acetate solutions, a precipitate appeared, and the reaction was also completed sooner, with the malonic derivative.

Oxaloacetic Ester.—With an 8% acetate solution the reaction began at once, and was finished in several minutes; with the chlorohydrate solution it was complete in about 5 minutes. The addition of hydrochloric acid of the concentration 0.5 *N* decreased the velocity somewhat, but a considerable precipitate had formed in 5 minutes, and, even after concentration to 10 *N* hydrochloric acid, the reaction was well advanced in a half hour.

The crystalline semicarbazone was crystallized several times from hot water, and then melted at 162°. For analysis it was dried at 100°.

Subs., 0.1546 g.; CO_2, 0.2508 g.; H_2O, 0.0885 g.

Calc. for $C_9H_{15}O_5N_3$: C, 44.1; H, 6.1. Found: C, 44.2; H, 6.4.

Benzoylacetic Ester.—Crystals appeared in about 30 minutes with an 8% acetate solution; with the monochloroacetate a slight precipitate in an hour, and the reaction was complete in 3 hours. With an 8% chlorohydrate solution a few crystals were shown in 2 hours, and, although the reaction was well advanced in 4 hours, it was not completed until 2 days.

This product was recrystallized from hot water, and then melted at 125° with dec.

Subst., 0.2661 g., dried at 100°; N, 39.1 cc. at 17° and 737 mm.

Calc. for $C_{12}H_{15}O_3N_3$: N, 16.8. Found: 16.6.

CAMBRIDGE, MASSACHUSETTS.

[CONTRIBUTION FROM THE KENT CHEMICAL LABORATORY OF YALE UNIVERSITY.]

THE PREPARATION AND HYDROLYSIS OF ESTERS DERIVED FROM THE SUBSTITUTED ALIPHATIC ALCOHOLS.

BY GEORGE R. BANCROFT.

Received November 20, 1918.

In a recent paper[1] published from this laboratory an account has been given of the preparation of esters derived from the α and β substituted ethyl alcohols and of an investigation of the effect of their constitution upon the rate of hydrolysis. It was shown by a study of α-chloroethyl acetate, α-chloroethyl propionate, and α-ethoxyethyl acetate that the substitution of halogen or an alkoxyl group in the α-position of the alkyl radical of an ester accelerates the decomposition of the ester to such an extent that the reaction velocity cannot be measured. In the case of all three esters of this type that were hydrolyzed acetaldehyde formed one of the hydrolysis products. It was further observed that the substitution of hydroxyl, methoxyl, ethoxyl, chlorine and bromine, in the β-position of the ethyl radical of ethyl acetate, produces a considerable retardation of the rate of hydrolysis. The hydroxyl and ethoxyl groups, and

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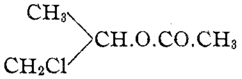
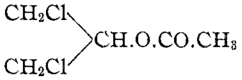
[1] *Am. J. Sci.*, 44, 371–380 (1917).

chlorine produced practically the same degree of retardation; methoxyl and bromine a somewhat smaller retardation. In preparing the esters necessary for this study it was found that the β-hydroxyethyl acetate may be obtained by refluxing equimolecular quantities of ethylene glycol and glacial acetic acid for eight hours over twice the theoretical quantity of anhydrous copper sulfate; and that β-ethoxyethyl alcohol is formed by digesting equimolecular quantities of β-bromoethyl acetate and sodium ethylate for half an hour in alcoholic solution.

In the present article this investigation has been extended to the study of esters derived from halogen substituted propyl alcohols, and the results are here given to show the effect of this substitution in the alkyl portion of the esters upon the rate of hydrolysis.

The following esters were prepared and hydrolyzed:

Unsymmetrical β-monochloroisopropyl acetate,	 $\begin{matrix}CH_3\\CH_2Cl\end{matrix}\!\!>CH.O.CO.CH_3$
Symmetrical β,β′-dichloroisopropyl acetate,	 $\begin{matrix}CH_2Cl\\CH_2Cl\end{matrix}\!\!>CH.O.CO.CH_3$
Unsymmetrical β,γ-dichloropropyl acetate,	$CH_2Cl.CHCl.CH_2O.CO.CH_3$
Unsymmetrical β,γ-dibromopropyl acetate,	$CH_2Br.CHBr.CH_2.O.CO.CH_3$

Preparation of Materials.

