A Facile Reduction of Certain Schiff Bases with Di- and Trichlorosilanes

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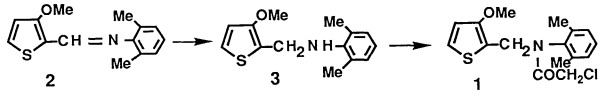
Synopsis. The reduction of *N*-[(3-methoxy-2-thienyl)methylene]-2,6-dimethylaniline (**2**) by use of trichlorosilane proceeded smoothly in the presence of a catalytic amount of BF_3·Et_2O. The trichlorosilane/BF_3·Et_2O combination was applicable to the reduction of various Schiff bases. In the case of dichlorosilane, the reduction of **2** proceeded with a 90% yield without any catalysts.

Recently we have found a highly active chloroacetamide herbicide (**1**) for paddy field rice.[1] Compound **1** has been synthesized in two steps from *N*-[3-methoxy-2-thienyl)methylene]-2,6-dimethylaniline (**2**) which involved a reducing step and a chloroacetylating step as shown in the following scheme.



On a laboratory scale, the above reduction proceeded easily by the use of $LiAlH_4$. However, $LiAlH_4$ is not suitable for industrial use because of the relatively high cost and the difficulty in handing. Common reducing agents such as hydrogen with a catalyst, sodium in methanol, and formic acid, did not afford the amine **3** in satisfactory yield probably due to the steric hindrance around the carbon–nitrogen double bond. In some cases, desulfurization in the thiophene ring was observed.

In this paper, we wish to report an excellent and economical reduction of the Schiff base **2** to the amine **3** by use of di- and trichlorosilanes.

Results and Discussion

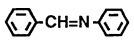
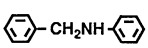
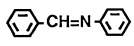
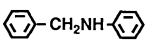
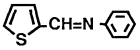
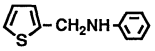
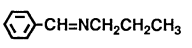
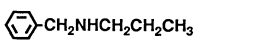
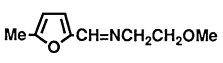
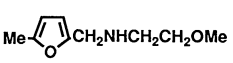
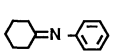
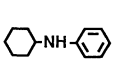
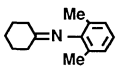
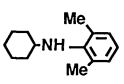
According to the literature, reduction of Schiff bases to the corresponding amines has been accomplished by various di- and tri-substituted silanes such as Et_3SiH/CF_3COOH,[2] Et_2SiH_2/Rh,[3] and $HSiCl_3$.[4] At first, we tried to reduce the Schiff base **2** using trichlorosilane in acetonitrile without any catalyst according to Benkeser's method.[4] However, the reaction mixture turned black and the desired amine **3** was not obtained at all after hydrolysis. This result indicated that Benkeser's method could not be applied to certain Schiff bases.

During the course of our investigation, we have found that the reduction of **2** with trichlorosilane proceeds to some extent with the use of benzene as a solvent and more smoothly on the addition of a Lewis acid (e.g. BF_3·Et_2O) as a catalyst. Thus, **2** was reduced with trichlorosilane in the presence of BF_3·Et_2O to afford **3** in a 61% yield.

$$\mathbf{2} \xrightarrow[C_6H_6]{HSiCl_3/BF_3\cdot Et_2O} \xrightarrow{KOH/aq\ EtOH} \mathbf{3}$$

We have extended this reduction with trichlorosilane to other Schiff bases. The results are shown in Table 1. As can be seen in the Table, the reduction of Schiff bases with trichlorosilane was proved to proceed satisfactorily

Table 1. Reduction of Schiff Bases to Amines with Trichlorosilane[a]

Entry	Schiff base	Catalyst	Amine	Yield/%[b]
1		None		17
2		BF_3·Et_2O		40
3		BF_3·Et_2O		37
4		BF_3·Et_2O		89
5		BF_3·Et_2O		82
6		BF_3·Et_2O		81
7		BF_3·Et_2O		61

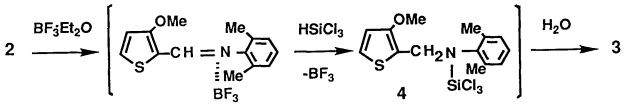
a) The reactions were carried out in benzene for 4 h, followed by hydrolysis using KOH in aqueous EtOH.
b) Yield was determined by GC and ^1H NMR.

in benzene in the presence of $BF_3 \cdot Et_2O$. The Schiff bases derived from alkylamines were converted into the corresponding amines in a better yield than those derived from arylamines (Entries 2, 3, 4, and 5). The reduction of the Schiff base prepared from cyclohexanone proceeded easily, in contrast to the Schiff base prepared from benzaldehyde (Entries 2 and 6). These results might be explained by considering that the lone pair of electrons on the nitrogen atom of the Schiff bases should play a role in complexing with trichlorosilane. A steric effect was noted in the comparison of Entry 6 and 7. The combination of trichlorosilane/$BF_3 \cdot Et_2O$ in benzene was found to be applicable to various Schiff bases.

