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Allyltin tribromide: A versatile reagent involved in the ring-opening of epoxides

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This paper presents a versatile reagent for epoxide cleavage. The allyltin tribromide could act as a novel and easily prepared allylation reagent and halide atom donor to convert epoxides to the corresponding homoallyl alcohols and halohydrins in high yields with excellent regioselectivities under mild reaction conditions, respectively. It could also act as a Lewis acid to catalyze the ring opening reactions of epoxides with alcohols.

versatile reagent, allyltin tribromide, ring opening of epoxides, room temperature

1 Introduction

Epoxides are the most useful and versatile substrates in organic synthesis due to their high reactivity [1–6]. A number of methods have been reported for the cleavage of epoxides with various nucleophiles, such as carbon-based nucleophiles [7, 8], halides [9], and alcohols [10, 11]. The corresponding β-substituted alcohol products are widely applied in the synthesis of natural products and pharmaceuticals [12]. However, only a few methods are known for the allylation of epoxides with allylmetal reagents. For example, allyl magnesium, allyl zinc and allylsilane were widely employed in the last century [13–15]. Recently, allylstannane has also been used in the allylation of epoxides. The allyltin reagents, such as allyl-tributyltin and tetraallyltin, solely act as allyl group donors with low atomic economy, and additives are required in Barbier-type reaction [16–18]. These methods suffer from a lack of efficiency and simplicity. Therefore, the development of simple and novel reagents, which are more efficient and provide convenient procedures with improved yields and high regioselectivity remains a challenge for synthetic organic chemists.

In continuation of our ongoing program on the allylation of carbonyl compounds mediated by an organotin reagent [19], we studied the further application of organotin reagents [20, 21]. Herein, we described the ring opening reaction of epoxides with allyltin tribromide as a new alternative method for allylation. We observed a byproduct, halohydrins, with a high yield, when the reaction conditions were screened. The allyltin tribromide could react with epoxides and yield halohydrins in high yields with complete regioselectivity. It could also act as a Lewis acid to catalyze the ring opening reactions of epoxides with alcohols (Figure 1).

2 Experimental

2.1 General methods

Chemicals were either prepared in our laboratories or purchased from chemical companies. Commercial solvents and reagents were distilled before use. Products were characterized by comparison of their physical data with those of the known samples. All yields refer to isolated products.

All reactions were monitored by TLC with silica gel

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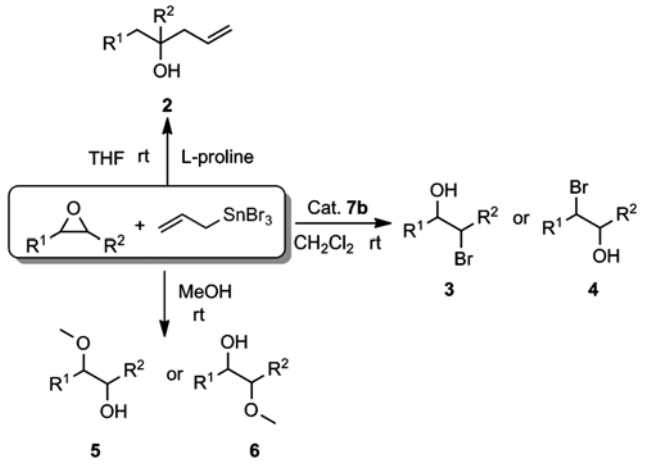


Figure 1 The ring-opening of epoxides with allyltin tribromides.

coated plates. Flash chromatography was performed using Merck silica gel 60 with freshly distilled solvents. Melting points (mp) were determined using a Fisher-Johns hot stage apparatus and are uncorrected. Specific optical rotations ([α]) were measured using a Perkin-Elmer 341 polarimeter at 20 °C with a sodium lamp (D line, 589 nm). ^{1}H NMR and ^{13}C NMR were obtained from a Varian Mercury 400 or Bruker Avance DPX 400 spectrometer in $CDCl_3$.

All the products are known compounds. The spectroscopic and physical data for all known compounds corresponded to those given in previous reports.