Symmetrical β,β′-dichloroisopropyl acetate was prepared by treating the β,β′-dichlorohydrin of glycerol, which was in stock, with acetyl chloride in slight excess of the theoretical amount by the method of Henry.[1] The pure ester boiling at 201–203° was obtained by fractionation. The halogen content of the ester was also determined as a further test of the purity of the substance.

Chlorine found: I, 41.45%; II, 41.92%. Chlorine calculated: 41.47%.

Unsymmetrical β,γ-dichloropropyl acetate was prepared by combining equimolecular quantities of the chlorohydrin and acetyl chloride according to R. de la Acena.[2] The ester purified by fractional distillation, boiled at 197–198°. The halogen content was found by analysis.

Chlorine found: I, 40.33%; II, 40.59%. Chlorine calculated: 41.47%.

β,γ-Dichloropropyl alcohol used in the preparation of this ester was obtained by passing dry chlorine gas into allyl alcohol at 0°, until the theoretical quantity of chlorine gas had been absorbed.

This method of preparation is discussed in the literature by Tollens,[3]

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[1] *Ber.*, **4**, 704 (1871); *Bull. sci. acad. roy. Belg.*, **42**, 261 (1906); *Rec. trav. chim.*, **26**, 89–105 (1907).

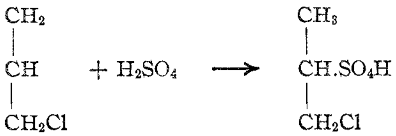
[2] *Compt. rend.*, **139**, 668 (1904).

[3] *Ann.*, **156**, 164 (1870).

Hübner and Müller,[1] Munder and Tollens.[2] The chlorohydrin was separated by fractionation, boiling at 182–183°. The yield from one hundred grams of allyl alcohol varied from eighteen to twenty-two grams. The allyl alcohol used was prepared by the method of Koehler.[3]

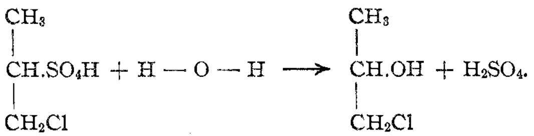
Unsymmetrical β,γ-dibromopropyl acetate was obtained by treating the β,γ-dibromohydrin, which was in stock, with acetyl chloride in slight excess. The ester purified by fractionation, boiled at 227–228°. Aschan[4] prepared this ester by treating the dibromohydrin with acetic anhydride.

β-Monochloroisopropyl alcohol was prepared from allyl chloride by the method of Oppenheim.[5] Two mols of concentrated sulfuric acid were gradually added to one mol of allyl chloride at 0°, when a thick reddish brown oily substance was formed, which became dark brown in color upon standing. The reaction seems to be additive in character, and may be represented by the following equation:



$$\begin{array}{l} \mathrm{CH_2} \\ | \\ \mathrm{CH} \\ | \\ \mathrm{CH_2Cl} \end{array} + \mathrm{H_2SO_4} \longrightarrow \begin{array}{l} \mathrm{CH_3} \\ | \\ \mathrm{CH.SO_4H} \\ | \\ \mathrm{CH_2Cl} \end{array}$$

The flask containing the reaction mixture was imbedded in snow and water, and after each addition of acid was shaken vigorously. The mixture was not permitted to warm up, because when the temperature was allowed to rise, clouds of hydrochloric acid gas were evolved and charring took place, indicating decomposition. After standing twenty-four hours, the dark-colored chloroisopropyl acid sulfate was diluted with eight to ten times its volume of water, and heated in a flask fitted with a reflux condenser on a water bath from one to two hours. The hydrolysis may be represented by the equation



$$\begin{array}{l} \mathrm{CH_3} \\ | \\ \mathrm{CH.SO_4H} \\ | \\ \mathrm{CH_2Cl} \end{array} + \mathrm{H-O-H} \longrightarrow \begin{array}{l} \mathrm{CH_3} \\ | \\ \mathrm{CH.OH} \\ | \\ \mathrm{CH_2Cl} \end{array} + \mathrm{H_2SO_4}.$$

The solution of the hydrolysis products was then distilled, and the distillate collected until a temperature of 128–130° was reached, when the distillation ceased and sulfur dioxide was evolved. The distillate was then neutralized with potassium carbonate, and the oily liquid separating was extracted with ether, salting out with sodium chloride. The ether

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[1] *Ann.*, **159**, 179 (1871).

