ON THE MECHANISM OF HYDROLYSIS.

THE ALKALINE SAPONIFICATIONS OF AMYL ACETATE.

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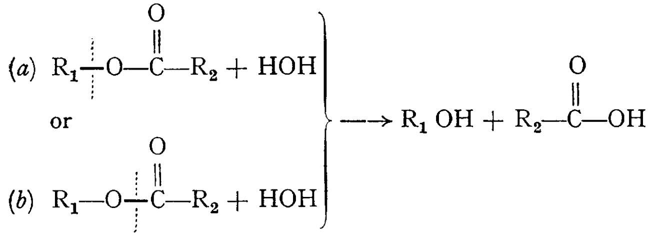
The present communication deals with a longstanding controversy regarding the mechanism of hydrolysis of esters. The question is, which of the two bonds of the oxygen bridge is split, that to the alkyl (according to (*a*) or to the acyl radical (according to *b*).



$$\left.\begin{array}{l}(a)\ R_1 \vdots O-\overset{O}{\overset{\|}{C}}-R_2 + HOH\\ \text{or}\\ (b)\ R_1-O \vdots \overset{O}{\overset{\|}{C}}-R_2 + HOH\end{array}\right\} \longrightarrow R_1\,OH + R_2-\overset{O}{\overset{\|}{C}}-OH$$

This question was first raised by Van't Hoff [1] and has been since frequently discussed. The evidence adduced was in the first place the variation of the reaction rate of hydrolysis when homologous series of radicals were substituted for R_1 and R_2 respectively (Van't Hoff [1] Skrabal,[2] Smith and Olsson,[3] Tronow [4]); other suggestions were based on the hydrolysis of those esters, in which the carbon atom of R_1 attached to the bridge oxygen is asymmetric (Holmberg); [5] still further conclusions were drawn from general considerations of the mechanism of organic reactions (Ferns and Lapworth,[6] Ingold and Ingold [7]). Of the opinions derived from these considerations we wish to refer only to those which apply to the *alkaline* hydrolysis, since our study was restricted to this case.

The suggestion of Van't Hoff was, that the reaction proceeds according to (*a*); Holmberg,[5] Ferns and Lapworth,[6] and Ingold and Ingold,[7] supported alternative (*b*); whereas Skrabal [2] and Smith and Olsson [3] concluded that the reaction proceeds along both lines (*a*) and (*b*).[8]

We propose to decide between (*a*) and (*b*) by using the following method.

The principle is to " mark " the oxygen of the hydrolysing water by shifting the ratio of the isotopes O^{16} and O^{18} contained in it, and determining after the hydrolysis, whether the " marked " oxygen goes to the alcohol or to the acid. This was carried out by dehydrating the alcohol, and determining the isotopic ratio of the oxygen in the water thus obtained. If the ratio is found to be normal, mechanism (*b*) is proved; if it has the shifted ratio of the " marked " oxygen, mechanism (*a*) must hold.

Obviously this implies the assumption that there is no great difference in the reaction velocity of H_2O^{18} and H_2O^{16}. This assumption appears sound enough, both from theoretical considerations, which show that the differences of reaction velocities between the isotopes of the heavier elements can only be small,[9] and by the well-known failures of attempts to separate the isotopes by chemical means.[10]

[1] J. H. Van't Hoff, Lectures, Part III. (1899).

[2] A. Skrabal and O. Ringer, *Monatsh.*, **42,** 38, 1921; A. Skrabal and A. M. Hugetz, *Monatsh.*, **47,** 17, 1926.

[3] L. Smith and H. Olsson, *Z. physik. Chem.*, **102,** 26, 1922; **118,** 99, 1925.

[4] R. Tronow, L. Djakonowa-Schulz, O. Guljewa and N. Nikoforowa, *Journ. Russ. Physik. Ges.*, **59,** 545, 1927.

[5] R. Holmberg, *Berichte*, **45,** 2997, 1912.

[6] I. Ferns and A. Lapworth, *J. Chem. Soc.*, **101,** 273, 1912.

