Syntheses of (*Z*)-allyl chlorides from Baylis–Hillman adducts with a trichlorotriazine/DMF system

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Stereoselective transformation of Baylis–Hillman adducts **1** into corresponding (*Z*)-allyl chlorides **2** have been achieved by treatment with 2,4,6-trichloro [1,3,5]triazine and *N*, *N*-dimethyl formamide. This novel approach proceeds readily at room temperature within a few hours with excellent yields and stereoselectivity.

Keywords: Baylis–Hillman adduct, (*Z*)-allyl chloride, trichlorotriazine/DMF

The Baylis–Hillman reaction is well known as one of the powerful carbon–carbon bond-forming methods in organic synthesis.[1-3] The adducts of the reactions, 3-hydroxy-2-methylene-alkanoates (derived from acrylate esters), have been utilised as important precursors for stereoselective synthesis of different multifunctional molecules.[4-7] Among these transformations, the preparation of 2-(halomethyl)alk-2-enoates from Baylis–Hillman adducts has received attention as these compounds are employed in the synthesis of various naturally occurring bioactive compounds and their analogues such as α-methylene-γ-butyrolactone, α-alkylidene-β-lactam and flavanoids.[8,9] The synthesis of the corresponding allyl bromides and the allylic iodide analogues from Baylis–Hillman adducts has been studied.[11-14] Recently, we have also developed a novel method to synthesise allylic iodides derivatives.[15] In contrast, the preparations of allylic chlorides has rarely been reported. Many traditional synthetic methods suffer from the use of strong acid (HCl) and low yields as well as poor stereoselectivity.[16-18] More recently, a new approach to allylic chlorides from Baylis–Hillman adducts has been provided by Krishna *et al.*[19] In the presence of $FeCl_3$, highly steroselective syntheses of allyl chlorides were obtained in good to excellent yields. Nevertheless, in such case the Baylis–Hillman adduct has to be acetylated before use, otherwise a large amount of the allylic alcohol is formed. As a result, to develop an alternative synthetic method without the acetylation of BH adduct is highly desirable. As a continuation of our interest in Baylis–Hillman reaction,[20-23] we report a new strategy to synthesise (*Z*)-allylic chlorides **2** from Baylis–Hillman adducts **1** promoted by the TCT/DMF system (Scheme 1).

In a typical procedure, the 2,4,6-trichloro[1,3,5]triazine (TCT) and DMF was mixed first, followed by the addition of CH_2Cl_2 solution of 1 equiv. Baylis–Hillman adduct **1**. As shown by Scheme 1 and Table 1, blending of BH adducts **1** with this system essentially led to the quantitative conversion to the corresponding allyl chlorides (Table 1). A series of substrates were examined to establish the generality, of the reaction. Most reactions proceeded smoothly under similar conditions. The experimental results showed that the present method was effective for substrates bearing either electron-donating or electron-withdrawing groups. Besides affording good yields, this process also exhibited excellent stereoselectivity. The *Z*-stereoconfiguration of the product was assigned by comparing the chemical shifts in ^{1}H NMR with reported ones and no *E*-isomer was observed from the spectra. Generally, the chemical shift value of the olefinic proton in ^{1}H NMR appears downfield to the aromatic ring proton, while the corresponding olefinic proton of *E*-isomer often mixes with aromatic ring proton or appears upfield.

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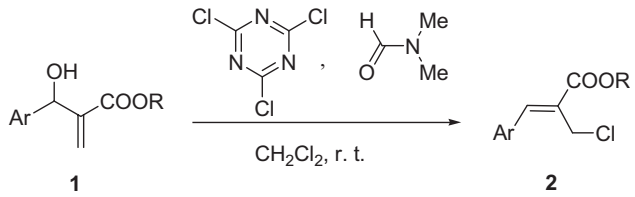


1 **2**

Scheme 1

Table 1 Stereospecific syntheses of (*Z*)-allyl chlorides **2** from Baylis–Hillman adducts **1**[a]

Entry	Ar	R	Product	Yield/%[b,c]
1	C_6H_5	Me	**2a**	89
2	2-ClC_6H_4	Me	**2b**	91
3	4-ClC_6H_4	Me	**2c**	94
4	4-$CH_3C_6H_4$	Me	**2d**	90
5		Me	**2e**	85
6	2-$NO_2C_6H_4$	Me	**2f**	95
7	3-$NO_2C_6H_4$	Me	**2g**	96
8	4-$NO_2C_6H_4$	Me	**2h**	97
9	C_6H_5	Et	**2i**	91
10	2-ClC_6H_4	Et	**2j**	92

