CHEMISTRY LETTERS, pp. 1097-1100, 1990.

# Gallium Chloride-Mediated Allylation of Dithioacetals with Allylstannanes

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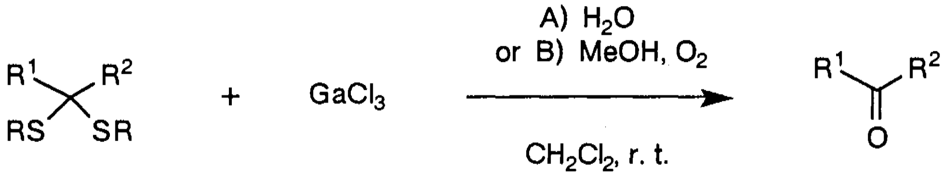
In the presence of gallium chloride, dithioacetals reacted with allylstannanes to give the corresponding homoallyl sulfides in high yields. The present method could be applied to the chemoselective allylation of bis(dithioacetal) of keto aldehyde, and the dithioacetal arising from keto function reacted with allylstannane exclusively.

Boron, aluminum, and thallium are very useful elements in organic synthesis. In contrast, gallium of the same group IIIA has been scarcely used.1) Gallium is a soft element compared with boron and aluminum. Then, a Lewis acid consisting of gallium is expected to activate soft functional groups effectively, which are difficult to activate with usual Lewis acids. In our effort to use gallium in organic synthesis, it was found that gallium chloride smoothly activated dithioacetals to achieve chemoselective hydrolysis to the corresponding ketones (Scheme 1).2) On the basis of this result, an application of gallium compounds to a carbon-carbon bond forming reaction was examined. We herein report that gallium chloride is an excellent Lewis acid activator in the allylation of dithioacetals with allylstannanes.



Scheme 1.

Concerning the preparation of homoallyl sulfides from dithioacetals and allylating reagents, a few methods have been reported so far.3) Particularly, it is known that an aliphatic aldehyde dithioacetal is difficult to be allylated in a high yield. Therefore, we tried the gallium compound-mediated allylation reaction of dithioacetals. At first, Lewis acid activators consisting of gallium were examined by using 3-phenylpropanal diethyl dithioacetal **1** and allyltributylstannane (**2**) (or tributylcrotylstannane (**3**)) as model compounds (Table 1). Among them, gallium chloride gave the corresponding allylated adduct in the highest yield. Next, the effects of solvent and stannyl group in allylating reagent were examined. As a result, dichloromethane was the most suitable solvent in this reaction (Table 1). The yield did not depend on the stannyl group ($^{n}Bu_3Sn$-, $Me_3Sn$-, or $Ph_3Sn$-). Moreover, the amount of gallium chloride and allylating reagent had a considerable effect on the yield of homoallyl sulfides (Table 2). In fact, the use of two equimolar amounts of gallium chloride and crotylstannane **3** considerably improved the yield.4)

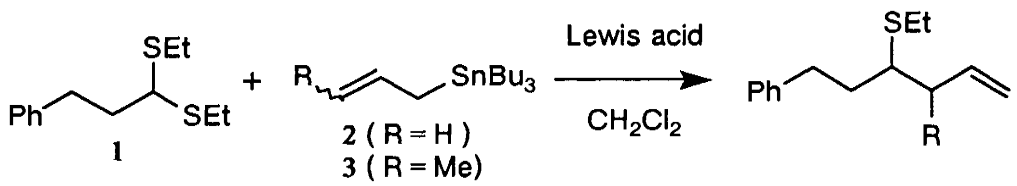


Table 1. Gallium Compound-Mediated Allylation Reaction of Dithioacetal 1 with Allylstannane 2[a)]

| Lewis acid | Solvent | Time/h | Yield/% |
|---|---|---|---|
| $GaCl_3$ | $CH_2Cl_2$ | 8 | 56 |
| | Toluene | 8 | 41 |
| | MeCN | 8 | 0 |
| | $Et_2O$ | 8 | 0 |
| $^iPr_2GaOTf$ | $CH_2Cl_2$ | 32 | 28 |
| $^iPrGa(OTf)_2$[b)] | $CH_2Cl_2$ | 7 | 16 |
| $Ga(OTf)_3$ | $CH_2Cl_2$ | 8 | 0 |

a) All the reactions were carried out at 0 °C. Molar ratio: 1 : 2 : Lewis Acid = 1 : 1 : 1.

b) Crotylstannane 3 was used instead of 2.

