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Remarkable rate acceleration of SmI_3-mediated iodination of acetates of Baylis-Hillman adducts in ionic liquid: facile synthesis of (*Z*)-allyl iodides*

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Abstract: Stereoselective transformation of Baylis-Hillman acetates **1** into corresponding (*Z*)-allyl iodides **2** has been achieved by treatment of **1** with samarium triiodide in THF. Remarkable rate acceleration of samarium triiodide-mediated iodination of **1** was found when ionic liquid 1-*n*-butyl-3-methyl-imidazolium tetrafluroborate ([bmim]BF_4) was used as reaction media in stead of THF. This novel approach proceeds readily at 50 °C within a few minutes to afford (*Z*)-allyl iodides **2** in excellent yields. A mechanism involving stereoselective iodination of the acetates of Baylis-Hillman adducts by samarium triiodide is described, in which a six-membered ring transition state played a key role in the stereoselective formation of **2**.

Key words: Baylis-Hillman adduct, (*Z*)-allyl iodide, Samarium triiodide, Ionic liquid
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INTRODUCTION

The Baylis-Hillman reaction has drawn much attention as a useful carbon-carbon bond-forming reaction in the last decades (Basavaiah *et al.*, 1996a; 2003). The adducts of the reaction, 3-hydroxy-2-methylene-alkanoates (derived from acrylate esters), have been widely utilized as important precursors for stereoselective synthesis of different multifunctional molecules (Cho and Krische, 2004; Kabalka *et al.*, 2003; 2004; Chung *et al.*, 2001). Among such transformations, the preparation of 2-(halomethyl)alk-2-enoates from Baylis-Hillman adducts has received much attention as these compounds are especially useful for the synthesis of various naturally occurring bioactive compounds and their analogs such as α-methylene-γ-butyrolactone, α-alkylidene-β-lactam and flavanoid (Hoffmann and Rabe, 1985; Buchholz and Hoffmann, 1991; Basavaiah *et al.*, 1998). The preparation of corresponding allyl chlorides and allyl bromides from Baylis-Hillman adducts is extensively studied up to now (Chavan *et al.*, 1997; Basavaiah *et al.*, 1995; 1996b). In contrast, the synthesis of corresponding allylic iodide analogs were rarely investigated, which limited to much extent their application in organic synthesis (Yadav *et al.*, 2001). Moreover, the traditional synthetic procedures for preparation of allylic iodide obviously suffer from the use of strong acid (HI-H_3PO_4) and long reaction time (4 d) (Ameer *et al.*, 1985). So development of an alternative synthetic method with high efficiency and operational simplicity is needed.

On the other hand, the so-called room temperature ionic liquids (RTILs), especially those derived from 1-*n*-alkyl-3-methylimidazolium cations, have been shown to have versatile applications in organic synthesis as reaction media (Wasserscheid and Keim, 2000; Welton, 1999; Sheldon, 2001). The attractive-

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ness of RTILs as green solvents lies in their wide liquid range, good solvating ability, tunable polarity, highly thermal stability, negligible vapor pressure, and easy recycleability.

As a continuation of our interest in Baylis-Hillman reaction (Li *et al.*, 2004; 2005a; 2005b; 2005c) and application of samarium reagents in organic synthesis (Zhang and Liu, 2001; Chen and Zhang, 2004; Lu and Zhang; 1999; Zhou and Zhang, 1997), we wish to report here that SmI_3 (Fan and Zhang, 2002; Ma and Zhang, 2003) as a Lewis acid can efficiently promote the conversion of Baylis-Hillman acetates **1** into the corresponding (*Z*)-allylic iodides **2** in ionic liquid.

METHODS

When Baylis-Hillman acetates **1** were treated with SmI_3 generated in situ in the ionic liquid 1-*n*-butyl-3-methyl-imidazolium tetrafluoroborate ([bmim]BF_4) at 50 °C for 10 min, (*Z*)-allyl iodides **2** were obtained in excellent yields (Fig.1). The *Z*-stereoconfiguration of the product was assigned by comparing the chemical shifts in ^1H NMR with the reported ones (Yadav *et al.*, 2001) and no *E*-isomer was observed from the spectra.

