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NUCLEOPHILIC SUBSTITUTIONS OF α-CHLOROKETONES

1-PHENYLMERCAPTO- AND 1-PHENYLSULFONYL-3-CHLOROPROPANONES

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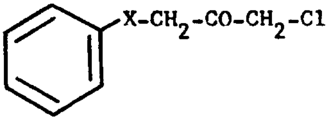
Recently it has been shown that α-chloroketones bearing in the α' position a heteroatom with a lone pair of electrons, such as oxygen or sulfur, undergo a new type of allylic rearrangement in the course of several nucleophilic substitutions; the rearrangements have been tentatively interpreted on the basis of a common ionic mechanism, involving the intervention of the lone electron pair of the heteroatom(1,2). In order to check the last point of the above mechanistic hypothesis, we have studied the behaviour towards nucleophiles of α-chloroketones (I) and (II), which differ essentially as to the electron availability on the sulfur atom.

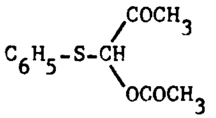


I : X = S
II : X = SO_2

1-phenylmercapto-3-chloropropanone (I,m.p. 46-7°) has been synthetized by reacting 1-phenylmercapto-3-diazopropanone (III) with an ethereal solution of dry HCl: its N.M.R. spectrum showed the following signals: 2,7 τ (m), aromatic protons; 5,75 τ (s) $-S-C\underline{H}_2-$; 6,15 τ (s) $-C\underline{H}_2-Cl$. The reaction of (I) with three moles of anhydrous CH_3COOK in glacial acetic acid gave the expected 1-acetoxy-1-phenylmercapto-propanone (IV); in addition, phenyl O-acetyl-thiol-α-lactate (V) and 3-acetoxy-1-phenylmercapto-propanone (VI) were obtained. The respective yields, estimated by V.P.C., were 60,6%, 37,4% and 1-2%.

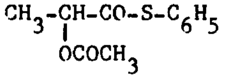
C_6H_5-S-CH_2-CO-CHN_2

(III)



C_6H_5-S-CH($COCH_3$)($OCOCH_3$)

(IV)



CH_3-CH($OCOCH_3$)-CO-S-C_6H_5

(V)

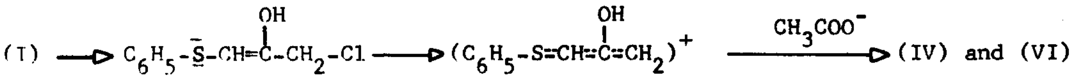
C_6H_5-S-CH_2-CO-CH_2-$OCOCH_3$

(VI)

The assignements of structures (IV), (V) and (VI) to the reaction products are fully consistent with the interpretation of the N.M.R. spectra. The data were the following. (IV): 2,40-2,88τ (m), aromatic protons; 3,93τ (s), -CH ; 7,85τ (s), -$COCH_3$; 7,87τ (s), -$OCOCH_3$. (V): 2,71τ (m), aromatic protons; 4,71τ (q), >CH-CH_3; 7,88τ (s), -$OCOCH_3$; 8,52τ (d), CH-CH_3. (VI): 2,77τ (m), aromatic protons; 6,29τ (s), -CH_2-S; 6,43τ (s), -CO-CH_2-O-; 7,97τ (s), -$OCOCH_3$.

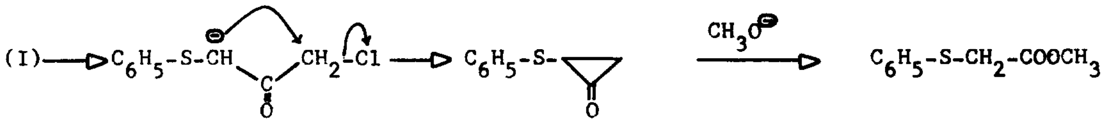
The structure of compound (V) has been confirmed through its indipendent synthesis from O-acetyl-α-lactyl chloride and sodium thiophenoxide.

The formation of the acetoxyketones (IV) and (VI) from (I) could be interpreted on the basis of the ionic mechanism previously proposed for the acetolyses of α'-aryloxy-α-chloroketones(1,2), although compound (VI) could also originate from a direct nucleophilic substitution.



