**Zn[aminoacid]_2 hybrid materials applied as heterogeneous catalysts in the synthesis of β-enaminones**

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**Abstract**

Hybrid materials have seized attention from scientific community mainly as heterogenic catalysts in organic reactions on a large scale succeeding in some organic compounds with high yields. One of the most important classes of hybrid materials used for this purpose involves the complexation of Zn and aminoacids. Herein, we introduced Zn[Pro]_2 and Zn[Gly]_2 in the synthesis of several β-enaminones via solvent free protocol and using an ultrasound device.

**Introduction**

There have been a growing interest in hybrid materials because of their application as heterogenic catalysts in various types of organic reactions, for example, in Prins condensation,¹ esters synthesis from alkyl aromatic compounds,² enantioselective catalysis,³ inter alia, as for other reactions applied in industry.⁴–⁶ Hybrid materials are classified in the literature according to the analysis of their structures and one of their most important classes is constituted by the interaction of both organic and inorganic fractions. One can classify two classes of organic/inorganic hybrid materials by the interaction between these two fractions: the hybrid materials with strong chemical bonds (ionic or covalent) inside its structure or the ones with week bonds (van der Walls or hydrogen bonds).⁷ Another example of class included in strong chemical bonds that have seized attention recently is the bis[proline-N,O]Zn or Zn[Pro]_2. This hybrid is an efficient, stable, inexpensive, recyclable, non-toxic Lewis acid catalyst which is soluble in water but insoluble in almost all the other organic solvents, enabling a simple and quantitative recovery of the catalyst. It has been extensively applied to various catalytic reactions including aldol condensation,⁸ direct nitro aldon condensation,⁸ Hantzsch reaction,¹⁰ Knoevenagel condensation,¹¹ Mannich reaction,¹² Friedlander condensation¹³ etc. It has also been used for the synthesis of 1,5-benzodiazepines,¹⁴ 1,2-disubstituted benzimidazoles,¹⁵ and pyrazoles,¹⁶ inter alia.¹⁷–²⁵ These heterogenic catalysts, such as Zn[Pro]_2, are mainly applied on the synthesis of compounds that present biological activity. Many of them presented nitrogen(s) in their structure, for example, the proteins. Therefore, there has been a growing interest in synthesized compounds containing nitrogen for example as starting point in library design.²³ Among the compounds containing nitrogen, the most used ones in organic chemistry as synthetic intermediates are the

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**Figure 1.** Yields obtained for each methodology during the β-enaminone synthesis.
β-enaminones which are widely applied mainly in organic reactions because of their versatile reactivity, as electrophiles and nucleophiles. Because of this remarkable property, nowadays, there are many research groups that have developed several numbers of preparations. The shortcoming of this procedure is that, in many cases, the catalysts are constituted of heavy metals, which is not in accordance with the principles of Green Chemistry. All in all, we proposed the insertion of Zn[Pro]$_2$ and bis[glycinate-N,O]Zn or Zn[Gly]$_2$ as a heterogenic catalyst on β-enaminones via solvent free synthesis using ultrasound protocol, aiming the acceleration of the process once it comes to an ecofriendly procedure.

**Results and discussion**

Firstly, we exposed the efficiency of the catalyst by carrying out the reaction involving the aniline and ethyl acetoacetate in four situations: (I) in the absence of catalyst using magnetic stirrer procedure (blank), (II) in the absence of catalyst but using the ultrasound device (US), (III) by inserting the catalyst Zn[Pro]$_2$, in 10% mol, using the ultrasound device, and finally (IV) by inserting the catalyst Zn[Gly]$_2$, in 10% mol, using the ultrasound device as well (Fig. 1).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Amine</th>
<th>Yield</th>
<th>Zn[Gly]$_2$</th>
<th>Zn[Pro]$_2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Aniline</td>
<td>90</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>p-Anisidine</td>
<td>65</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>p-Toluidine</td>
<td>72</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Benzylamine</td>
<td>92</td>
<td>65</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Butylamine</td>
<td>99</td>
<td>70</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Ciclohexylamine</td>
<td>96</td>
<td>67</td>
<td></td>
</tr>
</tbody>
</table>

* Yields obtained after purification on chromatographic column.
or the Zn[Gly]$_2$ here underlined their ability to promote the synthesis of 26 In our mechanism there is a nucleophylic pre-

<table>
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<th>Zn[Gly]$_2$</th>
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<tbody>
<tr>
<td>1</td>
<td>Aniline</td>
<td>93</td>
<td>93</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>p-Anisidine</td>
<td>87</td>
<td>60</td>
<td></td>
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</tbody>
</table>

$^a$ Yields obtained after purification on chromatographic column.

