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COMMUNICATION

An efficient synthetic method for allyl-epoxides *via* allylation of α-haloketones or esters with allylmagnesium bromide†

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A simple, efficient, and non-metal-catalyzed synthetic method for allyl-epoxides and diallyl-epoxides by allylation of α-haloketones and esters with allylmagnesium bromide in mild conditions is reported in this article. It inherited some advantages of the organomagnesium reagents such as availability, operational simplicity and low toxicity.

Epoxides are important synthetic intermediates for the synthesis of oxygen-containing natural and unnatural compounds, which can be converted to a variety of products.[1] Compounds containing reactive oxirane moieties are established building blocks in polymer science, and the most typical example is preparing epoxy resins. Furthermore, epoxides are well-known as carbon electrophiles capable of reacting with various nucleophiles and their ability to undergo regioselective ring-opening reactions contributes largely to their synthetic value.[2] In these ring-opening nucleophilic addition reactions, one of the useful transformations is the Meinwald rearrangement from epoxides to afford aldehydes or ketones with various reagents including a number of Lewis acids.[3]

In addition to the traditional synthetic method—epoxidation of olefins,[4] epoxides are often synthesized in many other ways: Darzens reaction,[5] catalytic reactions of α-haloketones with organometal reagents,[6] and so on.[7] Up to now, epoxides are still derived mainly by epoxidation of olefins, especially asymmetric epoxidation which is an area of interest at present. This method is the oxidation of olefins with organic peroxides in the presence of transition metal complexes or peracids.[8] However, among these catalytic epoxidation systems, difficulty of separation and recycling of the often expensive chiral catalysts, and the use of toxic solvents are the main drawbacks of this procedure. Furthermore, these methods by the epoxidation of olefins cannot be applicable to synthesize selectively epoxides which contain other functional groups. After further development and modifications, recently we have reported an original reaction of allylzinc bromide toward α-haloketones which can get three products by different conditions,[9] in addition we also covered epoxides with various functional groups by the scope of organozinc halides with α-haloketones.[10] This method has written a new chapter in the reaction of α-haloketones with organometallic reagents.

Magnesium has been proven to be an essential trace element in animal science. And organomagnesium reagents were first prepared over 100 years ago by Grignard and still occupy a central place in synthetic organic and organometallic chemistry. Moreover, they are strong nucleophiles and react with a broad range of electrophilic substrates. A series of reactions of α-halocarbonyl compounds with organomagnesium reagents have been investigated for a long time.[11] However, epoxides were obtained difficultly, and they often underwent rapid rearrangement or opened rings to generate aldehydes or alcohols.[12]

Based on our previous work,[9,10] we think the former reaction of α-halocarbonyl compounds with organomagnesium reagent[11,12] should be re-investigated to see whether the epoxide could be obtained. As we expected, epoxides with high yields were obtained in the reaction.

In our initial study, α-bromoacetophenone (**1a**) was chosen as a model substrate to react with organomagnesium bromide (**2a**) in THF at room temperature, and the corresponding epoxide (**3a**) was obtained. Encouraged by this efficient experimental result, we examined the scope of α-halocarbonyl compounds with allylmagnesium bromide. The results are summarized in Table 1.

Generally, the α-haloketones were treated with allylmagnesium bromide at room temperature in THF and the corresponding allylic epoxides **3a–l** were obtained in good yields except for **3g**. We investigated the factors of the electronic effect and steric hindrance at the phenyl- and halo-substituted compounds. From **1a** to **1f**, we can conclude that electron-deficient groups at the *para* position of phenyl ring were well tolerated in good yields (**3a–3c**, **3e–3f**). While an electron-donating group at the *para* position resulted in slightly lower yield (**3d**). We also found that sterically hindered epoxides can be obtained in good yields when more time was taken (Table 1, entries 6, 8, 9, 12, 13). For aliphatic series, when X = Cl, the reaction showed a lower product yield (80%) than X = Br of 86%. The reason is probably that the leaving ability of the Br atom is higher than that of the Cl (Table 1, entries 10–11).

Encouraged by the above nice results, we performed the reaction of allylmagnesium bromide with α-haloester which did not react with allylzinc bromide in our former work.[9,10] We were

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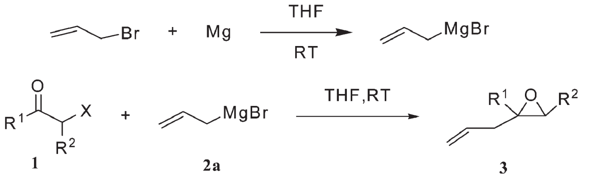
Table 1 Products obtained by the allylation of α-bromoketones with allylmagnesium bromide[a]



