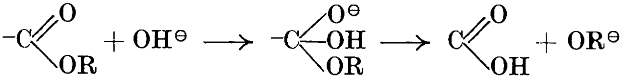
96. *Mechanism of the Hydrolysis of Carboxylic Esters with Special Reference to Acid Hydrolysis.*

By Edith Hilda Ingold and Christopher Kelk Ingold.

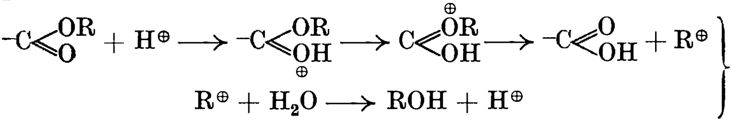
Modern views regarding the mechanisms of reactions leave little room to doubt that alkaline saponification of carboxylic esters is initiated by the addition of an anion to the carbonyl carbon atom :



$$\mathrm{OR}^{\ominus} + \mathrm{H_2O} \longrightarrow \mathrm{HOR} + \mathrm{OH}^{\ominus}$$

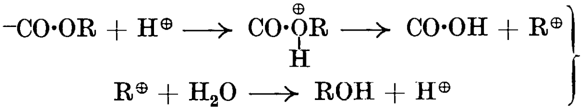
This mechanism has many known analogies, *e.g.*, the addition of cyanide ions to carbonyl compounds (Lapworth, J., 1903, **83**, 995; 1904, **85**, 1206, 1215), and it is consistent with the circumstance that a Walden inversion has never been observed during the saponification of carboxylic esters of such optically active alcohols as *sec.*-octyl alcohol (Kenyon, private communication).

On the other hand, the *a priori* application of the same theories of reaction mechanism does not appear uniquely to define the course pursued by acid hydrolysis. Thus it is known that the carbonyl oxygen atom has definite basic tendencies (compare Baker, J., 1931, 307), which polarisation of the carboxyl group, $\mathrm{O{-}C{=}O}$, would be expected to enhance. Therefore hydrolysis might conceivably be initiated at the carbonyl oxygen atom, the complete reaction, in which the last stage is analogous to 'onium salt decomposition, being as follows :

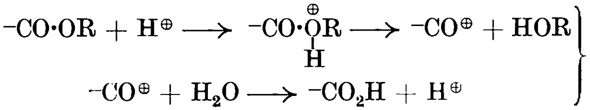


$$\left.\begin{array}{l} -\mathrm{C}{<}^{\mathrm{OR}}_{\mathrm{O}} + \mathrm{H}^{\oplus} \longrightarrow -\mathrm{C}{<}^{\mathrm{OR}}_{\underset{\oplus}{\mathrm{OH}}} \longrightarrow \mathrm{C}{<}^{\overset{\oplus}{\mathrm{OR}}}_{\mathrm{OH}} \longrightarrow -\mathrm{C}{<}^{\mathrm{O}}_{\mathrm{OH}} + \mathrm{R}^{\oplus} \\ \qquad \mathrm{R}^{\oplus} + \mathrm{H_2O} \longrightarrow \mathrm{ROH} + \mathrm{H}^{\oplus} \end{array}\right\} \mathrm{A}$$

The alternative hypothesis is that the reaction commences at the ethereal oxygen atom in conformity with the established basic character of singly linked bicovalent oxygen. In this case an 'onium structure would be produced, which could lead to the products of hydrolysis by fission in either of two directions :



$$\left.\begin{array}{l} -\mathrm{CO{\cdot}OR} + \mathrm{H}^{\oplus} \longrightarrow \mathrm{CO{\cdot}}\overset{\oplus}{\underset{\mathrm{H}}{\mathrm{O}}}\mathrm{R} \longrightarrow \mathrm{CO{\cdot}OH} + \mathrm{R}^{\oplus} \\ \qquad \mathrm{R}^{\oplus} + \mathrm{H_2O} \longrightarrow \mathrm{ROH} + \mathrm{H}^{\oplus} \end{array}\right\} \ldots \mathrm{B}$$



$$\left.\begin{array}{l} -\mathrm{CO{\cdot}OR} + \mathrm{H}^{\oplus} \longrightarrow -\mathrm{CO{\cdot}}\overset{\oplus}{\underset{\mathrm{H}}{\mathrm{O}}}\mathrm{R} \longrightarrow -\mathrm{CO}^{\oplus} + \mathrm{HOR} \\ \qquad -\mathrm{CO}^{\oplus} + \mathrm{H_2O} \longrightarrow -\mathrm{CO_2H} + \mathrm{H}^{\oplus} \end{array}\right\} \ldots \mathrm{C}$$

Thus theory suggests three possible modes of reaction, of which two (B and C) are identical as regards their method of initiation and two (A and B) are likewise identical in the manner of their completion.