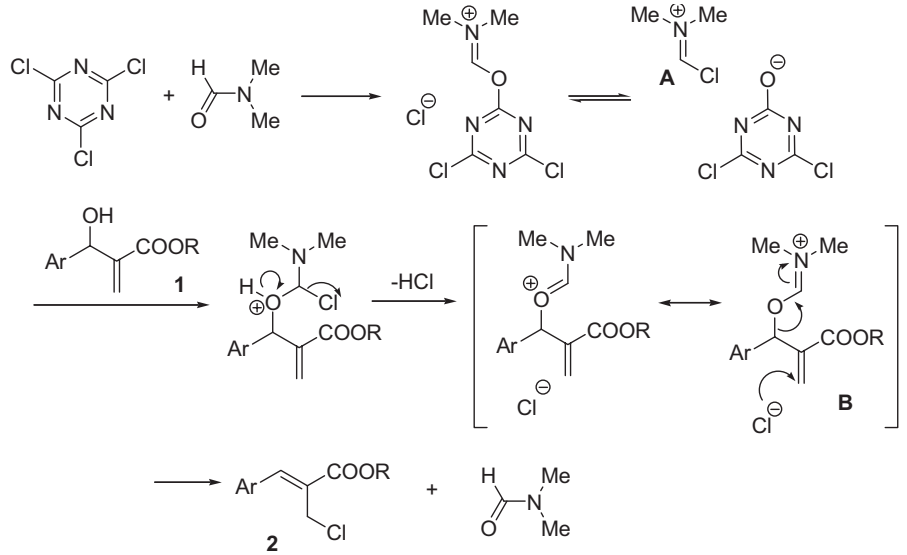
[a]All reactions were carried out with 1 mmol Baylis–Hillman adduct **1** at room temperature and finished within 1.5 h.
[b]Isolated yields based on substrate **1**.
[c]All new products were characterised by ^{1}H NMR, MS and IR.

The reaction mechanism, may follow the pathway depicted in Scheme 2. As suggested, the reactive Vilsmeier–Haack type complex **A** was firstly formed, which then combines with the hydroxyl oxygen of substrate **1** to give the resonance-stabilised cation intermediate.[24] Subsequent nucleophilic attack of a chloride anion toward the methylene carbon and the cleavage of C–O bond resulted in the formation of corresponding chlorides **2**.

In conclusion, we have provided a new method to synthesise (*Z*)-allylic chlorides **2** from the Baylis–Hillman adducts **1**.[25] The cheap reagents, experimental simplicity together with the excellent yields and good stereoselectivity make present method a good alternative to traditional methods.

Experimental

All reactions were conducted in the air. ^{1}H NMR spectra were recorded on a Bruker AC-400 instrument in $CDCl_3$ solutions using TMS as an internal standard. Chemical shifts (δ) were reported in ppm and coupling constants *J* are given in Hz. IR spectra were taken as thin films with a Bruker Vector-22 infrared spectrometer. EIMS spectra were obtained on a HP 5989B mass spectrometer. Melting points were uncorrected. Elemental analyses were performed on an EA-1110 instrument. All solvents were purchased from commercial sources and were used without further purification. All Baylis–Hillman adducts are prepared according to the literature.



Scheme 2

General procedure for the synthesis of (Z)-allylic chloride (**2**)
2,4,6-Trichloro [1,3,5]triazine (2.5 mmol) was added to DMF (0.5 ml) at room temperature. After the formation of a white solid, the reaction was monitored (TLC) until the disappearance of the TCT. Then CH_2Cl_2 (10 ml) was added as solvent, followed by the addition of the Baylis–Hillman adduct (1 mmol). After completion of the reaction, the reaction mixture was quenched with 0.1 M hydrochloric acid (5 ml) and extracted with ether (3 × 20 ml). The organic phase was successively washed with 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 using ethyl acetate and cyclohexane (1:5) as eluent.

(Z)-methyl 2-(chloromethyl)-3-phenylacrylate **(2a)**: Oil. IR (film)/cm^{-1}: 1721, 1625; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (1H, s), 7.41–7.55 (5H, m), 4.46 (2H, s), 3.88 (3H, s); MS: *m/z* (%) 196 (M^+, 100), 198 (M^+ + 2, 52), 261 (M^+–Cl, 64), 102 (31); Anal: Calcd.for $C_{11}H_{11}ClO_2$ C, 62.72; H, 5.26; Found C, 62.85; H, 5.37%.

(Z)-methyl 2-(chloromethyl)-3-(2-chlorophenyl)acrylate **(2b)**: White solid, m.p. 41–42°C. IR (KBr)/cm^{-1}: 1709, 1630, 1359; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (1H, s), 7.63-7.31 (4H, m), 4.33 (2H, s), 3.87 (3H, s); MS: *m/z* (%) 244 (M^+, 5.1), 209 (M^+–Cl, 100), 149 (12); Anal: Calcd.for $C_{11}H_{10}Cl_2O_2$ C, 53.90; H, 4.11; Found C, 54.05; H, 4.12%.