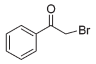
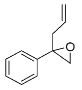
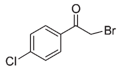
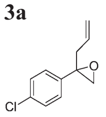
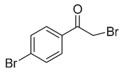
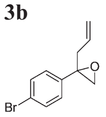
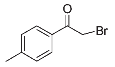
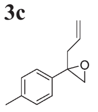
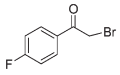
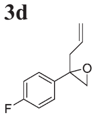
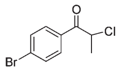
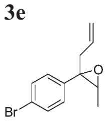
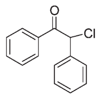
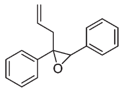
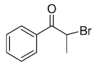
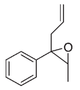
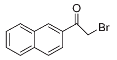
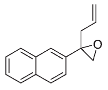
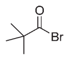
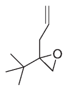
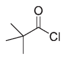
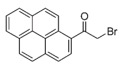
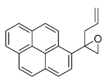
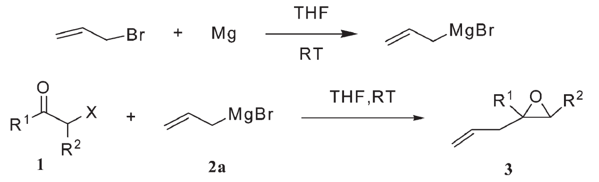
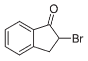
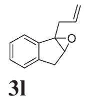
Entry	α-Haloketones	Time (h)	Product	Yield^{b,c} (%)
1	 **1a**	0.5	 **3a**	94
2	 **1b**	0.5	 **3b**	95
3	 **1c**	0.5	 **3c**	96
4	 **1d**	0.5	 **3d**	81
5	 **1e**	0.5	 **3e**	94
6	 **1f**	2	 **3f** dr = 72 : 28[c]	95
7	 **1g**	2	 **3g** dr > 20 : 1[c]	18
8	 **1h**	2	 **3h** dr = 95 : 5[c]	91
9	 **1i**	2	 **3i**	94
10	 **1j**	0.5	 **3ja**	86
11	 **1k**	2	**3jb**	80
12	 **1l**	2	 **3k**	75

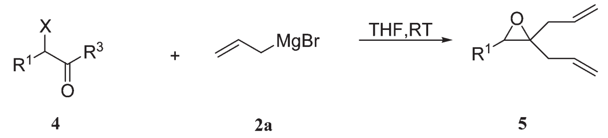
Table 1 *(Contd.)*

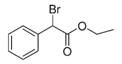
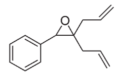
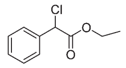
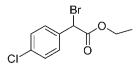
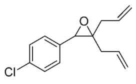
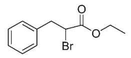
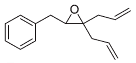
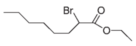
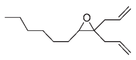
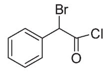
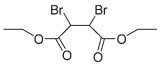
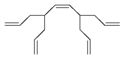


Entry	α-Haloketones	Time (h)	Product	Yield^{b,c} (%)
13	 **1m**	2	 **3l**	80

[a] Reaction conditions: α-haloketone (0.5 mmol), allylmagnesium bromide (1.0 mmol) and THF (5 mL) at room temperature under nitrogen. [b] Isolated yield based on **1** after silica gel chromatography. [c] Diastereomeric ratio (dr) determined by ^{1}H NMR analysis, relative stereochemistry not determined.

Table 2 Reactions of a variety of α-haloesters and allylmagnesium bromide[a]



Entry	α-Haloesters	Time (h)	Product	Yield^{b} (%)
1	 **4a**	1.5	 **5aa**	85
2	 **4b**	1.5	**5ab**	73
3	 **4c**	1.5	 **5b**	83
4	 **4d**	2	 **5c**	78
5	 **4e**	2	 **5d**	75
6	 **4f**	2	**5ac**	23
7	 **4g**	2	 **5e**	43

[a] Reaction conditions: α-haloesters (0.5 mmol), allylmagnesium bromide (1.25 mmol) and THF (5 mL) at room temperature under nitrogen. [b] Isolated yield based on **4** after silica gel chromatography.

surprised to find that the reaction was successfully extended to α-haloesters and α-halocarbonyl chlorides. The selected results are summarized in Table 2.

Compared to α-chloroester (**4b**), we found that α-bromoesters (**4a**, **4c–4e**) yielded epoxides with higher yields, because of the higher leaving ability of Br atom compared with Cl. For α-halocarbonyl chloride, the yield was very poor (Table 2, entry 6). Even when we tried to decrease the reaction temperature, the yield was still not improved. Finally, a special substrate—containing two α-bromoester groups—didn't yield the corresponding diallylic epoxide, but **5e** was obtained in acceptable yield.

In summary, a new method was developed to produce allylic and diallylic epoxides in mild conditions with good yields. Further studies are under way to expand a series of organomagnesium reagents which can react with α-haloketones and esters.

Acknowledgements

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