The idea that the initial stage in the hydrolysis of an ester is the formation of a complex ion seems to have originated with Kastle (*Amer. Chem. J.*, 1897, **19**, 894). It has been developed by Lapworth, Acree, Stieglitz, and others. Lapworth (Mellor's "Statics and Dynamics," 1904, p. 289) suggested two alternative mechanisms, one of which is identical with A above, whilst the other is related to C, differing therefrom in that the molecule of ROH is assumed to be eliminated in two parts, $OR^{\ominus}$ and $H^{\oplus}$, of which the former is ejected from the (hydrated) ester molecule without prior formation of the complex kation. Stieglitz (*Amer. Chem. J.*, 1908, **39**, 166) advanced a mechanism which, after the first stage, becomes equivocal and may be regarded as a generalised representation covering both the possibilities B and C. Acree (*Amer. Chem. J.*, 1907, **38**, 297) formulated the intermediate kation in a manner which appears to leave open all three possibilities A, B, and C. Later Lapworth interpreted (J., 1912, **101**, 273) the dissimilar behaviour of alkyl sulphonates and carboxylates, *e.g.*, towards amines and the Grignard reagent, on the basis of the hypothesis that the two types tend to divide in the parts $-SO_2-O-|-R$ and $-CO-|-OR$ respectively, the comparatively rapid alcoholysis of phenyl carboxylates being adduced as further support for this idea (P., 1914, 142). In this connexion specific reference was made to the acid hydrolysis of carboxylic esters, the alkoxyl groups of which were considered as being eliminated without separation into their components. Thus, as regards the completion of the reaction, the mechanism conforms to scheme C, but it has a certain similarity also with scheme A in relation to the initiation of the reaction, since the basicity of the hydrated carbonyl group as well as that of the ether-like oxygen atom is considered to be responsible for the formation of the intermediate kation. Thus it would appear that each of the alternatives which might at present be envisaged has been foreshadowed in earlier theories.

An attempt has been made to obtain evidence permitting a distinction between these theories on the basis of the following considerations. Mechanisms A and B involve the elimination of the alcoholic constituent R of the ester in the form $R^{\oplus}$. Let it be supposed that R is of the form $A-\overset{|}{C}H-CH{=}CHB$, the isomeric form $A-CH{=}CH-\overset{|}{C}H-B$ of this radical being designated R′. Now Burton (J., 1928, 1650) has shown that the anionotropic conversion of RX into R′X depends on the intermediate liberation of the kation, $R^{\oplus}{=}R'^{\oplus}$, common to these tautomerides. It should be stated that in thus equating the two representations of the tautomeric kation the writer is expressing acceptance of the view that such an ion, when freed from strong local electrostriction, possesses a distributed charge. Now let it be supposed that X is a carboxy-group, *e.g.*, acetoxyl. If, during the hydrolysis of the ester RX, the alcoholic radical ever becomes free as $R^{\oplus}$, then, since this ion is electromeric, its final combination with hydroxide ions should yield the same mixture of alcohols ROH and R'OH as would be obtained if either of these alcohols could be caused to ionise under corresponding conditions. Thus, provided it is known that the ester R—X and the alcohol ROH have not in themselves an appreciable tautomeric mobility (*i.e.*, tendency to ionise) in the solvent and at the temperature of the hydrolysis experiment, the recovery from each of the pure isomeric esters RX and R'X of an identical mixture of alcohols will be diagnostic of the liberation of the alcoholic residue as $R^{\oplus}$, whilst, if each ester gives only its own alcohol, this will indicate that the ion $R^{\oplus}$ has never at any stage been set free.

The forms chosen for experimental study were R equals $\overset{|}{\mathrm{C}}\mathrm{HMe{-}CH{=}CH_2}$ and R' equals $\mathrm{CHMe{=}CH{-}}\overset{|}{\mathrm{C}}\mathrm{H_2}$; for X the acetoxy-group was taken. It was clear from Baudrenghien's work (*Bull. Soc. chim. Belg.*, 1922, **31**, 160) that neither the alcohols ROH and R'OH nor the acetates RX and R'X would exhibit appreciable mobility under the conditions of hydrolysis contemplated, and this conclusion is fully confirmed by the results now recorded.

Crotyl acetate and α-methylallyl acetate were hydrolysed by 2*N*-sulphuric acid at 60°, and after upwards of 90% of hydrolysis had occurred the reactions were completed by alkaline saponification. The alcohols were then isolated and their physical properties examined. Each ester yielded its own alcohol.

This result would appear to exclude mechanisms A and B, and thus leave mechanism C as the only acceptable alternative. To this extent Lapworth's suggestion of 1912, regarding the point at which carboxylic esters undergo fission in their reactions generally, is confirmed by the work now described.

As to the alkaline hydrolysis of carboxylic esters a corresponding problem does not arise, because, as is explained above, one mechanism only is conceivable in the light of modern knowledge. Actually the proof of this by the method employed above in relation to acid hydrolysis is already completed, since Prévost has shown (*Ann. Chim.*, 1928, **10**, 147) that crotyl acetate and methylallyl acetate on alkaline hydrolysis yield exclusively their respective alcohols. Nevertheless, since this result was to be utilised in the experimental method described above, in which the incomplete acid hydrolyses were completed by alkaline saponification, prior to the isolation of the alcohols, it was deemed advisable to make certain that Prévost's finding was applicable to the conditions under which these saponifications were carried out. The record of this confirmation will be found in the experimental section.

