Organic Sulfur Compounds. XV. Asymmetric Oxidation of the Sulfoxides with Percamphoric Acid

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Asymmetric sulfoxide syntheses have been achieved, although in a low optical yield, by oxidizing the dissymmetric sulfoxides with such optically active peracids as percamphoric acid, perhydratorpic acid and α-substituted perglutaric acid.1-3) Sulfoxides can be oxidized further with peracids to the corresponding sulfones. It may be expected that one of the optical isomers of the symmetric sulfoxide will be oxidized faster than the other isomer in the reaction with the optically active peracids. When the racemic sulfoxide is treated with a 1/2-equivalent of the asymmetric peracid, one optical isomer of sulfoxide with a higher reactivity would be consumed faster than the other, resulting in a mixture of sulfone and sulfoxide, which is richer in the lower reactive

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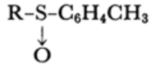
optical isomer of sulfoxide than the original 50%. Since the sulfones have no optical activity, having no molecular asymmetry, the sign of the rotation of this mixture will be determined by the sign of the rotation of the isomeric sulfoxide with a lower reactivity. If there exists an appreciable difference between the reactivities of two optical forms of the sulfoxide, this partial oxidation might be useful as a preparative method of the optically active sulfoxides. These optically active sulfoxides can usually be obtained by the Grignard synthesis,4) in which one epimer of the *l*-menthyl sulfinate is treated with the Grignard reagent, while an alkyl or aryl group of the Grignard reagent replaces the menthyloxy group in the formation of the sulfoxides with the inverted configuration. Although this method has the advantage of producing sulfoxides of very high optical purity, it can not be applied to the synthesis of sulfoxides with such reactive substituents as the nitro group, which reacts faster than the menthyloxysulfinyl group with the Grignard reagent.5)

In the present study, the partial oxidation of methyl *p*-tolyl sulfoxide and benzyl *p*-tolyl sulfoxide with *cis*-(+) percamphoric acid6) was investigated. To a solution of these sulfoxides in ether, cooled at −60°C, an ether solution of a 1/2-equivalent of percamphoric acid was added; the mixture was kept for 1—3 days at a low temperature (from −60 to −10°C) until all the peracid had disappeared. The reaction mixture was then washed repeatedly with a sodium hydrogen carbonate solution to remove camphoric acid, and the solvent was evaporated off. The optical rotation of the remaining mixture of sulfoxide and sulfone was measured in acetone. The composition of this mixture was estimated by infrared spectroscopy, and the optical purity of the remaining sulfoxides was calculated. In the case of benzyl *p*-tolyl sulfoxide, pure sulfoxide free from benzyl *p*-tolyl sulfone was obtained by elution chromatography on alumina with benzene; its optical activity was also determined. The results are shown in the following table.

THE OXIDATION OF SULFOXIDE 

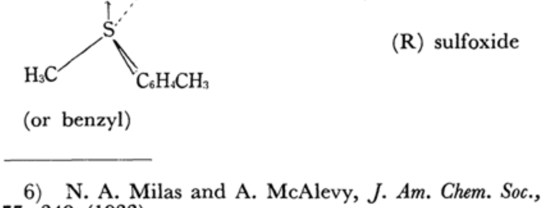
$R\text{-}\underset{\underset{\displaystyle O}{\downarrow}}{S}\text{-}C_6H_4CH_3$

R	$[\alpha]_D$ of pure sulfoxide	$[\alpha]_D^{15}$ of the remaining sulfoxide	Optical purity
Methyl	±145.5° 7)	+3.5°	2.4%
Benzyl	±252° 8)	+7.1°	2.8%

Since the optical purity of the sulfoxides formed is very low, as is indicated in the table, this partial oxidation is not practical for the preparation of the asymmetric sulfoxides.

However, it seems to be interesting that the sulfoxide remaining shows the positive sign of the optical rotation in both cases, indicating the lower reactivity of the optical isomer with the R configuration (plus rotation)7) towards *cis*-percamphoric acid, which has been known to possess the S configuration.

By speculating on the transition state, depicted below, in which the tetrahedral configuration around C-3 (indicated by an asterisk in the figure) takes the trans conformation with regard to the pseudotetrahedral configuration around the S atom, the preferential attack of *cis*-(S)-percamphoric acid on S-sulfoxide may be explained by the stronger repulsion between the *gem*-dimethyl group of percamphoric acid and the *p*-tolyl group of sulfoxide with the R configuration, than the repulsion between this *gem*-methyl and the methyl or benzyl group of S-sulfoxides. The transition state postulated above is somewhat similar to the Cram-Prelog model, which is used to explain the asymmetric synthesis of active mandelic acid from the optically active esters of benzoylformic acid and Grignard reagent.9) Due to the longer atomic distance between C-3 and the S atom, the potential barrier for the intramolecular rotation around the C-3 —S axis becomes smaller than that in the case of mandelic acid synthesis, resulting in a low optical yield.



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4) K. K. Andersen, *Tetrahedron Letters,* No. 3, 93 (1962).

5) For example, when an ether solution of methylmagnesium iodide was added to a solution of ethyl *p*-nitrobenzenesulfinate drop by drop at low temperature, a vigorous reaction took place but gave no methyl *p*-nitrophenyl sulfoxide.

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