A Convenient One Pot Allylation of Aldehydes with Allylic Halides Prepared in Situ from Allylic Alcohols in the Presence of Metallic Bismuth

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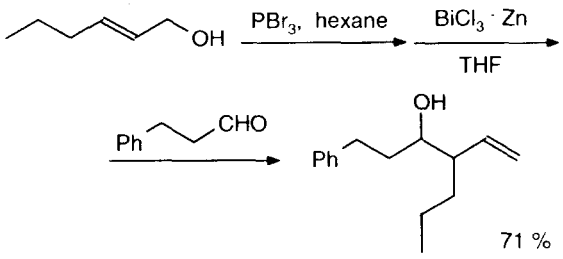
A convenient one pot allylation of aldehydes with allylic iodides prepared in situ from allylic alcohols by using trimethylsilyl chloride and sodium iodide proceeds smoothly in the presence of metallic bismuth to afford the corresponding homoallylic alcohols in good yields.

Allylation of carbonyl compounds is one of the most fundamental carbon–carbon bond forming reactions in organic synthesis. Numerous efficient methods by using allylic organometallics derived from a number of metallic elements have been reported.[1] Among them, the Grignard-type or Barbier-type reaction using metals or low-valent metallic compounds and allylic halides is one of the most useful and convenient methods for performing allylation reactions. Generally, commercially unavailable allylic halides have to be prepared from the halogenation of the stable and tractable corresponding allylic alcohols. Therefore, the development of direct allylation of aldehydes with allylic alcohols is an important theme. However, there are few reports so far about the allylation of aldehydes using allylic alcohols, involving the transformation of the functional group from an allylic alcohol to an allylic halide in situ.[2] This is because the halogenation of alcohols[3] is always carried out under strongly acidic conditions, which frequently cause rapid decomposition of allylic organometallic species which are produced by allylic halides and several metals.

In the course of our investigations on the reaction with bismuth compounds, we have already reported some allylations of aldehydes by the use of metallic bismuth or $BiCl_3$–Zn, Fe, Al or Mg.[4] These reactions proceeded smoothly in an aqueous environment as well as in anhydrous solvent; for example, the reaction took place not only in THF–H_2O but also in strongly acidic conditions using an acid such as TsOH or aq HCl and in strongly basic conditions using a base such as aq KOH, or in a buffer such as the frequently used aq KH_2PO_4.[4b] These results prompted us to try the allylation of aldehydes with allylic alcohols via the transformation from the alcohols to the halides in situ.

Results and Discussion

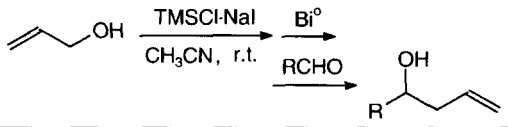
First, we examined the transformation of an allylic alcohol using phosphorus tribromide (PBr_3).[3] Namely, hexane solutions of PBr_3 and (*E*)-2-hexen-1-ol were added to the THF suspension of $BiCl_3$–Zn; after stirring for 30 min, 3-phenylpropanal was added to the reaction mixture. The corresponding homoallylic alcohol was obtained in good yield (Eq. 1). Unfortunately, the reaction yields were not reproducible, and the reaction did not take place when 2-propen-1-ol was used.

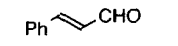
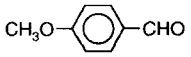
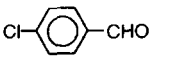
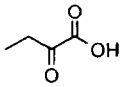
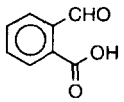


(1)

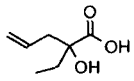
Thus, the iodination of allylic alcohols was carried out by using trimethylsilyl iodide (TMS-I) prepared in situ.[5] 2-Propen-1-ol was added to the acetonitrile suspension of trimethylsilyl chloride (TMS-Cl) and sodium iodide (NaI). After stirring for 12 h, metallic bismuth and an aldehyde were successively added to the reaction mixture to give the desired product. The scope and versatility of the present reaction were investigated by using various aldehydes. As shown in Table 1, both aliphatic and aromatic aldehydes reacted smoothly to afford the corresponding homoallylic alcohols in good yields (Entries 1—5). An α,β-unsaturated aldehyde such as cinnamaldehyde was allylated to give the 1,2-addition product as a sole product (Entry 6). When aldehydes having functional groups such as alkoxy, chloro, or olefinic groups were used, the corresponding homoallylic alcohols were obtained in moderate to good yields (Entries 7—9). Moreover, in this reaction system, 2-propen-1-ol was successfully used for the allylation of carbonyl compounds containing a carboxylic group such as 2-oxobutyric acid and phthalaldehydic acid, which are usually unusable substrates owing to rapid protonolysis of the allylating agent (Entries

