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CONCERNING THE REARRANGEMENT OF γ-HALOESTERS TO γ-LACTONES AND ALKYL HALIDES

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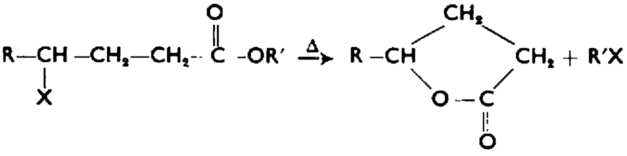
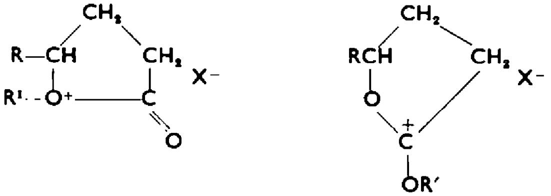
Abstract—Pyrolysis of cetyl γ-chlorobutyrate labeled with oxygen-18 in the carbonyl group gave γ-butyrolactone with all of the label in the ether oxygen of the lactone. This result shows that it is the carbonyl oxygen which participates in the ring formation.

THE pyrolytic conversion of γ-haloesters (I) to γ-lactones (II) and alkyl halides (III) is well known.[2] It seems quite clear that the reaction involves an intramolecular displacement process and that two intermediates, IV and V, merit consideration.


I II III

Weinstock[2b] has considered these two possibilities and on the basis of some very reasonable arguments has favored V. More recently Singh *et al.*[3] have studied the solvolysis of *o*-carbophenoxybenzhydryl bromide and showed that 3-phenylphthalide is formed. The fate of the phenoxy group was not determined. The results of their study implicate an intermediate similar to V.


IV V

Although IV is a less likely candidate than V, intramolecular participation by a methoxyl group is well recognized.[4] This is particularly facile when a five membered ring is formed. Indeed an intermediate IV is required to explain the transformation of

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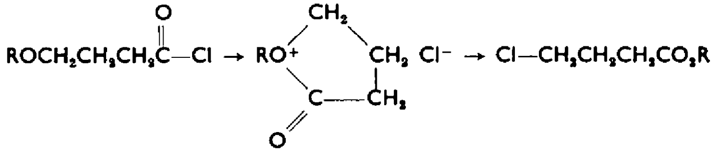
[2] [a] M. S. Kharasch, P. S. Skell and P. Fisher, *J. Amer. Chem. Soc.* **70**, 1055 (1948); [b] J. Weinstock, *Ibid.* **78**, 4967 (1956).

[3] A. Singh, L. J. Andrews and R. M. Keefer, *J. Amer. Chem. Soc.* **84**, 1179 (1962).

[4] S. Winstein, E. Allred, R. Heck and R. Glick, *Tetrahedron* **3**, 1 (1958).

γ-alkoxy acid halides into γ-halo esters.[5] It is important to note that collapse of the intermediate does not yield lactone,



however this may be strictly due to kinetic control. The transformation of the acid chlorides occurs under much more mild conditions than that of the γ-halo esters.

An approach to a definitive structural elucidation of the intermediates involved in these transformations involves the use of oxygen-18 labeled compounds. It is the purpose of this report to present results of such a study.

Methyl γ-chlorobutyrate (VI) labeled with oxygen-18 in the carbonyl group was prepared by esterification of labeled γ-chlorobutyric acid with methanol. Pyrolysis of VI in a sealed tube at 200° led to the formation of γ-butyrolactone and methyl chloride. The position of the label was determined by exchange of the carbonyl oxygen with water.[6] By this technique it was found that approximately half of the label was lost from the lactone. These results show that at sometime during the transformation the two oxygens have become equivalent. Such a result is not compatible with either IV or V, however, it does not eliminate either one of them since the equilibration could be unrelated to the formation of lactone. That this is the case was demonstrated by pyrolyzing an equimolar mixture of carbonyl labeled γ-butyrolactone and unlabeled methyl γ-chlorobutyrate. Oxygen-18 analysis of the lactone obtained followed by exchange with water and reanalysis showed that one half of the label was lost. This result clearly demonstrates that the lactone equilibrates under the conditions of the reaction. It does not prove that the equilibration necessarily occurred in this way.

Pyrolysis of a carbonyl labeled sample of cetyl γ-chlorobutyrate allowed removal of the lactone as rapidly as it was formed. Exchange of the lactone obtained from this reaction gave lactone which contained essentially all of the excess oxygen-18. These results show that the carbonyl oxygen of the ester becomes the ether oxygen of the lactone. Thus an intermediate (V) is clearly implicated and IV is eliminated as a lactone forming intermediate. Presumably carbonyl oxygen participation will be a common feature of neighboring ester group participation.

