

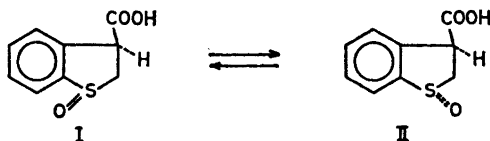
Equilibration and Racemization of Sulphoxides

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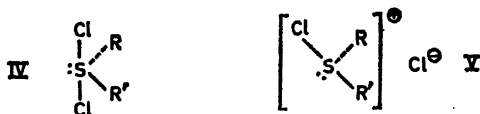
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Sulphoxides have been found to equilibrate and racemize in trifluoroacetic acid. Mineral acids and potassium nitrate catalyze the rearrangement. Water has a retarding effect on the rate. Racemization also takes place in acetic anhydride and the rate increases by adding acetic acid.

In a previous paper¹ the rearrangement of the *cis* sulphoxide I into the *trans* sulphoxide II was shown to be catalyzed by nitric acid in trifluoroacetic acid. It has now been found that other strong acids like sulphuric acid and perchloric acid catalyze the rearrangement of the sulphoxide group in trifluoroacetic acid. Potassium nitrate is also as effective as nitric acid in catalyzing the rearrangement. The rate is also highly dependent on the concentration of water which has a retarding effect. The end product in the case of I and II is an equilibrium mixture (45:55) and with optically active methyl *p*-tolyl sulphoxide (III) a racemization takes place. The result is interpreted as involving an oxysulphonium salt intermediate. Racemization of III was also found to take place in acetic anhydride in accordance with this mechanism.



Previously, sulphoxides have been reported to racemize in polyphosphoric acid,² concentrated sulphuric acid,³ and hydrogen chloride-organic solvent.⁴ The last method which is the one generally used to effect equilibration or racemization of sulphoxides is thought to involve the reversible formation of a sulphide dichloride intermediate with structure IV or V:



If the intermediate has structure V, racemization can be effected by a rapid exchange of chlorines *via* a transition state similar to the intermediate IV. These dihalides have been well known for a long time and several have been described. On hydrolysis they give the corresponding sulphoxides. A support for this mechanism is the fact that the rate of exchange of ^{18}O equals the rate of racemization in dioxan and 12 M HCl- H_2^{18}O . The rate of racemization is also highly dependent on the water content.

On the other hand sulphoxide salts of other mineral acids have not been much investigated although Saytzeff as early as 1867 prepared the solid 1:1 dimethyl sulphoxide-nitric acid adduct.⁵ No adduct with sulphuric acid has been reported but it was assumed to occur as an intermediate in the condensation reaction of methyl *p*-tolyl sulphoxide with alkyl aryl sulphides.⁶

Some typical rate constants of racemization of methyl *p*-tolyl sulphoxide are presented in Table 1. During the racemization with nitric acid and potassium nitrate as catalyst an oxidation to the sulphone stage took place. When the rotatory power had decreased by 85 % of the starting value 10–12 % sulphone was present as shown in samples analyzed by NMR. This means that 40–50 % of the catalyst had been consumed. The rate constants were therefore calculated from the first period of half-life. To check the order of the reaction a kinetic run was performed with the nitrate concentration twice that of sulphoxide. When concentrated sulphuric acid was used as catalyst a considerable decomposition of methyl *p*-tolyl sulphoxide occurred.

The equilibration of I and II was followed by NMR and the approach to equilibrium was strictly first-order. Starting either with *cis* I or *trans* II the same effective rate constants and the same composition of isomers were obtained. The rearrangement was effected in trifluoroacetic acid by nitric acid, sulphuric acid, and 70 % perchloric acid but the last reaction was accompanied by oxidation and decomposition. When the reaction was carried out in trifluoroacetic acid-D and nitric acid-D no deuterium transfer occurred which eliminates a mechanism involving an "enol" form of the sulphoxide in this case.