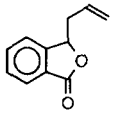
Table 1. Allylation of Various Aldehydes and a Keto Acid with Allyl Alcohol



Entry	Aldehyde	Yield/%[a]
1	PhCHO	68
2	$PhCH_2CHO$	74
3	$PhCH_2CH_2CHO$	91
4	$CH_3(CH_2)_7CHO$	67
5	c-Hexyl-CHO	76
6		55
7		50
8		90
9	$CH_2{=}CH(CH_2)_8CHO$	85
10		68[b]
11		89[b]

a) Isolated Yields. b) In Entries 10 and 11, the products were as fellows:

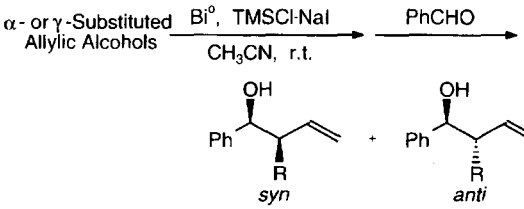
Entry 10; 

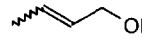
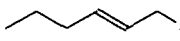
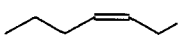
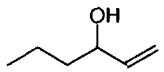
Entry 11; 

10 and 11). Noteworthy is the fact that the present reaction takes place smoothly without the protection of the carboxyl group.

Furthermore, we examined the regio- and diastereoselectivity of the present reaction by using α- or γ-substituted allylic alcohols. Table 2 summarizes the results of the reaction of benzaldehyde with allylic alcohols **1**, *E*-**2**, *Z*-**2**, and **3**. The same homoallylic alcohol was obtained with similar diastereoselectivities although *E*-**2** and *Z*-**2** were used (Entries 2 and 3). Then a similar result was obtained when secondary allylic alcohol **3** was used. The reaction between homoallylic alcohols *E*-**2**, *Z*-**2**, or **3** and TMSCl–NaI was monitored by ^{1}H NMR spectroscopy. We found that the same primary allylic iodide (*E*-form; the coupling constant of olefinic protons was J = 15.1 Hz) was prepared from allylic alcohol **2** (*E*-alcohol) and **4** (secondary alcohol), and the primary allylic iodide (*Z*-form; the coupling constant of olefinic protons was J = 10.3 Hz) was prepared from allylic alcohol **3** (*Z*-alcohol). Thus, we also found that the reaction proceeded on the internal carbon (secondary carbon) of the allylic system and that the *syn*-adducts were major products irrespective of the double bond geometry of allylic alcohols.[6] Although the reaction mechanism is not clear at the present stage, we propose an acyclic transition state for the stereochemical rationalization, as shown in our previous paper.[4c]

Table 2. Diastereoselectivity of Allylation of Benzaldehyde with α- or γ-Substituted Allylic Alcohols



Entry	Allylic alcohol[a]		Yield/%[b]	*syn* : *anti*[c]
1		**1**	82	88 : 12
2		*E*-**2**	87	75 : 25
3		*Z*-**2**	90	75 : 25
4		**3**	62	77 : 23

a) Allylic alcohol **1** ; E : Z = 86 : 14. Allylic alcohols *E*-**2**, *Z*-**2**, and **3**; stereochemically pure (> 98%). b) Isolated yields. c) The ratio of diastereoselectivity was determined by ^{1}H NMR spectra. See Refs. 2c and 7.

