254. *Reaction Kinetics and the Walden Inversion. Part III. Homogeneous Hydrolysis and Alcoholysis of α-Bromopropionic Acid, its Ester and Anion.*

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The kinetics-controlled stereochemical examination of the substitution of Hal by OR is here continued for a group of cases, in which, besides hydrogen and alkyl groups, a carboxyl group in one of its various modifications is attached to the seat of substitution. The reactions studied were the methoxylation or hydroxylation or both of methyl α-bromopropionate, non-ionised α-bromopropionic acid and the α-bromopropionate ion.

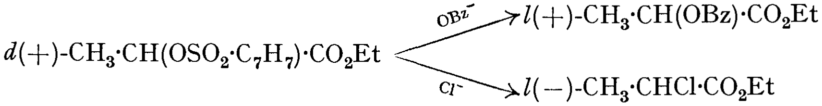
The determination of the relationship between configuration and sign of rotation, and the fixing of maximal rotatory powers, presented no difficulty. Each of the reactions to be examined for the optical effect was examined kinetically. A study was made of salt effects, which are shown, both experimentally and theoretically, to be opposite for bi- and uni-molecular substitutions, and to afford, therefore, an auxiliary criterion of mechanism, especially valuable when rates and reaction orders are not decisive. The methoxylation of methyl α-bromopropionate is a second-order reaction in alkaline solution, and first-order in acidic solution. In the alkaline hydroxylation and methoxylation of the anion, second- and first-order reactions take place side by side. The hydroxylation of the non-ionised bromo-acid is a first-order process. We here use, as is customary, the terms " second " and " first order " to indicate the type of kinetic equation which a reaction follows; the terms " bimolecular " and " unimolecular " relate to mechanism, as has already been illustrated (this vol., pp. 1177, 1187); we have also seen that there is not always a simple and exclusive correspondence between order and mechanism. In the present series of examples the kinetically second-order reactions are all mechanistically bimolecular, and so also are the first-order reactions of the ester and undissociated acid; but the first-order reactions of the anion are unimolecular.

The optical investigation was complicated by racemising processes independent of the substitution, and these had to be sorted out. This done, it was found that the

five bimolecular reactions invert configuration whilst the two unimolecular reactions retain it, and that in no case is there any detectable racemisation definitely attributable to substitution by any one mechanism; although, of course, the concurrence of two mechanisms which produce two opposite stereochemical effects will cause racemisation. Quantitative particulars are given, together with a conspectus of the results of Parts I—III.

In this communication we report on steric orientation, under conditions defined with respect to reaction kinetics, in hydrolytic and alcoholytic replacements of the halogen atom in α-bromopropionic acid, its anion, and methyl ester.

By definition, *d*-lactic acid is that lactic acid which gives dextrorotatory salts, $(+)CH_3{\cdot}CH(OH){\cdot}CO_2^-$. The acid itself is lævorotatory, $(-)CH_3{\cdot}CH(OH){\cdot}CO_2H$, but gives dextrorotatory methyl and ethyl esters $(+)CH_3{\cdot}CH(OH){\cdot}CO_2R$, dextrorotatory methyl and ethyl ethers, $(+)CH_3{\cdot}CH(OR){\cdot}CO_2H$, and dextrorotatory esters of these ethers, $(+)CH_3{\cdot}CH(OR){\cdot}CO_2R$. Its ethyl ester gives a dextrorotatory acetyl derivative, $(+)CH_3{\cdot}CH(OAc){\cdot}CO_2Et$, a lævorotatory benzoyl derivative, $(-)CH_3{\cdot}CH(OBz){\cdot}CO_2Et$, and a dextrorotatory *p*-toluenesulphonyl derivative, $(+)CH_3{\cdot}CH(OSO_2{\cdot}C_7H_7){\cdot}CO_2Et$. All these compounds can be prepared from lactic acid without exchanging a bond attached to the asymmetric carbon atom, and hence all must be configuratively related: they are "*d*"-derivatives. Kenyon, Phillips, and Turley have shown (J., 1925, **127**, 399) that the (+)*p*-toluenesulphonyl derivative on treatment with potassium benzoate yields the (+)benzoyl compound. This reaction involves an inversion, since its product belongs to the *l*-series, and it may therefore be assumed that the corresponding reaction with lithium chloride would also give a product belonging to the *l*-series:*