2.2 Representative procedure for the preparation of the starting material

Dibromodiallyltin ($(CH_2=CHCH_2)_2SnBr_2$)

To an oven dried 250 mL four-necked flask equipped with a magnetic stirring bar, a reflux condenser and a thermometer was added 150 mL toluene, tin powder (17.8 g, 150 mmol) and $HgCl_2$ (0.5 g, 1.85 mol). The mixture was refluxed for 30 min, and then cooled to room temperature freely. Triethylamine (0.2 g) was added into the resulting suspension, followed by 1-bromopropene (18.2 g, 150 mmol) within 30 min under reflux temperature. After the mixture was refluxed for an additional 2 h, the reaction mixture was cooled to room temperature, filtered, and concentrated in vacuo. The crude product was distilled under reductive pressure and resulted in 18.990 g of slightly yellow oil: yield 70%; b.p. 70–72 °C/0.5 mmHg; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.69–2.90 (m, 2H), 5.13–5.24 (m, 2H), 5.89–6.00 (m, 1H).

Allyltin tribromide ($CH_2=CHCH_2SnBr_3$)

A mixture of diallyltin dibromide (10.83 g, 30 mmol) and $SnBr_4$ (13.15 g, 30 mmol) was stirred in neat at room temperature for 2 h. Allyltin tribromide was obtained as slightly yellow oil: yield 100%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.25–3.27 (d, 2H), 5.31–5.55 (m, 2H), 5.91–6.0 (m, 1H).

2.3 Synthesis of 7a–7c

Methyl (S)-1-Arylpyrrolidine-2-carboxylates

To a solution of L-proline methyl ester hydrochloride (0.1 mol) in dry EtOAc was added triethylamine (0.2 mol), and the mixture was stirred at room temperature for 5 min. The solution was cooled to −10 °C and bromomethyl benzene (0.1 mol) was added through a cannula, and the mixture was further stirred for 20 h at room temperature. The reaction was then quenched with water (30 mL) and the contents were extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine and dried over anhydrous $MgSO_4$, filtered, and the solvent was removed at reduced pressure. The residue was used for the next reaction without further purification.

(S)-(1-Benzylpyrrolidin-2-yl)diphenylmethanol ***7a***

The phenylmagnesium bromide (0.125 mol) in THF was placed in a dry, three-necked, round-bottomed flask with a pressure-equalizing dropping funnel, a condenser, a rubber septum, and a magnetic stirrer bar under nitrogen. The flask was cooled to −10 °C with ice-salt bath, and the solution of methyl (*S*)-1-arylpyrrolidine-2-carboxylates (16 mmol) in THF (10 mL) was added dropwise through a pressure-equaliser. After the addition, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature and the contents were further stirred for 3 h at reflux. Aqueous NH_4Cl was added to the reaction mixture. The resulting mixture was concentrated under reduced pressure to remove THF and the resulting contents were extracted with Et_2O (3 × 30 mL). The combined organic layer was washed with brine and dried over anhydrous $MgSO_4$, filtered, and the solvents were removed at reduced pressure. The residue was recrystallized to yield the corresponding compound **7a**.

Colorless crystals; yield 65%; mp 115–116 °C, $[\alpha]_D^{20}$ = +70.2 (*c* 1, $CHCl_3$) (Lit. [26]: m.p. 120–122 °C, yield 72%, $[\alpha]_D^{29}$ = +73.7 (*c* 1, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.62–1.70 (m, 2H), 1.75–1.80 (m, 1H), 1.95–2.00 (m, 1H), 2.32–2.39 (m, 1H), 2.90–2.92 (m, 1H), 3.01–3.04 (d, J = 12 Hz, 1H), 3.20–3.23 (d, J = 12 Hz, 1H), 3.96–4.00 (m, 1H), 4.94 (br. s, 1H), 7.04–7.32 (m, 11H), 7.57–7.60 (m, 2H), 7.72–7.74 (m, 2H).