[2] *Z. angew. Chem.*, **14**, 252 (1871).

[3] *Bull. soc. chim.*, [4] **13**, 1103 (1913).

[4] *Ber.*, **23**, 1827 (1890).

[5] *Ann. spl.*, **6**, 367 (1868); *Rec. trav. chim.*, **21**, 535–36 (1902).

extract was then dried over freshly fused potassium carbonate. The ether was distilled off, the residue passing over at 120–130°, which, when redistilled, boiled definitely at 126–127°, as described by Henry.[1]

In the account of this work done by Oppenheim,[2] the details of the preparation of the chloroisopropyl acid sulfate are not given. After carrying out the distillation of the solution containing the products of hydrolysis Oppenheim separated the β-monochloroisopropyl alcohol from the distillate by saturating it with potassium carbonate. Much better results were obtained by the author by neutralizing the solution with potassium carbonate at this point and extracting with ether as described above.

The β-monochloroisopropyl acetate was prepared by causing equimolecular quantities of β-monochloroisopropyl alcohol and acetyl chloride to react. The resulting ester was purified by fractionation, boiling at 149–150°, the same temperature reported by Henry.[1]

The allyl chloride used in the preparation of the unsymmetrical β-monochloroisopropyl alcohol was prepared by the method of Tollens,[3] by treating three mols of allyl alcohol with one mol of phosphorus trichloride. The allyl alcohol was placed in a distilling flask connected with a Liebig's condenser, and the phosphorus trichloride was added through a dropping funnel, the flask being cooled with ice-water and shaken vigorously from time to time as the addition was carried on. The reaction may be represented by the following equation:

$$3CH_2 = CH.CH_2OH + PCl_3 \longrightarrow CH_2 = CH.CH_2Cl + H_3PO_3$$

When all the phosphorus trichloride had been added the temperature of the water bath was maintained at 40° until all the hydrochloric acid was evolved, then raised sufficiently to distil off the fraction of allyl chloride boiling at 45–50°. During the distillation the flask was shaken vigorously at intervals to assist in volatilizing the allyl chloride and separating it from the thick and heavy phosphorous acid.

In performing this fractionation it was found that if the temperature were permitted to rise to the vicinity of the boiling point of allyl alcohol, an explosion occurred wrecking the apparatus and setting free red phosphorus, which was distributed through the distillation apparatus, while at the same time a strong garlic odor of phosphine or hydrogen phosphide was formed. DeMole[4] and Béchamp[5] record the same difficulty in carrying on similar work.

When the distillation was completed, the distillate was washed with water; the allyl chloride forming a layer on the surface of the water-solu-

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[1] *Rec. trav. chim.*, **22**, 209–10 (1903).

[2] *Ann. spl.*, **6**, 367 (1868).

[3] *Ann.*, **156**, 154 (1870).

[4] *Rec. trav. chim.*, **9**, 48 (1876).

[5] *Compt. rend.*, **42**, 227 (1856).

tion was removed by a separatory funnel, dried over calcium chloride, and redistilled, boiling at 46–47°.

Meeting with the above-mentioned difficulty in the method of procedure just described, another treatment was adopted with satisfactory results. The procedure in this case was based upon the fact that allyl chloride is insoluble in water, while phosphorous acid is soluble. The allyl alcohol was placed in a flask fitted with a reflux condenser and the phosphorus trichloride was added by means of a dropping funnel supported by a grooved cork in the upper end of the condenser. The flask was held in a water bath filled with ice-water, and shaken at intervals during the addition of the chloride of phosphorus. When the addition was complete the reaction mixture was refluxed for an hour, permitted to cool, and washed with a sufficient quantity of water to remove the phosphorous acid. The allyl chloride was then separated, dried and redistilled as already described in the former procedure.

The latter method of treatment seemed to be very satisfactory, and the yield of this method showed a slight increase over that of the first, due to the fact that a small amount of the allyl chloride was held back from distillation by the phosphorous acid. This was shown by dissolving up the phosphorous acid left as a residue after the distillation in the first process. The yield obtained by treating allyl alcohol with the phosphorous trichloride varied from 39.4% to 37.8% of the theoretical.

Hydrolysis of Esters.