$$\begin{tikzcd} & l(+)\text{-}CH_3{\cdot}CH(OBz){\cdot}CO_2Et \\ d(+)\text{-}CH_3{\cdot}CH(OSO_2{\cdot}C_7H_7){\cdot}CO_2Et \arrow[ur, "OBz^-"] \arrow[dr, "Cl^-"'] & \\ & l(-)\text{-}CH_3{\cdot}CHCl{\cdot}CO_2Et \end{tikzcd}$$

The chloro-ester thus obtained was lævorotatory, and hence a dextrorotatory ethyl α-chloropropionate is configuratively related to *d*-lactic acid. Similar experiments with sodium bromide and potassium iodide as reagents showed that dextrorotatory ethyl α-bromopropionate and ethyl α-iodopropionate have the same kind of configuration as *d*-lactic acid. Dextrorotatory α-chloropropionic acid and dextrorotatory methyl and ethyl α-chloropropionates can be shown by hydrolysis, esterification, or preparation through a common acid chloride to be configuratively related. Dextrorotatory α-bromopropionic acid can be similarly connected with its dextrorotatory methyl and ethyl esters (part of the evidence is in this paper). Hence all these halogenopropionic acids and their esters, when dextrorotatory, are configuratively related to *d*-lactic acid. These are the conclusions on which we base the interpretation of our observations of rotatory power. Identical conclusions have been reached in other ways by Freudenberg, Markert, and Lux (*Ber.*, 1927, **60**, 2447; 1928, **61**, 1083), Kuhn and Wagner-Jauregg (*Ber.*, 1928, **61**, 481, 504), and Bancroft and Davis (*J. Physical Chem.*, 1931, **35**, 1624), and directly opposing conclusions by Levene and Haller (*J. Biol. Chem.*, 1929, **81**, 703; **83**, 185) and Clough (J., 1918, **113**, 551; 1926, 1674).

One of our main objects was to compare the steric orienting influence of an esterified and unesterified carboxyl group, since special effects were expected to arise from the development of an anionic charge on the latter. It was found impossible to displace the halogen atom in methyl α-chloro- or α-bromo-propionate by treatment with potassium hydroxide in aqueous acetone without first completely hydrolysing the carbomethoxyl group; and even α-chloropropionamide on treatment with aqueous alkali underwent almost complete hydrolysis with respect to the carboxylamide group before displacement of the

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* This type of argument distinguishes a number of Kenyon's later papers on other optically active compounds; it was not used explicitly in relation to the comparatively early work cited. It is employed or accepted by us always with the reservation that there must be definite reason for presuming that the reactions taken as analogous are actually of the same kinetic type. A case in which this requirement was not fulfilled was mentioned in Part II.

halogen could be observed. We therefore commenced this investigation with methoxylation instead of hydroxylation as the substitution process, since the former could be studied both for methyl α-bromopropionate and for the α-bromopropionate ion without altering the form of the carboxyl group in either compound. Later we devised an investigation of hydroxylation which confirms and supplements the study of methoxylation.

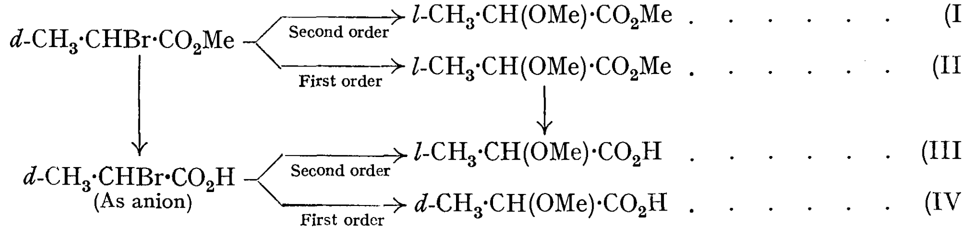
(A) *Methoxylation.*

It will be convenient to give a qualitative summary of the observed relations, and then, for each of the reactions mentioned, to add the necessary quantitative particulars.

