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Preparation of substituted allyl acetates and sulfones from Baylis–Hillman adducts in ionic liquid media

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Abstract—Reactions of potassium acetate and the sodium salt of p-toluenesulfinic acid with acetates of Baylis–Hillman adducts produce substituted allyl acetates and allyl sulfones respectively. Ionic liquids are utilized in place of conventional solvents. © 2003 Published by Elsevier Science Ltd.

There has been rapid growth in the use of room temperature ionic liquids as reaction media for organic transformations because they are air and moisture stable and can be used to replace volatile solvents.¹ Ionic liquids containing 1-alkyl-3-methylimidazolium cations are electrochemically stable, have negligible vapor pressure, and are chemically and thermally stable. They are useful as media for reactions of polar substrates which do not readily dissolve in conventional organic solvents.^{1,2}

The Baylis-Hillman reaction is an important carbon-carbon bond forming route which has been used in the synthesis of a variety of compounds.³ For example, acetates of Baylis-Hillman adducts have been utilized to prepare trisubstituted alkenes.³ As part of our studies of organic reactions in ionic liquid media,⁴ we examined the use of organoboronates as nucleophiles in reactions with acetates of Baylis-Hillman adducts.⁵ When potassium acetate was used as a base, we noted a product which formed via $S_N 2'$ substitution of the original acetate.⁶ For example, methyl 3-acetoxy-3phenyl-2-methylenepropanoate was converted to methyl (E)-2-(acetoxymethyl)-3-phenylprop-2-enoate in high yields (Scheme 1). Previously the isomerization of acetates of Baylis-Hillman adducts required catalysts such as TMSOTf,^{7a} DABCO^{7b} or montmorillonite K10 clay.^{7c} The present method utilizes simple protocols and provides high yields in an environmentally benign system.

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We first examined the reaction of methyl 3-acetoxy-3phenyl-2-methylenepropanoate with potassium acetate in various ionic liquids as well as conventional solvents (Table 1). Interestingly, the reaction proceeded well in ionic liquids, whereas little reaction occurred in conventional solvents (Table 1). The best results were obtained when butylmethylimidazolium tetrafluoroborate (BmimBF₄) was used as the reaction media.

In order to establish the generality of the reaction, we utilized various Baylis-Hillman acetate adducts (1 in



Scheme 1.

 Table 1. Reaction of KOAc with 3-acetoxy-3-phenyl-2methylenepropanoate in various solvents (Scheme 1)

Entry	Solvent	Isolated yield (%)
1	BmimBr	92
2	$BmimBF_4$	95
3	BmimPF ₆	52
1	Methanol	0
5	Ethanol	0
,	THF	0
	Dioxane	0
5	Acetonitrile	8
)	DMF	43
.0	Recycled BmimBF ₄	94

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Table 2) that had been prepared according to literature procedures.⁷ Similar reactions were observed for both ester and nitrile derivatives but stereochemical directive effects were reversed.^{3,7} Although no mechanistic studies have been carried out, related stereochemical reversals have been attributed to differences in the relative stabilities of the transition states.^{3e} E:Z ratios in all cases were greater than 9:1 (Table 2). The stereochemistry of the products was assigned on the basis of the ¹H NMR chemical shift values of the olefinic protons by comparison with the values reported in the literature.⁷

We applied the method to the preparation of allyl sulfones by allowing Baylis–Hillman acetate adducts to react with the sodium salt of *p*-toluenesulfinic acid. It is interesting to note that the reaction of acetates of Baylis–Hillman adducts with KOAc does not occur

when R is alkyl (Table 2). However, this is not a limitation when the reaction is carried out using the sodium salt of *p*-toluenesulfinic acid (Table 3). The product allylsulfones are important intermediates in organic synthesis⁸ and are generally prepared by displacement of halides by sodium arenesulfinates.⁹ The structures of the allylsulfones were established by comparing the ¹H NMR spectra values¹⁰ of olefin and methylene protons with those of related compounds.^{7,9a} The products were also prepared from known allyl acetates.¹¹ For example reactions of methyl (E)-2-(acetoxymethyl)-3-phenylprop-2-enoate (2a) with p-toluenesulfinic acid sodium salt in the presence of $Pd(PPh_3)_4$ and triphenylphosphine gave (Z)-(2-methoxycarbonylstyryl)tolylsulfone (4a). The preparation of substituted allylsulfones from Baylis-Hillman acetate adducts has not been reported.