(Z)-methyl 2-(chloromethyl)-3-(4-chlorophenyl)acrylate **(2c)**: Oil. IR (film)/cm^{-1}: 1718, 1631, 1591, 1490, 1437; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (1H, s), 7.50 (2H, d, *J* = 8.4 Hz), 7.43 (2H, d, *J* = 8.4 Hz), 4.44 (2H, s), 3.89 (3H, s); MS: *m/z* (%) 244 (M^+, 100), 246 (M^+ + 2, 52), 248 (M^+ + 4, 10), 209 (M^+–Cl, 76), 149 (67); Anal: Calcd.for $C_{11}H_{10}Cl_2O_2$ C, 53.90; H, 4.11; Found C, 53.97; H, 4.26%.

(Z)-methyl 2-(chloromethyl)-3-p-tolylacrylate **(2d)**: Oil. IR (film)/cm^{-1}: 1716, 1630, 1373; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (1H, s), 7.47 (2H, d, *J* = 8.0 Hz), 7.27 (2H, d, *J* = 8.0 Hz), 4.50 (2H, s), 3.88 (3H, s); MS: *m/z* (%) 224 (M^+, 67), 189 (M^+–Cl, 100), 129 (68); Anal: Calcd.for $C_{12}H_{13}ClO_2$ C, 64.15; H, 5.83; Found C, 63.96; H, 5.87%.

(Z)-methyl 2-(chloromethyl)-3-(furan-2-yl)acrylate **(2e)**: Oil. IR (film)/cm^{-1}: 1720, 1650, 1492, 1437; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 (1H, s), 7.51 (1H, s), 6.83–6.56 (2H, m), 4.72 (2H, s), 3.80 (3H, s); MS: *m/z* (%) 200 (M^+, 100), 202 (M^+ + 2, 41), 204 (M^+ + 4, 8.5); 165 (M^+–Cl, 56); Anal: Calcd.for $C_9H_9ClO_3$ C, 53.88; H, 4.52; Found C, 54.05; H, 4.57%.

(Z)-methyl 2-(chloromethyl)-3-(2-nitrophenyl)acrylate **(2f)**: Yellow solid, m.p. 47–49°C. IR (KBr)/cm^{-1}: 1718, 1631, 1591, 1490, 1437; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.24 (1H, d, *J* = 8.0 Hz), 8.12 (1H, s), 7.79 (1H, t, *J* = 7.6 Hz), 7.68 (1H, t, *J* = 7.6 Hz), 7.63 (1H, d, *J* = 8.0 Hz), 4.20 (2H, s), 3.92 (3H, s); MS: *m/z* (%) 255 (M^+, 4.7), 220 (M^+–Cl, 100), 204 (21); Anal: Calcd.for $C_{11}H_{10}ClNO_4$ C, 51.68; H, 3.94; Found C, 51.79; H, 4.12%.

(Z)-methyl 2-(chloromethyl)-3-(3-nitrophenyl)acrylate **(2g)**: Light yellow solid, m.p. 75–76°C. IR (KBr)/cm^{-1}: 1706, 1629, 1523, 1434; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40–8.26 (2H, m), 7.92 (1H, s), 7.89–7.67 (2H, m), 4.43 (2H, s), 3.92 (3H, s); MS: *m/z* (%) 255 (M^+, 77), 257 (M^+ + 2, 17), 220 (M^+–Cl, 100), 174 (41), 115 (91); Anal: Calcd.for $C_{11}H_{10}ClNO_4$ C, 51.68; H, 3.94; Found C, 51.76; H, 4.02%.

(Z)-methyl 2-(chloromethyl)-3-(4-nitrophenyl)acrylate **(2h)**: Yellow solid, m.p. 118–119°C. IR (film)/cm^{-1}: 1718, 1631, 1591, 1490, 1437; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (2H, d, *J* = 8.0 Hz), 7.89 (1H, s), 7.71 (2H, d, *J* = 8.0 Hz), 4.41 (2H, s), 3.92 (3H, s); MS: *m/z* (%) 255 (M^+, 56), 220 (M^+–Cl, 42), 174 (85), 160 (100); Anal: Calcd.for $C_{11}H_{10}ClNO_4$ C, 51.68; H, 3.94; Found C, 51.55; H, 3.82%.

(Z)-ethyl 2-(chloromethyl)-3-phenylacrylate **(2i)**: Oil (lit.[19]). IR (film)/cm^{-1}: 1718, 1628, 1591, 1457, 1056; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (1H, s), 7.58–7.42 (5H, m), 4.45 (2H, s), 4.34 (2H, q, *J* = 7.0 Hz), 1.40 (3H, t, *J* = 7.1 Hz); MS: *m/z* (%) 224 (M^+, 12), 189 (M^+–Cl, 100), 129 (31).

(Z)-ethyl 2-(chloromethyl)-3-(2-chlorophenyl)acrylate **(2j)**: Oil (lit.[19]). IR (film)/cm^{-1}: 1724, 1648, 1590, 1437; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (1H, s), 7.61–7.22 (4H, m), 4.38 (2H, q, *J* = 7.6 Hz), 4.30 (2H, s), 1.38 (3H, t, *J* = 7.6 Hz); MS: *m/z* (%) 258 (M^+, 100), 224 (M^+–Cl, 42), 136 (45), 111 (21).

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