The methoxylation of methyl and of sodium α-bromopropionate has been effected by means of sodium methoxide in absolute methyl-alcoholic solution. The following transformations have been realised :

SCHEME A.

Methyl Alcoholysis of Methyl and Sodium α-Bromopropionate.



In this scheme the symbols *d* and *l* represent, not only the rotations, but also the configurations. It will be seen that three of the methoxylation reactions lead to inversion and one to retention of configuration.

Reaction I (*Ester + Sodium Methoxide*).—We may now consider the methoxylation of the methyl ester in further detail. The reaction in the absence of sodium methoxide is extremely slow. In the presence of sodium methoxide (0·2—0·5*M*) the methoxylation is rather rapid and fairly accurately of the second order (reaction I), although the constants seem to be slightly higher in the more concentrated methoxide solutions. The specific rate at 25·0° may be taken as 0·00042 sec.^{-1} g.-mol.^{-1} l. over the range of concentrations used for the optical investigation. This means that if the original solution were 0·5*M* with respect to each reagent the period of half-change would be 80 minutes.

The optical effect is typically represented by the following record. A solution 0·478*M* with respect to both sodium methoxide and methyl α-bromopropionate having $\alpha_D^{20^\circ}$ (l = 10 cm.*) −53·2° was kept at 25° for 19 hours, by which time 93% of the material must have undergone reaction; the methoxy-ester, which was then isolated and purified, had $\alpha_D^{20^\circ}$ +1·94°. This figure requires correction for the incompleteness of conversion. We shall show later that during the methoxylation the bromo-ester independently undergoes racemisation, and does so at such a rate that the 7 mols. % remaining after 19 hours would be quite inactive. If this material also had been methoxylated the isolated product would have been diluted with a corresponding amount of inactive methoxy-ester, and the rotation would have been only 93% of what was found. We cannot describe this reduced value as the rotation which the methoxy-ester would have if isolated after infinite time, because the methoxy-ester itself undergoes a slow racemisation. Therefore we shall take as the corrected result that rotation which would be observed if the conversion proceeded naturally during the period of the experiment, and was then completed suddenly. The rotations are then as follows :

$$(\alpha_D^{20^\circ} -53{\cdot}2^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2Me \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2Me\ (\alpha_D^{20^\circ} +1{\cdot}80^\circ) \quad . \ . \ . \quad (I)$$

These figures indicate that much racemisation has occurred, and we can ascertain how much. A lower limit to the rotation of optically pure methyl α-bromopropionate is set by the fact that we have prepared a specimen having $\alpha_D^{20^\circ}$ +68·6°. A more accurate figure follows if we adopt Ramberg's carefully established value $\alpha_D^{20^\circ}$ 49° for the rotatory

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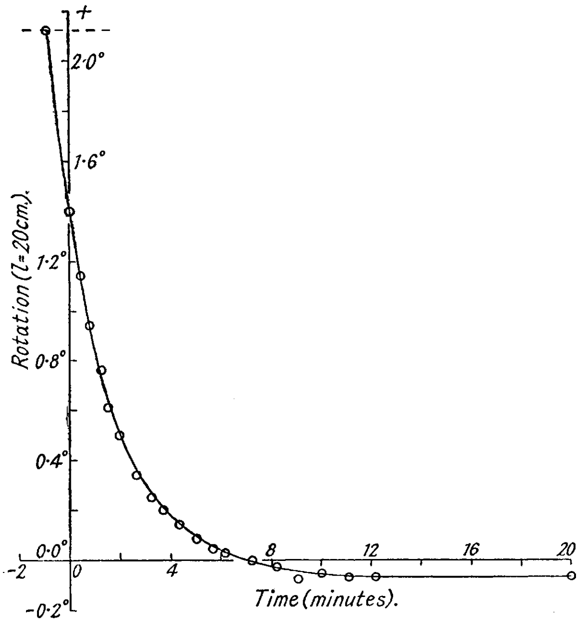
* All rotations relate to l = 10 cm. throughout, unless otherwise specified.

