ART. XXIX.—*On the Hydrolysis of Esters of Substituted Aliphatic Acids;* by W. A. DRUSHEL and E. W. DEAN.

[Contributions from the Kent Chemical Laboratory of Yale Univ.—ccxxxv.]

4. *Ethyl Esters of Glycollic Acid and of Methyloxy, Ethyloxy and Propyloxy Acetic Acids.*

PREVIOUS work on the hydrolysis of the esters of aliphatic acids has been reviewed in the first paper* of this series. The substances which had been previously studied were the methyl, ethyl and propyl acetates, the methyl and ethyl esters of chloracetic acid, and the ethyl esters of di- and trichloracetic acids. The velocity of hydrolysis of isobutyl acetate had also been measured.

It was shown in this paper that the introduction of halogen into the acetyl radical lowers the rate of hydrolysis. It was also shown that the esters of different alcohols and any one acid differ but little in their velocities of hydrolysis in acid solution. The substances studied were the methyl, ethyl, propyl and isobutyl chlor- and bromacetates. In a second paper† it was shown that ethyl cyanacetate hydrolyzes more slowly than the chloracetate. From these results it would seem probable that the rate of hydrolysis bears some relation to the strength of the acids in esters and that this is in accord with the rule‡ stated by Nernst for the degree of hydrolysis of salts in general. Cyanacetic acid is about two and a half times as strongly dissociated as chloracetic, which in turn is about eighty times as strong an acid as acetic. It was shown, however, that this factor does not entirely account for the difference in reaction velocity of the esters.

In a third paper§ the results of work with alpha and beta chlor- and brompropionic esters are published. It was found here that the ester of the beta acid hydrolyzes more slowly than that of the alpha acid in the cases of both bromine and chlorine substituted derivatives. This is apparently an exception to the theory mentioned above, as the beta acids are weaker than the corresponding alpha acids.

A study has been undertaken recently to show the effect of the presence of hydroxyl and alkyloxy groups in fatty acid radicals on the rate of hydrolysis. The following esters are considered in this paper: ethyl glycollate, $CH_2OH.COOC_2H_5$; ethyl methyloxy-acetate, $CH_2OCH_3.COOC_2H_5$; ethyl ethyloxy-acetate, $CH_2OC_2H_5.COOC_2H_5$, and ethyl propyloxy-acetate, $CH_2OC_3H_7.COOC_2H_5$.

---

* This Journal, xxx, 72.

† This Journal, xxxiii, 27.

‡ Nernst, Theoretical Chemistry, p. 521.

§ W. A. Drushel, this Journal, xxxiv, 69.

Preparation of the Esters.—The preparation of these esters was attended with some difficulty, largely due to the impossibility of employing any very effective methods of purification. The glycollic and methyloxy esters in particular are very soluble, rendering it impracticable to wash them with water. The last two esters of the series are more satisfactory in their preparation, although small yields were obtained by the methods employed.

The glycollic ester was prepared according to the method of Schreiner,* which depends upon heating together sodium glycollate, ethyl chloracetate and absolute alcohol in a sealed tube at 150° to 160° for a day. The tubes were then opened and the ester purified by fractional distillation. The first attempts to prepare glycollic ester by this method proved unsuccessful. There seemed to be a great tendency on the part of the ester to break down into glycollic acid and this was very difficult to remove, although its boiling point is 30° above that of the ester. The presence of small quantities of water or free acid in the glycollate appears to prevent almost entirely the formation of the ester. By the use of absolutely neutral and carefully dried sodium glycollate we were able to prepare a small quantity of the ester, which boiled at a constant temperature of about 155° and was proven free of halogen. The boiling point given in the literature is 160°, but the fractions we obtained boiling at this temperature generally contained free acid. It does not seem probable, however, that the presence of traces of glycollic acid can noticeably affect the hydrolysis, as it is one of the products formed in the reaction and is a very weak acid.

The alkyloxy acetic esters were all prepared by the same general method, the action of sodium alcoholate on ethyl chloracetate. The reaction proceeds according to the following equation:

$$CH_2Cl.COOC_2H_5 + NaOR \rightarrow CH_2OR.COOC_2H_5 + NaCl.$$

In one case the mixture was allowed to react in ethereal solution, in the others an excess of absolute alcohol was used. The yields were rather poor, varying from 30 per cent to 35 per cent in the different cases. It seems possible that this may have been due to loss of ester while the excess of alcohol or ether was being distilled off, as the reaction is one which should go to completion.

The boiling points of the esters are given as follows: ethyl glycollate, 160°; ethyl methyloxy-acetate, 130°; ethyl ethyloxy-acetate, 152°, and ethyl propyloxy-acetate, 184·5°. The solubilities are not given in the literature. All but the propyloxy ester seem to be very soluble; the latter dissolves with a little difficulty in the quantities used in the hydrolysis.