(2S)-1-Benzyl-2-(hydroxydiphenylmethyl)pyrrolidine 1-oxide ***7b***

To a solution of amino alcohol **7a** (8 mmol) and anhydrous K_2CO_3 (1.659 g, 12 mmol) in CH_2Cl_2 (80 mL) was added mCPBA (70.74%, 1.381 g, 9.6 mmol) at 78 °C under nitrogen. The resulting mixture was stirred at the same temperature for 10 h, and allowed to warm slowly to room temperature and filtered, then the solvent was evaporated at reduced pressure to yield a solid, which was purified by

silica gel column chromatography (EtOAc/petroleum ether = 1/1) to yield the corresponding compound **7b**.

White solid; yield: 90%; mp 190–193 °C, $[\alpha]_D^{20} = +58.2$ (*c* 0.55, $CHCl_3$) (Lit. [26]: mp 185–187 °C, yield 91%, $[\alpha]_D^{29} = +60.4$ (*c* 0.55, $CHCl_3$)); ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.74–1.79 (m, 1H), 2.04–2.09 (m, 1H), 2.27–2.30 (m, 1H), 2.51–2.54 (m, 1H), 2.84–2.89 (m, 1H), 3.20–3.24 (m, 1H), 3.57–3.60 (d, J = 7.2 Hz, 1H), 3.67–3.70 (d, J = 7.2 Hz, 1H), 4.47–4.52 (m, 1H), 7.16–7.36 (m, 11H), 7.57–7.60 (m, 2H), 7.86–7.89 (m, 2H), 11.96 (br. s, 1H).

8-Hydroxyquinoline 1-oxide ***7c***

8-hydroxyquinoline 1-oxide **7c** was prepared according to the previous report [27]. Hydrogen peroxide (4 mL, 30% in water) was added dropwise to a solution of commercially available 8-hydroxyquinoline (1.5 g, 10.35 mmol) in acetic acid (20 mL), and the solution was refluxed for 40 min. After completion of the reaction, as indicated by TLC, the mixture was allowed to warm slowly to room temperature and aqueous Na_2SO_3 was added. The resulting contents were extracted with dichloromethane (3 × 30 mL). The combined organic layers were washed with saturated $NaHCO_3$ aqueous solution, brine and dried over anhydrous $MgSO_4$. The solvent was evaporated at reduced pressure to yield a solid, which was purified by silica gel column chromatography (EtOAc/petroleum ether = 1/3) to yield the corresponding compound **7c**.

Yellow solid; yield 51%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04–7.07 (dd, ^3J = 7.9 Hz, ^4J = 0.9 Hz, 1H), 7.22–7.26 (m, 2H), 7.46–7.50 (t, ^3J = 8.0 Hz, 1H), 7.77–7.79 (d, ^3J = 8.4 Hz, 1H), 8.22–8.24 (d, ^3J = 6.0 Hz, 1H).

2.4 General procedure for allylation of epoxides with allyltin tribromide

To a stirred solution of allyltin tribromide (200 mg, 0.5 mmol) and L-proline (0.5 mmol, 1.0 equiv) in THF (3 mL) was added epoxide **1** (0.6 mmol, 1.2 equiv), and the reaction mixture was stirred at room temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with saturated sodium bicarbonate (2 mL) and extracted with chloroform (3 × 5 mL). The combined extracts were dried over anhydrous sodium sulfate, and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc, 10:1 as eluent) to yield the desired products.

1-Phenylpent-4-en-2-ol (Table 2, entry 1)

Colorless oil; yield 88%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.19–2.37 (m, 2H), 2.70–2.85 (m, 2H), 3.86–3.90 (m, 1H), 5.14–5.19 (m, 2H), 5.84–5.91 (m, 1H), 7.22–7.34 (m, 5H).

1-p-Tolylpent-4-en-2-ol (Table 2, entry 2)

Colorless oil; yield: 72%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.78 (br, 1H), 2.20–2.27 (m, 1H), 2.35 (s, 3H), 2.67–2.82 (dd, 2H), 3.85–3.88 (m, 1H), 5.15–5.19 (m, 2H), 5.83–5.93 (m, 1H), 7.12–7.24 (m, 4H).

1-(4-(Chloromethyl)phenyl)pent-4-en-2-ol (Table 2, entry 3)

White solid; yield 67%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.18–2.38 (m, 2H), 2.71–2.84 (m, 2H), 3.85–3.91 (m, 1H), 4.58 (s, 2H), 5.15–5.19 (m, 2H), 5.81–5.91 (m, 1H), 7.22–7.24 (d, 2H), 7.33–7.35 (d, 2H).

