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IBX/Sc(OTf)$_3$-promoted one-pot oxidative conjugate addition of allyltrimethylsilane to Baylis–Hillman adducts

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Abstract—Baylis–Hillman adducts undergo smooth one-pot oxidative Michael addition with allyltrimethylsilane in the presence of 2-iodoxybenzoic acid (IBX)/Sc(OTf)$_3$ under mild conditions to afford homoallyl β-ketoesters in good yields with high 1,4-selectivity.

The stereoselective addition of allylmetal reagents to carbon electrophiles is an important carbon–carbon bond forming reaction in organic synthesis.[1] In particular, Lewis acid catalyzed carbon–carbon bond forming reactions are of great significance in organic synthesis because of their high reactivity, selectivity and mild reaction conditions.[2] Baylis–Hillman adducts are well known carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo nucleophilic substitution reactions contributes largely to their synthetic value.[3–6] The versatility of the functionality in such Baylis–Hillman adducts makes them valuable synthetic intermediates for the synthesis of a variety of heterocycles such as quinolines, pyrimidones, isoxazolines, pyrazolones, pyrrolidines, indolizines, azetidinones, diazacyclophanes and chromanones as well as biologically active natural products including α-alkylidene-β-lactams, α-methylene-γ-butyrolactones and mikanecic acids, frontalin, trimethoprim, sarkomycin, ilmofosine nuciferol and many others.[7] However, there have been no reports on the conjugate addition of allyltrimethylsilane to Baylis–Hillman adducts via an oxidative addition.

Recently, the use of hypervalent iodine reagents as oxidants in organic synthesis has attracted increasing interest due to their mild, selective and environmentally benign oxidizing properties.[8] IBX is a versatile oxidizing agent due to its high efficiency, easy availability, mild reaction conditions and its stability to moisture and air.[9] A wide functional group tolerance and high-yielding reactions, without over oxidation have made IBX very familiar for the oxidation of alcohols even in the presence of olefins, thioethers and amino groups,[10] and in other elegant oxidative transformations.[11]

In this Letter, we report a direct, one-pot oxidative Michael reaction of Baylis–Hillman adducts with allyltrimethylsilane using IBX/Sc(OTf)$_3$ as a novel catalytic system. Initially, we examined the oxidative Michael reaction of ethyl 2-[hydroxyl(phenyl)methyl] acrylate (**1**) with allyltrimethylsilane (**2**) in the presence of 1.2 equiv of IBX and 10 mol % Sc(OTf)$_3$ in acetonitrile. The reaction proceeded smoothly at room temperature and the product, ethyl 2-benzoylhex-5-enoate (**3a**) was obtained in 84% yield (Scheme 1).

This result encouraged us to examine other substituted Baylis–Hillman adducts (Table 1). Interestingly, this method worked well with substrates derived from both aliphatic and aromatic aldehydes. The starting materials were prepared by using a known procedure.[12] In all cases, the reactions were clean and afforded the Michael adducts in good yields. The reaction conditions were compatible with various functionalities such as halides, aryl methyl ethers, esters and alkenes (Table 1). All the products were characterized by ^{1}H NMR, IR and mass spectroscopy. Of the various hypervalent iodine reagents examined, including iodosobenzene (PhIO), iodobenzene diacetate (PhI(OAc)$_2$) and Dess–Martin periodinane (DMP), 2-iodoxybenzoic acid (IBX) was found to be the best in terms of conversion. Other

Keywords: Baylis–Hillman adducts; Hypervalent iodine; Allylsilane; Conjugate addition.
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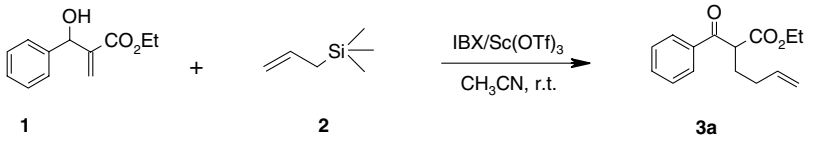
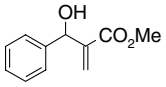
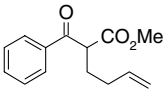
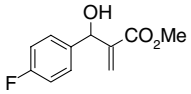
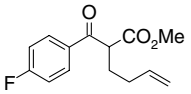
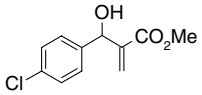
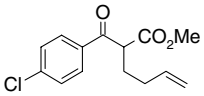
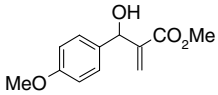
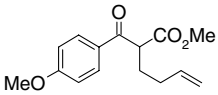
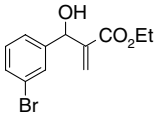
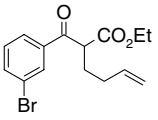
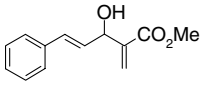
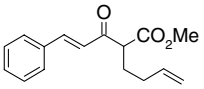
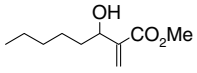
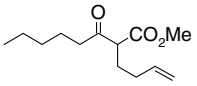
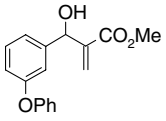
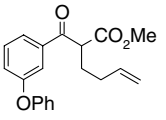
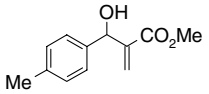
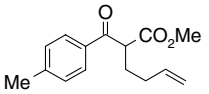
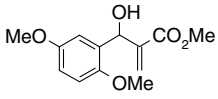
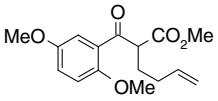
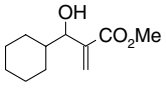
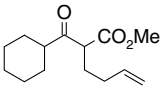
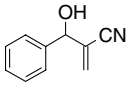
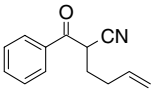


1 2 3a

Scheme 1.