It is important to evidence that all the reactions were performed in solvent free procedures. So, as expected, the changes in the systems resulted in substantial modifications of the β-enaminone yields. We observed, for the blank reaction, that β-enaminone was not obtained without the catalyst neither with the ultrasound device. Therefore, when we used it in the same synthesis, for 1 h, we observed the resulting β-enaminone in 12% yield. On the other hand, when we inserted in the reaction the Zn[Pro]$_2$ or the Zn[Gly]$_2$ we obtained the β-enaminone in good yields in 1 h (70% and 90%, respectively). We attributed this difference to the frame of the catal-
yst. The hybrid catalyst constituted by glycine is a bit smaller than the one with proline. So, compared to proline, the access to other amines keeping dicarbonyl compound as being ethyl aceto-

As previously mentioned, the reactions using Zn[Gly]$_2$ presented the best yields when we compare them to the ones with Zn[Pro]$_2$. To the best of our knowledge, we purposed a mechanism as presented in Figure 2. This mechanism was based on the one described by Siddiqui. 26 In our mechanism there is a nucleophylic attack of the nitrogen from the catalyst (red nitrogen, structure 1—Figure 2) on the ketone carbonyl. This attack produced the iminium ion (structure 3) which was attacked by the amine (blue nitrogen). The obtained N,N acetal (structure 4) produced the corresponding imine which finally rearranged itself resulting in the β-enaminone. It is worth mentioning that in both hybrid catalysts, we did not observe the nucleophylic attack on the ester carbonyl group.

Besides, it was not possible to observe the substituted effect of the phenyl group on the β-enaminones’ yield. For this reason, we concluded that the size of the catalyst was a determinant point linked to the yields as previously mentioned.

For this reason, we decided to change the dicarbonyl compound to acetylacetone and carry out the β-enaminone synthesis with some amines and acetylacetone. The yields for the use of hybrid catalysts Zn[Pro]$_2$ and Zn[Gly]$_2$ on the β-enaminone synthesis with some amines and acetylacetone are presented in Table 2 in which we observed the resulting β-enaminone in good yields in 1 h (70% and 90%, respectively). We attributed this difference to the frame of the catalyst. The hybrid catalyst constituted by glycine is a bit smaller than the one with proline. So, compared to proline, the access to other amines keeping dicarbonyl compound as being ethyl aceto-

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For this reason, we decided to change the dicarbonyl compound to acetylacetone and carry out the β-enaminone synthesis with some amines previously used. Data are presented in Table 2 in which we obtained the highest yields for almost all the β-enaminones except for the cases involving the p-anisidine and p-toluidine (entries 2 and 3) in which we obtained the lowest yields in the set because of the difficulty in separating the amine precursor and the corresponding β-enaminones.

### Conclusion

In short, synthetically versatile β-enaminones were prepared with the use of the hybrid catalysts Zn[Pro]$_2$ and Zn[Gly]$_2$ in a green protocol and using the ultrasound and solvent free conditions. This extension of the scope for the use of Zn[Pro]$_2$ and Zn[Gly]$_2$ here underlined their ability to promote the synthesis of β-enaminones with high yields, assuring the maintenance of other groups like esters.

### Acknowledgments

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### Supplementary data

Supplementary data (general experimental procedures and spectral data) associated with this article can be found, in the online version, at [http://dx.doi.org/10.1016/j.tetlet.2014.05.122](http://dx.doi.org/10.1016/j.tetlet.2014.05.122).

### References and notes