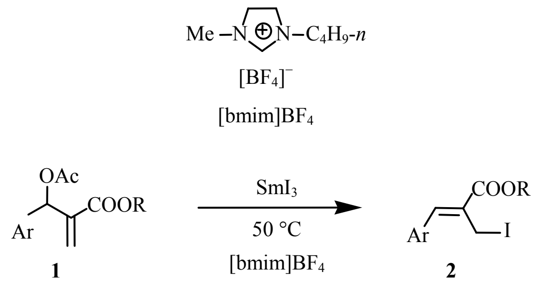
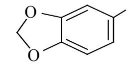


Fig.1 Iodination of the acetates of Baylis-Hillman adducts in ionic liquid

RESULTS AND DISCUSSION

The results are summarized in Table 1. Our previous study found that samarium and iodine can efficiently promote the iodination of the Baylis-Hillman acetates (Li *et al.*, 2005c). We propose that the above iodination reaction may proceed via the Sm(III) species, which prompted us to directly use SmI_3 as reagent for iodination of the Baylis-Hillman acetates. At first, when the reaction was carried out in THF, it gave very low yield of product even for long time at 50 °C (Entry 1). However, when ionic liquid 1-*n*-butyl-3-methyl-imidazolium tetrafluoroborate ([bmim]BF_4) was used as reaction media, in which remarkable acceleration of iodination of the Baylis-Hillman adducts was found to complete the reaction within 10 min at 50 °C.

Table 1 SmI_3-mediated synthesis of (*Z*)-allyl iodides 2 from the acetates of Baylis-Hillman adducts 1 in ionic liquid[a]

Entry	Ar	R	Product[b]	Yield (%)[c]
1	C_6H_5	Me	**2a**	0[d], 25[e]
2	C_6H_5	Me	**2a**	95
3	4-$CH_3C_6H_4$	Me	**2b**	99
4	2-ClC_6H_4	Me	**2c**	97
5	4-ClC_6H_4	Me	**2d**	91
6		Me	**2e**	92
7	3-$NO_2C_6H_4$	Me	**2f**	95
8	4-$NO_2C_6H_4$	Me	**2g**	90
9	2-Furyl	Me	**2h**	87
10	2-$CH_3OC_6H_4$	Me	**2i**	93
11	C_6H_5	Et	**2j**	89
12	2-ClC_6H_4	Et	**2k**	91

[a]All reactions were carried out with 1 equiv. SmI_3 in [bmim]BF_4 at 50 °C and finished within 10 min unless otherwise specially stated; [b]All products were characterized by ^1H NMR, MS and IR; [c]Isolated yields based on Baylis-Hillman acetates **1**; [d]The reaction was carried out in THF at room temperature for 5 h; [e]The reaction was carried out in THF at 50 °C for 5 h

A series of substrates were used in this reaction to establish the generality, and most reactions proceeded efficiently under similar conditions. The experimental results showed that the present method was effective for substrates bearing either electron-donating or electron-withdrawing groups. Besides good yields, this process also exhibited excellent stereoselectivity. Only *Z*-stereoconfiguration of the products was obtained while no *E*-isomers were observed from the spectra. In the following discussion, we will give some explanation for the excellent *Z*-stereoselectivity.

The reaction mechanism could be explained by a six-membered ring transition state. According to Concellón *et al.*(1999), chelation of Sm(III) with the carbonyl oxygen and another oxygen atom of the OAc group led to the formation of a six-membered ring

(Fig.2). Subsequently, the attack of iodine anion on the olefin methylene carbon followed by the elimination of OAc group resulted in the formation of new carbon-carbon double bond. Thus, the products allyl iodides **2** provided good *Z*-stereoselectivity.

CONCLUSION AND EXPERIMENTAL DETAILS

In conclusion, we have provided a new method to prepare (*Z*)-allylic iodides **2** from the acetates of Baylis-Hillman adducts **1** mediated by SmI_3 in ionic liquid media. The remarkable advantages of this process are its short reaction time, experimental simplicity, environmentally benign process, excellent yields and good stereoselectivity.

