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Short communication

Amberlyst-15: An efficient reusable heterogeneous catalyst for aza-Michael reactions under solvent-free conditions☆

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Abstract

The aza-Michael reactions of amines with α,β-unsaturated carbonyl and nitrile compounds have efficiently been carried out at room temperature using Amberlyst-15 as a heterogeneous reusable catalyst. The products were formed in short reaction times and in high yields.

Keywords: Aza-Michael reaction; Amine; α,β-Unsaturated carbonyl and nitrile compounds; Amberlyst-15; Heterogeneous reusable catalyst

The aza-Michael reaction involving the conjugate addition of a nitrogen nucleophiles to an α,β-unsaturated carbonyl or nitrile compounds constitutes an important reaction in organic synthesis for the construction of C–N bond and for the preparation of a β-amino carbonyl or nitrile compounds [1]. Various β-amino carbonyl compounds are present in bioactive natural products and are also useful for the synthesis of fine chemicals and pharmaceuticals [2]. The aza-Michael reactions are usually carried out under acid and base catalysis [3]. However, to avoid the problems associated with a strong acid or a base which may initiate the side reactions, various Lewis acids have been introduced [4]. Many of these Lewis acid induce several drawbacks, such as $Yb(OTf)_3$ [4a] and $CeCl_3{\cdot}7H_2O$–NaI [4c] require drastic reaction conditions and toxic solvent, MeCN, $CeCl_3{\cdot}7H_2O$–NaI [4c] is used in large excess and $InCl_3$ [4b] and Cu-salt [4f] complete the conversion in long reaction times. As the aza-Michael reaction is of versatile use in organic synthesis a mild, facile and eco-friendly protocol for this reaction is highly essential. In continuation of our work [5] on the application of Amberlyst-15 for development of useful synthetic methodologies we recently observed that it can catalyse efficiently the aza-Michael reactions of amines with α,β-unsaturated carbonyl and nitrile compounds at room temperature (Scheme 1). The reaction was conducted under solvent-free conditions. Initially, the reaction was attempted with different solvents (Table 1) but the yields were found to be better in absence of any solvent.

A series of β-amino carbonyl and nitrile compounds were prepared by direct treatment of amines with α,β-unsaturated carbonyl and nitrile compounds in the presence of Amberlyst-15 (Table 2). Both the primary and secondary aliphatic amines underwent the conversion smoothly. Primary amines, such as benzyl amine, phenylethyl amine or *n*-butyl amine reacted with an α,β-unsaturated carbonyl and nitrile compound to form only the corresponding mono-alkylated product. The method worked well for α,β-unsaturated esters, nitriles and ketons (acyclic or cyclic). The reaction was completed within 10–30 min. The yields of the products were high (76–98%) with aliphatic amines. However, when an aromatic amine, such as aniline, was treated with an α,β-unsaturated ester or nitrile the yield of the adduct was low (∼30% in 2 h) but the similar reaction with methyl vinyl ketone afforded the desired product in impressive yield (92% in 1 h). This difference in reactivity of aromatic amines with α,β-unsaturated esters or nitriles shows the chemoselectivity of conjugate addition of aliphatic amines in the present method.

Thus, when a mixture (1:1) of morpholine and aniline was treated with an excess methyl acrylate in the presence of

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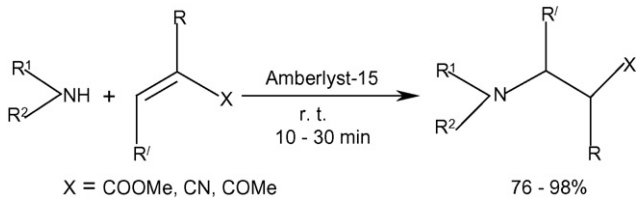


Scheme 1.

Amberlyst-15, only the morpholine adduct was formed as the sole product (Scheme 2).

The catalyst, Amberlyst-15, is commercially available, inexpensive and non-hazardous. It works under heterogeneous conditions and can easily be handled and removed by simple filtration. The recovered catalyst was recycled consecutively three times to produce the desired products with a little variation of their yields (Table 2).

In conclusion, we have developed an efficient general methodology for the preparation of β-amino carbonyl and nitrile compounds by applying aza-Michael reactions of amines and α,β-unsaturated carbonyl and nitrile compounds in the presence of Amberlyst-15. The simple experimental procedure, application of an inexpensive heterogeneous recyclable catalyst, solvent-free reaction conditions, short reaction times and high yields are the notable advantages of the protocol.

