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Complex Containing a Lewis Acid and Brønsted Acid for the Catalytic Reactions of Aza-Michael Addition[1]

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Abstract—The novel efficient complex catalyst containing a Lewis acid and a Brønsted acid have been prepared by the reaction of proline ion liquid and cuprous iodide. The catalyst was characterized by FT-IR techniques using pyridine as probe molecule. A fast, mild, and quantitative procedure for aza-Michael addition reactions between various amines and α,β-unsaturated carbonyl compounds and nitriles has been developed using the novel complex catalyst. The results showed that the novel catalyst owned high activities for the reactions with excellent yields within 1 min.

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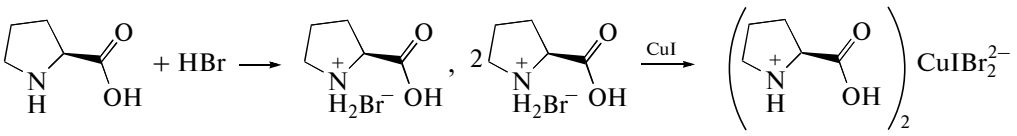
The aza-Michael reaction is an important reaction since it provides an easy route for obtaining β-amino carbonyl derivatives [1, 2], especially for the synthesis of C–N heterocycles [3]. It is a straightforward approach for the synthesis of substituted amines and their derivatives with 100% atom efficiency and without any by-product formation [4]. A number of alternative procedures have been reported recently using a variety of reagents such as Pd compounds [5], Lewis acids [6–8], clay [9], silica gel [10], lipase [11], ion liquid [12] etc. However, despite satisfactory results, many of these methods used heavy metal salts and hazardous organic solvents. Hence, the development of less expensive, simpler, "greener" procedures for the reactions are still highly desirable. Aiming to these advantages, we developed a novel solvent-free procedure for the aza-Michael addition of amines to electron deficient alkenes at room temperature (**r.t.**) using the proline cuprous iodide complex containing a Lewis acid and a Brønsted acid as catalyst [13] (Scheme 1). The results showed that the catalyst is very efficient for the reactions with high yields, and very short reaction time.



Scheme 1. The synthesis of the proline cuprous iodide complex catalyst.

EXPERIMENTAL

All organic reagents were commercial products of the highest purity available (>98%) and used for the reaction without further purification. Proline, cuprous iodide, acrylonitrile, butyl acrylate, methyl acrylate, methyl methacrylate, piperidine, diethylamine, morpholine, isopropylamine, cyclohexanamine were purchased from Shanghai Chemicals Co.

Synthesis of the Catalyst

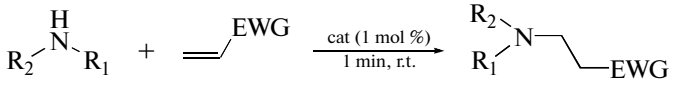
Proline and equimolar hydrobromic acid were mixed together and stirred magnetically for 2 h at 25°C. Then, the water was removed under reduced pressure and a light yellow ionic liquid was formed. It was used without further purification. A mixture of synthesized ionic liquid (20 mmol) and cuprous iodide (10 mmol) were placed in vacuum drying oven for 1 h.

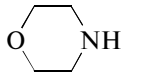
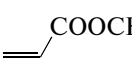
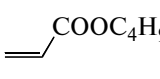
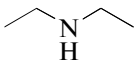
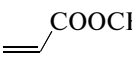
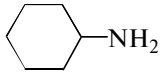
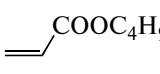
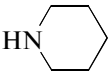
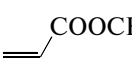
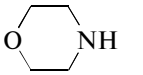
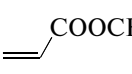
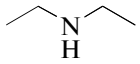
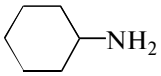
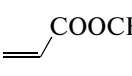
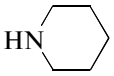
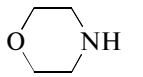
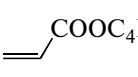
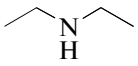
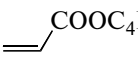
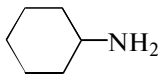
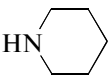
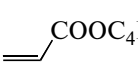
Catalytic Procedure for the Aza-Michael Addition

