A Simple and Efficient Protocol for Chlorination of Baylis–Hillman Adducts Using PPh_3/CCl_4[1]

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PPh_3/CCl_4 system has been employed for the stereoselective synthesis of (*Z*)- and (*E*)-allyl chlorides from Baylis–Hillman adducts in excellent yields.

The conversions of primary and secondary alcohols into the corresponding chlorides by treatment with PPh_3/CCl_4 proceed with high efficiency.[2] During our work[3] on the Baylis–Hillman adducts[4] **1** (3-hydroxy-2-methylene alkanoates) and **2** (3-hydroxy-2-methylene alkanenitriles), we have employed this reagent for chlorination of these adducts. A mixture of **1** or **2** and PPh_3/CCl_4 was refluxed for 2–3 h to produce the corresponding allyl chloride **3** or **4** in stereoselective manner (Scheme 1).

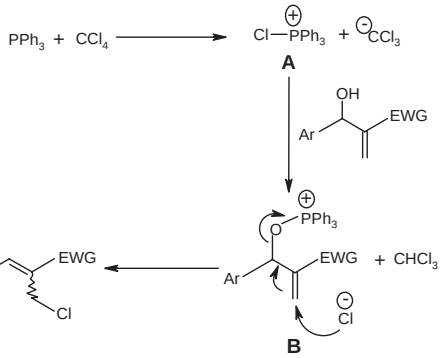
The allyl halides prepared from Baylis–Hillman adducts are utilized for the synthesis of different natural bioactive molecules and their analogues such as α-methylene-γ-butyrolactone, α-alkylidene-β-lactam, and flavonoids.[5] Generally, a strong acid or a metal halide is used for the conversion of a Baylis–Hillman adduct into the corresponding allyl halide.[5a,6] However, PPh_3/CCl_4 system has conveniently been utilized here for the preparation of allyl chlorides **3** and **4** from the adducts **1** and **2** respectively in high yields (83–98%).

A series of allyl chlorides have been prepared[7] from various Baylis–Hillman adducts having both ester and nitrile moieties (Table 1). Several functionalities such as halogen, nitro, ether, and ester remained intact. The adducts containing electron-donating as well as electron-withdrawing groups underwent the conversion smoothly. The reaction when carried out at room temperature afforded the products in poor yields even after 24 h. CCl_4 was used here both as a reagent and as a solvent. No additional solvent and catalyst were required. Though previously the halogenation of Baylis–Hillman adducts was performed[6c,8] using a halogen carrier and trialkyl or triphenylphosphine no systematic study on the preparation of allyl chloride from the adducts has been reported there. Moreover, the chlorination of the adducts with PPh_3/HCA produced both normal and rearranged products.[6c]

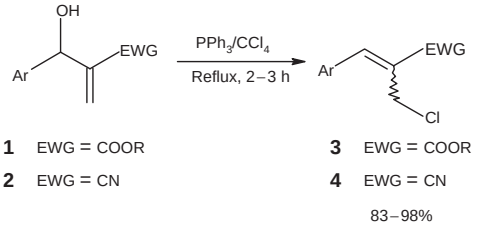
The present conversion was highly stereoselective. When an ester group was present in the adducts **1** the allyl chlorides with (Z) stereochemistry **3** were the sole products. However, if –CN group was present in the adducts **2** the allyl chlorides with (E) stereochemistry **4** were the major products. The structures and stereochemistries of **3** and **4** were easily settled from their spectral (^{1}H NMR and MS) data.[9] In the ^{1}H NMR spectrum the β-vinylic proton cis and trans to the ester group is known to resonate at ca. δ 7.5 and 6.5, respectively, while the same proton cis and trans to the nitrile group resonates at ca. δ 7.5 and 7.0, respectively.[6e,10] These reported ^{1}H NMR values were useful to determine the stereochemistry of the products.

In the present reaction PPh_3 reacts with CCl_4 to form the intermediate **A** which then reacts with a Baylis–Hillman adduct to produce the alkenylphosphonium salt **B**.[2] Chloride ion subsequently attacks this salt to furnish the allyl chloride and Ph_3PO (Scheme 2).