Table 1
Conjugate addition of morpholine and methyl acrylate under different reaction conditions[a]

Entry	Solvent	Isolated yield (%)
1	DCM	59
2	CH_3CN	62
3	THF	42
4	DMF	38
5	EtOH	41
6	Solvent free	79, 76, 74, 71[b]

[a] Reaction conditions: morpholine (2 mmol) and methyl acrylate (2.5 mmol); solvent (2 mL) or without any solvent; Amberlyst-15 dry (30%, w/w); *r*, *t*; 30 min.
[b] Catalyst was used over four runs.

Table 2
Conjugate addition of amines to α,β-unsaturated carbonyl and nitrile compounds catalysed by Amberlyst-15 under solvent-free condition[a]

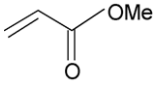
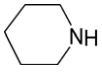
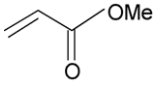
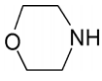
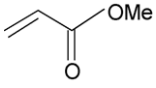
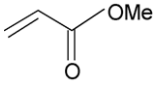
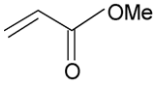
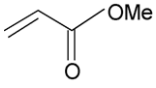
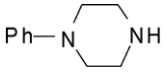
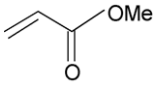
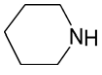
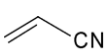
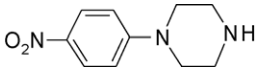
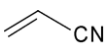
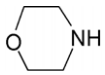
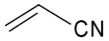
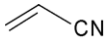
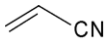
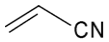
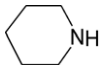
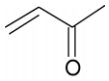
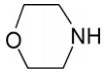
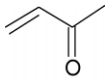
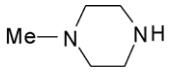
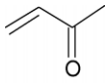
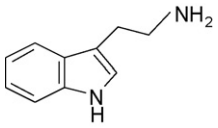
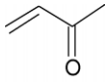
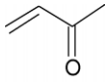
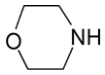
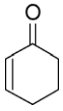
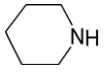
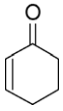
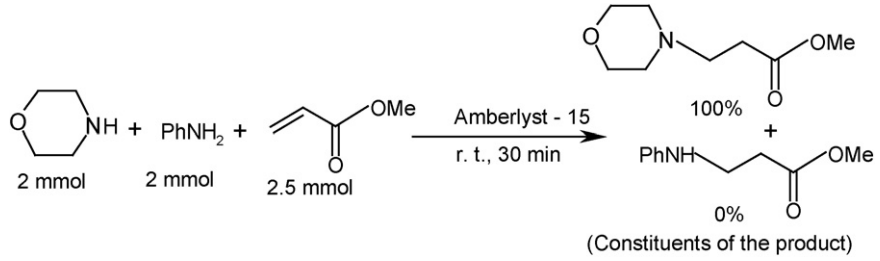
Entry	Amine	α,β-Unsaturated compound	Time (min)	Isolated yield (%)
1			25	94
2			30	87
3			30	79
4	$PhCH_2NH_2$		30	90
5	$PhCH_2CH_2NH_2$		30	87
6	*n*-$BuNH_2$		25	88
7			30	93
8			10	96
9			30	86

Table 2 (*Continued*)

Entry	Amine	α,β-Unsaturated compound	Time (min)	Isolated yield (%)
10			20	98
11	$PhCH_2NH_2$		15	92
12	$PhCH_2CH_2NH_2$		15	93
13	*n*-$BuNH_2$		15	95
14			25	77
15			25	89
16			30	91
17			30	78
18	$PhNH_2$		60	92
19			30	76
20			30	81

[a] The structures of the products were settled from the spectral (IR, ^1H NMR and MS) data.



Scheme 2.

1. Experimental

1.1. Typical experimental procedure

To a mixture of methyl acrylate (2.5 mmol) and Amberlyst-15 (65 mg, 30%, w/w) was added morpholine (2 mmol) and stirred at room temperature for 30 min. TLC indicated the completion of the reaction. CH_2Cl_2 (10 mL) was added and the catalyst was separated by filtration. The solvent was evaporated from the filtrate and the residue was subjected to column chromatography (silica gel, hexane-EtOAc) to obtain pure product (79%).

The recovered catalyst was recycled for consecutive three times for the above reaction to furnish the product with a little variation of its yield (Table 1).

Acknowledgement

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