power of α-bromopropionic acid (*Annalen*, 1909, **370**, 234); because we have hydrolysed the ester to the acid under conditions which preclude appreciable racemisation. The best value for the rotatory power of methyl α-bromopropionate is thus $\alpha_{\rm D}^{20^\circ}$ 74°. The rotation of optically pure methyl α-methoxypropionate is $\alpha_{\rm D}^{20^\circ}$ 95° (Purdie and Walker, J., 1899, **75**, 485; Irvine, J., 1906, **89**, 935). It follows that in the experiment recorded above, a bromo-ester having 72% of its maximal rotation has given a methoxy-ester with only 1·90% of its maximal rotation, and that therefore the optically pure bromo-ester would have given a methoxy-ester with 2·65% of its proper rotatory power.

Now this racemisation might occur in three ways, *viz.*, before, during, or after the substitution. All the compounds with which we are concerned in this paper contain a potentially ionising hydrogen atom (α- to carboxyl), and hence are capable of undergoing a racemisation, catalysed by methoxide ions, which is nothing to do with replacement in which the methoxide ions engage. In so far as the loss of optical activity under consideration does not accompany substitution, we expect it to take place mainly before this reaction, because Wilson has shown (J., 1934, 98) that the rates of racemisations which involve hydrogen-ionisation are regularly related to the electron-affinity of the groups joined to the asymmetric atoms; and, as bromine has a higher electron-affinity than methoxyl, the bromo-ester should be more rapidly racemised than the methoxy-ester. We must determine how much racemisation can be accounted for as having occurred before and after substitution, in order to isolate that part which essentially depends on the substitution.

Fig. 1.



Fall of rotation of a solution of methyl *d*-α-bromopropionate (0·5*M*) and sodium methoxide (0·5*M*) in methyl alcohol at 25°.

Fig. 1 shows the variation with time at 25° of the rotation of a solution initially 0·508*M* with respect to both methyl α-bromopropionate and sodium methoxide. From this curve it is qualitatively obvious that most of the racemisation observed in the substitution must have taken place in the bromo-ester before substitution occurred: the rotatory power falls to zero in 7·9 minutes when only 9·0% of material has undergone methoxylation; and after a further equal period it becomes practically constant although only 16·7% of substitution has occurred. The methoxy-ester which was isolated was formed in a reaction which occupied many hours, but its optical activity must have arisen entirely from the small amount that was formed in the first few minutes, when the bromo-ester still retained an appreciable activity.

Considering more quantitatively the experiment in which the change of rotation with time was followed, we note that rotation at any instant is the sum of two partial rotations, one due to the bromo-ester and the other to the methoxy-ester. The partial rotation of the bromo-ester can be considered to be the product of its instantaneous concentration and instantaneous rotatory power. We define rotatory power for this purpose as the rotation which would be observed in the same polarimeter tube if material of the same quality in unit concentration alone contributed to the rotation. The partial rotation of the methoxy-ester is a similar product of a concentration and a rotatory power. All four quantities, the two concentrations and the two rotatory powers, vary with time. In the case of rotatory powers, moreover, two kinds of instantaneous value must in general be distinguished, *viz.*, that belonging to the whole of the compound present at the instant under consideration, and that applying to a small increment of material produced at that instant. For the bromo-ester, which is being destroyed all the time, the two sorts of rotatory power, that of the whole and that of the (negative) increment, are the same; but for the methoxy-ester, which is being produced continuously from bromo-ester of varying rotatory power, they are in general different.

The time-variation of the concentration of bromo-ester is known, because we have studied the reaction kinetically. The time-variation of the rotatory power of the bromo-ester depends on an unknown rate-constant for the catalysed racemisation of this substance, and on the concentration of the catalysing methoxide ions. This concentration is time-variable, but the law of the variation is known from our kinetic results. Hence the whole function giving the time-variation of the partial rotation due to bromo-ester can be expressed with the inclusion of one unknown rate constant.

