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Journal of Molecular Catalysis A: Chemical 260 (2006) 32–34
JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL
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Short communication

A convenient highly stereoselective synthesis of allyl amides from Baylis–Hillman adducts using Amberlyst-15 as a heterogeneous reusable catalyst☆

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Received 7 June 2006; received in revised form 27 June 2006; accepted 28 June 2006
Available online 8 August 2006

Abstract

The Baylis–Hillman adducts have efficiently been converted into the corresponding allyl amides in stereoselective manner by heating in acetonitrile under reflux in the presence of Amberlyst-15 as a catalyst. The catalyst works under heterogeneous conditions and can be recycled.

Keywords: Baylis–Hillman adduct; Amberlyst-15; Allyl amides; Stereoselectivity; Heterogeneous recyclable catalyst

The Baylis–Hillman adducts (**1**) [1] which are densely functionalized molecules are highly useful in various chemical transformations and in synthesis of several bioactive compounds [1b,2]. We have utilized these adducts for the synthesis of trisubstituted alkenes present in different natural products [2,3]. In continuation of this work, the Baylis–Hillman adducts have now been applied for the stereoselective synthesis of allyl amides which are valuable intermediates for the synthesis of various pharmaceuticals [4]. These adducts when heated in MeCN under reflux in the presence of Amberlyst-15 afforded the corresponding allyl amides (Scheme 1).

The Baylis–Hillman adducts containing both ester and nitrile moieties underwent the conversion smoothly. The C–N bond formation occurred through Ritter reaction (Scheme 1) [5]. The adducts with electron-donating or electron-withdrawing groups in the aromatic rings afforded the desired products cleanly. Previously, Baylis–Hillman adducts were converted into allyl amides by treatment with a strong acid, methanesulfonic acid at 110 °C for 5 h [6]. The limitation of this method is that an adduct with an aromatic ring containing an electron-donating group at the 3-position affords a 2-benzazepines derivative instead of an allyl amide.

The present protocol is a high-yielding process for the synthesis of allyl amides with excellent stereoselectivity (Table 1). The products containing an ester moiety were formed with (*E*)-configuration, while those containing a nitrile had solely the (*Z*)-configuration. The structures and stereochemistry of the products were settled from their spectral (^{1}H NMR and MS) and analytical data. In the ^{1}H NMR spectrum of a trisubstituted alkene related to **2** the β-vinylic protons, *cis*- and *trans*- to the ester group is known [7a,b] to resonate at δ 7.5 and 6.5, respectively while the same proton *cis*- and *trans*- to a nitrile group appears [7c–e] at δ 7.6 and 7.2, respectively. These reported values are useful to determine the stereochemistry of the products.

The stereoselectivity of the present conversion can possibly be explained [2b] by considering the transition state models A, B and C (Fig. 1). Model A is more favoured than B when the EWG is an ester and (*E*)-products are formed exclusively. On the other hand, model C is more favoured than A when the EWG is a nitrile as, CN is linear and hence the (*Z*)-products are formed.

The catalyst, Amberlyst-15, is inexpensive and commercially available. It is a macroreticular sulfonic acid based polystyrene cation exchange resin [8]. It works under heterogeneous conditions. In recent years heterogeneous catalysts are gaining much importance due to their interesting reactivity as well as eco-

☆ Part 102 in the series "Studies on novel synthetic methodologies". IICT Communication No. 060625.