EXPERIMENTAL.

Preparation of Alcohols.—Crotyl alcohol was prepared by reducing crotonaldehyde with zinc-copper couple as described by Charon (*Compt. rend.*, 1896, **123**, 123), except that further additions of the couple were found necessary to complete the reduction. The material, twice dried with potassium carbonate in ether, twice fractionated through a column, and finally thrice distilled over barium oxide, with control by refractive index determinations, had b. p. 120—121°/763 mm., $n_{5461}^{15\cdot4^\circ}$ 1·4289; b. p. 119—122°/763 mm., $n_{5461}^{15\cdot7^\circ}$ 1·4287, $n_{5461}^{15\cdot4^\circ}$ 1·4282; b. p. 119—120°/759 mm., $n_{5461}^{18\cdot8^\circ}$ 1·4265, $n_{5461}^{19\cdot7^\circ}$ 1·4252 (Charon gives b. p. 122—123°; Baudrenghien, *loc. cit.*, gives 121·5—122°/763 mm.).

α-Methylallyl alcohol was prepared by the method of Wohl and Lösanitsch (*Ber.*, 1908, **41**, 3621), methylmagnesium bromide being used in place of methylmagnesium iodide. The alcohol, isolated and purified exactly as described above for the case of crotyl alcohol, had b. p. 97°/763 mm., $n_{5461}^{15\cdot6^\circ}$ 1·4182, 1·4183; b. p. 96—97°/759 mm., $n_{5461}^{19\cdot6^\circ}$ 1·4156, $n_{5461}^{18\cdot6^\circ}$ 1·4167 (Baudrenghien, *loc. cit.*, gives b. p. 97°/763 mm.; Wohl and Lösanitsch give b. p. 96—97°/756 mm.).

Preparation of Acetates.—Crotyl acetate was prepared by heating equimolecular quantities of crotyl alcohol and acetic anhydride for 6 hours on the water-bath. The solution was shaken with 6—7 times its volume of water until 5 minutes after the odour of acetic anhydride completely disappeared, and then extracted twice with ether. The ethereal solution was washed twice with a small amount of water and dried with calcium chloride. After the removal of the ether through a fractionating column, the residue was subjected to a long series of fractionations, controlled by determinations of refractive index, an efficient Dufton column being used. It then had b. p. 132°/761 mm., $n_{5461}^{15\cdot5^\circ}$ 1·4214, $n_{5461}^{15\cdot6^\circ}$ 1·4210 (Found: C, 62·9; H, 8·9. Calc.: C, 63·1; H, 8·8%).

α-Methylallyl acetate was prepared from α-methylallyl alcohol by the preceding method, except that the mixture was heated for 8 hours and the product was fractionated thrice only. It had b. p. 112—114°/766 mm., $n_{5461}^{15\cdot3^\circ}$ 1·4065; b. p. 110—115°/766 mm., $n_{5461}^{15\cdot2^\circ}$ 1·4064.

Acid Hydrolysis of Crotyl Acetate.—0·2*N*-Sulphuric acid was employed, and the quantity of crotyl acetate was such that on complete hydrolysis the solution would have been 0·3*N* with regard to acetic acid. The mixture was kept at 61° and frequently shaken until it became homogeneous; thereafter the course of the reaction was followed by withdrawing samples for titration. After 8 hours, when 91% of the ester had been hydrolysed, the reaction was completed by adding enough potassium hydroxide solution, previously warmed to 61°, to make the mixture 0·2*N* with regard to alkali. The alkaline mixture was kept for 0·5 minute at 61°, rapidly cooled, and extracted five times with half its volume of ether each time. The ethereal solution was dried with potassium carbonate, and the greater part of the ether removed through a long Dufton column. The remainder of the solvent was removed through a short Dufton column and the residue was dried and distilled over barium oxide. It had b. p. 118—120°/736 mm., $n_{5461}^{15\cdot7^\circ}$ 1·4272.

Acid Hydrolysis of α-Methylallyl Acetate.—This hydrolysis was carried out by the preceding method (thermostat temperature 62°). After 8·5 hours, when 93% of the ester had reacted, the hydrolysis was completed and the product isolated as above described. In a duplicate experiment (thermostat temperature 61°) the alkali was added after 8 hours, when 92% had been hydrolysed. The product had b. p. 93—99°/765 mm., $n_{5461}^{15\cdot2^\circ}$ 1·4172; $n_{5461}^{19\cdot6^\circ}$ 1·4131; $n_{5461}^{19\cdot4^\circ}$ 1·4132.

Alkaline Hydrolysis of α-Methylallyl Acetate.—The ester was hydrolysed with sufficient 0·5*N*-potassium hydroxide to render the solution 0·2*N* with respect to alkali after the completion of hydrolysis. The mixture was shaken at 60° until it became homogeneous (5—6 minutes), kept at this temperature for a further minute, and worked up in the manner illustrated in connexion with the experiments on acid hydrolysis. The product had b. p. 94—98°/756 mm., $n_{5461}^{15\cdot2^\circ}$ 1·4161.

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