Esters Derived from Halogen Substituted Propyl Alcohols.—These esters were hydrolyzed in decinormal hydrochloric acid by the methods already outlined[1] in connection with the hydrolysis of ester derived from the β-substituted ethyl alcohols. Hydrolysis measurements were made of the β,β′-dichloropropyl acetate and the β,γ-dichloropropy acetate at 25°, 35° and 45°, and of the β-monochloroisopropyl acetate at 35° and 45°, and constants were calculated for these esters as may be seen in Table I, and these results are further summarized in Table II.

Table I.—Hydrolysis of Chloro-Substituted Propyl Acetates in Decinormal Hydrochloric Acid.

Temperature.	35°.	45°.	25°.	35°.	45°.	25°.	35°.	45°.
Time in minutes..........	1325	438	2877	630	216	3146	630	210
$k \times 10^5$..................	75.5	(158)	26.4	(36.6)	(78)	(29.7)	(67.4)	(165)
	74.4	182	25.2	65.3	165.0	27.5	83.3	202
	75.4	184	26.6	67.7	166.0	27.8	84.9	201
	74.8	184	27.6	66.6	165.0	27.9	83.1	200
	75.5	188	26.3	67.7	165.0	28.5	83.1	203
	75.0	185	26.6	65.7	167.0	27.9	83.0	206
	75.6	186	26.0	67.1	166.0	..	..	...
Averages.................	75.2	185	26.4	66.7	166.0	27.9	83.4	202
Averages (duplicate).......	75.5	186	26.8	66.8	165.0	27.8	83.2	203

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[1] *Am. J. Sci.*, **44**, 371–380 (1917).

TABLE II.—SUMMARY.

	$k \times 10^5$.			Temperature coefficients.	
Temperature.	25°.	35°.	45°.	25–35°.	35–45°.
Ethyl acetate	64.7	162.1	379	2.5	2.3
	64.8	161.9	376		
β-Chloroethyl acetate	46.5	117.6	275	2.5	2.3
	47.2	117.6	275		
β-Bromoethyl acetate	55.1	134.5	298	2.4	2.2
	56.5	134.8	298		
Propyl acetate	67.1	167.8	386	2.5	2.3
	66.8	167.0	384		
β-Chloroisopropyl acetate	..	75.2	185	...	2.4
	..	75.5	186		
Symmetrical β,β′-dichloroisopropyl acetate	26.4	66.7	166	2.5	2.5
	26.8	66.8	165		
Unsymmetrical β,γ-dichloropropyl acetate	27.9	83.4	202	2.9	2.4
	27.8	83.2	203		

The dichloro-substituted propyl acetates were found to be soluble in water only to the extent of about four cubic centimeters per liter. The β,γ-dibromopropyl acetate was much less soluble, making it impossible to dissolve enough of this ester in decinormal hydrochloric acid to make satisfactory velocity measurements. The β-monochloroisopropyl acetate proved to be more soluble than the dichloro-substituted propyl acetates, eight cubic centimeters of this ester dissolving in one liter of water.

In the case of the dichloro-substituted propyl acetates one cubic centimeter of each ester was dissolved in 250 cm³. of decinormal hydrochloric acid previously warmed in the thermostat to the required temperature. The flask was then vigorously shaken, and as soon as the ester was completely dissolved, 25 cm³. of the reaction mixture were withdrawn and titrated with decinormal sodium hydroxide, using phenolphthalein as an indicator. Further titrations were made from time to time as already described[1] in the preceding series of esters hydrolyzed, from which constants were determined. By making occasional titrations with decinormal silver nitrate it was shown that there was no splitting out of halogen at 25°, 35° and 45°.

Two cubic centimeters of the β-monochloroisopropyl acetate were dissolved in 250 cm³. of decinormal hydrochloric acid, and hydrolysis measurements were made as in case of the other esters. On titrating the portions of the reaction mixture withdrawn at the intervals recorded in Table I, with decinormal sodium hydroxide and then with silver nitrate, it was found that no halogen was liberated in the titrations made at 35°. At 45° in the final titration there was a small amount of halogen acid set free, for which correction was made in calculating the constants.

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[1] *Am. J. Sci.*, [4] **44**, 371–380 (1917).