General procedure: Under a nitrogen atmosphere, Sm powder (0.15 g, 1.0 mmol) and I_2 (0.37 g, 1.5 mmol) were added to a 10-ml flask charged with 5 ml $[bmim]BF_4$. The mixture was stirred at room temperature for 30 min. Then to the in situ generated SmI_3 was added Baylis-Hillman acetates **1** (1.0 mmol). The resulting mixture was stirred at 50 °C for 10 min. At the end of the reaction, the resulting mixture was extracted with ether (3×20 ml). The organic phase was successively washed with saturated $Na_2S_2O_3$ (15 ml), brine (15 ml) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure to give the crude products, which were purified by preparative TLC (thin layer chromatography) using ethyl acetate and cyclohexane (1:5) as eluent.

2a: solid, m.p. 49~51 °C; δ_H ($\times10^{-6}$) 3.88 (s, 3H), 4.34 (s, 2H), 7.40~7.57 (m, 5H), 7.73 (s, 1H); ν_{max} (cm^{-1}) 2843, 1716, 1620, 1269, 1069, 770; *m*/*z* (%) 303 (37.59, M^++1), 175 (100, M^+–I), 143 (26.26); Anal. calcd. for $C_{11}H_{11}IO_2$: C 43.73; H 3.67. Found: C 43.61; H 3.74.

2b: solid, m.p. 52~53 °C; δ_H ($\times10^{-6}$) 2.39 (s, 3H), 3.88 (s, 3H), 4.37 (s, 2H), 7.28 (d, 2H, *J*=8.0 Hz), 7.47 (d, 2H, *J*=8.0 Hz), 7.71 (s, 1H); ν_{max} (cm^{-1}) 1704, 1605, 1508, 1066, 811, 761; *m*/*z* (%) 317 (0.17, M^++1), 189 (58.94, M^+–I), 129 (100), 115 (38.51); Anal. calcd. for $C_{12}H_{13}IO_2$: C 45.59; H 4.14. Found: C 45.78; H 4.08.

2c: oil; δ_H ($\times10^{-6}$) 3.89 (s, 3H), 4.20 (s, 2H), 7.33~7.70 (m, 4H), 7.82 (s, 1H); ν_{max} (cm^{-1}) 2952, 1722, 1627, 1437, 1074, 735; *m*/*z* (%) 337 (14.53, M^++1), 209 (66.96, M^+–I), 149 (55.74), 115 (100); Anal. calcd. for $C_{11}H_{10}ClIO_2$: C 39.26; H 2.99. Found: C 39.40; H 2.95.

2d: solid, m.p. 37~39 °C; δ_H ($\times10^{-6}$) 3.78 (s, 3H), 4.17 (s, 2H), 7.31 (d, 2H, *J*=8.8 Hz), 7.37 (d, 2H, *J*=8.8 Hz), 7.54 (s, 1H); ν_{max} (cm^{-1}) 2950, 1716, 1620, 1592, 1067, 767; *m*/*z* (%) 337 (23.36, M^++1), 209 (100, M^+–I), 149 (29.32), 115 (59.34); Anal. calcd. for $C_{11}H_{10}ClIO_2$: C 39.26; H 2.99. Found: C 39.13; H 3.03.

2e: solid, m.p. 71~72 °C; δ_H ($\times10^{-6}$) 3.87 (s, 3H), 4.36 (s, 2H), 6.04 (s, 2H), 6.89~7.10 (m, 3H), 7.63 (s, 1H); ν_{max} (cm^{-1}) 2949, 1708, 1602, 1511, 828; *m*/*z* (%) 347 (4.15, M^++1), 219 (100, M^+–I), 189 (95.57), 159 (85.47), 115 (48.69); Anal. calcd. for $C_{12}H_{11}IO_4$: C 41.64; H 3.20. Found: C 41.80; H 3.25.

2f: oil; δ_H ($\times10^{-6}$) 3.92 (s, 3H), 4.28 (s, 2H), 7.68 (t, 1H, *J*=8.0 Hz), 7.74 (s, 1H), 7.89 (d, 1H, *J*=8.0 Hz), 8.26 (d, 1H, *J*=8.0 Hz), 8.41 (s, 1H); ν_{max} (cm^{-1}) 3063, 2919, 1662, 1605, 1573, 1447, 1410; *m*/*z* (%) 348 (1.09, M^++1), 220 (53.68, M^+–I), 174 (60.60), 115 (100).