1-(4-Bromophenyl)pent-4-en-2-ol (Table 2, entry 4)

White solid; yield 53%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16–2.37 (m, 2H), 2.65–2.79 (m, 2H), 3.83–3.87 (m, 1H), 5.14–5.18 (m, 2H), 5.78–5.89 (m, 1H), 7.09–7.11 (d, 2H), 7.42–7.44 (d, 2H).

1-(4-Chlorophenyl)pent-4-en-2-ol (Table 2, entry 5)

Colorless oil; yield 29%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.16–2.36 (m, 2H), 2.67–2.81 (m, 2H), 3.83–3.85 (m, 1H), 5.14–5.18(m, 2H), 5.81–5.88(m, 1H), 7.15–7.17 (d, 2H), 7.26–7.29 (d, 2H).

2.5 General procedure for ring-opening of epoxides with allyltin tribromide in the presence of catalyst 7b

To a stirred solution of allyltin tribromide (0.25 mmol, 0.50 equiv) and compound **7b** (0.275 mmol, 0.55 equiv) in CH_2Cl_2 (3 mL) was added epoxide **1** (0.5 mmol), and the reaction mixture was stirred at room temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with saturated sodium bicarbonate (2 mL) and extracted with chloroform (3 × 5 mL). The combined extracts were dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc, 6:1 as eluent) to yield the corresponding products.

2-Bromo-2-phenylethanol (Table 4, entry 1)

Colorless oil; yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51 (br s, 1H), 3.93–4.09 (dd, 2H), 5.03–5.07 (m, 1H), 7.33–7.43 (m, 5H).

2-Bromo-2-(4-(chloromethyl)phenyl)ethanol (Table 4, entry 2)

Colorless oil; yield 80%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.60 (br s, 1H), 3.95–4.04 (m, 2H), 4.58 (s, 3H), 5.04 (m, 1H), 7.38–7.43 (m, 4H).

2-Bromo-1,2-diphenylethanol (Table 4, entry 3)

Colorless oil; yield 89%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.09 (br s, 1H), 5.04–5.16 (m, 2H), 7.12–7.24 (m, 10H).

1-Bromo-3-phenoxypropan-2-ol (Table 4, entry 4)

Colorless oil; yield 96%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.85–2.87 (m, 1H), 3.61–3.69 (m, 2H), 4.08–4.22 (m, 3H),

6.92–7.03 (m, 3H), 7.30–7. 34 (m, 2H).

1-Bromo-3-(4-methoxyphenoxy)propan-2-ol (Table 4, entry 5)

Colorless oil; yield 75%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.72–2.74 (m, 1H), 3.56–3.67 (m, 2H), 3.77 (s, 3H), 4.02–4.06 (m, 2H), 4.16 (m, 1H), 6.85 (m, 4H).

2-Bromo-1-(4-nitrophenyl)ethanol (Table 4, entry 6)

Colorless oil; yield 98%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.90 (br s, 1H), 3.50–3.55 (m, 1H), 3.66–3.69 (m, 1H), 5.05 (m, 1H), 7.57–7.59 (d, 2H), 8.22–8.24 (d, 2H).

2.6 General procedure for ring-opening of epoxides with methanol in the presence of allyltin tribromide

To a stirred solution of epoxide **1** (0.5 mmol) in MeOH (2 mL) was added allyltin tribromide (0.1 mmol, 0.20 equiv), and the reaction mixture was stirred at room temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was quenched with saturated sodium bicarbonate (2 mL) and extracted with chloroform (3×5 mL). The combined extracts were dried over anhydrous sodium sulfate, and concentrated in vacuo. The residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc, 6:1 as eluent) to yield the desired products.

2-Methoxy-2-phenylethanol (Table 6, entry 1)

Colorless oil; yield 95%; ^{1}HNMR (400 MHz, $CDCl_3$): δ 3.19 (br s, 1H), 3.30 (s, 3H), 3.59–3.72 (m, 2H), 4.34 (dd, 1H), 7.29–7.37 (m, 5H).

