Communications

A Convenient Synthesis of 2-Methylenealkanoates and Alkanenitriles from the Acetates of the Baylis-Hillman Adducts

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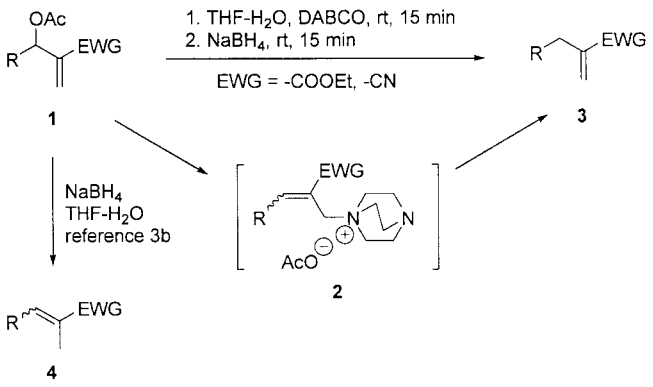
The Baylis-Hillman reaction provides a simple atom economic synthesis of β-hydroxy-α-methylene esters, ketones, nitriles, etc. The versatility of the functionality have made these adducts valuable synthetic intermediates.[1-3] One of the interesting transformations of the Baylis-Hillman adducts is the reduction either to 2-methylenealkanoates[3a] or α-methyl cinnamates.[3b] Synthesis of these compounds is important in view of their versatile applications as synthons in the synthesis of various biologically active molecules.[4]

During the research program on the Baylis-Hillman chemistry,[2] we found that the Baylis-Hillman acetates **1** make salts **2** readily with DABCO,[3a,3d-f] DBU[5] or DMAP[5] at room temperature within 15 min quantitatively. The salts can be attacked by the hydride ion from $NaBH_4$ to form 2-methylenealkanoates and alkanenitriles **3** in good yields (Scheme 1 and Table 1). Direct reduction of **1a** with $NaBH_4$ gave ethyl α-methylcinnamate in good yield as reported by Basavaiah.[3b] Such a discrepancy in the reaction of the Baylis-Hillman acetates with nucleophiles, depending on the presence or absence of DABCO, was originally reported by Drewes *et al.* for their reaction with 2-formylimidazole.[3e]

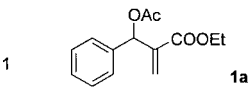
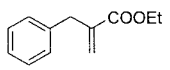
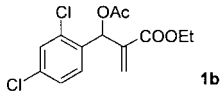
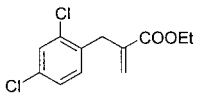
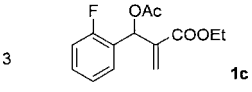
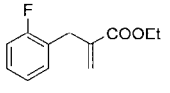
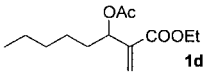
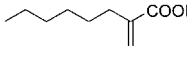
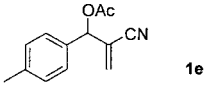
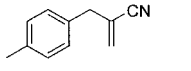
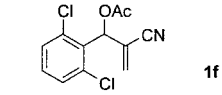
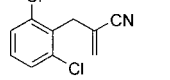
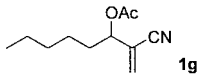
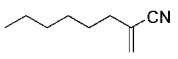
The synthesis of ethyl 3-phenyl-2-methylenepropanoate (**3a**) is typical: To a stirred solution of the acetate **1a** (496 mg, 2 mmol) in aqueous THF (4 mL, THF/H_2O, 3 : 1) was added DABCO (224 mg, 2 mmol) at room temperature and stirred during 15 min. Sodium borohydride (76 mg, 2 mmol) was added at once to the reaction mixture and stirred further 15 min. After the usual workup and column purification, pure **3a** was isolated as a clear oil (370 mg, 97%).[6] As shown in Table 1, the reaction works well irrespective of the substituents, ester or nitrile, on the Baylis-Hillman acetates in short time.

The synthesis of 2-methylenealkanoates from (2*Z*)-2-(bromomethyl)alk-2-enoates with $NaBH_4$ have been reported recently by Basavaiah *et al.*[3a] In their elegant paper, the salts of DABCO with the allylic bromides were easily reduced to 2-methylenealkanoates in short time. We think that the Basavaiah's concept and ours are the same in respect that both methodology used the allylic tertiary amine (DABCO) salts as precursors for the reduction. However, the use of acetates is more convenient than allylic bromides as starting materials in view of the following reasons: (1) Baylis-Hillman acetates **1** can be prepared in higher yields from the



Scheme 1

Table 1. Synthesis of 2-methylenealkanoates and alkanenitriles **3**

Entry	Substrate (1)	Product (3)	Yield (%)[a]
1	 **1a**	 **3a**	97
2	 **1b**	 **3b**	99
3	 **1c**	 **3c**	93[b]
4	 **1d**	 **3d**	99
5	 **1e**	 **3e**	97
6	 **1f**	 **3f**	98
7	 **1g**	 **3g**	77

[a]Isolated yield. [b]82% when DMAP was used.

Baylis-Hillman adducts than the allylic bromides,[1,7] (2) the reaction conditions for the preparation of acetates (Ac_2O/pyridine) is milder than for allylic bromides (HBr/H_2SO_4 or PBr_3),[7] and (3) the yields of 2-methylenealkanoates and alkanenitriles **3** were higher than the reported method in all cases.[3a]

In conclusion. we have developed an efficient method for the preparation of 2-methylenealkanoates and alkanenitriles from the regioselective reduction of the acetates of the Baylis-Hillman adducts.

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5. The salts derived from the acetates **1** and DBU decomposed slowly in aqueous THF. When we use DMAP instead of DABCO, similar salt formation and clear reduction was observed. However, the use of DABCO is better in view of yields (see entry 3 in Table 1) and reaction time.
6. The structure of prepared 2-methylenealkanoates and alkanenitriles **3** was identified by ^{1}H NMR, ^{13}C NMR, and IR.[3a] As an example, selected spectroscopic data of **3a** was presented: 370 mg (97%); clear oil; IR ($CHCl_3$) 1718 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, J = 7.1 Hz, 3H), 3.63 (s, 2H), 4.17 (q, J = 7.1 Hz, 2H), 5.44 (s, 1H), 6.23 (s, 1H), 7.18-7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.07, 38.03, 60.65, 125.85, 126.23, 128.32, 128.99, 138.76, 140.39, 166.84.
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