2g: solid, m.p. 112~114 °C; δ_H ($\times10^{-6}$) 3.92 (s, 3H), 4.26 (s, 2H), 7.71 (d, 2H, *J*=8.0 Hz), 7.74 (s, 1H), 8.33 (d, 2H, *J*=8.0 Hz); ν_{max} (cm^{-1}) 1722, 1593, 1514, 1273, 874; *m*/*z* (%) 348 (1.51, M^++1), 220 (15.39, M^+–I), 174 (100), 115 (90.34); Anal. calcd. for $C_{11}H_{10}INO_4$: C 38.06; H 2.90. Found: C 38.23; H 2.84.

2h: oil; δ_H ($\times10^{-6}$) 3.78 (s, 3H), 4.60 (s, 2H),

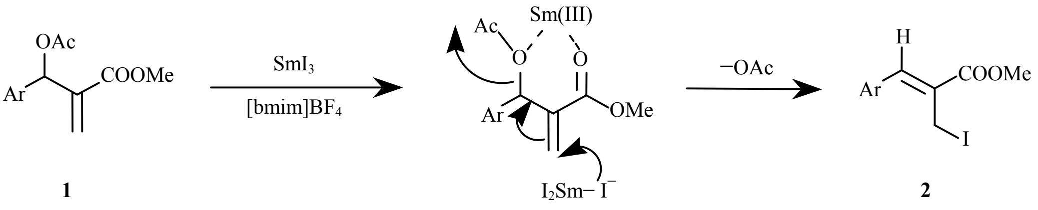


Fig.2 Stereoselective iodination of the acetates of Baylis-Hillman adducts by SmI_3

6.48~6.74 (m, 2H), 7.35 (s, 1H), 7.61 (s, 1H); $\nu_{\max}$ (cm^{-1}) 1714, 1614, 1529, 1437, 1351, 1209; *m*/*z* (%) 293 (0.07, M$^+$+1), 254 (100), 165 (28.68, M$^+$–I), 127 (59.51); Anal. calcd. for $C_9H_9IO_3$: C 37.01; H 3.11. Found: C 36.91; H 3.16.

2i: solid, m.p. 93~95 °C; δ_H (×10^{-6}) 3.90 (s, 3H), 3.91 (s, 3H), 4.35 (s, 2H), 6.96~7.73 (m, 4H), 7.97 (s, 1H); $\nu_{\max}$ (cm^{-1}) 2943, 1707, 1597, 1025, 817; *m*/*z* (%) 333 (0.83, M$^+$+1), 205 (75.69, M$^+$–I), 145 (100), 115 (33.66); Anal. calcd. for $C_{12}H_{13}IO_3$: C 43.39; H 3.95. Found: C 43.47; H 3.88.

2j: oil; δ_H (×10^{-6}) 1.44 (t, 3H, *J*=7.2 Hz), 4.37~4.42 (m, 4H), 7.45~7.62 (m, 5H), 7.78 (s, 1H); $\nu_{\max}$ (cm^{-1}) 2978, 1706, 1609, 1510, 1022, 814; *m*/*z* (%) 317 (2.71, M$^+$+1), 189 (100, M$^+$–I), 145 (18.57), 117 (71.45); Anal. calcd. for $C_{12}H_{13}IO_2$: C 45.59; H 4.14. Found: C 45.38; H 4.09.

2k: oil; δ_H (×10^{-6}) 1.39 (t, 3H, *J*=7.0 Hz), 4.20 (s, 2H), 4.35 (q, 2H, *J*=7.0 Hz), 7.33~7.70 (m, 4H), 7.82 (s, 1H); $\nu_{\max}$ (cm^{-1}) 2981, 1717, 1599, 1508, 1369, 1205, 1053; *m*/*z* (%) 351 (26.91, M$^+$+1), 223 (67.66, M$^+$–I), 151 (55.33), 115 (100); Anal. calcd. for $C_{12}H_{12}ClIO_2$: C 41.11; H 3.45. Found: C 41.24; H 3.53.

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