In conclusion, the Barbier-type allylation reactions are usually carried out using allylic halides which are prepared in advance from the corresponding allylic alcohols. In the present reaction, it is noteworthy that in the presence of metallic bismuth the Barbier-type allylation of carbonyl compounds with allylic halides prepared in situ from allylic alcohols by using TMS-I proceeds smoothly to afford the corresponding homoallylic alcohols in good yields.

Experimental

General Method. ^{1}H NMR spectra were recorded with JEOL EX-90A (90 MHz) and JEOL EX-400 (400 MHz) spectrometers; chemical shifts (δ) were reported in ppm using tetramethylsilane as an internal standard. IR spectra were taken on a Horiba FT-IR 210 spectrometer. Tetrahydrofuran (THF) was freshly distilled from sodium diphenylketyl before use. Preparative thin layer chromatography (TLC) was performed on silica gel (Wakogel B-5F). All other reagents were commercially available and were used without further purification.

General Procedure for the Preparation of 1-Phenyl-5-hexen-3-ol by Using Trimethylsilyl Chloride and Sodium Iodide. Under an argon atmosphere, 2-propen-1-ol (150 mg, 2.58 mmol) was added to the acetonitrile (10 ml) suspension of TMS–Cl (264 mg, 2.43 mmol) and NaI (431 mg, 2.88 mmol) at room temperature. After stirring for 12 h, metallic bismuth (542 mg, 2.59 mmol) was added to the reaction mixture. After stirring for 1 h at room temperature, 3-phenylpropanal (134 mg, 1.00 mmol) was added. After stirring for 22 h, the reaction mixture was quenched with an aqueous 1 M hydrochloric acid (10 ml) (1 M = 1 mol dm^{-3}). The organic materials were extracted with diethyl ether (30 ml×3), and the combined organic layer was washed successively with water, 5% aq $KHSO_3$ and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvents, the residue was purified by TLC (hexane : ethyl acetate = 4 : 1) to give the corresponding homoallylic alcohol, 1-phenyl-5-hexen-3-ol (160 mg, 91% yield). This product was identified by comparison with the literature.[4c,8] The spectral data of the products are as follows.

1-Phenyl-3-buten-1-ol. 68% yield. This product was identified by comparison with the literature.[4c,8]

1-Phenyl-4-penten-2-ol. 74% yield. ^{1}H NMR (90 MHz, $CDCl_3$) δ = 1.88 (1H, s), 2.01—2.78 (4H, m), 3.85 (1H, quint, J = 5.4 Hz), 5.05—5.21 (2H, m), 5.64—6.01 (1H, m), 7.25 (5H, s). IR (neat) 3404, 2950, 1641, 1496, 1454, 1080, 744, 700 cm^{-1}. This product was identified by comparison with an authentic sample prepared from the known procedure.[9]

1-Dodecen-4-ol. 67% yield. This product was identified by comparison with the literature.[4c]

1-Cyclohexyl-3-buten-1-ol. 76% yield. This product was identified by comparison with the literature.[8]

1-Phenyl-1,5-hexadien-3-ol. 55% yield. This product was identified by comparison with the literature.[8]

1-(4-Methoxyphenyl)-3-buten-1-ol. 50% yield. This product was identified by comparison with the literature.[4c]

1-(4-Chlorophenyl)-3-buten-1-ol. 90% yield. This product was identified by comparison with the literature.[4c]

Tetradeca-1,13-dien-4-ol. 85% yield. This product was identified by comparison with literature.[2c]

2-Ethyl-2-hydroxy-4-pentenoic Acid. 68% yield. This product was identified by comparison with the literature.[4b]

3-Allylphthalide. 89% yield. This product was identified by comparison with the literature.[4b]

1-Phenyl-4-propyl-5-hexen-3-ol. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.87 (3H, t, J = 7.3 Hz), 1.12—1.50 (4H, m), 1.51—1.86 (3H, m), 2.02—2.16 (1H, m), 2.58—2.89 (2H, m), 3.45—3.50 (1H, m), 5.04—5.18 (2H, m), 5.51—5.68 (1H, m), 7.15—7.29 (5H, m). IR (neat) 3369, 3064, 2929, 1639, 1603, 1496, 1049, 914, 748, 700 cm^{-1}. The diastereomeric ratio was not determined. This product was identified by comparison with an authentic sample prepared by a known procedure.[9]