When the Schiff base **2** was treated with dichlorosilane instead of trichlorosilane, the desired amine **3** was obtained in a 90% yield without a catalyst as described below.

$$2 \xrightarrow[C_6H_6]{H_2SiCl_2} \xrightarrow{KOH/aq\ EtOH} 3$$

The proposed mechanism of the addition of trichlorosilane to a Schiff base in acetonitrile was that the lone pair of electrons of the Schiff base nitrogen reacted with trichlorosilane to form a complex, followed by an intramolecular hydride transfer to give a *N*-trichlorosilyl compound.[4] To clarify this reduction mechanism, we have measured the ^1H NMR spectrum in C_6D_6. When $BF_3 \cdot Et_2O$ was mixed with trichlorosilane, the spectrum was a mere combination of each signal ascribed to both compounds. However, when $BF_3 \cdot Et_2O$ was mixed with **2**, the signal at 8.48 ppm (CH=N) disappeared and a signal appeared at 9.32 ppm. A small amount of solid, which was regarded as a Schiff base-BF_3 complex, was obtained. On the basis of these facts, a rational mechanism can be proposed in the following Scheme.



At first, $BF_3 \cdot Et_2O$ would locate close to the Schiff base to form a certain complex which then reacts with trichlorosilane to form the *N*-silyl compound **4** which affords the amine by hydrolysis. On the other hand, dichlorosilane can form **4** smoothly without a catalyst probably due to the steric factor.

The method described in this report might be useful for the synthesis of a secondary amine from a Schiff base.

Experimental

The ^1H NMR spectra were measured with a Hitachi R1500 spectrometer using tetramethylsilane as an internal standard. The GC Mass spectra were obtained on a Hitachi M80 spectrometer.

Reduction of 2 to 3 with Trichlorosilane. A one-hundred milliliter flask containing **2** (2.48 g, 10 mmol) in benzene (15 ml) was cooled in an ice bath. After trichlorosilane (3.98 g, 29 mmol) and $BF_3 \cdot Et_2O$ (0.1 ml) were added slowly, the resulting mixture was heated to reflux temperature for 7 h. After being cooled to room temperature, the mixture was treated with KOH (3.3 g) in 80% aqueous EtOH (45 ml) in an ice bath and stirred at room temperature for 12 h. The organic layer was extracted with ether and dried over anhydrous sodium sulfate. The solvent was then distilled out and the resulting pale yellow liquid (1.50 g, 61% yield) was composed of **3** which boiled at 122 °C/0.15 mmHg (1 mmHg=133.322 Pa). ^1H NMR ($CDCl_3$) δ=2.25 (6H, s, CH_3), 3.30 (1H, brs, NH), 3.71 (3H, s, OCH_3), 4.14 (2H, s, CH_2), and 6.68—7.03 (5H, aromatic H); IR (KBr) 3380 cm^{-1} (NH); MS *m/z* 247 (M^+). Found: C, 68.08; H, 6.78; N, 5.58%. Calcd for $C_{14}H_{17}NOS$: C, 68.01; H, 6.88; N, 5.67%.

Reduction of Various Schiff Bases with Trichlorosilane. A typical procedure is as follows. A flask containing *N*-benzylidenepropylamine (1.47 g, 10 mmol) in benzene (8 ml) was cooled in an ice bath. After trichlorosilane (1.60 g, 12 mmol) in benzene (2 ml) and $BF_3 \cdot Et_2O$ (0.1 ml) were added slowly, the resulting mixture was heated to reflux temperature for 4 h. After being cooled to room temperature, the mixture was treated with KOH (4.0 g) in 80% aqueous EtOH (35 ml) in an ice bath and stirred at room temperature for 12 h. The organic layer was extracted with ether and dried over anhydrous sodium sulfate. Removal of the solvent in vacuo gave *N*-benzylpropylamine as a pale yellow liquid (1.33 g). The yield was 89% (Table 1, Entry 4).

Other reductions were carried out in a manner similar to that described above and the products were comfirmed by GC, GCMS, and ^1H NMR. In the cases of the reactions resulting in good yields (Entries 4, 5, and 6), the obtained amine was obtained in pure form without any purification. In each case of the reaction resulting in a low yield (Entries 1, 2, 3, and 7), unreacted Schiff base was recovered along with the expected amine.

Reduction of 2 to 3 with Dichlorosilane. A one-hundred milliliter glass autoclave was charged with **2** (2.48 g, 10 mmol) in benzene (15 ml) and cooled in a dry ice–methanol bath. Dichlorosilane (2.81 g, 28 mmol) was introduced and the resulting solution was warmed to room temperature. The reaction mixture was stirred for 8 h in an oil bath (50 °C), treated with KOH (4.0 g) in 80% aqueous MeOH (35 ml) in an ice bath and stirred at room temperature for 12 h. The organic layer was extracted with ether and dried over anhydrous sodium sulfate. The solvent was removed in vacuo and the residue was distilled to give **3** as a pale yellow liquid (2.22 g, 90% yield).

References

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2) D. N. Kursanov, Z. N. Parnes, and N. M. Loin, *Synthesis*, **1974**, 633.
3) I. Ojima and T. Kogure, *Tetrahedron Lett.*, **1973**, 2475.
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