Table 1. Oxidative allylation of Baylis–Hillman adducts using the IBX/$Sc(OTf)_3$ system

Entry	Substrate	Product[a]	Reaction time (h)	Yield[b]
a			24	84
b			20	82
c			22	78
d			30	76
e			22	79
f			24	70
g			36	82
h			26	83
i			26	82
j			30	88
k			32	80
l			26	78

[a] All products were characterized by ^1H NMR, IR and mass spectroscopy.
[b] Yield refers to pure products after column chromatography.

oxidants such as Oxone®, CAN, MnO_2 and $KBrO_3$ failed to produce the desired product. The oxidation of secondary alcohols was only observed when using IBX alone. In the absence of $Sc(OTf)_3$, no allyl addition occurred with IBX even after long reaction times (9–13 h) under reflux conditions. Various catalytic systems

such as IBX/$InCl_3$, IBX/$InBr_3$ and IBX/$CeCl_3{\cdot}7H_2O$ were screened but none gave satisfactory yields of products. As solvent, acetonitrile gave the best results. The by-product, iodosobenzoic acid was separated by a simple filtration and could be reoxidized to IBX. The scope of the IBX promoted oxidative Michael reaction was investigated with respect to various Baylis–Hillman adducts and the results are presented in Table 1.[13]

In conclusion, we have described an efficient protocol for the one-pot oxidative conjugate addition of allyltrimethylsilane to Baylis–Hillman adducts using IBX/$Sc(OTf)_3$ as a novel catalytic system. The method offers several advantages such as operational simplicity, mild reaction conditions, cleaner reaction profiles, simple work-up procedure and the use of inexpensive and readily available reagents, which makes it a useful and attractive strategy for the preparation of homoallyl β-ketoesters in a single step operation.

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13. *Experimental procedure*: A mixture of Baylis–Hillman adduct (1 mmol) and IBX (1.2 mmol) in acetonitrile (10 ml) was stirred at room temperature until complete oxidation took place. Allyltrimethylsilane (1.5 mmol) and $Sc(OTf)_3$ (10 mol %) were added sequentially and the reaction stirred at room temperature. The reaction mixture was then diluted with saturated aqueous $NaHCO_3$ solution (15 ml) and extracted with EtOAc (3×10 ml). The combined organic layers were washed with brine (1×10 ml), dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The resulting product was purified by silica gel column chromatography using a gradient mixture of hexane/ethyl acetate (9.5:0.5) as eluent to afford the pure Michael adduct. *Spectral data for selected compounds*: **3e**: Colourless oil: IR (neat): υ 3072, 2925, 2853, 1737, 1690, 1565, 1418, 1287, 1191, 1023, 915, 758 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.19 (t, 3H, $J = 6.8$ Hz), 2.01–2.16 (m, 4H), 4.07–4.30 (m, 2H), 4.97–5.05 (m, 2H), 5.69–5.83 (m, 1H), 7.34 (t, 1H, $J = 8.3$ Hz), 7.68 (d, 1H, $J = 8.3$ Hz), 7.87 (d, 1H, $J = 8.3$ Hz), 8.04 (s, 1H), 8.02 (s, 1H). ESIMS: m/z: 325 $(M+H)^+$, 347 $(M+Na)^+$. HRMS calcd for $C_{15}H_{17}O_3NaBr$: 347.0258. Found: 347.0266. **3g**: Colourless oil: IR (neat): υ 2955, 2930, 2860, 1744, 1715, 1640, 1438, 1355, 1248, 1167, 915, 746 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.89 (t, 3H, $J = 6.8$ Hz), 1.20–1.44 (m, 6H), 1.47–1.63 (m, 2H), 1.86–2.04 (m, 2H), 2.34–2.58 (m, 2H), 3.40 (t, 1H, $J = 6.8$ Hz), 3.71 (s, 3H), 4.95–5.05 (m, 2H), 5.64–5.80 (m, 1H). ESIMS m/z: 227 $(M+H)^+$. HRMS calcd for $C_{13}H_{22}O_3Na$: 249.1466. Found: 249.1478. **3j**: Colourless oil: IR (neat): υ 2925, 1740, 1670, 1593, 1492, 1274, 1221, 1164, 1042, 761 cm^{-1}. ^1H NMR ($CDCl_3$, 200 MHz): δ 1.73–2.00 (m, 4H), 3.49 (s, 3H), 3.63 (s, 3H), 3.67 (s, 3H), 4.10 (t, 1H, $J = 6.6$ Hz), 4.75–4.89 (m, 2H), 5.49–5.71 (m, 1H), 6.69 (d, 1H, $J = 9.1$ Hz), 6.84 (dd, 1H, $J = 2.4$ and 8.3 Hz), 7.13 (d, 1H, $J = 2.4$ Hz). ESIMS: m/z: 293 $(M+H)^+$, 315 $(M+Na)^+$. HRMS calcd for $C_{16}H_{20}O_5Na$: 315.1208. Found: 315.1203.