

# ZnNaY zeolite catalysed reaction of $\beta$ -dicarbonyl compounds with ethyl cyanoformate under solventless conditions

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A simple and environmentally friendly procedure has been developed for the reaction of  $\beta$ -dicarbonyl compounds with ethyl cyanoformate. The corresponding unsaturated aminoesters were synthesised in good yields (60–95%) and excellent selectivities (96–98%) by carrying out the reaction under solventless conditions in the presence of a Zn-exchanged NaY zeolite. The catalyst can be recovered and reused.

## Introduction

In light of stringent and growing environmental regulations, the chemical industry needs to re-examine the most important synthetic processes and to develop more eco-compatible synthetic methodologies.<sup>1</sup> To this purpose heterogeneous catalysis plays a fundamental role, mainly due to its economic and environmental advantages (*i.e.* minimum execution time, low corrosion, waste minimisation, recycling of the catalyst, easy transport and disposal of catalysts).<sup>2</sup>

Another important goal in green chemistry is represented by the elimination of volatile organic solvents; in fact solvent-free organic reactions make syntheses simpler, save energy, and prevent solvent wastes, hazards, and toxicity.<sup>3</sup>

Of course the combination of heterogeneous catalysis with the use of solventless conditions represents a suitable way towards the so-called ideal synthesis.<sup>4</sup> Since the revision of fundamental synthetic reactions under environmentally friendly conditions has been the subject of our research over the last decade,<sup>5</sup> we have recently examined the reaction of  $\beta$ -dicarbonyl compounds with ethyl cyanoformate under zeolite catalysis. This reaction produces unsaturated aminoesters that are useful intermediates for the synthesis of heterocycles,<sup>6</sup> of amino acid derivatives and of other multi-functional derivatives.<sup>7</sup>

Under homogeneous conditions the process is usually carried out in the presence of stoichiometric amounts of Lewis acids<sup>8</sup> or catalytic quantities of zinc or nickel acetylacetonates.<sup>7,9</sup>

## Results and discussion

In a first series of experiments we decided to carry out the model reaction between benzoylacetone **1a** (10 mmol) and ethyl cyanoformate **2** (10 mmol) in methylene chloride (5 ml) in the presence of various metal acetates (5% mol) in order to find out the best metal promoter (Scheme 1).

Results concerning the yield and the selectivity of product **3a** are given in Table 1.

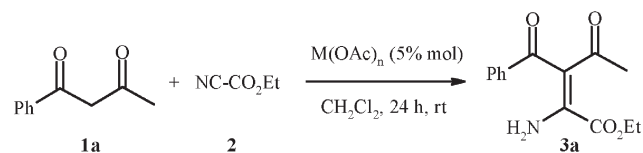
In all cases the reactions are highly selective affording the (Z)-isomer; by employing zinc acetate (Table 1, entry c), a good yield was also achieved.

On the basis of these preliminary results, we decided to prepare a Zn-exchanged zeolite to be used as catalyst to perform the reaction under heterogeneous conditions. We singled out zeolite NaY<sup>10</sup> due to its large pores (7.8 Å) that can allow the diffusion of both reactants and products.<sup>11</sup> The zeolite was exchanged with Zn(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O following the methodology reported in the literature;<sup>12</sup> the final content of Zn in the zeolite was 0.6 mmol g<sup>-1</sup>.

The model reaction was carried out in the absence of the solvent and was optimised by taking into account the following parameters: reaction time, reaction temperature, and reagents : Zn ions molar ratio. At first, a comparison of the concentration of product **3a** vs. time was made (Fig. 1) by carrying out the reaction at 75 °C with 10 mmol of each reagent and 0.50 g of zeolite.

Results show that the maximum production of **3a** occurs during the first 1.5 hours (~60% yield); then the reaction proceeds slowly and the yield reaches its maximum value of 78% after 4 hours.

If the reaction temperature is increased to 100 °C, the product can be isolated in 85% yield.



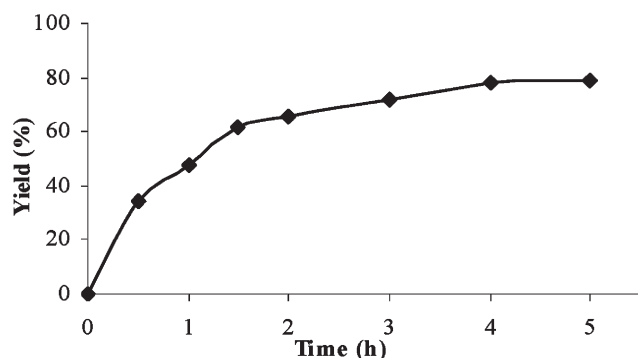
**Scheme 1** Reaction of benzoylacetone with ethyl cyanoformate in the presence of various metal acetates.

