

A Rapid and Efficient Stereoselective Synthesis of (*Z*)- and (*E*)-Allyl Bromides from *Baylis–Hillman* Adducts Using Bromo(dimethyl)sulfonium Bromide¹⁾

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Treatment of *Baylis–Hillman* adducts **1** with bromo(dimethyl)sulfonium bromide, $\text{Br}(\text{Me}_2)\text{S}^+\text{Br}^-$, in MeCN was found to stereoselectively afford (*Z*)- and (*E*)-allyl bromides **2**. The reaction is rapid at room temperature, high-yielding, and highly stereoselective.

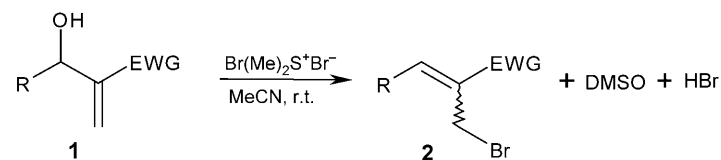
Introduction. – The *Baylis–Hillman* reaction involving the coupling of an activated vinylic system with electrophiles in the presence of a catalytic amount of tertiary amine (usually DABCO) is a useful carbon–carbon bond-forming process in synthetic organic chemistry [1]. The resulting adducts **1** (see below), 3-hydroxy-2-methylidene-alkanoates (derived from acrylate esters) or 3-hydroxy-2-methylidene-alkanenitriles (derived from acrylonitrile), have frequently been used for the stereoselective synthesis of different functionalized molecules [1b][2]. The allyl halides prepared from these adducts have been used in the synthesis of various natural and biologically active molecules and their analogues such as α -methylidene- γ -butyrolactones [2a], α -alkylidene- β -lactams [2b], and flavonoids [2c]. The direct conversion of the *Baylis–Hillman* adducts into their corresponding halides has been previously accomplished with different halogen-containing reagents including strong acids ($\text{HBr}/\text{H}_2\text{SO}_4$, $\text{HI}/\text{H}_3\text{PO}_4$) [2a][3a], organic acid halides (oxalyl chloride, MsCl) [3b,c], HCA/PPh_3 [3a], *Lewis* acids (FeCl_3 , InCl_3) [3d,e], and metallic (Na and Li) halides [3f,g]. However, unsatisfactory yields, low stereoselectivities, prolonged reaction times, and harsh reaction conditions are often drawbacks in many of these methods.

Results and Discussion. – In continuation of our work [3d,g][4] on the synthesis of configurationally defined, trisubstituted alkenes from *Baylis–Hillman* adducts, we have recently discovered that these adducts can easily be converted into the corresponding allyl bromides by treatment with bromo(dimethyl)sulfonium bromide ($\text{Br}(\text{Me}_2)\text{S}^+\text{Br}^-$) in MeCN at room temperature (*Scheme 1*).

Several allyl bromides were now prepared in yields of 83–99% from different *Baylis–Hillman* adducts containing either ester (MeOOC , EtOOC) or cyano (CN) groups (*Table*). The adducts with either electron-donating or withdrawing groups in the aryl

¹⁾ Part 81 in the series ‘Studies on Novel Synthetic Methodologies’, IICT Communication No. 060703.

Scheme 1



R = Aryl, alkyl

EWG = EtOOC, MeOOC, CN

(Ar) moiety underwent the conversion smoothly. The reaction time required for the conversion of adducts containing aryl groups with electron-rich substituents was only 0.2–1.0 h. For aromatic substrates with electron-withdrawing groups, the reaction time was somewhat longer (*ca.* 3 h).

The structures and configurations of the prepared allyl bromides were derived from their ^1H -NMR and MS data, and by comparison of the spectroscopic values with those reported for known compounds [3f,g]. The allyl bromides were formed with excellent stereoselectivities. The compounds with ester moieties as electron-withdrawing groups (EWG) were obtained with (*Z*)-configuration, while those with CN groups were (*E*)-configured exclusively. In the ^1H -NMR spectrum of a trisubstituted alkene, the β -vinylic H-atom *cis* and *trans* to the ester group is known to resonate at $\delta(\text{H})$ 7.5 and 6.5, respectively, when the substituent R is aromatic [5a,b]. The same H-atom *cis* and *trans* to an ester group resonates at $\delta(\text{H})$ 6.8 and 5.7, respectively, when R is alkyl [5c,d]. Similarly, the β -vinylic H-atom *cis* and *trans* to the CN group resonates at $\delta(\text{H})$ 7.6 and 7.2, respectively, when R is aryl [3g][5e,f]; the same H-atom *cis* and *trans* to a CN group resonates at $\delta(\text{H})$ 6.8 and 6.3, respectively, when R is alkyl [3g][5g,h]. Based on these reported chemical shifts, the (*Z*)- and (*E*)-isomers of the prepared allyl bromides could be readily identified.