2-(4-(Chloromethyl)phenyl)-2-methoxyethanol (Table 6, entry 2)

Colorless oil; yield 82%; ^{1}HNMR (400 MHz, $CDCl_3$): δ 3.15 (br s, 1H), 3.27 (s, 3H), 3.56–3.67 (m, 2H), 4.29–4.32 (m, 1H), 4.55 (s, 2H), 7.28–7.30 (d, 2H), 7.36–7.37 (d, 2H).

2-Methoxy-1,2-diphenylethanol (Table 6, entry 3)

Colorless oil; yield 80%; ^{1}HNMR (400 MHz, $CDCl_3$): δ 3.32(s, 1H), 3.64(br s, 1H), 4.14–4.16 (d, 1H), 4.67–4.69 (d, 1H), 7.02–7.07 (m, 4H), 7.18–7.24 (m, 6H).

1-Methoxy-3-phenoxypropan-2-ol (Table 6, entry 4)

Colorless oil; yield 61%; ^{1}HNMR (400 MHz, $CDCl_3$): δ 3.19 (br s, 1H), 3.41 (s, 3H), 3.52–3.61 (m, 2H), 4.01–4.02 (m, 2H), 4.18 (m, 1H), 6.92–6.97 (m, 3H), 7.27–7.31 (m, 2H).

1-Methoxy-3-(4-methoxyphenoxy)propan-2-ol (Table 6, entry 5)

Colorless oil; yield 47%; ^{1}HNMR (400 MHz, $CDCl_3$): δ 2.69 (br s, 1H), 3.41 (s, 3H), 3.51–3.59 (m, 2H), 3.76 (s, 3H), 3.95–3.97 (m, 2H), 4.14 (m, 1H), 6.81–6.87(m, 4H).

2-Methoxy-2-(4-nitrophenyl)ethanol (Table 6, entry 7)

White solid; yield 35%; ^{1}HNMR (400 MHz, $CDCl_3$): δ2.38 (br s, 1H), 3.35 (s, 3H), 3.63–3.66 (m, 2H), 4.40–4.43 (m, 1H), 7.49–7.51 (d, 2H), 8.22–8.24 (d, 4H).

3 Results and discussion

In our initial study, the catalysts and solvents were screened in the ring opening reaction of styrene oxides with allyltin tribromides. As shown in Table 1, there was no apparent difference in yields with 10 mol% catalyst or without any catalyst (Table 1, entries 1–7). In view of the cost and availability, CH_3COOH and L-proline were selected for further examination (Table 1, entries 8–14). As a result, L-proline, which was widely used owing to its availability, stability and low cost, was found to be the most efficient catalyst. The homoallylic alcohol product could be obtained in 88% yield when 1 equiv of L-proline was used (Table 1, entry 14,) in half an hour. The similar yield was achieved with longer reaction time (Table 1, entry 15). With further investigation of the solvents and temperature, no improvement of yield was observed (Table 1, entries 16–19).

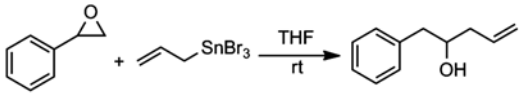
Afterwards the generality of the reaction was tested with a variety of epoxides (Table 2) catalyzed by 1 equiv L-proline at ambient temperature in THF. In the cases of styrene oxide and various 4-substituted aryl epoxides, the corresponding rearrangement products homoallyl alcohols could be obtained in moderate to high yields (Table 2, entries 1–5, 29%–88%). However, with regard to the stilbene oxide (Table 2, entry 6) and epoxides bearing solely aliphatic substituents (Table 2, entries 7, 8), the reactions yielded no homoallyl alcohols but halohydrins under the same condition. The isomerization of stilbene oxide and aliphatic epoxides to the carbonyl compound with the present procedure is not very encouraging.

Presumably, owing to the large steric factor and much less stabilization, the incipient carbocations formed by the initial cleavage of epoxides are much less stabilized in stilbene oxides and alkyl-substituted epoxides.

