# A Rapid and Efficient Stereoselective Synthesis of (*Z*)- and (*E*)-Allyl Bromides from *Baylis–Hillman* Adducts Using Bromo(dimethyl)sulfonium Bromide[1])

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Treatment of *Baylis–Hillman* adducts **1** with bromo(dimethyl)sulfonium bromide, $Br(Me_2)S^+Br^-$, 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 $\alpha$-methylidene-$\gamma$-butyrolactones [2a], $\alpha$-alkylidene-$\beta$-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 ($HBr/H_2SO_4$, $HI/H_3PO_4$) [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 ($Br(Me_2)S^+Br^-$) 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

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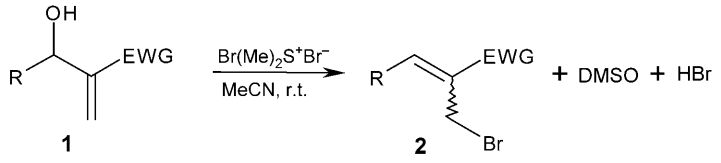
*Scheme 1*




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 $^1$H-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 $^1$H-NMR spectrum of a trisubstituted alkene, the *β*-vinylic H-atom *cis* and *trans* to the ester group is known to resonate at *δ*(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 *δ*(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 *δ*(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 *δ*(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 $Br(Me_2)S^+Br^-$ to form species **A**. Then, $Br^-$ attacks the methylidene 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*

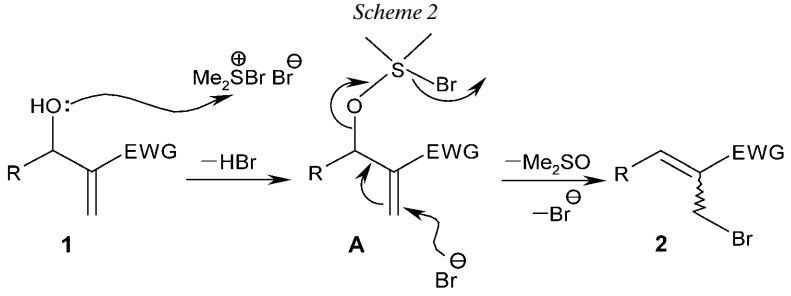
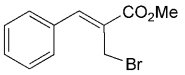
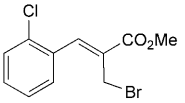
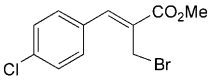
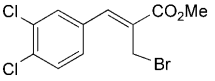
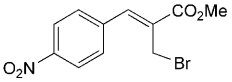
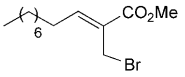
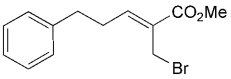
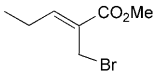
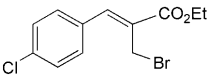
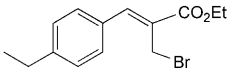
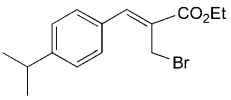
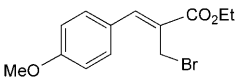
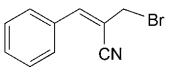
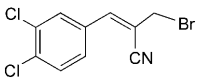
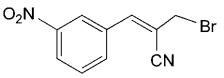


Table. *Preparation of (Z)- and (*E*)-Allyl Bromides* **2a**–**o** *from* Baylis–Hillman *Adducts Using* $Br(Me_2)S^+Br^-$ . For synthetic details and compound characterization, see text and *Exper. Part.*

| Series | R | EWG[a]) | Product[b]) | Time [h] | Yield [%][c]) |
|---|---|---|---|---|---|
| **a** | $C_6H_5$ | $CO_2Me$ |  | 0.3 | 98 |
| **b** | 2-Cl–$C_6H_4$ | |  | 0.5 | 93 |
| **c** | 4-Cl–$C_6H_4$ | |  | 0.5 | 95 |
| **d** | 3,4-$(Cl)_2$–$C_6H_3$ | |  | 0.5 | 90 |
| **e** | 4-$O_2N$–$C_6H_4$ | |  | 3.0 | 85 |
| **f** | $Me(CH_2)_7CH_2$ | |  | 0.5 | 95 |
| **g** | $C_6H_5(CH_2)_2$ | |  | 0.5 | 93 |
| **h** | Et | |  | 1.0 | 89 |
| **i** | 4-Cl–$C_6H_4$ | $CO_2Et$ |  | 0.5 | 92 |
| **j** | 4-Et–$C_6H_4$ | |  | 0.2 | 99 |
| **k** | 4-i-Pr–$C_6H_4$ | |  | 0.2 | 99 |
| **l** | 4-MeO–$C_6H_4$ | |  | 0.5 | 94 |
| **m** | $C_6H_5$ | CN |  | 0.5 | 91 |
| **n** | 3,4-$(Cl)_2$–$C_6H_3$ | |  | 1.0 | 88 |
| **o** | 3-$O_2N$–$C_6H_4$ | |  | 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.

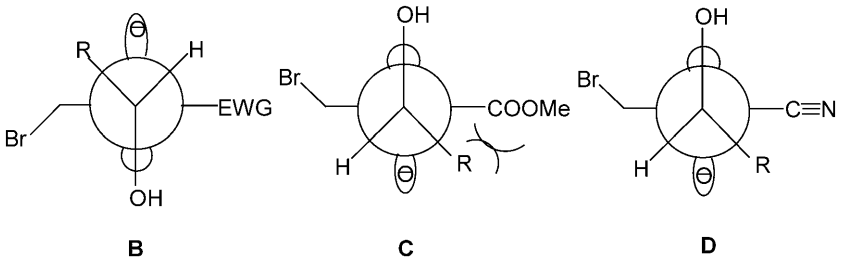



Figure. *Conformational transition-state analysis for the rationalization of the observed stereoselectivity in the reaction leading to the allyl bromides* **2**. For details, see text.

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.

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## Experimental Part

*General Procedure.* To a soln. of the adduct **1** (5 mmol) in MeCN (5 ml), $Br(Me_2)S^+Br^-$ (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, $H_2O$ (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 ($SiO_2$; 5–10% AcOEt in hexane) to afford the pure allyl bromide. Selected anal. data of some representative allyl bromides **2** are given below.

*Methyl (2Z)-2-(Bromomethyl)-3-(2-chlorophenyl)prop-2-enoate* (**2b**). Semisolid. $^1$H-NMR (200 MHz, $CDCl_3$): 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 $C_{11}H_{10}BrClO_2$: C 45.67, H 3.46; found: C 45.72, H 3.40.

*Methyl (2Z)-2-(Bromomethyl)pent-2-enoate* (**2h**). Semisolid. $^1$H-NMR (200 MHz, $CDCl_3$): 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 $C_7H_{11}BrO_2$: 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. $^1$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 $C_{14}H_{17}BrO_2$: 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. $^1$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 $C_{15}H_{19}BrO_2$: C 57.88, H 6.11; found: C 57.94, H 6.08.

*(2*E*)-2-(Bromomethyl)-3-(3-nitrophenyl)prop-2-enenitrile* (**2o**). Semisolid. $^1$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 $C_{10}H_7BrN_2O_2$: C 44.94, H 2.62; found: C 44.72, H 2.64.

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