A plausible mechanism for the above conversion is shown in Scheme 2. It involves attack of the electron pair of the OH group of the adduct **1** to the S-atom of $\text{Br}(\text{Me}_2\text{S})^+\text{Br}^-$ to form species **A**. Then, Br^- attacks the methyldiene C=C bond, which results in isomerization under concomitant detachment of the C(3)–O bond and formation of the allyl bromide **2**.

Scheme 2

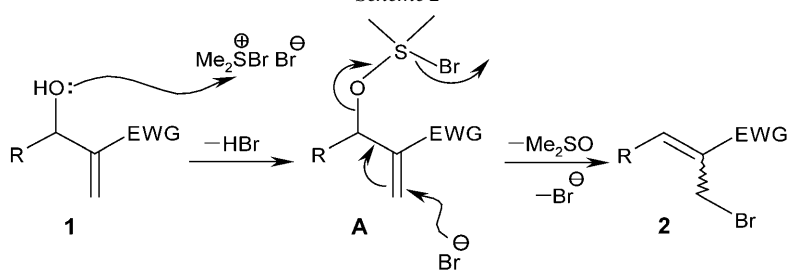
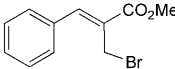
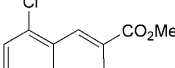
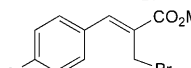
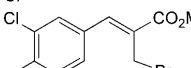
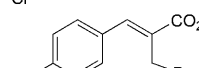
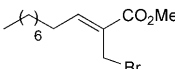
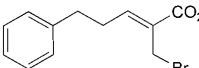
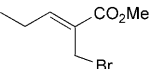
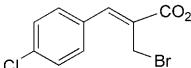
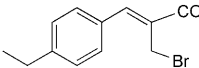
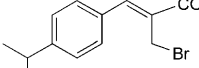
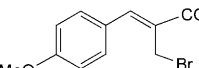
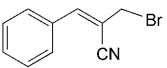
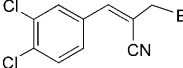
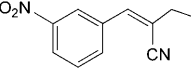


Table. Preparation of (Z)- and (E)-Allyl Bromides **2a–o** from Baylis–Hillman Adducts Using $Br(Me_2S)^+ Br^-$. For synthetic details and compound characterization, see text and *Exper. Part*.

Series	R	EWG ^{a)}	Product ^{b)}	Time [h]	Yield [%] ^{c)}
a	C ₆ H ₅	CO ₂ Me		0.3	98
b	2-Cl-C ₆ H ₄			0.5	93
c	4-Cl-C ₆ H ₄			0.5	95
d	3,4-(Cl) ₂ -C ₆ H ₃			0.5	90
e	4-O ₂ N-C ₆ H ₄			3.0	85
f	Me(CH ₂) ₇ CH ₂			0.5	95
g	C ₆ H ₅ (CH ₂) ₂			0.5	93
h	Et			1.0	89
i	4-Cl-C ₆ H ₄	CO ₂ Et		0.5	92
j	4-Et-C ₆ H ₄			0.2	99
k	4-i-Pr-C ₆ H ₄			0.2	99
l	4-MeO-C ₆ H ₄			0.5	94
m	C ₆ H ₅	CN		0.5	91
n	3,4-(Cl) ₂ -C ₆ H ₃			1.0	88
o	3-O ₂ N-C ₆ H ₄			3.0	83

^{a)} Electron-withdrawing group. ^{b)} Compounds **2h**, **2j**, and **2k** are new products [3f,g]. ^{c)} Isolated yield.

The configuration of the products **2** can possibly be rationalized by considering the transition state (TS) models **B–D** (Figure). TS **B** is more favored than **C** when the EWG is an ester: in this case, (*Z*)-products are obtained solely. However, the TS model **D** is more favored than **A**, when the substituent is a (linear) CN group, which gives rise to (*E*)-configured products.

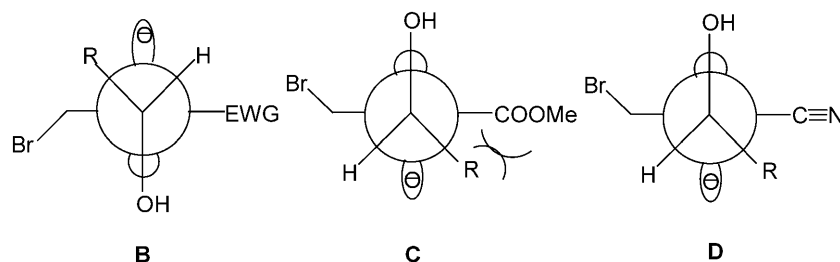


Figure. Conformational transition-state analysis for the rationalization of the observed stereoselectivity in the reaction leading to the allyl bromides **2**. For details, see text.

