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THE MECHANISM OF SULFOXIDE HALOGENATION

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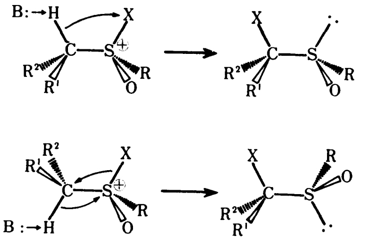
A general mechanism for the halogenation of open-chain and cyclic sulfoxides is proposed. This mechanism gives an account for all the seemingly contradictory experimental results found by various groups, including the chirality of the products.

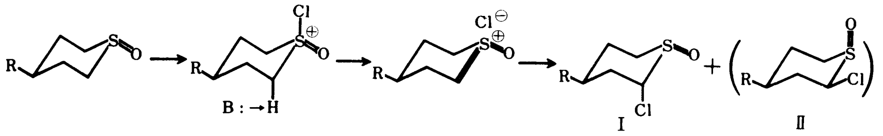
The kinetic2) and stereochemical3) study of the α-halogenation of sulfoxides and the observation that the steric course4) at sulfur and carbon during this reaction is either retention-retention or inversion-inversion or a mixture of the two led4) to the proposal of two concurrent concerted mechanisms (1) and (2) for this reaction. According to both mechanisms, the halogen remains at the same side of the plane containing the C-S bond and perpendicular to the H-C-S-X plane.



$S_{RET}C_{RET}$ (1)

$S_{INV}C_{INV}$ (2)

The last conclusion was proved incorrect by the studies of thiane oxides halogenation.5,6,7) Thiane oxides trans-substituted at C_4 introduced the α-halogen trans to the position where it was axially located in the intermediate chlorosulfoxonium ion. The position of chlorine on sulfur and its configuration in this intermediate was confirmed8) by internal trapping with suitably located functional groups. Despite this a retention on carbon and sulfur was the result of the reaction. An axial deuterium was abstracted preferentially5) to an equatorial hydrogen despite the considerable deuterium isotope effect. Acidity of the proton did not promote its abstraction5) when equatorial. A trans antiperiplanar diaxial elimination of HCl from the intermediate chlorosulfoxonium ion (3), leading to a positively charged ylide,5,7) was proposed as an essential step in this reaction. This ylide was then attacked axially by the chloride anion, yielding the product I.



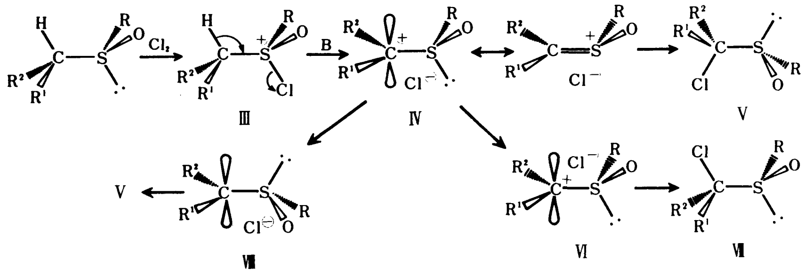
(3)

However, an additional isomer II with an axial oxygen and equatorial halogen was also found in the product of the reaction.[6,7] The amount of this last compound was increased in the presence of silver nitrate.[9] The occurence of anti elimination of HBr was confirmed[10] for the bromination of the rigid trans-2-thiahydrindan 2-oxide, but bromide attacked on the same side where it was in the bromosulfoxonium ion, leading to inversion-inversion.

It was already pointed out by us[5] that the inversion-inversion and retention-retention relation for sulfur and carbon in the steric course of halogenation does not necessarily require a migration of the halogen concerted with proton abstraction. It is sufficient to postulate hindered rotation in the positively charged ylide and a stereospecific anti attack of chloride on this ylide in such a manner that the lone-pair in the halogenated sulfoxide finds itself anti to the halogen. Such a course of the reaction is reasonable for compounds capable of configurational stability of the lone pair. It is found for example in the addition of anions to acetylenes, where a vinylic anion with the pair of electrons trans to the entering group is formed.

A planar $>C=\overset{\oplus}{S}\begin{smallmatrix}\nearrow R\\ \searrow O\end{smallmatrix}$ group could explain the relative stereochemistries at sulfur and carbon and the formation of a racemic or inverted product, but not the retention-retention observed in uncatalyzed reactions. Chirality at sulfur in the intermediate ylide was inferred to explain such a course of the reaction.[5] This symmetry argument can justify the chirality at sulfur and carbon on the halogenated sulfoxide, but for the understanding of the reasons, why in some cases retention and in other inversion occurs, a detailed mechanism of the reaction is now presented.