In the above reactions, halohydrin byproduct **3** or **4a** was observed, even as the main product in some reactions. Inspired by the results, we further examined the synthetic potential of this reagent. In order to realize the desymmetrization of either meso- or racemic-epoxides, several chiral catalysts were tested (Table 3). At the outset of this study, we still selected L-proline as a model catalyst, but the reaction yielded the corresponding product 4a in only 10% yield.

To improve the conversion efficiency, this reaction was conducted with other L-proline derivatives (Figure 2). It was found that the product's yield was largely increased up to 98% when 1 equiv N-oxide compound **7b** was used (Table 3, entry 3). With reducing amount of compound **7b** (0.55 equiv) and allyltin tribromide (0.5 equiv) simultaneously, the reaction could still proceed effectively and the product was obtained in 96% yield (Table 3, entry 4). In entry 4, we found that two bromo atoms of tribromoallyltin

Table 1 Optimization of reaction conditions

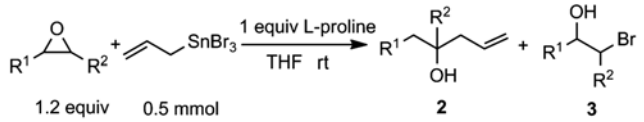


1a 0.5 mmol **2a**

Entry	Cat. (equiv)	Solvent	Time (h)	Yield (%) [a]
1	–	THF	10	45
2	–	reflux	5	64
3	$InCl_3$(0.1)	THF	5	41
4	CsF (0.1)	THF	5	47
5	CF_3COOH (0.1)	THF	5	47
6	CH_3COOH (0.1)	THF	5	48
7	L-proline (0.1)	THF	5	45
8	CH_3COOH (0.2)	THF	5	59
9	CH_3COOH (0.5)	THF	5	60
10	CH_3COOH (1)	THF	3	62
11	L-proline (0.2)	THF	5	65
12 [b]	L-proline (0.2)	THF	4	64
13	L-proline (0.5)	THF	5	68
14	L-proline (1)	THF	0.5	88
15	L-proline (1)	THF	5	87
16	L-proline (1)	CH_2Cl_2	8	22
17	L-proline (1)	CH_3CN	8	5
18	L-proline (1)	Et_2O	8	19
19	L-proline (1)	Hexane	8	21
20 [c]	L-proline (1)	MeOH	8	5

Reactions were performed with styrene oxide (0.6 mmol) and allyltin tribromide (0.5 mmol) in the presence of a catalyst at room temperature in the solvent (3 mL). a) Isolated yield. b) 50 °C. c) β-Methoxy alcohol was obtained in 62% yield.

Table 2 Reaction of epoxides with allyltin tribromides

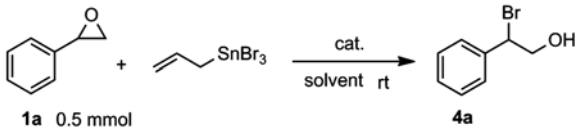


1.2 equiv 0.5 mmol **2** **3**

Entry	R^1	R^2	Time (h)	Product	Yield (%) [a]
1	Ph	H	0.5	**2a**	88
2	*p*-$CH_3C_6H_4$	H	1	**2b**	72
3	*p*-$ClCH_2C_6H_4$	H	11	**2c**	67
4	*p*-BrC_6H_4	H	18	**2d**	53
5	*p*-ClC_6H_4	H	18	**2e**	29
6	Ph	Ph	15	**3f**	85
7	$PhOCH_2$	H	10	**3g**	96
8	*p*-$MeOC_6H_4OCH_2$	H	10	**3h**	75

a) Isolated yield.

