α-Chlorination of Sulfoxides by Chlorine

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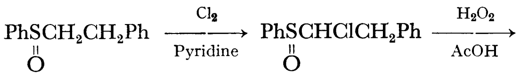
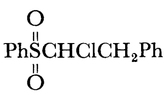
Although α-halogenation of carbonyl compound is the well-established reaction in synthetic chemistry, a similar halogenation of sulfoxides was believed to be difficult until very recently.[1,2] It is now known that α-chlorination of sulfoxides can be achieved by using specific reagents such as p-toluenesulfonyl chloride,[1] nitrosyl chloride,[2] iodobenzene dichloride,[3] and t-butyl hypochlorite.[4] No research has been reported, however, on the halogenation of sulfoxides by molecular halogen. In this communication, we would like to report that sulfoxides can be easily α-chlorinated by chlorine and the reaction proceeds fairly stereo- and regioselectively.

When sulfoxides were treated with chlorine, difficulty was encountered by the evolution of hydrogen chloride which causes Pummerer-type rearrangement of sulfoxides. This was overcome by the addition of an excess amount of pyridine. Chlorine gas (5.3 mmol) was bubbled with stirring into the methylene dichloride solution (30 ml) of 2-phenylethyl phenyl sulfoxide (**1**) (5.3 mmol) and dry pyridine (10.6 mmol) for one hour at 0°C. The usual work-up gave 1-chloro-2-phenylethyl phenyl sulfoxide (**2**)[5] in 92% yield, which proved to be homogeneous by NMR and TLC. **2**: mp 60°C; MS, M$^+$ 264; NMR, τ 7.55 (1H, q), 6.45 (1H, q), 5.44 (1H, q), 2.81 (5H, s), and 2.3—2.6 (5H, m).



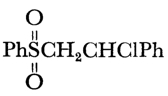
$$\text{Ph}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{CH}_2\text{CH}_2\text{Ph} \xrightarrow[\text{Pyridine}]{\text{Cl}_2} \text{Ph}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{CHClCH}_2\text{Ph} \xrightarrow[\text{AcOH}]{\text{H}_2\text{O}_2}$$

1 **2**



$$\text{Ph}\overset{\overset{\text{O}}{\|}}{\underset{\underset{\text{O}}{\|}}{\text{S}}}\text{CHClCH}_2\text{Ph}$$

3



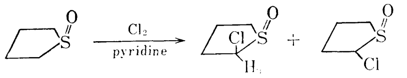
$$\text{Ph}\overset{\overset{\text{O}}{\|}}{\underset{\underset{\text{O}}{\|}}{\text{S}}}\text{CH}_2\text{CHClPh}$$

4

The structure of **2** was confirmed by converting **2** to the corresponding sulfone (**3**, mp 67—67.5°C). 2-Chloro-2-phenylethyl phenyl sulfone (**4**, mp 88.5—89.5°C) was synthesized according to the method in literature,[6] and from the inspection of their spectral data, **3** was proved to be the positional isomer of **4**.

It is striking that the position alpha to sulfinyl is much more susceptible to chlorination than the benzyl position, and only one diastereomer was obtained although the reaction could produce two diastereomers of **2**.

A similar reaction of tetrahydrothiophene-1-oxide (**5**) afforded 2-chlorotetrahydrothiophene-1-oxide (**6**) in 65% yield: mp 42—43°C; MS, M$^+$ 138; NMR, τ 7.1—8.1 (5H, m), 6.65—6.95 (1H, m), and 4.85 (1H, q). The product consists of two diastereomers in a ratio of 8 : 2, and a study of the NMR solvent-induced shift of H_a proton[7] revealed that the major isomer is *cis*-**6**.

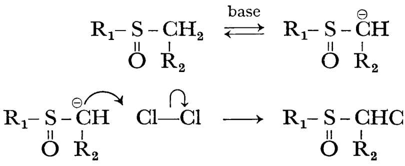


5 *cis*-**6** *trans*-**6**

In this case, the hydrogen atom *cis* to oxygen of sulfinyl group appears to be substituted preferentially.

Similarly, the reaction of methyl p-tolyl sulfoxide, ethyl phenyl sulfoxide, and dimethyl sulfoxide gave chloromethyl p-tolyl sulfoxide (mp 61.5—62°C), 1-chloroethyl phenyl sulfoxide (bp 83—84°C/1mmHg), and chloromethyl methyl sulfoxide (bp 63—68°C/0.2 mmHg, lit,[2] bp 65°/0.05 mmHg) in 70, 85, and 75% yields, respectively. Thus, this method of chlorination will provide a general route for synthesizing α-chlorosulfoxides.

The following scheme seems plausible for this reaction.



$$\text{R}_1\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-}\underset{\underset{\text{R}_2}{|}}{\text{CH}_2} \xrightleftharpoons{\text{base}} \text{R}_1\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-}\underset{\underset{\text{R}_2}{|}}{\overset{\ominus}{\text{C}}\text{H}}$$

$$\text{R}_1\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-}\underset{\underset{\text{R}_2}{|}}{\overset{\ominus}{\text{C}}\text{H}} \quad \text{Cl—Cl} \longrightarrow \text{R}_1\text{-}\underset{\underset{\text{O}}{\|}}{\text{S}}\text{-}\underset{\underset{\text{R}_2}{|}}{\text{C}}\text{HCl} + \text{Cl}^{\ominus}$$

Sulfuryl chloride with pyridine can also be used as an α-chlorinating agent for sulfoxides, nearly equal to chlorine. Detailed studies on the mechanism of these chlorinations are in progress.

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1) M. Hojo and Z. Yoshida, *J. Amer. Chem. Soc.*, **90**, 4496 (1968).

2) R. N. Loeppky and D. C. K. Chang, *Tetrahedron Lett.*, **1968**, 5415.

3) M. Cinquini, S. Colonna and F. Montanari, *Chem. Commun.*, **1969**, 607.

4) S. Iriuchijima and G. Tsuchihashi, *Tetrahedron Lett.*, **1969**, 5259.

5) Satisfactory data of elemental analysis were obtained for all the new compounds reported here.

6) M. Assher, D. Vofsi and A. Katchalsky, Belg. 654544 (1965); *Chem. Abstr.*, **65**, 5404e (1966).

7) E. T. Strom, B. S. Snowden, Jr, and P. A. Toldan, *Chem. Commun.*, **1969**, 50.