Bromo(dimethyl)sulfonium bromide [6] is an inexpensive reagent that can be used under mild reaction conditions. Previously, it was used to carry out some synthetic conversions [6], mainly as a catalyst, but its utility has not fully been explored yet.

In conclusion, we have developed a simple and efficient synthesis of both (*Z*)- and (*E*)-allyl bromides from unmodified *Baylis–Hillman* adducts by treatment with bromo(dimethyl)sulfonium bromide in MeCN at room temperature. The method is characterized by mild reaction conditions, short conversion times, high yields, and excellent stereoselectivities.

The authors thank CSIR and UGC, New Delhi, for financial assistance.

Experimental Part

General Procedure. To a soln. of the adduct **1** (5 mmol) in MeCN (5 ml), Br(Me₂)S⁺Br[−] (6 mmol), prepared according to [6], was added. The mixture was stirred at r.t., and the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure, H₂O (10 ml) was added to the residue, and the mixture was extracted with AcOEt (3 × 10 ml). The extract was concentrated, and the crude residue was purified by column chromatography (SiO₂; 5–10% AcOEt in hexane) to afford the pure allyl bromide. Selected anal. data of some representative allyl bromides **2** are given below.

Methyl (2*Z*)-2-(Bromomethyl)-3-(2-chlorophenyl)prop-2-enoate (2b). Semisolid. ¹H-NMR (200 MHz, CDCl₃): 7.81 (s, 1 H); 7.64 (d, *J* = 8.0, 1 H); 7.61 (d, *J* = 8.0, 1 H); 7.41 (t, *J* = 8.0, 1 H); 7.22 (t, *J* = 8.0, 1 H); 4.15 (s, 2 H); 3.81 (s, 3 H). EI-MS: 292, 290, 288 (*M*⁺). Anal. calc. for C₁₁H₁₀BrClO₂: C 45.67, H 3.46; found: C 45.72, H 3.40.

Methyl (2*Z*)-2-(Bromomethyl)pent-2-enoate (2h). Semisolid. ¹H-NMR (200 MHz, CDCl₃): 6.94 (t, *J* = 7.0, 1 H); 4.21 (s, 2 H); 3.83 (s, 3 H); 2.31 (q, *J* = 7.0, 2 H); 0.83 (t, *J* = 7.0, 3 H). EI-MS: 208, 206 (*M*⁺). Anal. calc. for C₇H₁₁BrO₂: C 40.58, H 5.31; found: C 40.69, H 5.25.

Ethyl (2Z)-2-(Bromomethyl)-3-(4-ethylphenyl)prop-2-enoate (2j). Semisolid. $^1\text{H-NMR}$ (200 MHz, CDCl_3): 7.76 (s, 1 H); 7.49 (d, $J=8.0$, 2 H); 7.28 (d, $J=8.0$, 2 H); 4.38 (s, 2 H); 4.30 (q, $J=7.0$, 2 H); 2.70 (q, $J=7.0$, 2 H); 1.39 (t, $J=7.0$, 3 H); 1.28 (t, $J=7.0$, 3 H). EI-MS: 298, 296 (M^+). Anal. calc. for $\text{C}_{14}\text{H}_{17}\text{BrO}_2$: C 56.57, H 5.72; found: C 56.64, H 5.63.

Ethyl (2Z)-2-(Bromomethyl)-3-[4-(1-methylethyl)phenyl]prop-2-enoate (2k). Semisolid. $^1\text{H-NMR}$ (200 MHz, CDCl_3): 7.75 (s, 1 H); 7.52 (d, $J=8.0$, 2 H); 7.30 (d, $J=8.0$, 2 H); 4.39 (s, 2 H); 4.32 (q, $J=7.0$, 2 H); 2.93 (m, 1 H); 1.40 (t, $J=7.0$, 3 H); 1.27 (d, $J=7.0$, 6 H). EI-MS: 312, 310 (M^+). Anal. calc. for $\text{C}_{15}\text{H}_{19}\text{BrO}_2$: C 57.88, H 6.11; found: C 57.94, H 6.08.

(2E)-2-(Bromomethyl)-3-(3-nitrophenyl)prop-2-enenitrile (2o). Semisolid. $^1\text{H-NMR}$ (200 MHz, CDCl_3): 8.46 (d, $J=2.0$, 1 H); 8.33 (dd, $J=8.0$, 2.0, 1 H); 8.28 (dd, $J=8.0$, 2.0, 1 H); 7.68 (dd, $J=8.0$, 2.0, 1 H); 7.21 (s, 1 H); 4.20 (s, 2 H). EI-MS: 268, 266 (M^+). Anal. calc. for $\text{C}_{10}\text{H}_7\text{BrN}_2\text{O}_2$: C 44.94, H 2.62; found: C 44.72, H 2.64.

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Received May 29, 2006