Table 2. The Effect of Molar Ratio in the Reaction of Dithioacetal 1 and Crotylstannane 3[a)]

| 1 : | 2 : | $GaCl_3$ | Temp/°C | Yield/% | Diastereomer ratio[b)] |
|---|---|---|---|---|---|
| 1 : | 1 : | 1 | -45 | 25 | 74 : 26 |
| 1 : | 1.5 : | 1.5 | -45 | 66 | 73 : 27 |
| 1 : | 2 : | 2 | -23 | 77 | 69 : 31 |

a) All the reactions were carried out in the presence of $GaCl_3$ for 30 h.

b) Determined by 400 MHz $^1H$-NMR. The stereochemistry was not determined.

Under these optimized conditions, the allylation of various dithioacetals was carried out. The results are shown in Table 3. Each dithioacetal reacted smoothly with allylstannanes to afford the corresponding homoallyl sulfides in high yields. Especially, it is noteworthy that, by the reaction of aliphatic aldehyde dithioacetals with allyltributylstannanes, homoallyl sulfides were obtained in high yields, compared to the conventional methods.[3,6)]

A typical experimental procedure is as follows: To a solution of 1,1-bis(ethylthio)-3-phenylpropane (1, 114 mg, 0.47 mmol) in $CH_2Cl_2$ (2 ml) was added a solution of gallium chloride in $CH_2Cl_2$ (2.8 $mol{\cdot}l^{-1}$, 0.33 ml, 0.93 mmol) at -23 °C under an argon atmosphere. Then, a solution of tributylcrotylstannane (3, 328 mg, 0.95 mmol) in $CH_2Cl_2$ (1 ml) was added dropwise at -23 °C over a period of 5 min. Stirring was continued for 30 h at the same temperature. The reaction mixture was quenched by addition of 0.2 $mol{\cdot}l^{-1}$ aqueous sodium citrate (10 ml). After filtration through Celite pad, the organic layer was separated and the aqueous layer was extracted with $CH_2Cl_2$ (3 × 2 ml). The combined organic layers were dried with $K_2CO_3$, and the solvent was removed under reduced pressure. The remaining residue was purified by preparative TLC (eluent: $CH_2Cl_2$ : hexane (v/v) = 3 : 17) to afford 4-ethylthio-3-methyl-6-phenyl-1-hexene (85 mg, 0.36 mmol, 77%).

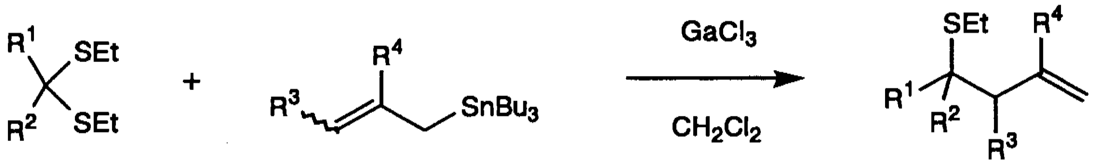
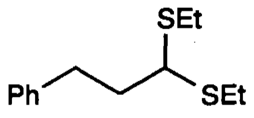
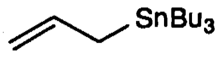
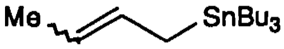
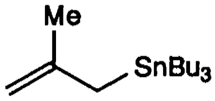
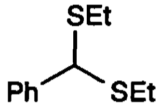
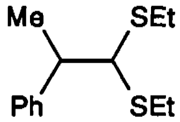
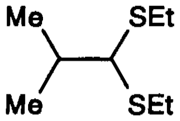
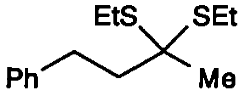


Table 3. Gallium Chloride-Mediated Allylation of Dithioacetals

| Dithioacetal | Allylstannane | Temp / °C | Time / h | Yield / %[a] (Diastereomer ratio)[b] |
|---|---|---|---|---|
|  1 |  2 | -23 | 30 | 84 |
| |  3 | -23 | 30 | 77 ( 69 : 31 )[c] |
| |  | -23 | 30 | 60 |
|  | 2 | -45 | 2 | 87 |
| | 3 | -78 | 5 | 86 ( 57 : 43 )[c] |
|  | 2 | -45 | 30 | 73 ( 81 : 19 ) |
|  | 2 | -45 | 30 | 68 ; 86[d] |
|  | 2 | -45 | 3 | 82 |