Table 3 Optimization of reaction conditions



1a 0.5 mmol **4a**

Entry	Allyltin tribromide	Catalyst 1 equiv	Solvent	Time (h)	Yield (%) [a]
1 [b]	1 equiv	L-proline	CH_2Cl_2	24	10
2 [b]	1 equiv	**7a**	CH_2Cl_2	15	30
3	1 equiv	**7b**	CH_2Cl_2	6	98
4	0.5 equiv	**7b** (0.55 equiv)	CH_2Cl_2	5	96
5	0.5 equiv	**7b** (0.50 equiv)	CH_2Cl_2	6	83
6	0.5 equiv	**7b** (0.20 equiv)	CH_2Cl_2	24	15
7 [c]	0.5 equiv	**7b** (0.20 equiv)	CH_2Cl_2	24	17
8	0.5 equiv	**7b** (0.55 equiv)	THF	26	47
9	0.5 equiv	**7b** (0.55 equiv)	CH_3CN	26	5
10	0.5 equiv	**7b** (0.55 equiv)	Et_2O	26	29
11	0.5 equiv	**7b** (0.55 equiv)	hexane	28	4
12	0.5 equiv	**7b** (0.55 equiv)	$bmimBF_4$	26	50
13	0.5 equiv	**7c** (0.55 equiv)	CH_2Cl_2	30	70

Reactions were performed with styrene oxide (0.5 mmol) and allyltin tribromide in the presence of a catalyst at room temperature in the solvent (3 mL). a) Isolated yield. b) The Main product was homoallyl alcohol. c) At reflux.

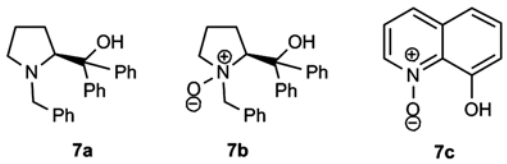


Figure 2 Screening of various catalysts.

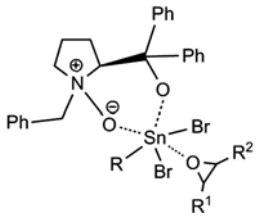


Figure 3 The proposed active intermediate.

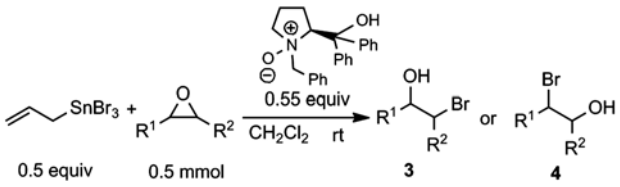
were involved in this reaction. However, with further decreasing the amount of compound **7b** (0.50 equiv and 0.20 equiv), **3** or **4a** was generated in very low yield even under reflux condition (Table 3, entries 5 and 6).

Taking into account the impact of solvent on the reaction, we examined several other solvents. Except for CH_2Cl_2, lower yields of halohydrins were obtained in other solvents, such as THF, CH_3CN, Et_2O, hexane, and $bmimBF_4$ (Table 3, entries 8–12). In all cases, the halohydrin products were obtained in high yields with excellent regioselectivity but low enantioselectivity (ee < 20%). Thus, we attempted to use achiral N-oxide compound **7c** as the catalyst and found that it could also yield the halohydrin product in good yield (Table 3, entry 13). It was deduced that the oxide in catalyst **7b** or **7c** is essential for the conversion of epoxides to halohydrins compared to catalyst **7a**. The reaction was considered to proceed via an active intermediate (Figure 3), and the Sn-Br bond was activated by the coordination of tin and oxygen atoms, and bromo anions could more easily attack the epoxide to form halohydrins. According to these studies, the reaction was found to be effective at room temperature using 0.5 equiv allyltin tribromide and 0.55 equiv compound **7b**.

Under the best reaction conditions, other epoxides were investigated. The results are summarized in Table 4. Except for the reaction of 2-(4-nitro-phenyl)oxirane (Table 4, entry 6), which produced a mixture of regioisomers, the reactions of other epoxides were found to be highly regioselective yielding a single product in good to excellent yields varying from 75% to 96%. As to the unsymmetrical epoxides, the direction of ring opening was probably dictated by steric and electronic factors. In the case of styrene oxide (Table 4, entries 1 and 2), the attack of nucleophile to the more hindered carbon showed that electronic effect controlled the course of the reaction. However, in other cases, the ring opening of epoxides was probably dominated by steric factors.