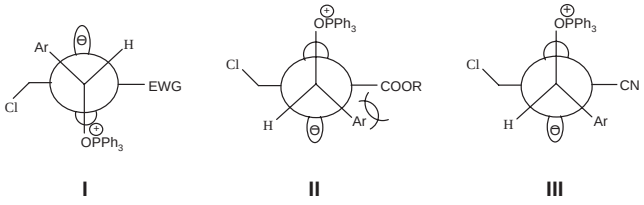
The stereochemistry of the present conversion can be explained by considering the transition state models **I**, **II**, and **III** (Scheme 3). Model **I** is more favoured than **II** when EWG is an ester and (Z) products are produced predominantly. However, model **III** is more favoured than **I** when EWG is –CN as it is a linear group. The steric effect in **III** due to the proximity of Ar and –CN is less compared to that in **I** resulting from the proximity of Ar and $-CH_2Cl$ groups. Thus the (E) compounds are the major products in this case.



Scheme 2.

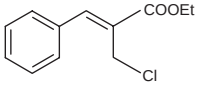
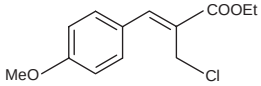
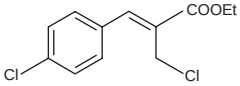
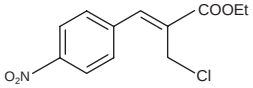
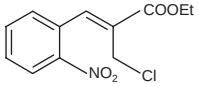
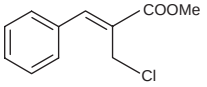
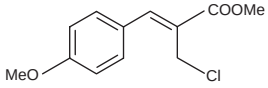
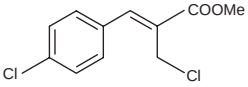
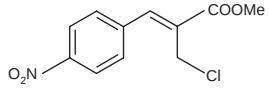
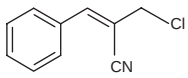
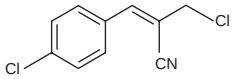
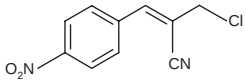


Scheme 1.



Scheme 3. Transition state models of the present reaction.

Table 1. Synthesis of (*Z*)- and (*E*)-allyl chlorides using PPh_3/CCl_4[a]

Entry	Product (**3** or **4**)	Time/h	Yield[b]/%	Z:E
a		2	98	100:0
b		2	98	100:0
c		2	97	100:0
d		3	96	100:0
e		3	95	100:0
f		2	97	100:0
g		2	98	100:0
h		2	97	100:0
i		3	96	100:0
j		3	86	4:96
k		3	85	5:95
l		3	83	4:96

[a]The structures of the products were settled from their spectral (IR, ^{1}H NMR, and MS) data. [b]The total yields of the products (Z + E isomers) after purification.

In conclusion, we have successfully employed a simple and inexpensive reagent, PPh_3/CCl_4 for stereoselective synthesis of (*Z*)- and (*E*)-allyl chlorides from the Baylis–Hillman adducts under acid and metal-free conditions. The operational simplicity, no requirement of additional catalyst, excellent yields, short reaction times, and high stereoselectivity are the great advantages of the present protocol.

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References and Notes

1 Part 168 in the series, Studies on novel synthetic methodologies.

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7 General experimental procedure: To a solution of the Baylis–Hillman adduct (2 mmol) in CCl_4 (10 mL) PPh_3 (3 mmol) was added. The mixture was stirred under reflux and the progress of the reaction was monitored by TLC. After completion the solvent was evaporated under reduced pressure. The product was extracted with EtOAc (2 × 10 mL), concentrated and chromatographed over silica gel to obtain the corresponding allyl chloride.

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9 The spectral (^{1}H NMR and MS) data of some representative products are given below.
3c: ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.32 (2H, d, J = 8.0 Hz), 7.89 (1H, s), 7.70 (2H, d, J = 8.0 Hz), 4.35 (2H, s), 4.32 (2H, q, J = 7.0 Hz), 1.37 (3H, t, J = 8.0 Hz); FABMS: m/z 281, 283, 285 $[M + Na]^+$.
3g: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.82 (1H, s), 7.55 (2H, d, J = 8.0 Hz), 6.98 (2H, d, J = 8.0 Hz), 4.51 (2H, s), 3.86 (6H, s); FABMS: m/z 263, 265 $[M + Na]^+$.
3i: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.51 (2H, d, J = 8.0 Hz), 7.41 (2H, d, J = 8.0 Hz), 7.24 (1H, s), 4.39 (2H, s), 3.88 (3H, s); FABMS: m/z 278, 280 $[M + Na]^+$.
4k: ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.79 (2H, d, J = 8.0 Hz), 7.44 (2H, d, J = 8.0 Hz), 7.18 (1H, s), 4.28 (2H, s); FABMS: m/z 234, 236, 238 $[M + Na]^+$.

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