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ANCHIMERIC ASSISTANCE IN ACID-CATALYZED HYDROLYSIS OF N-(p-TOSYL)-SULFIMIDES

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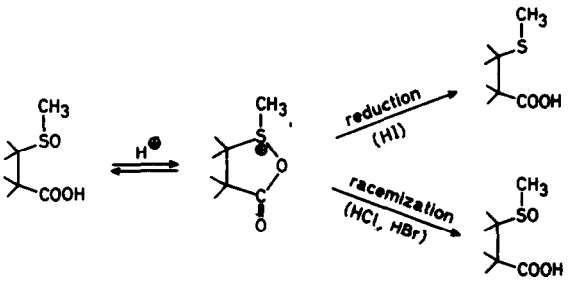
During our investigation on the reduction and racemization of sulfoxides in hydrohalic acid media[1], it was found that the reactions were anchimerically assisted by a neighbouring carboxyl substituent. These assisted reactions were assumed to involve a reactive cyclic acyloxysulfonium ion intermediate as formulated in Scheme 1.



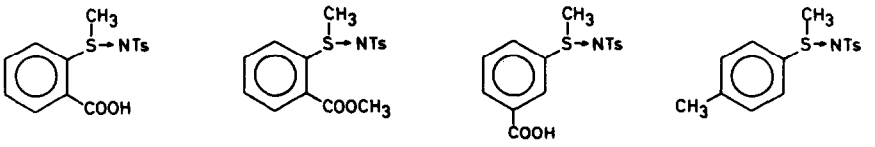
Scheme 1

The intermediate could in principle be formed along two different mechanistic pathways: either by an intramolecular displacement of water from the protonated carboxyl group by the sulfinyl-oxygen, leaving the configuration at sulfur unchanged, or by substitution at sulfur, with inversion, in the protonated sulfoxide by an attack of the carboxyl group.

Recently some results have appeared which give strong support to the latter mechanism: the investigation on the reduction and racemization of 2-methylsulfinylbenzoic acid and its methyl ester by Landini and Torre[2] and the determination of oxygen-exchange vs. racemization rates of ^{18}O-labelled 2-alkylsulfinylbenzoic acids in sulfuric acid by Oae et al[3], later confirmed by Landini and Rolla[4].

We have found further evidence for this type of mechanism from a kinetic investigation of the acid-catalyzed hydrolysis of N-(p-tosyl)methyl-2-carboxyphenylsulfimide (I). Our results show that this reaction is anchimerically assisted by the neighbouring carboxyl group and that its stereochemistry is controlled by

a double inversion mechanism giving over-all retention. The only products of the reaction are the corresponding sulfoxide and p-tosylamide.



The optically active compounds I-III were studied polarimetrically in a 2.0 M perchloric acid-acetone mixture (to 1.0 ml 4.0 M perchloric acid, acetone was added to give a volume of 2.0 ml). The reaction showed pseudo first-order kinetics and the observed rate constant for compound I was 1.0×10^{-4} sec^{-1} at $25.0 \pm 0.1^{\circ}C$ (Fig. 1). A stereospecificity of > 99 % retention was estimated from the observed value of α_{∞}. The racemization rate of the corresponding sulfoxide was found to be quite negligible under the same condition. For compounds II and III, however, where no assistance is possible, the change in optical rotation was very slow and resulted in a completely inactive final state. Therefore no rate constant for the sulfimide hydrolysis could be determined with certainty in these cases. A safe conclusion is, however, that hydrolysis of compound I is faster than of the compounds II and III by the factors $k_I/k_{II} > 300$ and $k_I/k_{III} > 50$.