Typical procedure for the conjugate addition of amines was the next. A mixture of amine (4 mmol), alkene (4.8 mmol) and the catalyst (15 mg) was stirred at room temperature for 1 min. The residue was filtered and condensed under reduced pressure. The process of the reaction was monitored by GC analysis.

[1] The article is published in the original.

The aza-Michael additions of various amines with alkenes*



Entry	Amines	Alkenes	Yield, %	Entry	Amines	Alkenes	Yield, %
1			98.4	9			99.7
2			99.7	10			93.7
3			99.7	11			99.9
4			95.7	12			99.4
5			99.9**	13			99.6
6			99.9	14			98.9
7			98.7	15			99.7**
8			98.2				

* The reaction conditions: amine 4 mmol, alkenes 4.8 mmol, catalyst 15 mg, r.t. (25°C), reaction time 1 min. The yield was estimated by GC analysis.

** Reaction time 2 min.

RESULTS AND DISCUSSION

Characterization of Catalyst

FT-IR absorption spectra of pyridine adsorbed on metal oxides have been widely described in the literature [13]. Pyridine adsorbed on Lewis acid sites (**L-Py**), yields two bands at 1460–1445 and 1610–1600 cm^{-1} whereas Brønsted acid sites (**B-Py**) are usually observed at 1540 and 1640–1630 cm^{-1} [14, 15]. The IR spectrum corresponding to pyridine adsorbed on the proline cuprous iodide complex is shown on Fig. 1. We can see that coordinated pyridine on Lewis acid sites is

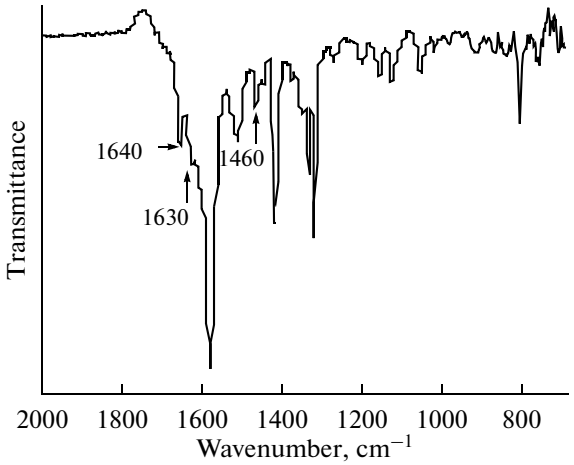


Fig. 1. FT-IR spectrum of pyridine adsorbed on proline cuprous iodide complex.

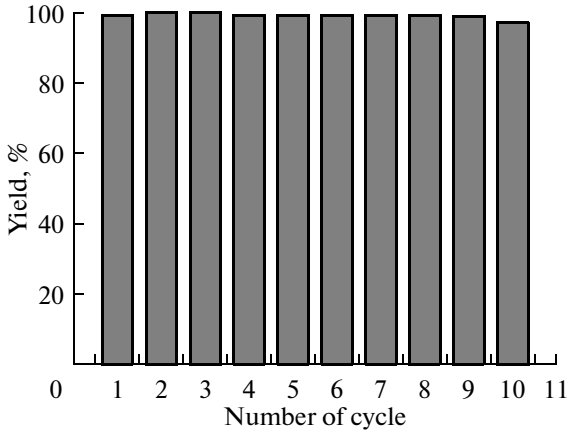


Fig. 2. The reuse of the proline cuprous iodide complex catalyst.

observed at 1460 cm^{-1}, and the presence of stretching mode at 1630 and 1640 cm^{-1} were assigned to Brønsted acid sites.

