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## Selective reduction of thioacetal to sulfide by gallium(II) chloride

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Abstract—The reaction of dithioacetals with gallium(II) chloride followed by the acid treatment afforded sulfides in good yields. © 2005 Elsevier Ltd. All rights reserved.

Group XIII elements are among the most useful metals for synthetic organic chemistry. Yet, the use of gallium compounds in organic chemistry has so far rarely been studied. In a recent study, gallium(III) chloride was used for thioacetal activation,<sup>1</sup> vinylation reaction,<sup>2</sup> isocyanide cycloaddition,<sup>3</sup> allylation reaction,<sup>4</sup> and acetal activation.<sup>5</sup> However, the utilization of gallium(II) chloride has mostly been limited to the reductive Friedel–Crafts reaction.<sup>6</sup> Since gallium(II) chloride has both Lewis acidity and reducing ability, we further explored the reaction of gallium(II) chloride.

When benzaldehyde bis(ethylthio)acetal was treated with gallium(II) chloride at 0 °C, benzyl ethyl sulfide was obtained after treatment with concd hydrochloric acid in 20% yield. Since the selective reduction of thio-acetal to sulfide without the formation of hydrocarbon is a rare transformation,<sup>7</sup> we optimized the reduction conditions for an efficient transformation to sulfide as shown in Table 1.

1-Naphthaldehyde bis(ethylthio)acetal was used as the substrate. A strongly acidic condition, that is, trifluoroacetic acid, 6 M sulfuric acid, and concd hydrochloric acid, is essential for the work-up. When 2 equiv of gallium(II) chloride were used, sulfide was obtained in high yield. It is not clear why 2 equiv of gallium(II) chloride was necessary.

Although the reaction proceeded even at lower temperature, the yield tended to decrease when the reaction was carried out at reflux conditions in dichloromethane. Therefore, the following reactions were carried out at 0 °C. When polar solvent was used, the yield decreased considerably, indicating that the Lewis acidity of gallium(II) chloride played an essential role in the reduction reaction. However, the reaction in cyclohexane resulted in a low sulfide yield because of the low solubility of gallium(II) chloride in cyclohexane.

Under the above optimized conditions, the reduction of various thioacetals was carried out.8 The results are shown in Table 2. Both aromatic and aliphatic thioacetals reacted smoothly with gallium(II) chloride to afford the corresponding sulfide in moderate to good yields. In every case, the starting material was completely consumed, and hydrocarbon was not observed, although by-product was not clear. Although the ether group was tolerated by the reaction conditions, the ester or nitro group reacted with gallium(II) chloride to give a low or poor product yield. Dithioketal gave the corresponding sulfide in rather low yield. Since bis(phenylthio)acetal was more reactive than bis(ethylthio)acetal, the use of excess gallium(II) chloride decreased the yield in certain cases. Further, cyclic dithioacetal also reacted with gallium(II) chloride to give monoalkylated dithiol. However, when acetal or O,S-acetal was used as the substrate, a complex mixture was obtained probably because of the simultaneous Friedel-Crafts reaction.

A plausible reaction mechanism is illustrated in Scheme 1. Gallium(II) chloride acts as the double salt of gallium(I) chloride and gallium(III) chloride.<sup>9</sup> Gallium(III) chloride, which is Lewis acid with high affinity to sulfur, activates thioacetal. The insertion of gallium(I) chloride

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Table 1. Reduction of 1-naphthaldehyde bis(ethylthio)acetal