The time-variation of the partial rotation of the methoxy-ester is due to two causes: first, the ester is being produced from bromo-ester of continually changing rotatory power; secondly, no sooner is the methoxy-ester formed than it begins to racemise. We have seen how to calculate the rotatory power of the bromo-ester present at any moment. The rotatory power of a small increment of methoxy-ester produced from the bromo-ester at that moment will bear a constant ratio to the rotatory power of the bromo-ester from which it is derived; it is indeed this ratio which we are chiefly interested to determine. The rotatory power of a newly formed increment of methoxy-ester will therefore be expressed by a function involving two unknown constants, the unknown rate-constant previously mentioned for racemisation of the bromo-ester and the required ratio of rotatory powers characterising the substitution. At a later time the rotatory power of this same small increment of methoxy-ester will have diminished on account of its racemisation, and we can calculate by how much, because, as mentioned later, we have determined the rate constant for the catalysed racemisation of the methoxy-ester by direct experiment, and we know the law of variation with time of the concentration of the catalysing methoxide ions. The whole amount of methoxy-ester present at any time contains the increments formed at all previous times, and hence a suitable integration will give the partial rotation of the methoxy-ester in terms of the two unknown constants.

Adding together the expressions for the two partial rotations we obtain an equation for the curve of Fig. 1; and by comparison with the experimental results we can evaluate the unknown constants.

As stated above, we directly determined the rate of racemisation of methyl α-methoxypropionate as catalysed by methoxide ions: the specific rate in methyl alcohol at 25° was 0·00000803 sec.$^{-1}$ g.-mol.$^{-1}$ l. The time of half-change in a solution 0·5*M* with respect to sodium methoxide would be 47·9 hours. Since in the methoxylation experiment half the original methoxide ions disappear in the first 80 minutes, it is qualitatively evident that racemisation of the methoxy-ester does not account for more than a small proportion of the total observed loss of optical activity.

As the detailed calculation corresponding to the foregoing analysis of the curve in Fig. 1 is rather complicated, we relegate it to an appendix. By fitting the theoretical equation to the curve we find the value 0·0148 sec.$^{-1}$ g.-mol.$^{-1}$ l. for the specific rate of racemisation of the bromo-ester by methoxide ions in methyl alcohol at 25°. If no methoxylation occurred, the time of half-change for the racemisation of the bromo-ester in a solution 0·5*M* with respect to sodium methoxide would be 1·55 minutes, a figure which may be compared with the 80 minutes half-change period for methoxylation.

The other unknown quantity, *viz.*, the ratio of rotatory powers characteristic of the substitution, is found to be substantially equal to the ratio of rotatory powers of the optically pure compounds, but with a negative sign on account of the inversion. We can calculate how much racemisation occurred in the bromo-ester and in the methoxy-ester under the conditions of the experiment in which after conversion the latter was isolated. If the original bromo-ester had been optically pure, then its racemisation prior to substitution would have led in a completed substitution to a methoxy-ester with 2·7% of its maximal optical activity. The racemisation of the methoxy-ester after its formation by substitution up to the moment at which the experiment was stopped must reduce the optical activity further to 2·6% of the maximum. Any racemisation *accompanying* substitution would reduce it further still. The observed optical activity, calculated to correspond to optically pure starting material, was 2·65% of the maximum. This activity leaves no margin for the occurrence of any appreciable racemisation in the act of substitution, which must therefore have taken place with a substantially complete inversion of configuration.