**Table 1** Reaction of benzoylacetone with ethyl cyanoformate in the presence of various metal acetates<sup>a</sup>

Entry	Catalyst	Yield (%)	Selectivity (%)
a	Ni(OAc) <sub>2</sub> ·4H <sub>2</sub> O	54	98
b	Mn(OAc) <sub>3</sub> ·2H <sub>2</sub> O	5	97
c	Zn(OAc) <sub>2</sub>	61	97
d	Co(OAc) <sub>2</sub> ·4H <sub>2</sub> O	46	96

<sup>a</sup> Reaction conditions according to ref. 9.

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**Fig. 1** Reactivity of benzoylacetone with ethyl cyanoformate in the presence of ZnNaY zeolite at 75 °C as a function of time.

The effect of the catalyst amount was then investigated. To this end the same model reaction was carried out in the presence of 0.10 g, 0.25 g, 0.50 g and 1.00 g of ZnNaY zeolite at 100 °C for 4 hours; product **3a** was obtained in 26%, 59%, 84% and 85% yields respectively. These data show that the optimum catalyst : reagents ratio was 0.25 g : 10 mmol.

To explore the general validity of this process, different  $\beta$ -dicarbonyl compounds, namely  $\beta$ -diketones,  $\beta$ -ketoesters and  $\beta$ -diesters were reacted with ethyl cyanoformate by stirring the mixture at 100 °C for 4 hours in the presence of ZnNaY zeolite; results are given in Table 2.

The reaction is of general applicability and affords good yields with  $\beta$ -diketones and  $\beta$ -ketoesters. On the contrary, due to the lower reactivity of  $\beta$ -diesters, the corresponding products were isolated in poor yield; moreover, in all cases excellent selectivity was observed (>96%).

Finally we faced the problem of catalyst leaching and recycling. The actual heterogeneity of the process was examined by following the standard procedure suggested by Lempers and Sheldon.<sup>13</sup> Thus the reaction mixture was filtered at 100 °C after 1 hour (when product **3a** had been produced in 50% yield) and the filtrate was heated at 100 °C for a further 3 hours. Product **3a** was detected in 52% total yield (50% + 2%). In contrast, addition of both reagents (10 mmol each) to the recovered solid catalyst and heating at 100 °C for 4 hours afforded the unsaturated aminoester **3a** in

85% yield. These results confirm that the reaction really occurs on the supported metal sites.

In addition, after filtration, washing with methanol and acetone, and drying, the ZnNaY zeolite was reused for three times affording the product with the same high yield (reaction: 87%; 1st recycle: 85%; 2nd recycle: 84%; 3rd recycle: 85%).

## Conclusions

In conclusion, we have reported a new, effective and environmentally friendly methodology for the preparation of variously substituted unsaturated aminoesters starting from  $\beta$ -diketones or  $\beta$ -ketoesters and ethyl cyanoformate. These compounds can be synthesised in high yield and with excellent selectivity by using a zinc-exchanged NaY zeolite and avoiding the use of any solvent. In addition the catalyst can be recovered by filtration and utilised at least four times without lowering its activity.

## Experimental

### Typical procedure

A mixture of the selected  $\beta$ -dicarbonyl compound (10 mmol), ethyl cyanoformate (10 mmol) and ZnNaY zeolite (0.25 g) was heated in an oil bath at 100 °C for 4 hours, with magnetic stirring. The flask was equipped with an air condenser and left open throughout the course of the reaction. After cooling to rt, the catalyst was removed by filtration and washed with methanol (20 ml) and acetone (10 ml); the solvents were distilled off and the crude product was purified by crystallisation from ethyl acetate. Satisfactory IR, MS, <sup>1</sup>H NMR, and mp data were obtained for all the unsaturated aminoesters **3**, results were consistent with those found in the literature.<sup>7,14</sup>

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**Table 2** Synthesis of variously substituted unsaturated aminoesters **3**

$  \begin{array}{c}  \text{R}^1 \text{---} \text{C}(=\text{O}) \text{---} \text{CH}_2 \text{---} \text{C}(=\text{O}) \text{---} \text{R}^2 + \text{NC-CO}_2\text{Et} \xrightarrow[4 \text{ h, } 100^\circ\text{C}]{\text{ZnNaY zeolite}} \text{R}^1 \text{---} \text{C}(=\text{O}) \text{---} \text{C}(\text{H}_2\text{N})=\text{C}(\text{CO}_2\text{Et}) \text{---} \text{R}^2 \\  \text{1} \qquad \qquad \text{2} \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \qquad \text{3}  \end{array}  $			
Entry	R <sup>1</sup>	R <sup>2</sup>	<b>3</b> Yield [sel.] (%)
a	Ph	Me	<b>3a</b> 84 [97]
b	Me	Me	<b>3b</b> 99 [99] <sup>a</sup>
c	Me	OEt	<b>3c</b> 70 [98]
d	OEt	Ph	<b>3d</b> 65 [96]
e	Me	OMe	<b>3e</b> 72 [97]
f	OMe	OMe	<b>3f</b> 10 [98]
g	OEt	OEt	<b>3g</b> 12 [98]

<sup>a</sup> Reaction carried out at rt.

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