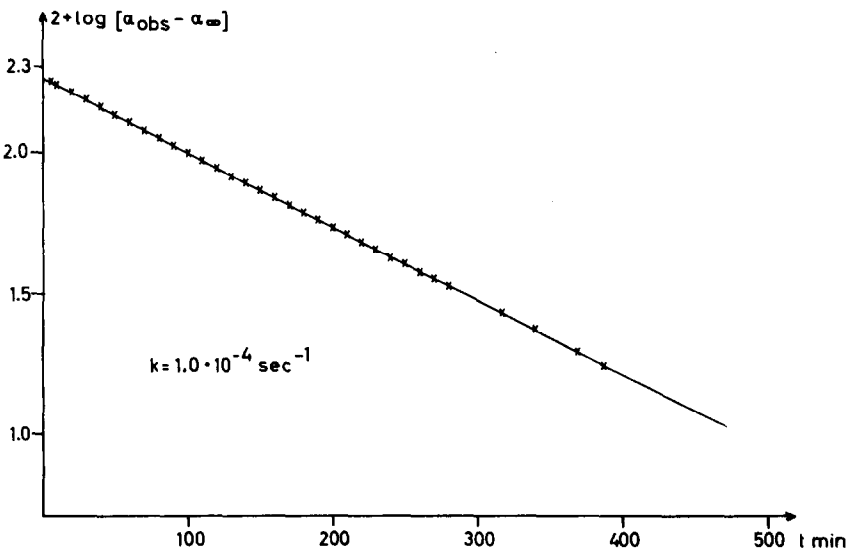
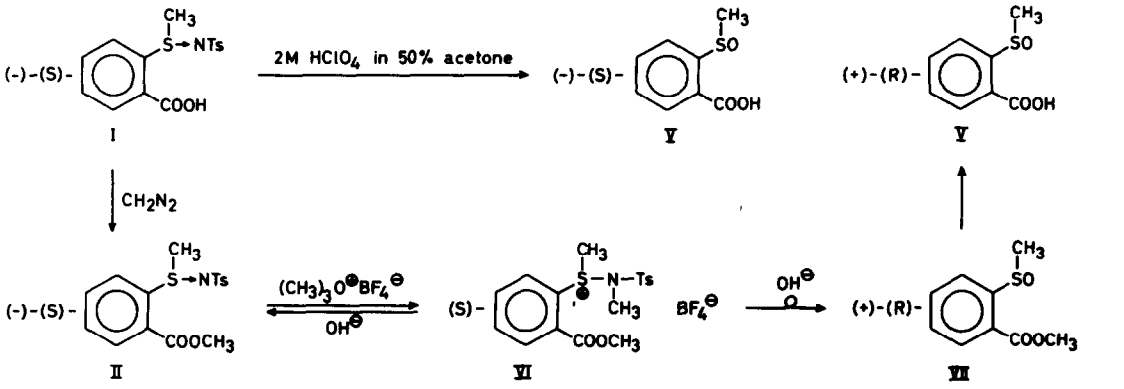


Fig. 1. Pseudo first-order plot for the hydrolysis of I.

The acidic hydrolysis reaction of N-(p-tosyl)sulfimides has previously been investigated[5-7]. Cram and collaborators[5] found that solvolysis of (-)-(S)-N-(p-tosyl)methyl-p-tolylsulfimide (IV) in concentrated sulphuric acid for two minutes took place with the formation of sulfoxide with 65 % inverted configuration. No attempts were made, however, to improve the stereospecificity.

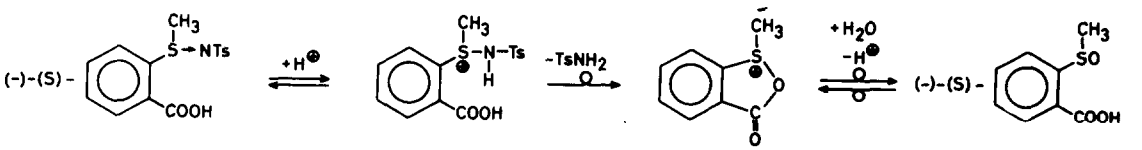
The stereochemical course of the acidic hydrolysis reaction for sulfimide I was determined by the use of a reaction reported by Johnson and Rigau[8] (Scheme 2).



Scheme 2

Esterification of I with diazomethane followed by N-methylation with trimethyloxonium tetrafluoroborate yielded the N-tosylaminosulfonium salt (VI). When this compound was treated with aqueous sodium hydroxide some regenerated sulfimide (II) was obtained together with methyl 2-methylsulfinylbenzoate (VII). The latter reaction proceeds with inversion[8]. The ester (VII) was then hydrolyzed by base. The over-all stereospecificity was 74 %.

This reaction sequence makes it possible to determine the relative configuration of the sulfoxide and the sulfimide. Thus, the acidic hydrolysis reaction of I must take place with over-all retention due to a double inversion process according to the mechanism in Scheme 3. Further with the knowledge of the absolute configuration of sulfoxide V[9], the absolute configuration of sulfimide I could be determined (Scheme 2).



Scheme 3

This mechanism is consistent with the results from a kinetic investigation by Kucsman et al[6] on uncarboxylated sulfimides. They suggested a protonation step followed by an attack of a molecule of water. In our assisted reaction, however, expulsion of tosylamide from the N-protonated sulfimide is facilitated by an intramolecular attack at sulfur by the carboxyl group yielding the cyclic intermediate with inverted configuration. The latter is then easily opened by a new attack at sulfur by a water molecule, resulting in another inversion.

The preparation and resolution of the substrates will be published elsewhere.

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