In order to estimate the degree of consistency obtainable by means of this derivation we carried out a second experiment with dextrorotatory bromo-ester and different initial concentrations. A solution 0·245*M* with respect to both sodium methoxide and the bromo-ester was kept at 25° for 70·0 hours, and the methoxy-ester was isolated and purified; it had $\alpha_D^{20^\circ}$ −1·06°. The bromo-ester, which originally had $\alpha_D^{20^\circ}$ +32·2°, must have been methoxylated to the extent of 96%. Correcting the rotation of methoxy-ester for incompleteness of conversion under the conventions used for the previous experiment, we find:

$$(\alpha_D^{20^\circ}\ +32{\cdot}2^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2Me \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2Me\ (\alpha_D^{20^\circ}\ -1{\cdot}02^\circ) \quad . \quad . \quad . \quad (I)$$

In this experiment a bromo-ester the rotation of which is 43% of its maximum gives a methoxy-ester with a rotation which is only 1·07% of its maximum; therefore under these conditions the optically pure bromo-ester would give a methoxy-ester with a rotation equal to 2·5% of its maximal value. Calculation shows that in this case the racemisation of an initially optically pure bromo-ester prior to substitution would lead to the formation of a methoxy-ester with 2·8% of its maximal rotation; and that racemisation of the methoxy-ester after its formation by substitution would reduce this value to 2·6%. In this case also, therefore, the experimental result leaves no margin for appreciable racemisation in the act of substitution.

Reaction II (*Ester + Methyl Alcohol*).—The first-order methoxylation of methyl α-bromopropionate (reaction II) is so slow in comparison with the second-order process that we could not observe the former in the presence of appreciable amounts of sodium methoxide; nor could it be studied at so low a temperature as 25°. It was therefore investigated in the absence of sodium methoxide and at 100°; the solution of the bromo-ester, although originally neutral, is acid with liberated hydrobromic acid throughout the course of the change. We have proved experimentally that under these conditions the reaction is kinetically of the first order, the rate constant being 0·00000295 sec.$^{-1}$: the period of half-change is 67 hours. However, although the rate law is obeyed fairly accurately over most of the reaction, disturbances affect the later stages in prolonged experiments. This is due to the action of the liberated hydrogen bromide on the solvent methyl alcohol, which it converts into methyl bromide and methyl ether, the water set free in this process causing hydrolysis of the methyl α-methoxypropionate and any remaining methyl α-bromopropionate with the production of free carboxylic acids. The etherification is catalytic in the sense that, given sufficient time, more methyl alcohol can be converted into ether than corresponds stoicheiometrically to the quantity of hydrogen bromide responsible for the change: the hydrogen bromide originally consumed in the formation of methyl bromide must be regenerated in the stage in which the ether is produced, the whole cycle resembling that which obtains in etherification with sulphuric acid as catalyst.

Experiments with optically active material were carried out in the first place by heating the bromo-ester at 100° for shorter times than those at which the disturbance mentioned becomes appreciable. The substitution was then only partial, and the methyl α-methoxypropionate and residual methyl α-bromopropionate were only partly separated. It was found that the methyl α-methoxypropionate produced from *d*-methyl α-bromopropionate was lævorotatory, even although the specimen examined still contained residual dextrorotatory bromo-ester. This showed qualitatively that substitution is accompanied by an inversion of configuration. In order to obtain quantitative results, we allowed the substitution to proceed nearly to completion, although, as explained above, hydrolysis of the carbomethoxyl group takes place under these conditions. However, preliminary experiments having shown that the bromo-ester is at least largely methoxylated before it is appreciably hydrolysed, we were able to carry the conversion of the bromo-ester through to the methoxy-acid, and to treat the optical results as relating essentially to a substitution of the bromo-ester.

Methyl α-bromopropionate having $\alpha_D^{20°}$ +29·6° was methoxylated by heating a 0·60*N*-solution in methyl alcohol at 100° for 230 hours. From the known rate of substitution it can be calculated that methoxylation should have taken place to the extent of 91%. During the subsequent isolation of the methoxy-acid a part of the remaining 9 mols.% of bromo-acid was eliminated: analysis showed the presence of 7·0% by weight or 4·5 mols.% of this substance. The rotation of the specimen, which therefore contained 95·5 mols.% of methoxy-acid, was $\alpha_D^{20°}$ —2·72°. The experiments and calculations described below will show that bromo-ester present in this specimen would not contribute appreciably to the observed rotation, and hence we can calculate the rotation which the methoxy-acid would have exhibited if the bromo-acid, an optically inactive diluent, had been completely removed. The proportion by volume of the diluent is 4·5%, and hence the corrected rotation of the methoxy-acid is —2·85°. However, the value in which we are really interested is, not the rotation of the methoxy-acid formed after 230 hours, but the rotation with which the acid would be found after completion of the substitution. Completion would replace the 9 mols.% of inactive bromo-compound by 9 mols.% of inactive methoxy-acid, and hence the rotation of the total methoxy-acid formed in a complete substitution would be only 91% of —2·85°. Our corrected result is therefore as follows:

