyclohexanone.

in excess with respect to the CEC of the clay in the exchanging solution, a high degree of substitution is not expected when exchanging only once with these cations. Higher degrees of substitution may be reached by repeating the exchange processes, but the amounts of Li^+ and Cs^+ incorporated to the clays were considered acceptable for the purpose of the study.

The X-ray diffraction patterns of the exchanged solids show the usual patterns of well-ordered saponites (Fig 1). The intensity of the Na^+-saponite diffractogram, included for comparison, is very similar to that of the $<2\,\mu m$ fraction of the natural clay, and compared with them, Li^+-SA has a more intense (001) reflection peak, while the Cs^+-SA has a less intense and wider reflection. Thus, exchanging with Li^+ produces an increased ordering of the layers, while the exchanging with Cs^+ has an opposite effect. At the same time, the basal spacing of the Na^+-saponite and Cs^+-SA is close to 12.5 Å, while for the Li^+-SA this spacing is close to 14.7 Å, the same as for the natural clay, which mainly has alkaline-earth cations in exchangeable positions. The basal spacings agree with the presence of a monolayer (Na-saponite and Cs^+-SA) or a bilayer (natural saponite and Li^+-SA) sheet of water molecules in the interlayer space of the clays, the higher hydration degree in the Li^+-exchanged sample being related to the high hydration capacity of this cation. Although the amounts of Li^+ and Cs^+ are relatively low, their presence clearly influences the shape of the diffractograms. In conclusion, both catalysts used in this study are well-ordered saponites, more crystalline in the case of the Li sample.

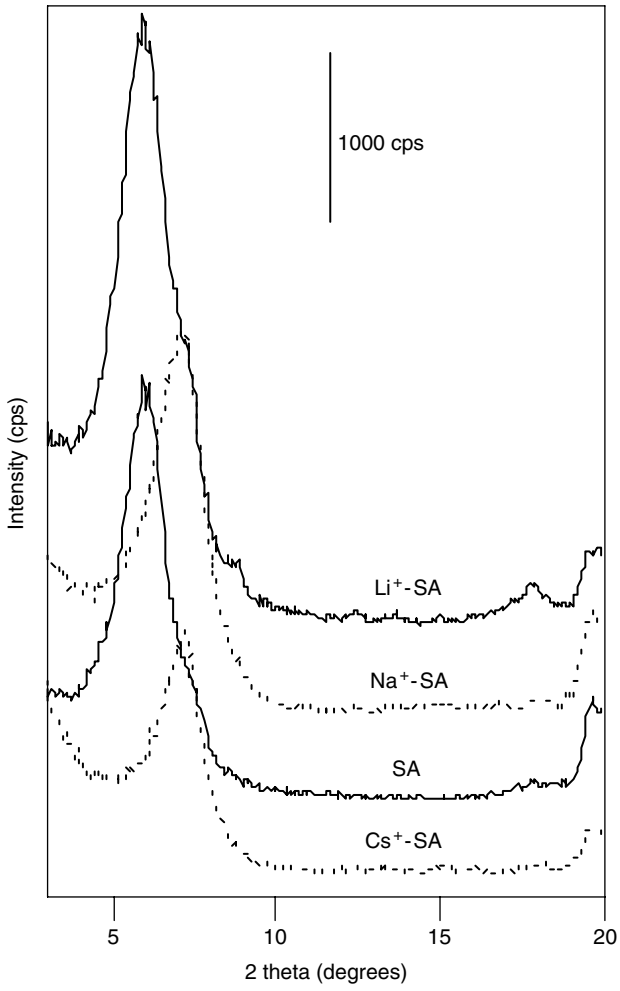


Figure 1. X-ray diffractograms of the natural saponite, SA ($\leq 2\,\mu m$ fraction), and of the Na^+-, Li^+- and Cs^+-exchanged solids.