In the reaction of the chlorinating agent with the sulfoxide, the chlorine atom is introduced into the position "occupied" previously by the lone pair.[9] The second step involves an anti elimination of a proton and chloride anion[3] III → IV, brought about by a base in solution in the rate-determining step, to yield the positively charged ylide IV. In this reaction the chloride leaves with the pair of electrons and another pair of electrons from the C-H bond is introduced into the C-S bond. The sulfur and its three ligands are not in one plane and it maintains its original configuration after an anti elimination. The sharing of two electrons by sulfur and the vacant p orbital on carbon introduces a barrier to rotation around the C-S bond.



The relative configuration at carbon and sulfur is determined during the addition of the chloride anion to IV. The attack of IV by the chloride from the same side where it was eliminated will lead to the α-chlorosulfoxide V, in which the carbon and the sulfur have a configuration inverse to that in the starting sulfoxide. This step is energetically not easy since it involves an inversion on sulfur in the intermediate IV due to the introduction of the lone pair anti to the forming C-Cl bond. Instead, another process can take place: the migration of the anion from one side of the cation to the other (or a rotation of the cation by 180° with the position of the anion unchanged). This process also has a sizable energy barrier, as shown by Cram[11] for proton abstractions, necessary to overcome the electrostatic attraction between two ions of oposite charges for their at least partial separation that will permit such a migration. The new ion-pair VI has probably an energy slightly different from that of IV, but for simplicity sake we shall assume these energies to be identical (Fig. 1).

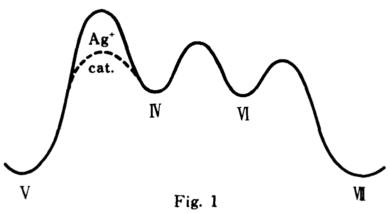
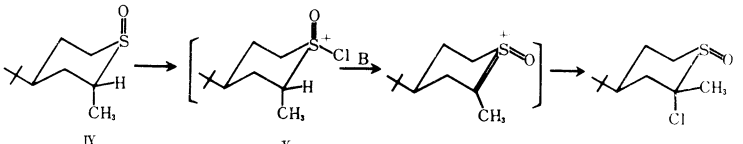


Fig. 1

The attack of chloride on the positively charged ylide in VI is much easier than in IV, since no inversion on sulfur is involved. Such an attack will give retention at sulfur and carbon, i.e. the course of noncatalyzed reactions. The steric course of the reaction could be changed, if the barrier for inversion at sulfur were lowered. The effect of silver nitrate is by coordination with the oxygen, thus lowering the activation energy for the inversion at sufur or in a concerted addition of the Ag-Cl bond to $>\overset{\oplus}{C}\text{-S=O}$. Concerted additions of metal-hetero atom bonds to double bonds have been suggested to occur.[12] The lowering of the barrier for inversion at sulfur could also be brought about by raising the energy of IV and/or by lowering the energy of the transition state due to other reasons. Both these effects occur probably in the bromination of trans-2-thiahydrindan 2-oxide, where trans elimination and inversion-inversion were observed.[10] It should be noted that the barrier for migration of the anion IV → VI will not be lowered since it will not depend on internal strain in the cation. The IV → V becomes therefore faster than IV → VI.

It is possible that the processes of attack by chloride and inversion are separate and a condition for the attack of the ylide by the chloride anion from the half-space to which it was eliminated is that it should be preceded by an inversion at sulfur IV → VIII. The competition will therefore be between an inversion at sulfur IV → VIII. and a migration of the chloride to the other half-space IV → VI, the rotation around $>C=\overset{\oplus}{S}(O)R$ remaining the slowest process.

syn-Elimination of a proton and a halogen anion seems also to occur in some special cases. The relief of strain due to an axial methyl in X and the additional stabilization due to a tertiary carbenium ion or conversely to a more substituted double bond, promotes the syn abstraction of the proton geminal to the methyl.



IX X XI

The strange exception to the general rule in the halogenation of benzyl methyl sulfoxide, where retention at carbon and inversion at sulfur occurred[13] could be explained by syn elimination.

References and Notes

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