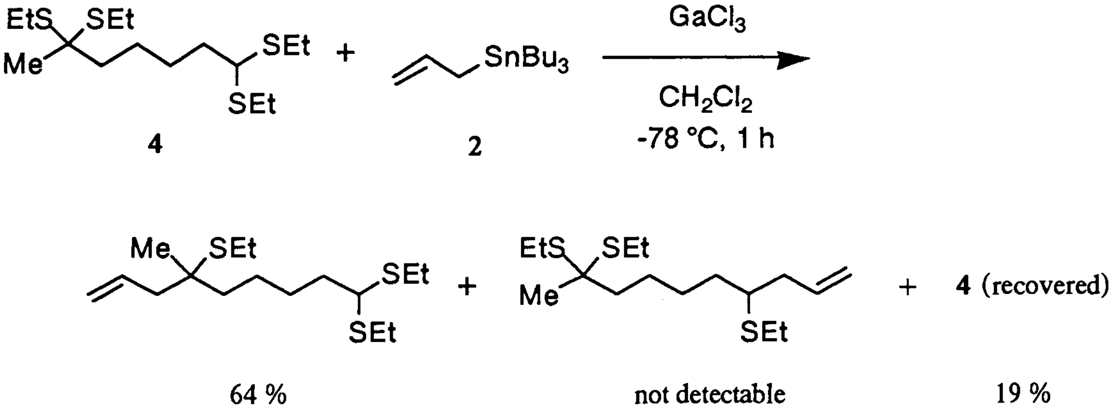
a) Isolated yield unless otherwise stated.

b) Determined by 400 MHz $^1$H-NMR. The stereochemistry was not determined.

c) No regioisomer was detectable.

d) Determined by GLC analysis.

As shown in Table 3, the dithioacetal derived from ketone reacted much faster than that of aldehyde. Therefore, gallium chloride is considered to induce the chemoselective allylation of bis(dithioacetal) of keto aldehyde such as **4**. Actually, the allylation of **4** proceeded chemoselectively at the dithioacetal arising from keto function. The adduct, of which the dithioacetal of aldehyde function was allylated, was not detectable by $^{13}$C-NMR (Scheme 2).



Scheme 2.

In conclusion, homoallyl sulfides, which are important synthetic intermediates in organic synthesis, are conveniently prepared in high yields by using gallium chloride. This method is also useful for the chemoselective allylation of bis(dithioacetal) of keto aldehyde. Moreover, our studies suggest that gallium element is useful in organic synthesis.

We thank Mitsubishi Metal Corporation for the gift of gallium chloride.

## References

1) For example, M. Falorni, L. Lardicci, and G. Giacomelli, *Tetrahedron Lett.*, **26**, 4949 (1985); S. Araki, H. Ito, and Y. Butsugan, *Appl. Organomet. Chem.*, **2**, 475 (1988); Y. Yamamoto and T. Furuta, *Chem. Lett.*, **1989**, 797.

2) K. Saigo, Y. Hashimoto, N. Kihara, H. Umehara, and M. Hasegawa, *Chem. Lett.*, **1990**, 831.

3) B. M. Trost and T. Sato, *J. Am. Chem. Soc.*, **107**, 719 (1985); I. Mori, P. A. Bartlett, and C. H. Heathcock, *J. Am. Chem. Soc.*, **109**, 7199 (1987); see also, T. Sato, S. Okura, J. Otera, and H. Nozaki, *Tetrahedron Lett.*, **28**, 6299 (1987).

4) It is suggested by Keck *et al.* that crotylstannane reacts with tin(IV) chloride and titanium(IV) chloride to afford trichlorocrotylstannane and trichlorocrotyltitanium, respectively.$^{5)}$ The same reaction may occur in the case of gallium chloride and afford crotylgallium species, which is less effective than gallium chloride for the activation of dithioacetals. This side reaction consumes gallium chloride, so that the use of one equimolar amount of gallium chloride may be not enough to activate dithioacetals effectively.

5) G. E. Keck, D. E. Abbott, E. P. Boden, and E. J. Enholm, *Tetrahedron Lett.*, **25**, 3927 (1984).

6) The same reaction was also tried using tin(IV) chloride or trityl tetrafluoroborate$^{7)}$ as an activator instead of gallium chloride. As a result, it was found that the highest yield was achieved with gallium chloride.

7) M. Ohshima, M. Murakami, and T. Mukaiyama, *Chem. Lett.*, **1985**, 1871; **1986**, 1593.

( Received April 12, 1990 )