Catalytic activity

Prior to the catalytic tests, a Knoevenagel test reaction had been applied to measure the basicity of the clays.[3] As expected, it was found that the basicity increases with the radius of the alkaline dopant (Li^+-SA < Cs^+-SA), both saponites having basic sites able to abstract protons of $9.0 \leq pK_a \leq 16.5$, thus being able to abstract protons from malononitrile, $pK_a = 11.0$. Thus, the catalysts were tested in the Knoevenagel condensation of this nitrile with benzaldehyde and cyclohexanone (Scheme 2), which represents industrial interest for the preparation of α,β-unsaturated nitriles.

Table 1 displays the conversion to α,β-unsaturated nitrile **(1)** during the condensation of benzaldehyde with malononitrile in the presence of Li^+-SA and Cs^+-SA at 308 K under sonochemical activation and under thermal activation in a batch reactor. The

Table 1. Condensation of benzaldehyde with malononitrile using Li^+-SA and Cs^+-SA as catalysts (reaction temperature: 308 K)

	Conversion (%)			
	Li^+-SA		Cs^+-SA	
Time (min)	Batch	Ultrasound	Batch	Ultrasound
5	4.2	6.3	5.7	15.0
15	9.1	16.4	10.9	30.7
30	10.0	25.1	14.4	57.5
45	13.5	31.3	24.3	65.7
60	19.0	35.6	34.1	71.0
120	31.3	51.5	49.0	97.0

mass spectra of the reaction products confirm that **1** [MS m/s: 145 (M^+), (100), 127, 103, 76, 50] is the only product obtained. Other side reactions, such as oxidation, Michael addition or decarboxylation may occur together with condensation; however in our case the only product formed is the α,β-unsaturated nitrile, therefore providing a selectivity of 100%. Thus, the yield values to the nitrile are the same as the conversion values. It is observed that, for all reaction times, the conversion is higher when using Cs^+-SA instead of Li^+-SA, and also higher when the reaction is activated by ultrasound irradiation than when carried out under thermal activation.

To study the influence of the type of carbonylic compound (aldehyde or ketone) cyclohexanone was also used as reactant. The results for the condensation between cyclohexanone and malononitrile are listed in Table 2, both under conventional heating and under ultrasound irradiation. The mass spectra of the reaction products confirm that derivative **(2)** [MS m/s: 146 (M^+), 131, 55 (100), 41] is the only product formed. As in the case of benzaldehyde, the conversion is also higher when using ultrasound irradiation and Cs^+-SA.

From Tables 1 and 2 it can be concluded that, in general, ultrasonic activation performs much better than thermal activation, since higher yields are reached in the same reaction times. The enhancement of the activity is more significant in the case of Cs^+-SA than in the case of Li^+-SA. A yield value of around 100% is achieved in 120 min under ultrasound activation

Table 2. Condensation of cyclohexanone with malononitrile using Li^+-SA and Cs^+-SA as catalysts (reaction temperature: 308 K)

	Conversion (%)			
	Li^+-SA		Cs^+-SA	
Time (min)	Batch	Ultrasound	Batch	Ultrasound
5	2.2	6.4	5.1	10.5
15	5.3	13.1	10.3	23.3
30	7.1	16.8	18.6	35.1
45	9.7	19.7	23.9	47.8
60	13.6	22.9	25.8	55.6
120	23.1	39.2	43.7	71.4

in the case of benzaldehyde when Cs^+-SA is used as catalyst. The basicity of the clay clearly influences the catalytic activity, the more alkaline solid (Cs^+-SA) having a higher activity than the less alkaline (Li^+-SA). The conversion could be influenced by the amount of alkaline element fixed during the cation exchange, but considering that the number of meq of Li^+ fixed is higher than that of Cs^+, it is clear that the activity is controlled by the basicity of the solids and not by the amount of alkaline cation.

On the other hand, it is well known that, under conventional heating, the reactivity of the carbonylic group of aldehydes is higher than that of ketones.[12] From the results presented in Tables 1 and 2, it can be concluded that this order of reactivity is maintained under ultrasound activation.