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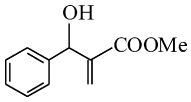
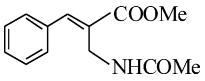
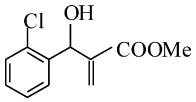
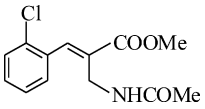
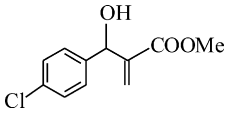
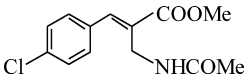
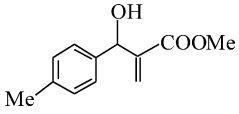
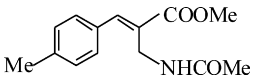
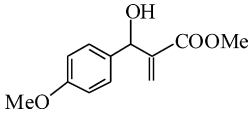
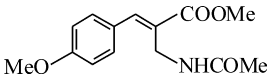
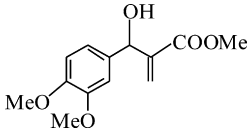
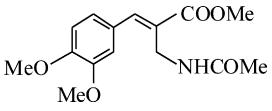
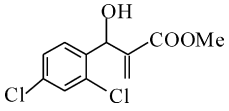
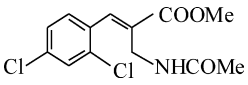
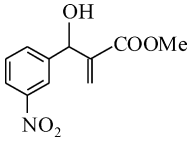
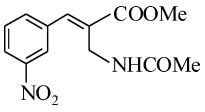
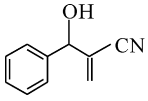
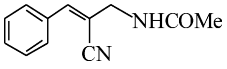
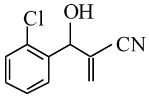
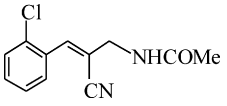
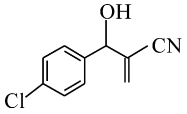
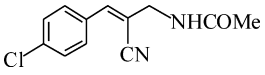
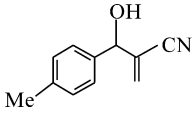
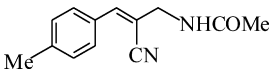
doi:10.1016/j.molcata.2006.06.051

Table 1
Synthesis of allyl amides using Amberlyst-15[a]

Entry	Adduct (**1**)	Product (**2**)	Time (h)	Isolated yield (%)
a			3.5	80
b			3.0	82
c			3.0	79
d			3.5	78
e			3.5	73
f			4.0	71
g			3.0	80
h			3.0	84
I			3.5	78
j			3.0	81
k			3.0	84
l			3.5	83

[a] The structures of the allyl amides were settled from their spectral (IR, ^{1}H NMR and MS) and analytical data.

nomic and ecological benefits. Amberlyst-15 can conveniently be handled and after reaction can be removed by simple filtration. The recovered catalyst showed almost equal efficiency in consecutive three cycles of the present conversion. In absence of the catalyst no allyl amide was formed. In earlier conversion of Baylis–Hillman adducts into allyl amides the reaction was catalyzed by methanesulfonic acid which is soluble in water and its recovery is a problem.

In conclusion, we have developed a simple stereoselective synthesis of both (*E*)- and (*Z*)-allyl amides from Baylis–Hillman adducts employing Amberlyst-15 as a heterogeneous reusable catalyst.

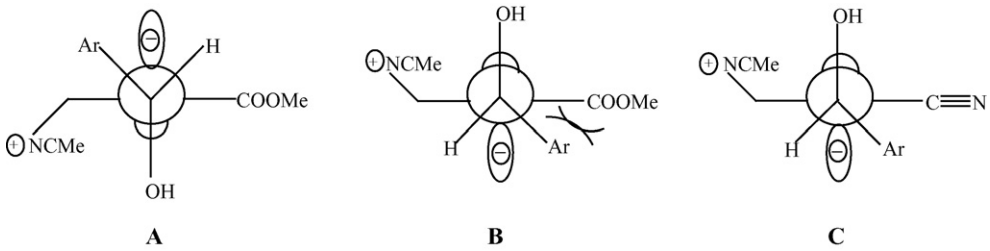
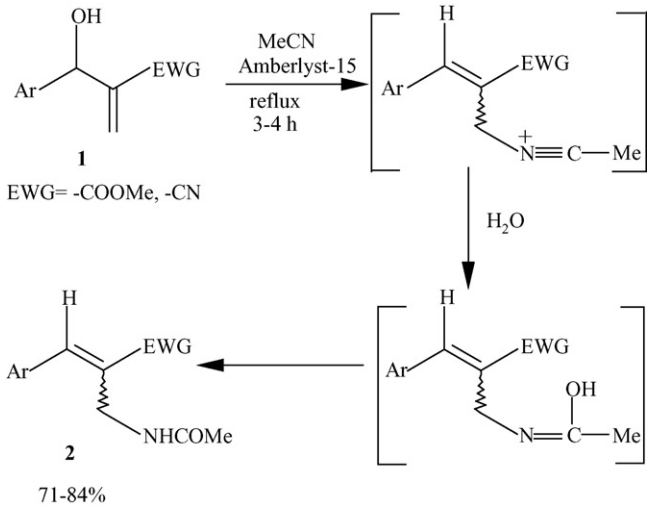


Fig. 1. Transition state models of the formation of allyl amides from Baylis–Hillman adducts.