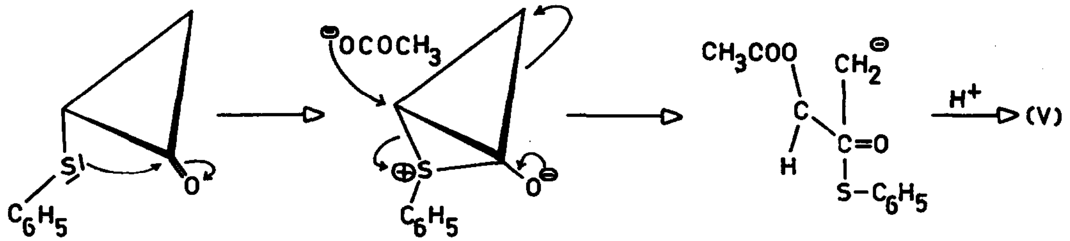
(A) (B)

The formation of thiol-ester (V) very probably involves the cyclopropanone intermediate (C): this possibility seems to be supported by the fact that by treatment with sodium methoxide in absolute methanol, (I) undergoes the Favorskij rearrangement, giving methyl 3-phenylmercapto-propionate (VII):



(C) (VII)

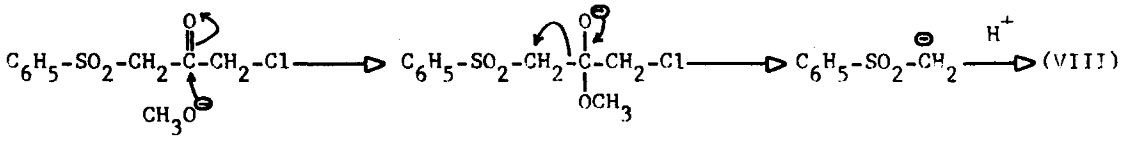
with a weaker nucleophile such as CH_3COO^- the cyclopropanone intermediate (C) could undergo an internal nucleophilic attack by the lone electron pair of the sulfur atom, immediately followed by,or simultaneous with, the nucleophilic attack of CH_3COO^- on the electron deficient carbon atom.



1-phenylsulfonyl-3-chloropropanone (II, m.p. 99°) has been prepared through the reaction of diazomethane with phenylsulfonyl-acetyl chloride followed by treatment with hydrogen chloride. The N.M.R. spectrum of II (CD_3COCD_3) showed the following signals: 1,88-2,4τ(m), aromatic protons; 5,3τ(s), -C$\underline{H}_2$-; 5,35τ (s), -C$\underline{H}_2$-.

Chloroketone (II) did not react with a solution of CH_3COOK in glacial acetic acid, even after prolonged heating, while with sodium methoxide in methanol it gave methyl-phenylsulfone (VIII, m.p. 87-8°; lit.$^{(3)}$88°), isolated in 70% yield.

The formation of methyl-phenylsulfone can be interpreted in terms of the following reaction mechanism:



$$C_6H_5\text{-}SO_2\text{-}CH_2\text{-}\underset{CH_3O^{\ominus}}{\overset{O}{\overset{\|}{C}}}\text{-}CH_2\text{-}Cl \longrightarrow C_6H_5\text{-}SO_2\text{-}CH_2\text{-}\underset{OCH_3}{\overset{O^{\ominus}}{\overset{|}{C}}}\text{-}CH_2\text{-}Cl \longrightarrow C_6H_5\text{-}SO_2\text{-}\overset{\ominus}{C}H_2 \xrightarrow{H^+} (VIII)$$

The different reactivity of chloroketones (I) and (II) towards alkali acetates in acetic acid solution clearly confirms the intervention of the lone electron pair of the heteroatom in the above allylic rearrangement. According to the above mechanism such intervention may develop as a simple mesomeric effect stabilizing the incipient primary carbonium ion; however an alternative possibility may involve the anchimeric assistance of the neighbouring group to the ionisation of the chloroketone or of its enol (A).

A similar ionic mechanism very probably is operating also in the acetolysis of diazoketone (III),which,by simple boiling in acetic acid, gave a mixture of acetoxy-ketones (IV) and (V), the yields being 51,5% and 40,5% respectively (estimated by V.P.C. analysis): in fact, these results are consistent with the reaction mechanism proposed for the acetolysis of some α'aryloxy-α-diazoketones(2)

Satisfactory analyses were obtained for all new compounds. Melting points were not corrected. All N.M.R. spectra (in $CDCl_3$ solution, if not differently stated) were recorded on a Perkin Elmer spectrometer mod. R 10 employing T.M.S. as internal standard.

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