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OPENING OF THE 1,3-OXATHIOLANE RING IN ACIDIC MEDIUM

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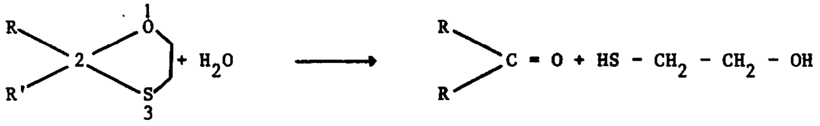
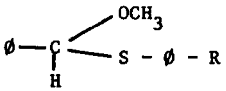
Recently several publications have been devoted to the mechanism of hydrolysis of 1,3-oxathiolanes, with conflicting conclusions :

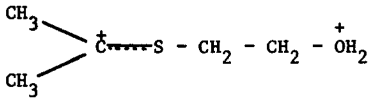


DE and FEDOR [1], on the basis of the solvent isotope effects, decide on an A_2 mechanism with rupture of the C - O bond ; whereas FIFE and JAO [2] predict an A_1 mechanism with rupture of the C - S bond. FIFE and ANDERSON [3] support this latter hypothesis by comparing the rates of formation of methanol and thiophenol in the acid hydrolysis of the following thioacetals :



Both the question of the opening of the ring and of the mechanism of hydrolysis remain unsettled. Furthermore, it appears dangerous to extend to all oxathiolanes results obtained with a particular family, and to use as model compounds products where the substituent on the sulfur atom is very different from that on the oxygen atom.

We have shown [4] that the protonation of 2,2-dimethyl-1,3-oxathiolane in FSO_3H-SbF_5 leads to the exclusive formation of the carbonium-sulfonium cation (note 1) :

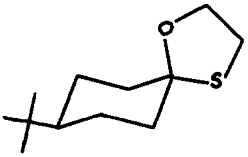


Note 1 : *Bromination seems to favor the rupture of the C - S bond. This result is to be compared with the catalytic effect of Hg^{++} ions observed by DE and FEDOR [1] ; Hg^{++}, Br and R - S - R are classified as soft acids and base according to PEARSON's theory [10];*

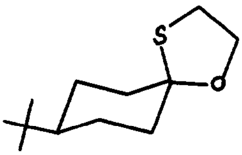
However the extreme conditions which we have used differ markedly from those of acid hydrolysis cited above. Also, if, due to its stability, the carbonium-sulfonium ion appears to the most probable intermediate of hydrolysis, it remains to be shown whether or not a solvent molecule takes part in the transition state of this reaction [5].

RESULTS

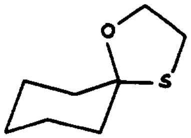
In an attempt to resolve these problems, we have prepared the oxathiolanes (I,II) derived from 4-tert-butylcyclohexanone [6] and their α, α'-tetradeuterated counterparts.



I

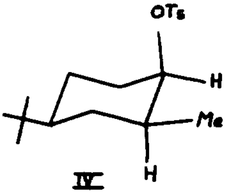


II

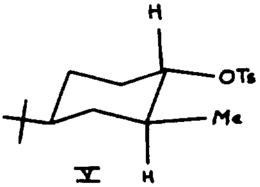


III

We have measured the kinetic deuterium isotope effect in acid-catalysed hydrolysis. TICHY, HAPALA and SICHER [7] have shown that, in the case of compounds IV and V, the deuterium isotope effect is decidly greater with the cis axial compound IV ($k_H/k_D = 2.08$) than with the trans equatorial compound V($k_H/k_D = 1.19$). This difference is due to the much greater stabilisation of the intermediate carbocation by the axial hydrogens or deuteriums.



IV



V

According to these results, if acid hydrolysis proceeds via rupture of the C – O bond first, the isotope effect should be much greater with compound I than with compound II. If however the C – S bond breaks first, the reverse will be true. Moreover, the presence or absence of an important isotope effect will give us some insight into the mechanism : for an A_2 mechanism the rate determining step would involve a bimolecular substitution on the conjugate acid of the substrate ; if this is the case, the kinetic isotope effect will be very small [8].

Our results carried out in a 20 – 80 water-isopropanol mixture (by volume), at 35° C, in presence of HCl 1.5 N are shown below (Table 1).

Table 1

	k_H	k_D	k_H/k_D
I	1.235	0.935	1.32
II	1.718	1.545	1.11
III	1.559	1.328	1.17_5

The value in Table 1 are mean values of three measurements with a reproducibility of ± 0.5 %.

DISCUSSION

These results appear to us to be devoid of ambiguity. The deuterium isotope effect is three times greater for compound I, where the C - O bond is axial, than for compound II. It is even greater than the value of 1.25 reported by SHINER and CROSS [9] in the acid hydrolysis of the ketal of phenoxyacetone for which an A_1 mechanism is admitted. Yet this value is the highest ever reported for acid hydrolysis of ketals.

We can therefore confirm our earlier observation [4] and conclude that the acid hydrolysis of alkyl 1,3-oxathiolanes proceeds through the A_1 mechanism with rupture of the C - O bond. The large isotope effect leads us to believe that the transition state is close to the carbonium-sulfonium cation.

The oxathiolane derived from cyclohexanone (III) is an equilibrium mixture of conformers with the sulfur atom axial and equatorial. The value of the isotope effect and therefore the reactivity falls between those of the two rigid compounds I and II. The calculation of the equilibrium constant by the usual kinetic method ($K_{eq.} = 0.49$) indicates that the axial sulfur conformation is preponderant (67 %). This is in accord with the results of ELIEL and PILATO [6]. The length of the C - S bond (1.81 Å), longer than the C - O bond (1.42 Å), makes it easier for the sulfur atom to avoid the interactions with the axial hydrogens in positions 3 and 5.

REFERENCES

1. N.C. De and L.R. Fedor, J. Amer. Chem. Soc. 90, 7266, (1968)
2. T.H. Fife and L.K. Jao, *ibid.* 91, 4217, (1969)
3. T.H. Fife and E. Anderson, *ibid.* 92, 5464, (1970)
4. F. Guinot, G. Lamaty and H. Münsch, Bull. Soc. Chim. France, 541 (1971)
5. F. Guinot and G. Lamaty *ibid.* in press
6. E.L. Eliel, L.A. Pilato and V.G. Badding, J. Amer. Chem. Soc., 84, 2377, (1962)
7. M. Tichy, J. Hapala and J. Sicher, Tetrahedron Letters, 3739 (1969)
8. G.A. Russel and E.R. Talaty, J. Amer. Chem. Soc., 87, 4867, 1965)
9. V.J. Shiner, Jr, and S. Cross, *ibid.* 79, 3599, (1957)
10. R.G..Pearson in "Survey of Progress in Chemistry", Volume 5 Ed. by F. Scott, Academic Press, New York, 1969, p1.