In the above allylation reaction of epoxides, β-alkoxy alcohol was unexpectedly obtained in good yield (62%) when methanol was used as the solvent instead of THF. It may be due to that the rate of the nucleophilic attack of methanol was much faster than that of the rearrangement of

Table 4 Reaction of epoxides with allyltin tribromides



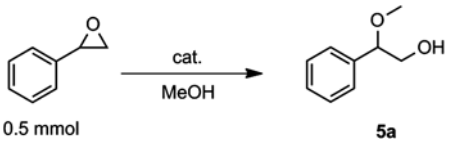
Entry	R^1	R^2	Time (h)	Product	Yield (%) [a]
1	Ph	H	5	**4a**	96
2	*p*-$CH_2ClC_6H_4$	H	7	**4c**	80
3	Ph	Ph	7	**4f**	89
4	$PhOCH_2$	H	10	**3g**	96
5	*p*-$MeOC_6H_4OCH_2$	H	4	**3h**	75
6	*p*-$NO_2C_6H_4$	H	6	**3i** + **4i**	98

a) Isolated yield.

epoxides. Nevertheless, this insight promoted us to explore the versatile function of the allyltin tribromide as a Lewis acid in the methoxylation of epoxides based on reports about the ring-opening reaction of epoxides with alcohol as the nucleophile [22–25].

As shown in Table 5, in the absence of allyltin tribromide, the reaction of styrene oxide with methanol did not proceed even under reflux conditions after a long reaction time (2 days) (Table 5, entries 1 and 2). Using 0.1 equiv of allyltin tribromide as a catalyst, the reaction of styrene oxide with methanol as both the substrate and solvent, could proceed smoothly and yielded the corresponding product in 85% yield (Table 5, entry 3). The yield could be improved to 95% by increasing the amount of the allyltin tribromide to 0.2 equiv (Table 5, entry 4). However, no improvement was observed by further increasing the catalyst loading (Table 5, entry 5). Therefore, the best reaction condition was styrene oxide (0.5 mmol) and allyltin tribromide (0.2 equiv) as a catalyst at room temperature in methanol (2 mL).

Table 5 A survey of the catalyst loading and temperature in the reaction of epoxides with methanol



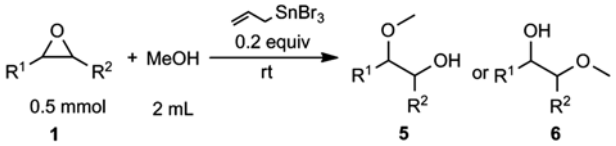
Entry	Allyltin tribromide	Temp (℃)	Time (h)	Yield (%) [a]
1	–	rt	48	–
2	–	reflux	48	–
3	0.1 equiv	rt	5	85
4	0.2 equiv	rt	0.5	95
5	1 equiv	rt	1	74

a) Isolated yield.

Subsequently, various epoxides reacted smoothly with methanol in the presence of allyltin tribromide (Table 6). Almost in each case, the reaction could yield the corresponding products in moderate to good yields except for the epoxide with strong electron-withdrawing groups.

In conclusion, allyltin tribromide could act as a useful and versatile reagent for the ring opening reactions of epoxides. Using L-proline as a catalyst the corresponding products could be obtained via a cascade epoxide rearrangement-aldehyde allylation process. The reaction might also smoothly proceed catalyzed by **7b** via an active intermediate transition (Figure 3), which might activate the Sn-Br bond, and yield halohydrins as the main product. It is noteworthy that two bromo atoms could be utilized well in a tribromoallyltin reagent. In the third type reaction, the allyltin tribromide could also act as a Lewis acid and yield the β-alkoxy alcohols in good yields without homoallyl alcohols. It might be due to that the rate of the nucleophilic attack of methanol was much faster than that of the rearrangement of epoxides. Ongoing studies are directed at providing supports for the hypothesis. The asymmetric ring-opening reactions of epoxides with this allyltin reagent are underway in our research group.

Table 6 Reaction of epoxides with methanol



Entry	R^1	R^2	Time (h)	Product	Yield (%) [a]
1	Ph	H	0.5	**5a**	95
2	*p*-CH_2ClPh	H	11	**5c**	82
3	Ph	Ph	2	**5f**	80
4	$PhOCH_2$	H	10	**6g**	61
5	*p*-$MeOPhOCH_2$	H	15	**6h**	47
6 [b]	$-(CH_2)_4-$	–	6	**5j**	82
7	*p*-NO_2Ph	H	24	**5k**	35

a) Isolated yield. b) GC yield.

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