General Procedure for the Preparation of 2-Methyl-1-phenyl-3-buten-1-ol. Under an argon atmosphere, (*E*)-2-buten-1-ol (180 mg, 2.50 mmol; contains 14% (*Z*)-form) was added to the acetonitrile (10 ml) suspension of metallic bismuth (522 mg, 2.50 mmol), TMS–Cl (274 mg, 2.52 mmol) and NaI (386 mg, 2.58 mmol) at room temperature. After stirring for 30 min at room temperature, benzaldehyde (106 mg, 1.00 mmol) was added. After stirring for 20 h, the reaction mixture was quenched with an aqueous 1 M hydrochloric acid (10 ml). The organic materials were extracted with diethyl ether (30 ml×3), and the combined organic layer was washed successively with water, 5% aq $KHSO_3$ and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvents, the residue was purified by TLC (hexane : ethyl acetate = 4 : 1) to give the corresponding homoallylic alcohol, 2-methyl-1-phenyl-3-buten-1-ol (133 mg, 82% yield).

This product was identified by comparison with the literature.[7] The diastereomeric ratio was calculated by the integration of the signals of the methine proton (C<u>H</u>–OH) in the 400 MHz ^{1}H NMR spectrum of the product. In this data, the signals of δ = 4.31 (0.12H, d, J = 7.8 Hz) and 4.55 (0.88H, d, J = 5.6 Hz) were assigned to the methine protons of *anti*-adduct and *syn*-adduct, respectively, according to the literature.[7]

1-Phenyl-2-propyl-3-buten-1-ol. This product was identified by comparison with the literature.[2c] The diastereomeric ratio was calculated by the integration of the signals of the methine proton (C<u>H</u>–OH) in 400 MHz ^{1}H NMR spectrum of the product. In this data, the signals of δ = 4.34 (0.25H, d, J = 7.3 Hz) and 4.52 (0.75H, d, J = 5.9 Hz) were assigned to the methine protons of *anti*-adduct and *syn*-adduct, respectively, according to the literature.[2c]

The Examination of the Reaction between Allylic Alcohol 2, 3, or 4 and TMSCl–NaI by ^{1}H NMR Spectroscopy. In the Case of the Reaction Using (*E*)-2-Hexen-1-ol. Under an argon atmosphere, (*E*)-2-hexen-1-ol (85 mg, 0.85 mmol) was added to the acetonitrile-d_3 (3 ml) suspension of TMS–Cl (92 mg, 0.85 mmol) and NaI (125 mg, 0.83 mmol) at room temperature. After stirring for 30 min at room temperature, the reaction mixture was monitored by ^{1}H NMR spectroscopy. ^{1}H NMR (400 MHz, CD_3CN) δ = 0.88 (3H, t, J = 7.3 Hz), 1.38 (2H, sext, J = 7.3 Hz), 1.95—2.05 (2H, m), 3.95 (2H, d, J = 5.8 Hz), 5.72 (1H, dt, J = 15.1, 6.3 Hz), 5.79 (1H, dt, J = 15.1, 5.8 Hz).

In the Case of the Reaction Using (*Z*)-2-Hexen-1-ol. ^{1}H NMR (400 MHz, CD_3CN) δ = 0.92 (3H, t, J = 7.3 Hz), 1.43 (2H, sext, J = 7.3 Hz), 2.08 (2H, dq, J = 7.3, 1.5 Hz), 3.99 (2H, d, J = 8.8 Hz), 5.55 (H, dt, J = 10.3, 7.8 Hz), 5.77 (1H, dtt, J = 10.3, 8.8, 1.5 Hz).

In the Case of the Reaction Using 1-Hexen-3-ol. The ^{1}H NMR specrtum of this reaction was almost the same as that of the reaction by using (*E*)-2-hexen-1-ol.

We thank the Center for Cooperative Research, The University of Tokushima, for the measurements of 400 MHz ^{1}H NMR spectra. The present work was partially supported by Grants-in-Aid for Scientific Research No. 10640524 (M. W.) and No. 09740474 (N. M.) from the Ministry of Education, Science, Sports and Culture, and a grant from Mitsubishi Chemical Corporation (M. W.).

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