Table 2. Reaction of acetates of Baylis–Hillman adducts (1) with KOAc in $BmimBF_4^{a}$

	R OAc CN 3	$\begin{array}{c} \text{KOAc} & \text{OAc} \\ \hline \text{BmimBF}_{4} & \text{F}_{4} \\ \text{50 °C, 2 hr} & 1 \end{array}$	$\xrightarrow{\text{KOAc}} H \xrightarrow{\text{COO}} R \xrightarrow{\text{BmimBF}_4} 0$	Me DAc	
R	Z	Product	Yield (%) ^b	E:Z ratio ^c	
Phenyl	COOMe	2a	95	96.4	
4-Chlorophenyl	COOMe	2b	92	94:6	
3-Nitrophenyl	COOMe	2c	92	91:9	
4-Nitrophenyl	COOMe	2d	93	100	
Octyl	COOMe	2e	0		
Phenyl	CN	3a	91	95:5	
4-Chlorophenyl	CN	3b	92	96:4	
Octyl	CN	3c	0		

^a All reactions were carried out at 50°C for 2 h.

^b Isolated yields.

^c E/Z ratio determined by ¹H NMR.

Table 3. Reaction of acetates of Baylis–Hillman adducts (1) with $TolSO_2Na$ in BmimBF₄^a

		$\frac{\text{NaSO}_2\text{Tol}}{40 \text{ °C},} \qquad \text{R} \stackrel{\text{OAc}}{\longleftarrow} Z$ mimBF ₄ , 90 min	NaSO ₂ Tol 40 °C, BmimBF ₄ , 90 min	H R SO ₂ Tol	
	5	1		4	
R	Z	Product ^b	Yield (%) ^c	E/Z ratio ^d	
Phenyl	COOMe	4 a	97	3:97	
4-Chlorophenyl	COOMe	4b	96	5:95	
3-Nitrophenyl	COOMe	4c	96	8:92	
4-Nitrophenyl	COOMe	4d	95	10:90	
Octyle	COOMe	4e	90	6:94	
Phenyl	CN	5a	94	92:8	
4-Chlorophenyl	CN	5b	95	94:6	
Octyl ^e	CN	5c	91	95:5	

^a Reactions were carried out at 40°C for 90 min.

^b All structures were characterized by NMR spectroscopy and elemental analyses.

^c Isolated yields.

^d E/Z ratio determined by ¹H NMR.

^e Reaction time was 3 h.

Reaction yields are very high. Product isolation can be achieved by distillation but, for convenience, we extracted the product using diethyl ether. Pure products were obtained and the ionic liquid can be reused without loss in reaction yield (Table 1, entry 10). No catalyst is required and the procedure is very straightforward. In conclusion, we have developed an environmentally benign procedure for the transformation of acetates of Baylis–Hillman adducts into trisubstituted alkenes using ionic liquids as reaction media.

General experimental procedure:

A mixture of the acetate of the Baylis–Hillman adduct (1 mmol) and $BmimBF_4$ (500 mg) was placed in a 10 ml round-bottomed flask followed by addition of potassium acetate or sodium *p*-toluenesulfinate (1.5 mmol). The mixture was stirred at the appropriate temperature until the reaction was complete (TLC), the product extracted into diethyl ether (3×5 ml), and purified by column chromatography (hexane and ethyl acetate). The ionic liquid was dried under vacuum and reused.

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- 10. In the crude ¹H NMR spectrum of 4, the β -vinylic proton, *cis* to the ester group (Z-isomer) appears at δ 7.09 and a minor peak for the *E*-isomer appears at δ 6.08 when R is alkyl. Similarly, the same proton appears at δ 7.90 and δ 6.85 for Z- and E-isomers, respectively, when R is aryl. Purification of the major isomer is readily achieved by column chromatography. Spectral data for 4a: ¹H NMR (250 MHz, CDCl₃); δ 2.36 (3H, s, Ar-CH₃), 3.60 (3H, s, -COOCH₃), 4.47 (2H, s, -CH₂-SO₂-Ar), 7.25 (2H d, J=8.0 Hz, Ar-H) 7.30–7.45 (5H, m, Ar-H), 7.68 (2H, d, J=8.0 Hz, Ar-H), 7.90 (1H, s, vinylic H; (Z)-isomer); ¹³C NMR: δ 21.3, 52.1, 54.8, 120.8, 126.9, 127.5, 128.4, 128.7, 129.4, 133.3, 136.9, 144.5, 145.7 and 166.6. In the crude ¹H NMR spectrum of 5, the α -vinylic proton *trans* to the nitrile group (*E*-isomer) appears at δ 6.33 and a minor peak for Z-isomer appears at δ 6.60 when R is alkyl. Similarly, the same proton appears at δ 7.08 and δ 7.48 for the *E*- and *Z*-isomers, respectively, when R is aryl. Spectral data for **5a**: ¹H NMR (250 MHz CDCl₃); δ 2.45 (3H, s, Ar-CH₃), 4.04 (2H, s, -CH₂-SO₂-Ar), 7.08 (1H, s, vinylic H; (E-isomer) 7.37 (2H, d, J=8.0 Hz, Ar-H), 7.39–7.68 (5H, m, Ar-H), 7.78 (2H, d, J=8.0 Hz, Ar-H). ¹³C NMR: 21.6, 61.3, 96.1, 117.1, 128.7, 128.9, 129.2, 130.1, 131.4, 132.4, 134.5, 145.7, 151.7.
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