Tetrahedron Letters No.8, pp. 599-601, 1970. Pergamon Press. Printed in Great Britain.

NUCLEOPHILIC SUBSTITUTIONS OF α-CHLOROKETONES. IX.

MECHANISM OF FORMATION OF PHENYL d,l-O.ACETYL-THIOL-α-LACTATE IN THE ACETOLYSIS OF 1-CHLORO-3-PHENYLMERCAPTO-PROPANONE.

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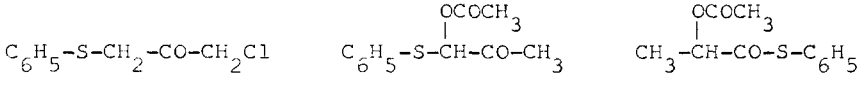
Recently it has been shown that 1-chloro-3-phenylmercapto-propanone (I) in refluxing acetic acid in the presence of potassium acetate gives 1-acetoxy--1-phenylmercapto-propanone (II)and phenyl d,l-O. acetyl-thiol-α-lactate (III) as major products.[1,2] We now wish to report some experimental results which clarify the mechanism of formation of the thiolester (III).



(I) (II) (III)

The previous hypothesis, by which the formation of (III) proceeded through a cyclopropanone intermediate[1,2] had to be reconsidered when it was ascertained that the acetoxyketone (II) is actually a precursor of the thiolester. In fact, (II) is stable in refluxing acetic acid, but in the presence of potassium acetate at 120° (III) is formed along with phenyl thiolacetate. The latter has

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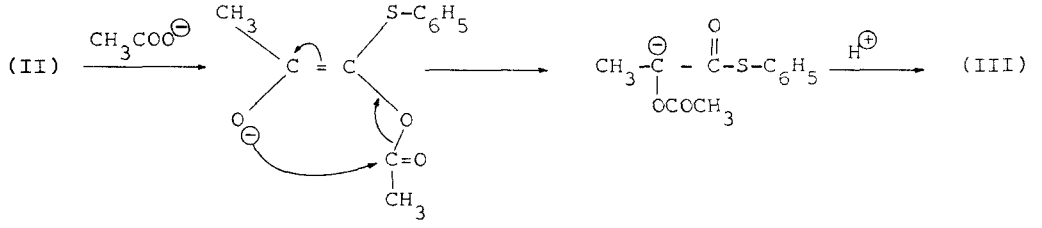
also been shown to originate from the same thiolester (III), by the action of potassium acetate in boiling acetic acid.

The formation of the thiolester (III) from the acetoxyketone (II) could also be explained in terms of an intramolecular oxidation-reduction of the hemiacetal and carbonyl functions of (II) :



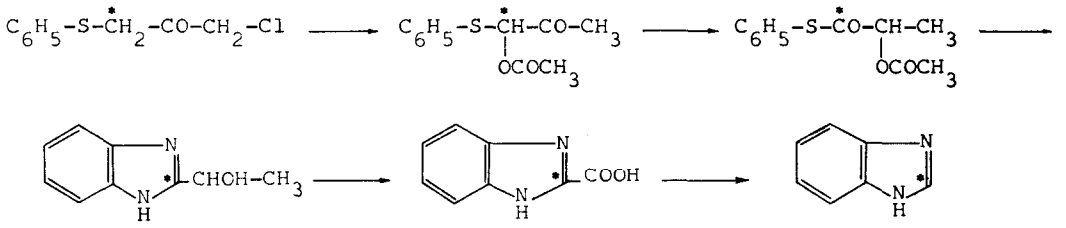
The above reaction mechanism was proved to be correct by the degradation of the thiolester (III) isotopically labelled. The method previously described by Roseman[3] for the degradation of lactic acid has been followed.

α-Chloroketone (I) labelled with ^{14}C at the α' carbon atom (activity: 8.95×10^8 DPM/mole)(*) was synthetized starting from chloroacetic acid labelled on the methylene (activity: 9.15×10^8 DPM/mole), according to the method previously described.[2] Isotopically labelled (I) after three hours heating in acetic acid at 120° in the presence of three moles of potassium acetate gave thiolester (III) with an activity of 8.65×10^8 DPM/mole. The reaction of (III) with o.phenylendiamine in the presence of phosphoric acid afforded 2-(α-hydroxyethyl)--benzimidazole (m.p. 177-9°; lit. 180-1°[3]), having an activity of $8,22 \times 10^8$ DPM/mole. The latter by permanganic oxidation furnished benzimidazol-2-carboxylic acid (m.p. 168-9°; lit. 169°[4]), which by thermal decomposition at its melting point gave benzimidazole (m.p. 170-1°; lit. 171-2°[5]) with an activity of 7.88×10^8 DPM/mole. The latter activity accounts for 88% of that of the starting α-chloroketone (I) and 91% of that of thiolester (III).

(*) Radioactivity measurements were made using a Tricarb Packard, 3CCC Series, counting apparatus.

The above results are fully consistent with the newly proposed mechanism, as illustrated by the reaction sequence of Chart I. The intramolecular oxidation--reduction which is involved closely resembles the isomerization of unsymmetrical α-hydroxyketones under basic catalysis.[6,7]

Chart I



The degradation study of labelled thiolester (III) strongly support the analogous reaction mechanism previously proposed for the formation of phenyl 2-acetoxy--thiolacrylate and phenyl 2,3-diacetoxy-thiolpropionate by acetolysis of 1-acetoxy--3-chloro-1-phenylmercapto-propanone.[8]

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REFERENCES

1) V.Rosnati, G.Pagani and F.Sannicolò, Tetrahedron Letters, 46, 4545 (1967)

2) V.Rosnati, F.Sannicolò and G.Pagani, Gazz. Chim. Ital., 99, 152 (1969)

3) S.Roseman, J. Am. Chem. Soc., 75, 3854 (1953)

4) A.Bistrzyki and G. Przeworski, Ber., 45, 3483 (1912)

5) C.F.Huebner, R.Lohmar, R.J.Dimler, S.Moore and K.P.Link, J.Biol.Chem., 159, 503 (1945)

6) Organic Reactions, Vol. IV, pag. 282, John Wiley, New York, 1948

7) G.Guillot and P.Rumpf, C.R.Acad.Sci., Paris, Ser. C, 264, 1985 (1967)

8) V.Rosnati, F.Sannicolò and G.Zecchi, Gazz. Chim. Ital., 99, 651 (1969)