[7] E. H. Ingold and C. K. Ingold, *J. Chem. Soc.*, **1932,** 756.

[8] Tronow's work is only concerned with acid hydrolysis.

[9] E. Cremer and M. Polanyi, *Z. physik. Chem.*, **19B,** 443, 1932; H. Eyring, *Proc. Nat. Acad. Sc.*, **19,** 78, 1933; C. E. H. Bawn and G. Ogden, *Trans. Faraday Soc.*, 1934.

[10] See *e.g.*, F. W. Aston, " Isotopes," 3rd edn., Edward Arnold & Co., London, 1934; H. A. Urey and G. M. Murphy (*Physic. Rev.*, **38,** 515, 1931) found that

Results.

Alkaline hydrolysis of primary amyl acetate by water with "shifted" oxygen produced an amyl alcohol containing normal oxygen. This proves that the hydrolysis follows mechanism (*b*), *i.e.*, the oxygen bridge is broken on the side of the acid.

The shifted water used was kindly given to us by Professor G. Hertz in Berlin, who had prepared it by his method of fractional diffusion.[11] Its density was 1·00033 compared with ordinary water at the same temperature. This corresponds to an excess of about 0·35 atomic per cent. of O^{18} over the ordinary abundance of this isotope, which is estimated to be 0·15 to 0·2 atomic per cent.

Our experiments were carried out with about 5½ millimols. (100 mg.) of water, to which about 2 millimols. of metallic sodium and 1·8 millimols. of ester were added. After the hydrolysis had taken place, the alcohol was isolated and dehydrated by passing it over heated bauxite. The water thus obtained was again isolated and purified and its density was measured.

A number of hydrolyses were carried out in the same way with ordinary water. Two of these blank tests are presented in the accompanying table, together with three runs made with "shifted" oxygen water.

1.	2.	3.
No. and Date of Experiment.	Density Shift of Hydrolysing Water in Millionths.	Density Shift of Water Obtained from Alcohol in Millionths.
1. 19/3—24/3 1934	0	− 3
2. 24/3—29/3 ,,	+330	+ 1
3. 6/4—12/4 ,,	+330	+ 2
4. 7/4—13/4 ,,	0	− 6
5. 13/4—18/4 ,,	+330	+13

The density shifts of the water obtained by the dehydration of the amyl alcohol formed in the hydrolyses all lay within the limits of error[12] so that the oxygen in the alcohol is to be considered as normal. Hence this oxygen does not come from the hydrolysing water, but originates from the bridge of the ester.

Experimental.

Primary Amyl Acetate.—This ester was prepared from the corresponding alcohol, by heating it for some hours with concentrated acetic acid and sulphuric acid. The product was poured into water, separated, taken up in ether, washed with soda, water, calcium chloride solution, dried and fractionated. Bp. 139-141° C.

Shifted Oxygen Water.—The experiments of Professor Hertz which resulted in the production of the water used by us were carried out with a modified form of his diffusion apparatus, described by H. Harmsen.[13] The question might be raised as to whether the increased density of the water thus prepared is not due to the accumulation of HDO or D_2O. As

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samples of NO prepared by different methods have the same isotopic composition; a slight shift in the isotopic ratio of oxygen seems to be apparent in the decomposition of lead peroxide (W. R. Smythe, *Physic. Rev.*, **45**, 299, 1934).

[11] G. Hertz, *Z. Physik*, **79**, 108, 1932.

[12] The densities were measured with the micro-pyknometer of Gilfillan and Polanyi (*Z. physik. Chem.*, **166A**, 254, 1933), which has been greatly improved by Dr. J. Horiuti since its original construction.