Catalytic Procedure for the Aza-Michael Addition

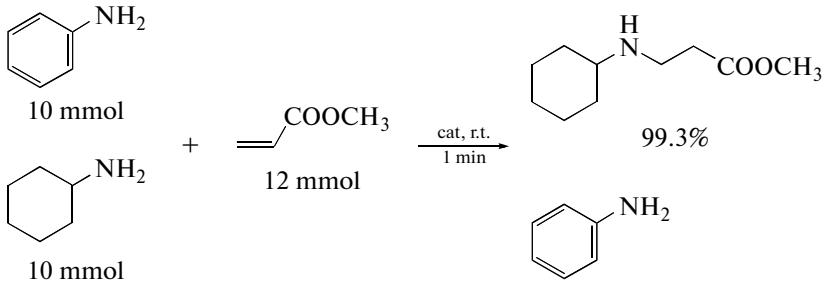
The aza-Michael additions of various amines with alkenes under solvent-free condition were investigated (table). The results showed that the reactions underwent smoothly at room temperature just within one or two minutes. The cyclohexanamine showed a low activity for all kinds of electron deficient alkenes with 2 min reaction time (entries 5, 15). The primary amines underwent the single substitution reaction under the reaction condition. The reaction conditions are mild and not sufficient enough to cause double substitution reaction. The multi-substitution reactions could also be activated when more alkenes (2.4 equiv) and high temperature (80°C) applied, then the double substituted products were obtained with high yields (88%) after 2 h. As to the alkenes, the reactivity was affected by the electronic withdrawing groups (EWG) and the steric hindrance around the double bond also had the certain effect on the reaction.

The Reuse of the Catalyst

The catalyst has been used in the heterogeneous catalytic process. Thus, recovery of the catalyst is very convenient. After reactions, the reaction mixture was filtered, and the catalyst was washed with acetone (5 ml) and dried. The complex catalyst could be reused without any further disposal. The recovered activities were investigated through the reaction of diethylamine and methyl acrylate carefully (Fig. 2). The yield remained unchanged even after the catalyst had been recycled for ten times.

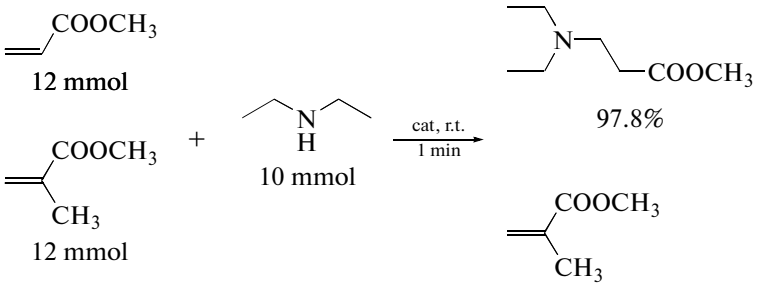
The Selectivity of the Catalyst

It is noteworthy that aromatic amines could not be transformed to the corresponding products under the same reaction conditions (Scheme 2). This result indicated that the present protocol could be applicable to the selective addition of aliphatic amines in the presence of aromatic amines.



Scheme 2. The selectivity of the proline cuprous iodide complex catalyst.

It was also found that methyl methacrylate could not be transformed to the corresponding products (Scheme 3). The reaction activity was greatly influenced by the steric hindrance of the methyl at the double bond of the methyl methacrylate.



Scheme 3. The selectivity of the proline cuprous iodide complex catalyst.

In conclusion, a novel efficient catalyst has been prepared for the aza-Michael addition of amines to electron deficient alkenes. FT-IR spectra indicated that the new catalyst contains both a Lewis acid site and a Brønsted acid site. The novel efficient procedure has been developed. Low cost and possibility of reuse of the catalyst, excellent selectivity, high yields are the key features of this methodology.

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