Scheme 1.

1. Experimental

1.1. General procedure for the synthesis of allyl amides

To a solution of Baylis–Hillman adduct (**1**) (1 mmol) in MeCN (5 ml), Amberlyst-15 (100 mg) was added. The mixture was heated under reflux and the reaction was monitored by TLC. After completion, the mixture was cooled to room temperature. The total material was filtered and the catalyst was recovered. The filtrate was concentrated and the residue was subjected to column chromatography over silica gel using 10% EtOAc in hexane to obtain pure allyl amide.

The recovered catalyst, after activation, was reused consecutively three times with minimum variation of the yield of the products. As for an example, with fresh catalyst allyl amide, **2b** was obtained in an yield of 82% and subsequently with the recovered catalyst in three cycles the yields of this compound was 80, 79, and 77%.

The spectral (IR, ^{1}H NMR and MS) and analytical data of some representative allyl amides are given below.

2c: IR (KBr): ν_{max} 3284, 1718, 1653, 1539 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.68 (1H, s), 7.52 (2H, d, J = 8.0 Hz), 7.39 (2H, d, J = 8.0 Hz), 6.41 (1H, t, J = 6.0 Hz), 4.24 (2H, d, J = 6.0 Hz), 3.82 (3H, s), 1.93 (3H, s); FABMS: m/z 270, 268 $[M+H]^+$; Anal. Calcd. for: $C_{13}H_{14}ClNO_3$: C, 58.32; H, 5.23; N, 5.23%; Found: C, 58.38; H, 5.27; N, 5.18%.

2f: IR (KBr): ν_{max} 3371, 1712, 1657, 1602, 1516 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.82 (1H, d, J = 2.0 Hz), 7.57 (1H, s), 7.24 (1H, d, J = 8.0 Hz), 6.99 (1H, dd, J = 8.0, 2.0 Hz), 6.23 (1H, t, J = 6.0 Hz), 4.31 (2H, d, J = 6.0 Hz), 3.86 (3H, s), 3.82 (3H, s), 3.73 (3H, s), 1.90 (3H, s); FABMS: m/z 294 $[M+H]^+$; Anal. Calcd. for: $C_{15}H_{19}NO_5$: C, 61.43; H, 6.49; N, 4.78%. Found: C, 61.38; H, 6.54; N, 4.84%.

2h: IR (KBr): ν_{max} 3417, 1717, 1638, 1531 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.72 (1H, s), 7.70–7.46 (4H, m), 6.21 (1H, t, J = 6.0 Hz), 4.25 (2H, d, J = 6.0 Hz), 3.88 (3H, s), 2.01 (3H, s); FABMS: m/z 279 $[M+H]^+$; Anal. Calcd. for: $C_{13}H_{14}N_2O_5$: C, 56.12; H, 5.04; N, 10.07%. Found: C, 56.25; H, 5.13; N, 10.12%.

2k: IR (KBr): ν_{max} 3352, 2215, 1664, 1547 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.68 (2H, d, J = 8.0 Hz), 7.36 (2H, d, J = 8.0 Hz), 7.22 (1H, s), 6.42 (1H, t, J = 6.0 Hz), 4.09 (2H, d, J = 6.0 Hz), 2.01 (3H, s); FABMS: m/z 237, 235 $[M+H]^+$; Anal. Calcd. for: $C_{12}H_{11}ClN_2O$: C, 61.41; H, 4.69; N, 11.94%. Found: C, 61.52; H, 4.74; N, 11.82%.

Acknowledgement

The authors thank UGC and CSIR, New Delhi for financial assistance.

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