[13] H. Harmsen, *Z. Physik*, **82**, 589, 1933.

to the latter, its concentration is about 4×10^{-6}, *i.e.*, about 200 times lower than that of H_2O^{18}. Only 1/200 of the density shift can therefore be due to an accumulation of D_2O. On the other hand, for HDO, which has about 1/10 of the abundance of H_2O^{18} the "separation factor" is 4·3 times smaller than for H_2O^{18}. Therefore only about 2·3 per cent. of the density shift can be due to an accumulation of HDO. To make it quite sure that the shift was not due to an accumulation of the diplogen in the water, we have tested the hydrogen which was evolved, when metallic sodium was dissolved in the water in the course of the experiment. It is known that about 60 per cent. of the diplogen of the decomposed water goes into the hydrogen thus produced. The test was made in conjunction with experiments Nos. 3 and 5. The results were clearly negative; the water samples produced by burning [14] the hydrogen showed density shifts of -13 and $+3$ parts in a million respectively, which is within the limit of error.

Hydrolysis.—Of the substances participating in the hydrolysis, the metallic sodium was introduced first into the reaction vessel. This was done by electrolysing 2 millimols. of sodium through the wall of an evacuated glass vessel.[15] The amount of sodium was computed from the quantity of electricity passed through the cell. Next, 100 mg. of water was distilled into the vessel containing the sodium, and (in experiments 3 and 5) the escaping hydrogen burnt in a copper oxide oven, to test its diplogen content. Last, 1·8 millimols. of amyl acetate was distilled into the vessel, containing now a concentrated solution of sodium hydroxide. The vessel was then sealed off and heated for two days at about 70° C. Blank tests have shown that by this treatment practically complete hydrolysis is obtained.

Isolation of the Alcohol.—The hydrolysis being completed the reaction vessel was again attached to a vacuum apparatus and the excess of water, the amyl alcohol as well as any residues of unhydrolysed amyl acetate were distilled out; sodium acetate and excess of sodium hydroxide staying behind. The organic constituents of the distillate were extracted with pentane and pipetted out, the water remaining behind. The pentane solution was then introduced into a vacuum system and the pentane distilled off at $-80°$ C.

Dehydration of the Alcohol.—The amyl alcohol obtained on the evaporation of the pentane (possibly with some impurities of undecomposed amyl acetate and pentane in it) was evaporated and dehydrated by repeatedly passing it by means of a circulation pump over bauxite at 400° C. In this process a mixture of pentene and water was formed, from which the water was isolated by condensation at low temperatures, the pentene being pumped off.

Purification of the Water.—The water thus obtained still contains traces of organic compounds, which interfere with the density measurement. We successfully eliminated these impurities by repeatedly passing the water vapour by means of a circulation pump over a platinum wire heated to 1200° C. The gases formed in this process were pumped off and the water collected in a part of the apparatus unpolluted by organic vapours. The water thus produced contains traces of colloidal mercury from the pumps, manometers, etc. The mercury was removed by distilling the water into a vessel containing sulphur, and leaving it in contact with the sulphur over night. Finally the water was distilled from the sulphur at $-10°$ C. into a vessel cooled to $-30°$ C., from which it was subsequently distilled into the micropyknometer.

We are greatly indebted to Professor O. Hertz for his gift of the "shifted oxygen" water of which we made use in these experiments.

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[14] The burning of the hydrogen was kindly carried out by Dr. J. Horiuti by means of a copper oxide oven.

[15] We followed the procedure of L. Márton and E. Rostás (*Z. techn. Physik*, **10**, 52, 1929), which we found to be very convenient.

Summary.

A new method is described for the investigation of the mechanism of hydrolysis. It consists in the use as a hydrolysing agent of water containing an excess of the isotope O^{18}, and the subsequent determination of the isotopic ratio in the oxygen of the alcohol thus obtained.

In the case of the alkaline hydrolysis of primary amyl acetate it could be shown that the oxygen of the alcohol obtained was of ordinary isotopic composition, which proves that it is the acid-oxygen bond of the ester molecule which is broken in the hydrolysis.

Incidentally, our results prove that amyl alcohol, when subjected to a prolonged treatment with a concentrated solution of sodium hydroxide in water at 70° C. does not exchange its hydroxyl group with that of the water.

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