

$\alpha$ -CHLORINATION OF SULFOXIDES BY t-BUTYL HYPOCHLORITE

S. Iriuchijima and G. Tsuchihashi

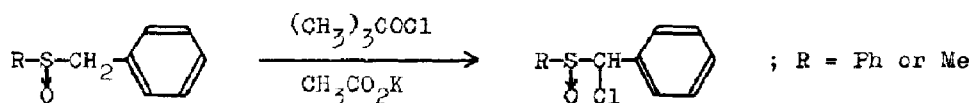
Sagami Chemical Research Center

Ohnuma, Sagamihara, Kanagawa 229 Japan

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$\alpha$ -Chlorination of sulfoxides in the presence of pyridine by nitrosyl chloride(1), p-toluenesulfonyl chloride(2), and iodobenzene dichloride(3) is known. Although the chlorination of benzyl phenyl sulfoxide could conceivably lead to a mixture of diastereomeric  $\alpha$ -chlorobenzyl phenyl sulfoxides, the reaction with nitrosyl chloride is reported to yield only one isomer. Benzyl methyl sulfoxide was chlorinated with iodobenzene dichloride to produce benzyl chloromethyl sulfoxide and  $\alpha$ -chlorobenzyl methyl sulfoxide in 32 and 30% yield, respectively. It was established that the latter compound consists of one isomer and that the proton, diastereotopic to the proton which is preferentially exchanged by deuterium in NaOD-D<sub>2</sub>O(4), is replaced with chlorine stereospecifically.

We now wish to report the free radical chlorination of benzyl phenyl sulfoxide and benzyl methyl sulfoxide by t-butyl hypochlorite(5) and the identification of the diastereomeric  $\alpha$ -chlorobenzyl phenyl sulfoxides.



Benzyl phenyl sulfoxide was allowed to react with a 50% excess of t-butyl hypochlorite in the presence of anhydrous potassium acetate in ethanol-free chloroform with stirring at 0° for 3 to 4 hrs. After the near-disappearance of the starting material was confirmed by thin-layer chromatography, the solvent was removed under reduced pressure and the residue was passed through silica gel using a 2:8 mixture of n-hexane and benzene as eluent.  $\alpha$ -Chloro-

benzyl phenyl sulfoxide was obtained in 45-50% yield. The nmr spectrum showed that the product was a 30:70 mixture of the diastereomers. Silica gel chromatography of the mixture with hexane-benzene ranging from 4:6 to 2:8 and collection of the latter half of the elution gave a 20:80 mixture(nmr) from which a major isomer crystallized out of cyclohexane. Recrystallization from n-hexane-cyclohexane yielded a pure isomer: mp 101-101.5°; ir(CS<sub>2</sub>) 1060, 1073, 1085, and 1096cm<sup>-1</sup>; Anal. Calcd for C<sub>13</sub>H<sub>11</sub>ClOS: C, 62.27; H, 4.42; Cl, 14.14; S, 12.79%. Found: C, 62.20; H, 4.65; Cl, 14.27; S, 12.83%.

Chlorination of benzyl phenyl sulfoxide by the previously studied reagents, nitrosyl chloride, p-toluenesulfonyl chloride, and iodobenzene dichloride, produced in our laboratory the mixtures of 90:10, 85:15, and 95:5, respectively, after passage through silica gel, in contrast with the ratio of 30:70 obtained from our free radical agent. Recrystallization from cyclohexane of the product from the nitrosyl chloride reaction gave another isomer which possesses a higher melting point, 122.5-123°, as reported in (1). The chemical shifts( $\delta$ ) of the  $\alpha$ -proton of these isomers in various solvents are shown in the Table.

Table. Nmr Chemical Shifts( $\delta$ )\* of a Benzylic Proton of the Diastereomeric  $\alpha$ -Chlorobenzyl Phenyl Sulfoxides.