The velocity constants recorded in Table I were calculated by using the titration formula for monomolecular reactions:

$$k = 2.3/t\ [\log (T\infty - T_o) - \log (T\infty - T_n)]$$

where T_o is the initial titration, $T\infty$ the final titration, and T_n an intermediate titration all expressed in cubic centimeters of decinormal sodium hydroxide, and t represents the time interval in minutes between the initial titration T_o and that represented by T_n.

Discussion.

In this work, as has been found in previous experience, the substitution of halogen in the β-position of the alkyl radical of the ester produces a marked retardation on the rate of hydrolysis. This retardation is further increased by the substitution of two chlorine atoms in the β,γ-position, and becomes still greater when the chlorine atoms occupy the β,β′-position. The degree of the effect of these substitutions upon the rate of hydrolysis can be readily seen on consulting Table II.

On making a comparison of the respective rates of hydrolysis of β-chloroethyl acetate and β-chloroisopropyl acetate with those of their corresponding unsubstituted esters it is seen that the retardation in the case of the β-chloroisopropyl acetate is much greater. This may be attributed to the iso-character of this ester. It is also to be observed that the more effective retarding influences of the dichloro-substitution in the β,β′-position may be due to the iso-structure of the ester in this case. E. W. Dean[1] in his study of the effect of the substitution in the acyl radical of an ester upon the rate of hydrolysis found that substituted and unsubstituted isobutyrates decompose more slowly than the corresponding normal esters. This investigation seems to furnish further evidence of the retarding influence of the iso-structure upon the rate of hydrolysis of the ester.

The retarding effect produced by the substitution of halogen in the β-position of the alkyl radical forms a striking contrast to the accelerating influence produced by substitution in the α-position, where the decomposition of the ester is promoted to such an extent that the rate of hydrolysis is not measurable. As a result of this study it is seen that the position of the halogen with respect to the carboxyl group has an important influence upon the hydrolysis. On making a comparison of the results found in this investigation with those obtained by Drushel,[2] in studying halogen substitution of the acyl radical of an ester, it is interesting to note that substitution in the α-position of either the alkyl or the acyl radical of an ester produces a decided acceleration of the rate of hydrolysis, but that this acceleration is much greater in the case of the alkyl substitution.

[1] *Am. J. Sci.*, [4] **37**, 331–338 (1914).

[2] *Idem.*, [4] **34**, 69–74 (1912).

The temperature coefficients for an increase of ten degrees show very little variation. An exception is found in the case of the β,γ-dichloropropyl acetate between 25° and 35°, where the coefficient seems to be 2.9.[1]

Summary.

1. A convenient method of procedure is introduced for the treatment of allyl alcohol with phosphorus trichloride in the preparation of allyl chloride based upon the insolubility of allyl chloride and the solubility of the phosphorous acid produced in the process.

2. In preparing β-monochloroisopropyl alcohol, Oppenheim brought about the separation of this alcohol by saturating the distillate obtained from the solution of hydrolysis products with potassium carbonate. It was found in performing this operation that a more convenient and complete separation was effected by salting out the alcohol with sodium chloride, and extracting with ether.

3. Substitution of chlorine in the β-position of the alkyl radical of the ester produces a marked retardation of the rate of hydrolysis. Substitution of two chlorine atoms in the β,γ-position produces a greater and in the β,β'-position a still greater retardation.

4. Evidence is furnished to show that the iso-structure in the molecule of an ester produces a retarding influence on the rate of hydrolysis.

The writer is indebted to Professor W. A. Drushel for his coöperation in this work.

[CONTRIBUTION FROM THE COLOR LABORATORY, UNITED STATES BUREAU OF CHEMISTRY, WASHINGTON, D. C.]

THE PREPARATION OF SODIUM *p*-HYDROXYPHENYLARSONATE.

BY JAMES B. CONANT.

Received November 22, 1918.

The importance of the aromatic arsenic acids is every day becoming more evident. Many of them have been found to be useful drugs. Their preparation is a necessary step in the synthesis of many other aromatic arsenic compounds which have the most valuable therapeutic properties, for example, the widely used Arsphenamine ("Salvarsan"). The reaction by which the arylarsenic acids may be prepared are, thus, of considerable practical interest. About seven different methods have been employed with more or less success, depending largely on the particular compound desired. Of these methods the most direct is the replacement of hydrogen by the arsenic acid group, a reaction which takes place when certain aromatic substances (phenols and amines) are heated with arsenic

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[1] See Table II.