The positive catalytic effect of the clay solids in the reaction needs to be verified, because it must be considered that ultrasonic waves can, themselves, exert a strong catalytic effect. This was done by studying the condensation of malononitrile with both carbonylic compounds under ultrasonic activation in the absence of any catalyst. The results obtained are compared in Fig 2 with those obtained using Li^+-SA and Cs^+-SA. It is confirmed that ultrasound exerts by itself, a catalytic effect on the production of α,β-unsaturated nitriles; with yields around 19% and 11% of **1** and **2**, respectively, achieved after 120 min when no catalyst is employed. Nevertheless, these values are significantly lower than those obtained under ultrasonic activation with the clay catalysts. The combination of both factors, the alkaline saponites and the ultrasound waves, affords a remarkable increase in the yields.

The influence of solvent under ultrasonic activation was investigated by carrying out the reaction in acetone. The condensation of malononitrile with both carbonylic compounds was considered, choosing the catalyst with higher activity, ie Cs^+-SA. The results obtained (Fig 3) clearly show that the conversion is higher when the reaction is performed in the absence of solvent, being around twice as high. This is a very interesting result from both the economic and the

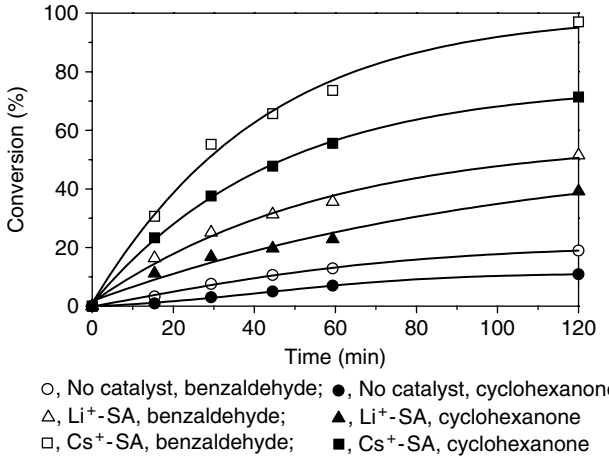


Figure 2. Condensation of malononitrile with benzaldehyde or cyclohexanone under ultrasound activation, at 308 K.

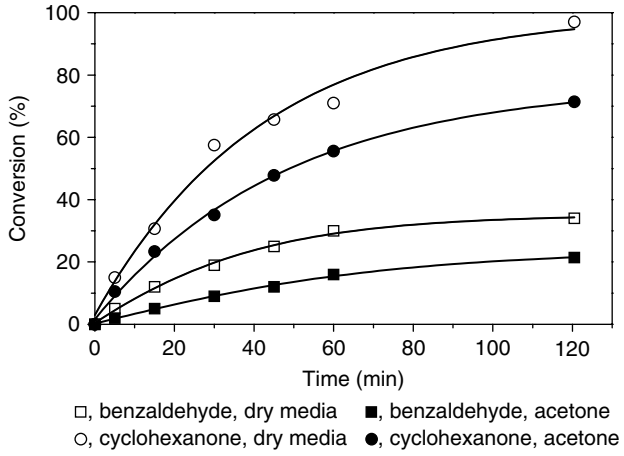


Figure 3. Condensation of malononitrile with benzaldehyde or cyclohexanone using Cs^+-SA as catalyst, and carrying out the reaction in dry media or in acetone.

environmental points of view, the cost of the reactions and their environmental impact may be considerably reduced.

CONCLUSIONS

Two basic saponites (Li^+-SA and Cs^+-SA) have been shown to be active and selective catalysts for the Knoevenagel condensation of benzaldehyde or cyclohexanone with malononitrile (synthesis of α,β-unsaturated nitriles). Ultrasonic activation has been employed to enhance the activity of the catalysts. The ultrasound waves exert a positive effect on the reactivity, improving the conversion values when compared with those obtained in a batch reactor under thermal activation. In general, better results are obtained using benzaldehyde instead of cyclohexanone as carbonylic compound. The highest yields are obtained for the Cs^+-SA, which possesses higher basicity than Li^+-SA. The use of a solvent (acetone) has a clear deleterious effect on the conversion of the reaction. Enhancement effects on the conversions, by combining the basicity of the clay catalyst and the ultrasonic waves, is presented as an alternative method for the synthesis of α,β-unsaturated nitriles, which can be easily produced with high yield and under very mild conditions.

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