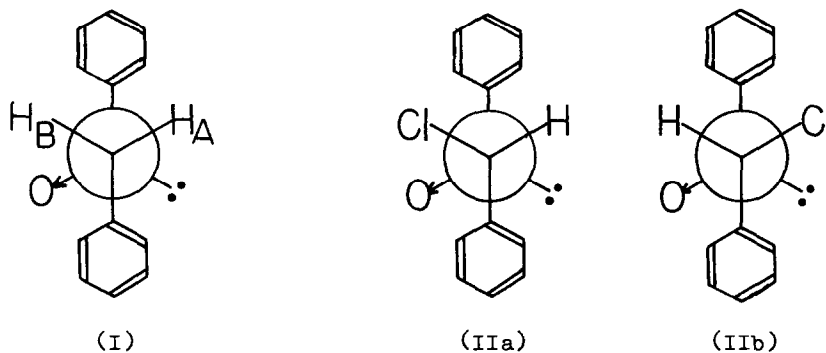
Solvent	Higher Melting Isomer	Lower Melting isomer
CCl <sub>4</sub>	5.39	5.25
CDCl <sub>3</sub>	5.45	5.45
Benzene	5.16( $\Delta$ +0.23)	5.16( $\Delta$ +0.09)
CF <sub>3</sub> CO <sub>2</sub> H	5.82( $\Delta$ -0.43)	5.93( $\Delta$ -0.68)

\* The nmr spectra were measured at a concentration of 10-15mg in 0.4ml with TMS as an internal standard using a Varian HA-100 spectrometer.  $\Delta = \delta(\text{CCl}_4) - \delta(\text{benzene or CF}_3\text{CO}_2\text{H})$ .

On the assumption that conformer I, with phenyl groups trans, predominates at room temperature, the signals for H<sub>A</sub> and H<sub>B</sub> were identified by analogy with fused ring systems(6). It was found that the signal for H<sub>B</sub>(trans to the sulfur lone pair) was shifted downfield on changing the solvent from methyl iodide to trifluoroacetic acid to a greater degree than was the signal for H<sub>A</sub>(trans to the sulfinyl oxygen). The same method using benzene-induced

shifts and trifluoroacetic acid-induced shifts relative to carbon tetrachloride was applied to the structural assignment of diastereomeric  $\alpha$ -methylbenzyl phenyl sulfoxides(7).

Figure. Benzyl Phenyl Sulfoxide(I) and the Assigned Structures of Higher Melting  $\alpha$ -Chlorobenzyl Phenyl Sulfoxide(IIa) and Its Lower Melting Isomer(IIb).



When these benzene- and trifluoroacetic acid-induced solvent shifts are applied to our  $\alpha$ -chlorobenzyl phenyl sulfoxides, the structures, IIa and IIb, can be assigned to the higher melting isomer from the ionic reagents and the lower melting isomer from the free radical agent, respectively. This assignment is very reasonable if one thinks that the free radical reaction takes place preferentially at the open lone pair side, when t-butoxy radical abstracts hydrogen from benzyl phenyl sulfoxide or when the radical  $(\text{Ph}-\overset{\cdot}{\text{S}}-\text{CH}-\text{Ph})$  thus formed abstracts chlorine from  $(\text{CH}_3)_3\text{COCl}$  or  $\text{Cl}_2$ .

Reaction of benzyl phenyl sulfoxide with a double amount of t-butyl hypochlorite in the presence of pyridine instead of potassium acetate gave a somewhat interesting result. The nmr spectrum of the product(45-50% yield) revealed that it is composed of 75% IIa and 25% IIb, a converse ratio to the experiment with potassium acetate and similar to the reaction with nitrosyl chloride. Reaction with t-butyl hypochlorite in the presence of pyridine thus seems to be ionic rather than free radical. This view is in accord with the fact that the chlorination of benzyl methyl sulfoxide in the presence of pyridine occurs preferentially at the methyl group, yielding benzyl chloro-

methyl sulfoxide, mp 65-67° (lit.(3), mp 54-55°), and  $\alpha$ -chlorobenzyl methyl sulfoxide in 45 and 15% yield, respectively, whereas with potassium acetate the benzylic position is chlorinated exclusively, producing onyl  $\alpha$ -chlorobenzyl methyl sulfoxide in 40% yield. On recrystallization, a diastereomer of  $\alpha$ -chlorobenzyl methyl sulfoxide, mp 56-56.5° (lit.(3), mp 50-51°), was obtained, which is identical on the basis of the nmr spectra with the compound isolated as a minor product from the chlorination by iodobenzene dichloride.

Thus, t-butyl hypochlorite appears to be a good potential chlorinating reagent for sulfoxides. The use of this reagent is advantageous from the viewpoint that the chlorination can proceed through either a free radical or an ionic pathway according to the reaction conditions chosen: i.e., in the presence of potassium acetate, it is a free radical agent, producing the products characteristic of such reagents, while with pyridine, it is an ionic reagent similar to nitrosyl chloride, p-toluenesulfonyl chloride, and iodobenzene dichloride.

Bromination with t-butyl hypobromite in a similar way gave  $\alpha$ -bromosulfoxides, whose synthesis, to our knowledge, is without precedent.

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