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A highly efficient stereoselective synthesis of (*Z*)- and (*E*)-allyl iodides from Baylis–Hillman adducts☆

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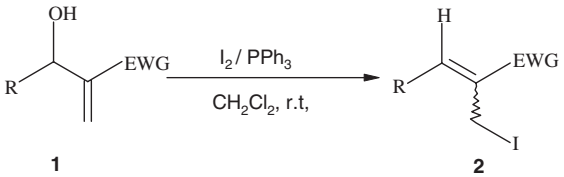
Abstract—A highly efficient synthesis of (*Z*)- and (*E*)-allyl iodides has been accomplished by treatment of Baylis–Hillman adducts with iodine and triphenylphosphine in methylene chloride at room temperature. The method is associated with mild reaction conditions, high yields and excellent stereoselectivity.

The Baylis–Hillman reaction is an important carbon–carbon bond forming method in organic synthesis.[1] The adducts of the reaction, 3-hydroxy-2-methylene-alkanoates (derived from acrylate esters) or 3-hydroxy-2-methylene-alkanenitriles (derived from acrylonitrile) are useful precursors for streoselective synthesis of multifunctional molecules.[1b,2] Allyl halides prepared from these adducts have been employed for the synthesis of various naturally occurring bioactive compounds and their analogues, such as α-methylene-γ-butyrolactones,[2a] α-alkylidene-β-lactams[2b] and flavanoids.[2c] Thus, the direct conversion of Baylis–Hillman adducts into the corresponding allyl chlorides and bromides has been thoroughly studied using various strong acids ($HBr–H_2SO_4$),[2a,b] organic acid halides (oxalyl chloride, MsCl),[3a,b] NCS/NBS–Me_2S,[3c–e] PBr_3[3f] and Lewis acids ($FeCl_3$, $InCl_3$).[3g,h] On the other hand, the methods of preparation of allyl iodides from Baylis–Hillman adducts are limited.

The documented methods have applied strong acids ($HI–H_3PO_4$),[4a] microwaves,[4b] reflux temperature[4c] and a catalyst ($NaHSO_4{\cdot}SiO_2$),[4d] which has to be prepared at the time of use. Recently a method utilizing TMSCl/NaI was reported[4e] for the preparation of (*Z*)-allyl iodides containing an aryl group only.

In continuation of our work[3g,4d,5] on the conversion of Baylis–Hillman adducts into trisubstituted alkenes, we recently observed that treatment of these adducts with iodine and PPh_3 in methylene chloride at room temperature afforded the corresponding allyl iodides in high yields (Scheme 1).

Baylis–Hillman adducts containing both ester and nitrile moieties underwent the conversion smoothly. The generality and efficiency of the reaction were established by studying various substrates (Table 1). Allyl iodides having both aryl and alkyl groups were prepared. Aryl groups containing electron-donating as well as electron-withdrawing functionalities were compatible. However, substrates possessing aryl groups with electron-withdrawing functionalities reacted more slowly and the yields of the products were reduced. Earlier older



1 **2**

R = alkyl, aryl
EWG = -COOMe, -CN

Scheme 1.

Keywords: Baylis–Hillman adduct; (*Z*)- and (*E*)-allyl iodides; I_2/PPh_3; Stereochemistry.

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Table 1. Preparation of (*Z*)- and (*E*)-allyl iodides from Baylis–Hillmann adducts using I_2/PPh_3[a]

Entry	R	EWG	Time (h)	Isolated yield (%)
a	C_6H_5	COOMe	0.5	98
b	2-Cl–C_6H_4	COOMe	1	95
c	4-Cl–C_6H_4	COOMe	1	94
d	2,4-Cl_2–C_6H_3	COOMe	1	93
e	4-Me–C_6H_4	COOMe	0.5	94
f	4-MeO–C_6H_4	COOMe	1	91
g	4-NO_2–C_6H_4	COOMe	6	55
h	3-NO_2–C_6H_4	COOMe	5	60
i	CH_3–$(CH_2)_6$	COOMe	1	92
j	C_6H_5	CN	1	92
k	4-Cl–C_6H_4	CN	1	90
l	2,4-Cl_2–C_6H_3	CN	1	91
m	3-NO_2–C_6H_4	CN	5	58
n	CH_3–$(CH_2)_6$	CN	1	89

[a] The structures of the alkenes were determined from their spectral (IR, ^{1}H NMR and MS) and analytical data. The alkenes in entries a–i were formed with (*Z*)-configuration while those of entries j–n were formed with (*E*)-configuration.

methods had failed to produce allyl iodides from such substrates.[4e]