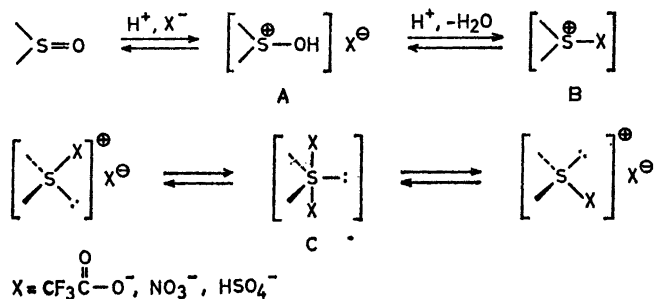
Table 1. Pseudo first-order rate constants of racemization of methyl *p*-tolyl sulphoxide at 38.0°. 0.35 g (2.3 mmole) of sulphoxide in 5 ml of trifluoroacetic acid.

Catalyst	mmole catalyst	mmole H_2O	$k_{\text{obs}}^a \times 10^4 \text{ min}^{-1}$
—	—	—	1.7
HNO_3	1.1	4	56
H_2SO_4	0.9	—	53 ^b
KNO_3	1.1	—	296
KNO_3	1.1	4	48

^a $k_{\text{obs}} = \ln a/t$.

^b 25 % racemization.

To explain the course of these reactions the following mechanism is proposed:

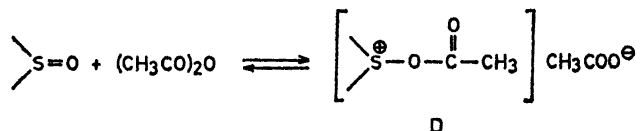


The rate-determining step is thought to be the formation of the oxysulphonium ion B which through a transition state C racemizes by a rapid exchange of acid anions. Water shifts this equilibrium toward salt A and, as can be seen from Table 1, small amounts of water have a marked effect on the rate. On the other hand small amounts of water have a slight effect on the formation of salt A because sulphoxide salts with nitric acid have been found to be surprisingly stable even to water.⁷

The existence of cyclic acyloxysulphonium ions as intermediates has been demonstrated by Allenmark⁸ in the reduction of sulphoxide acids by iodide ion and recently the oxidation of sulphides by iodine has been shown to proceed over oxysulphonium salts.⁹

Racemization of sulphoxides in concentrated sulphuric acid was shown by Oae *et al.*³ to proceed with oxygen exchange with the solvent thus demonstrating the formation of a new sulphur-oxygen bond during this reaction.

The first step to give acyloxy sulphides in the Pummerer reaction between sulphoxides and hot acid anhydrides is thought to involve an acyloxysulphonium salt intermediate (D).^{10,11} Therefore optically active methyl *p*-tolyl sulphoxide was dissolved in acetic anhydride at 38° and at that low temperature no reaction with the anhydride occurred but a slow racemization took place. After a few days the rotatory power had decreased by 85 % and after adding dilute sodium hydroxide solution 95 % of starting sulphoxide was recovered with 15 % of the original activity. When acetic anhydride-acetic acid (75:25) was used as solvent the rate of racemization was faster.



These results indicate that there is an exchange of acyloxy groups in acyloxysulphonium salts similar to the exchange of alkoxy groups in alkoxy-sulphonium salts, a possibility which has been suggested by Johnson and Phillips.¹² This interchange also explains the data of ¹⁸O exchange obtained by Oae *et al.*¹³ in their study of the Pummerer reaction.

EXPERIMENTAL

The NMR-spectra were recorded with a Varian model A-60 spectrometer. *cis* and *trans* Dihydrothianaphthene-3-carboxylic acid 1-oxides (I and II) were prepared as described earlier.¹

(+)-Methyl *p*-tolylsulphoxide (III) was prepared from (-)-menthyl (-)-*p*-toluenesulphinate and methylmagnesium iodide according to Mislow *et al.*¹⁴ The isolation of the sulphoxide after hydrolysis of the reaction mixture was simplified by first extracting the menthol with ether and then the sulphoxide with chloroform. After three recrystallizations from ether the sulphoxide had m.p. 78–79°. (Lit. 73–74.5°). $[\alpha]_D^{25} = +154^\circ$ (ethanol).

Kinetic measurements. The racemization of methyl *p*-tolyl sulphoxide was followed with a Perkin-Elmer Model 141 Polarimeter. The cell was thermostated at 38.0°. The composition of the different runs is given in Table 1. To isolate the products after a kinetic run the acidic solution was neutralized with 2 M sodium hydroxide and then extracted with chloroform. The products were identified by means of IR, NMR, and melting points.

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