The randomization of the label in the lactone was not studied further but could be due to ring opening to γ-chlorobutyric acid by traces of hydrogen chloride. Ring closure would regenerate lactone and hydrogen chloride.

EXPERIMENTAL

Oxygen-18 analyses were conducted by the method of W. E. Doering and E. Dorfman, *J. Amer. Chem. Soc.* **75**, 5595 (1953) as modified by D. B. Denney and M. A. Greenbaum, *Ibid.* **79**, 979 (1957). IR spectra were obtained with a Perkin–Elmer Infracord. Gas-liquid phase chromatographic analyses were performed with a F and M model 500 Gas Chromatograph.

[5] This conversion is reviewed and discussed in detail by D. S. Noyce and H. I. Weingarten, *J. Amer. Chem. Soc.* **79**, 3093 (1957).

[6] F. A. Long and L. Friedman, *J. Amer. Chem. Soc.* **72**, 3692 (1950).

*Oxygen-*18 *labeled γ-chlorobutyric acid.* γ-Chlorobutyryl chloride, 18·5 g (0·13 mole) was added dropwise with stirring and cooling to 40 ml water (ca. 1·3 atom % oxygen-18). After stirring overnight at room temp, the aqueous solution was extracted repeatedly with ether. After drying ($CaCl_2$) the ether was removed and the residue was distilled, b.p. 70–72° (0·1 mm), lit.[7] 114°, 11 mm.

Preparation and pyrolysis of VI. Esterification of the labeled γ-chlorobutyric acid was conducted by boiling a methanolic solution in the presence of *p*-toluenesulfonic acid for 2 hr. Isolation was effected by standard techniques. The labeled ester, 2·0 g, was heated in a sealed tube at 200° for 6 days. The product was distilled, b.p. 110–115° (12 mm). The IR spectrum was identical to that of an authentic sample of γ-butyrolactone. Samples for oxygen-18 analysis were further purified by glpc using a 10 ft. 6 M Carbowax column at 200° and 60 ml He/min. The retention time was 10·6 min and only one component was detected. An authentic sample had the same retention time. Oxygen-18 analysis showed 0·46 atom % excess oxygen-18.

Exchange of a 1·0 ml sample of the labeled lactone with 5 ml water was effected by the procedure of Long and Friedman.[6] The exchanged lactone was molecularly distilled, analytical samples were obtained by glpc. The oxygen-18 content was 0·27 and 0·28 atom % excess oxygen-18.

Pyrolysis of a mixture of labeled γ-butyrolactone and VI. Carbonyl labeled γ-butyrolactone[6] was prepared by exchange with oxygen-18 enriched (1·7%) water. Oxygen-18 analysis showed 0·67; 0·65 atom % excess oxygen-18.

A mixture of 1·0 g (0·0116 mole) of the lactone and 1·57 g (0·0116 mole) of methyl γ-chlorobutyrate was heated at 200° for 6 days. The product was molecularly distilled and analytical samples were prepared by glpc. The oxygen-18 content was found to be 0·40; 0·39 atom % excess oxygen-18. The lactone was exchanged and reanalyzed. There was found 0·24; 0·22 atom % excess oxygen-18.

Labeled cetyl γ-chlorobutyrate. A solution of 11·8 g (0·049 mole) of cetyl alcohol, 6·0 g (0·049 mole) of oxygen-18 labeled γ-chlorobutyric acid and a catalytic amount of *p*-toluenesulfonic acid in 150 ml benzene was heated under reflux for 12 hr. The benzene solution was extracted (Na_2CO_3 aq) dried and distilled. The ester, 12 g (70%), had b.p. 174° (0·05 mm). The IR spectrum was identical to that of an unlabeled sample which had been analyzed. (Found: C, 69·94; H, 11·51; Cl, 10·45. $C_{20}H_{39}OCl$ requires: C, 69·28; H, 11·33; Cl, 10·23%).

Pyrolysis of labeled cetyl γ-chlorobutyrate. The ester, 9·0 g (0·026 mole) was pyrolyzed at 250° (bath) for 2 days. The volatile materials were distilled as formed. The volatile fraction was molecularly distilled, b.p. 110–115° (12 mm). The IR spectrum was identical to that of γ-butyrolactone. Oxygen-18 analysis of samples further purified by glpc showed 0·55, 0·55 atom % excess oxygen-18.

The lactone was exchanged with water and reanalyzed for oxygen-18, 0·52, 0·53 atom % excess oxygen-18 was found.

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[7] H. Wohlgemath, *Ann. Chim.* **2**, 305 (1914).