The present method[6] proceeds with excellent stereoselectivity. Allyl iodides containing an ester moiety were formed with the (*Z*)-configuration while those containing a nitrile had solely the (*E*)-configuration. The ^{1}H NMR spectra of the products were used[6] to establish their structures and stereochemistry by comparison with reported data for known compounds.[4d] In the ^{1}H NMR spectrum of a trisubstituted alkene the β-vinylic protons, *cis*- and *trans*- to the ester group are known to resonate at δ 7.5 and δ 6.5, respectively, when R is aryl.[7a,b] The same proton *cis*- and *trans*- to an ester group appears at δ 6.8 and δ 5.7, respectively, when R is alkyl.[7c,d] Similarly, the β-vinylic protons *cis*- and *trans*- to a nitrile group resonate at δ 7.6 and δ 7.2, respectively, when R is aryl,[4d,7e,f] while protons *cis*- and *trans*- to the nitrile group appear at δ 6.8 and δ 6.3, respectively, when R is alkyl.[4d,7g,h] The stereoselectivities of the present conversions can be explained[2b] by considering the transition state models **A**, **B** and **C** (Fig. 1). Model **A** is more favoured than **B** when the EWG is an ester and (*Z*)-products are formed exclusively. On the other hand, model **C** is more favoured than **A** when the EWG is a nitrile as –CN is linear and hence the (*E*)- products are formed.

In conclusion, we have described a highly efficient and stereoselective synthesis of both (*Z*)- and (*E*)-allyl iodides from Baylis–Hillman adducts by treatment with I_2/PPh_3 in CH_2Cl_2 at room temperature.

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6. General procedure for the preparation of allyl iodides: A solution of iodine (1 mmol) and PPh_3 (1 mmol) in CH_2Cl_2 (10 ml) was stirred at room temperature for 5 min. The alcohol **1** (1 mmol) dissolved in CH_2Cl_2 (10 ml) was added and the stirring continued. After completion (TLC) the reaction mixture was washed with saturated aqueous

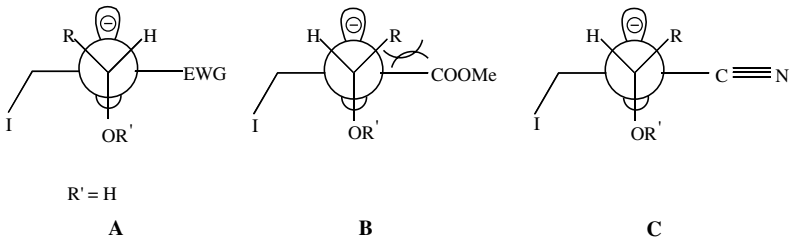

Figure 1.

sodium thiosulphate solution (3×10 ml), brine (3×10 ml) and water (3×10 ml) and subsequently dried over anhydrous Na_2SO_4. The volatiles were evaporated to give a crude product, which was purified by column chromatography over silica gel using 4% EtOAc in hexane to yield the pure allyl iodide.

Spectral and analytical data of unknown allyl iodides are given below.

Compound **2d**: IR (KBr): 1719, 1629, 1584, 1467, 1229 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.73 (1H, s), 7.70 (1H, d, $J = 8.0$ Hz), 7.49 (1H, d, $J = 2.0$ Hz), 7.42 (1H, dd, $J = 8.0$, 2.0 Hz), 4.16 (2H, s), 3.91 (3H, s); EIMS: m/z 243 ($M^{+\cdot}$-I); Anal. Calcd for $C_{11}H_9Cl_2IO_2$: C, 35.58; H, 2.43. Found: C, 35.52; H, 2.36.

Compound **2i**: IR (KBr): 1722, 1637, 1438, 1276, 1160 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 6.81 (1H, t, $J = 7.0$ Hz), 4.06 (2H, s), 3.74 (3H, s), 2.12 (2H, q, $J = 7.0$ Hz), 1.57–1.41 (2H, m), 1.39–1.18 (8H, m), 0.84 (3H, t, $J = 7.0$ Hz); EIMS: m/z 197 ($M^{+\cdot}$-I); Anal. Calcd for $C_{12}H_{21}IO_2$: C, 44.44; H, 6.48. Found: C, 44.38; H, 6.43.

Compound **2l**: IR (KBr): 2223, 1609, 1581, 1469, 1291 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.02 (1H, d, $J = 8.0$ Hz), 7.52 (1H, d, $J = 2.0$ Hz), 7.38 (1H, dd, $J = 8.0$, 2.0 Hz), 7.25 (1H, s), 4.17 (2H, s); EIMS: m/z 210 ($M^{+\cdot}$-I); Anal. Calcd for $C_{10}H_6Cl_2IN$: C, 35.50; H, 1.78; N, 4.14. Found: C, 35.42; H, 1.73; N, 4.18.

Compound **2n**: IR (KBr): 2222, 1628, 1460, 1163 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 6.43 (1H, t, $J = 7.0$ Hz), 3.90 (2H, s), 2.37 (2H, q, $J = 7.0$ Hz), 1.58–1.42 (2H, m), 1.38–1.21 (8H, m), 0.89 (3H, t, $J = 7.0$ Hz); EIMS: m/z 164 ($M^{+\cdot}$-I); Anal. Calcd for $C_{11}H_{18}IN$: C, 45.36; H, 6.19; N, 4.81. Found: C, 45.31; H, 6.13; N, 4.77.

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