		EtS_SEt -	1) Ga₂Cl₄ 2) H <sup>+</sup> → solvent	SEt		
Entry	Ga <sub>2</sub> Cl <sub>4</sub> (equiv)	Solvent	$\mathrm{H}^+$	Temp (°C)	Time (h)	Yield (%)
1	1	$CH_2Cl_2$	H <sub>2</sub> O	0	4	4
2	1	$CH_2Cl_2$	CH <sub>3</sub> COOH	0	5	9
3	1	$CH_2Cl_2$	CF <sub>3</sub> COOH	0	4	58
4	1	$CH_2Cl_2$	6 M HCl	0	4	56
5	2	$CH_2Cl_2$	CF <sub>3</sub> COOH	0	5	84
6	2	$CH_2Cl_2$	1 M H <sub>2</sub> SO <sub>4</sub>	0	4	4
7	2	$CH_2Cl_2$	$6 \text{ M H}_2 \text{SO}_4$	0	5	89
8	2	$CH_2Cl_2$	6 M H <sub>2</sub> SO <sub>4</sub>	-48	8	88
9	2	$CH_2Cl_2$	6 M H <sub>2</sub> SO <sub>4</sub>	rt	4	90
10	2	$CH_2Cl_2$	6 M H <sub>2</sub> SO <sub>4</sub>	Reflux	3	81
11	2	CH <sub>3</sub> CN	CF <sub>3</sub> COOH	0	4	11
12	2	THF	CF <sub>3</sub> COOH	0	3	15
13	2	PhCl	CF <sub>3</sub> COOH	0	2	77
14	2	ClCH <sub>2</sub> CH <sub>2</sub> Cl	CF <sub>3</sub> COOH	0	4	64
15	2	CHCl <sub>3</sub>	CF <sub>3</sub> COOH	0	3.5	33
16	2	CCl <sub>4</sub>	CF <sub>3</sub> COOH	0	5	33
17	2	Cyclohexane	CF <sub>3</sub> COOH	0	4	41

## Table 2. Reduction of various acetals

	SR'	1) 2 eq. Ga <sub>2</sub> Cl <sub>4</sub> 2) 6 M H <sub>2</sub> SO <sub>4</sub>	,SR'	
	SR'	CH <sub>2</sub> Cl <sub>2</sub>	R—/	
Entry	Substrate	Temp (°C)	Time (h)	Yield (%)
1	SEt SEt	0	5	73
2	SEt	0	7	56
3	MeO-	0	5	52
4		rt	4	57
5	MeO O SEt	rt	12	17
6	O <sub>2</sub> N-	rt	24	Complex mixture
7	SEt	0	20	52
8	SEt SEt	rt	12	68
9	Ph SEt SEt	rt	10	27
10 <sup>a</sup>	SPh SPh	0	5	79
11 <sup>a</sup>	PhS_SPh	0	0.5	32

 Table 2 (continued)

Entry	Substrate	Temp (°C)	Time (h)	Yield (%)
12	SPh SPh	rt	24.5	94
13 <sup>a</sup>	S S	rt	4.5	30 <sup>b</sup>
14		0	4.5	Complex mixture
15	⟨S	0	7	Complex mixture

<sup>a</sup> Ga<sub>2</sub>Cl<sub>4</sub> 1 equiv.

<sup>b</sup>1-NpCH<sub>2</sub>SCH<sub>2</sub>CH<sub>2</sub>SH.



Scheme 1.

into the activated C–S bond affords organogallium intermediate, which is then converted to sulfide by the protonation of the C–Ga bond. Because of the low polarity of the C–Ga bond, highly acidic conditions are necessary for hydrolysis.

In summary, we have developed a novel method for the reduction of thioacetal to sulfide by the action of gallium(II) chloride. The application of intermediary organogallium species is in progress.

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- 8. Typical procedures for the reduction of 1-naphthaldehyde bis(ethylthio)acetal: Under a nitrogen atmosphere, 1-naphthaldehyde bis(ethylthio)acetal: (87.7 mg, 0.334 mmol) in dichloromethane (4.00 ml) was added to a suspension of gallium(II) chloride (190 mg, 0.675 mmol) in dichloromethane (4.00 ml) at room temperature, and the mixture was stirred at the temperature for 4 h. After 6 M sulfuric acid (10.0 ml) was added, the mixture was stirred for about 10 min. The organic materials were extracted with chloroform. The organic layer was washed with satd. CuSO<sub>4</sub> aq, brine, dried over MgSO<sub>4</sub>, and concentrated. The residue was purified by column chromatography (hexane/chloroform = 4/1) to give ethyl 1-naphthylmethyl sulfide (60.7 mg, 0.300 mmol, 90%).
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