---

* Ann. d. Chem. u. Pharm., cxcvii, 5.

Procedure.—The hydrolysis experiments were carried on in the thermostat described in the first paper[*] of the series. The temperature was regulated so that variations were never more than a tenth of a degree. The esters were hydrolyzed in 250^{cm^3} flasks, which were filled to the mark with decinormal hydrochloric acid and warmed to the temperature of the thermostat before starting the reaction. The esters were measured out in quantities of about $2·5^{cm^3}$ from a graduated pipette. At regular intervals 25^{cm^3} portions of the reaction mixture were removed by means of a pipette, run into cold water, and immediately titrated with decinormal barium hydroxide solution. Phenolphthalein was used as an indicator.

Experiments were carried on at 25·2°, 35°, and 45°, duplicates being obtained in all the cases. Calculations were made by using the titration formula for reactions of the first order. Figures are given below for the series which gave the most regular constants. Averages of duplicate series are also recorded.

TABLE I.

Hydrolysis at 25·2°. N/10 HCl.

Time (minutes)	Ethyl Acetate 10^5K	Ethyl Glycollate 10^5K	Ethyl Alkyloxy Acetates		
			Methyloxy 10^5K	Ethyloxy 10^5K[†]	Propyloxy 10^5K[†]
120	63·6	71·0	---	37·4	34·1
240	67·0	69·5	36·3	36·4	36·0
360	64·9	69·6	39·9	36·5	35·6
600	64·2	(79·8)	41·8	35·4	35·7
840	64·9	71·9	36·7	36·3	36·3
1380	65·6	69·9	38·2	36·5	36·9
2040	65·0	70·6	37·7	35·2	35·9
3180	---	---	36·0	---	---
Averages...	64·7	70·4	38·1	36·2	35·8
Averages... (duplicate)	64·9	68·5	38·9	36·1	35·8
Hydrolysis at 35°					
90	(155·5)	171·1	89·5	(80·5)	(71·8)
180	158·8	184·0	89·5	85·3	(78·9)
360	163·7	183·1	88·4	87·2	82·1
600	162·1	176·1	90·9[‡]	88·3[‡]	85·4[‡]
900	162·8	168·0	90·4	87·2	85·3
1440	166·4	166·9	90·5	87·5	86·8
2160	(174·0)	160·5	92·3	87·9	86·8
Averages..	162·7	172·8	90·2	87·2	85·3
Averages.. (duplicate)	162·6	166·2	90·0	87·5	84·0

[*] Loc. cit.

[†] These constants for 25·2° are calculated from series run at 25·0°. Time intervals are slightly different.

[‡] Time interval, 700 minutes.

TABLE I (continued).

Hydrolysis at 45°.

30	372	(366)	(252)	227	(174)
60	377	(360)	232	218	205
90	378	391	230	214	205
150	375	390	225	218	215
270	(338)	391	227	217	215
450	376	394	226	215	217
630	366	393	225	216	216
Averages	374	392	227	218	212
Averages (duplicate)	374	385	226	217	212

The constants in parentheses are not counted in the averages.

TABLE II. Summary.

Temperature	25·2°		35°		45°	
	10^5K I	10^5K II	10^5K I	10^5K II	10^5K I	10^5K II
Ethyl acetate	64·7	64·9	162·7	162·6	374	374
Ethyl glycollate	70·4	68·5	172·8	166·2	392	385
Ethyl methyloxy-acetate	38·1	38·9	90·2	90·0	227	226
Ethyl ethyloxy-acetate	36·2	36·1	87·2	87·5	218	217
Ethyl propyloxy-acetate	35·8	35·8	85·3	84·0	212	212

The temperature coefficient varies between 2·3 and 2·5 for an increase of ten degrees. Average, 2·4.

Summary.

(1) Ethyl glycollate has a greater reaction velocity than ethyl acetate when hydrolyzed in acid solution. This would indicate that the presence of the hydroxyl group in an ester accelerates its decomposition.

(2) The methyloxy, ethyloxy, and propyloxy esters hydrolyze more slowly than the acetate, indicating a retardation caused by the presence of an alkyloxy group. This retardation increases with the size of the alkyl radical in the substituted group, the difference, however, being less marked between the ethyloxy and propyloxy than between the methyloxy and ethyloxy esters.

In a later paper we expect to show the effect of the presence of a second hydroxyl group in the acyl radical, and also the result of changing the substituted group from the alpha to the beta position. This work will involve the hydrolysis of esters of glyceric, lactic, and hydracrylic acids.