$$(\alpha_D^{20°}\ +29{\cdot}6°)\ CH_3{\cdot}CHBr{\cdot}CO_2Me \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2H\ (\alpha_D^{20°}\ -2{\cdot}60°)\quad . \quad . \quad . \quad (II)$$

Evidently much racemisation has occurred. The rotation of optically pure methyl α-bromopropionate is $\alpha_D^{20°}$ 74° (p. 1211). Purdie and Irvine determined the rotation of optically pure methyl α-methoxypropionate, and we have hydrolysed the methyl ester to the acid under conditions which preclude perceptible racemisation. Combining the results, we find the maximal rotation of the acid to be $\alpha_D^{20°}$ 93·5°. From these data it can be calculated that under the conditions of the above experiment an optically pure bromo-ester would have given a methoxy-acid with 7·0% of its full rotation.

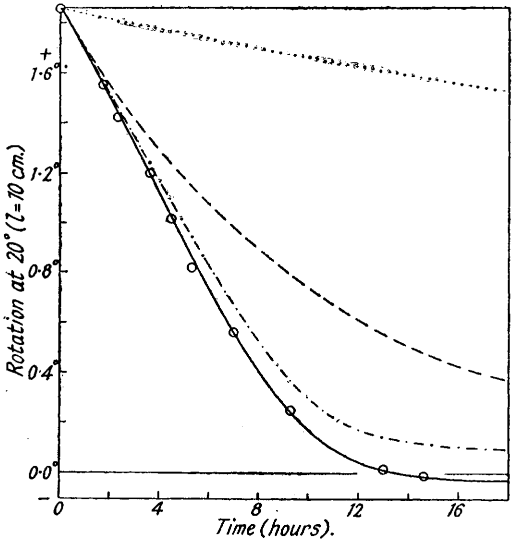
We have now to decide how much of the loss of optical activity represented by this figure occurs before, during, and after the substitution. Actually none occurs after substitution, the methoxy-ester and acid being optically stable under the experimental conditions. In order to find out how much takes place before substitution, it is necessary to know the rate of racemisation of the bromo-ester, and to this end we have studied the variation with time of the rotation of a methyl-alcoholic solution of the bromo-ester placed under the same experimental conditions. A solution, 0·60*N* with respect to the bromo-ester, was kept at 100°; and from time to time samples were withdrawn for the measurement of their rotation at the room temperature. The results are shown in Fig. 2.

It is qualitatively evident that most of the racemisation observed in the methoxy-compound which was isolated after 230 hours must have taken place prior to the substitution. The rotation–time curve falls to zero rotation in 14 hours, when, as we can calculate from the known rate of substitution, only 14% of the bromo-ester has been methoxylated. At this point the lævorotation of the methoxy-ester formed compensates the dextrorotation still remaining in the bromo-ester; but the former contribution must be small, as the " isolation " experiment shows, and hence the latter must be small also. It is not difficult to see that more than 90% of the optical activity of the bromo-ester must have been destroyed in 14 hours, even although 86% of the ester still remained unsubstituted.

We may next qualitatively consider the shape of the rotation curve, which is unusual: the curve runs nearly straight for much of its course, as though it represented a reaction of zero order; and then it turns rather sharply into the direction of the time axis.

We may simplify qualitative discussion by disregarding the small contribution of the methoxy-ester to the rotation, and considering the experimental curve as though it represented only the destruction of optically active bromo-ester by racemisation and substitution. We shall show eventually that the curve for partial rotation due to the bromo-ester runs as indicated by the chain-line in Fig. 2; but it is obvious at present that this curve will be quite close to the experimental curve, being, in fact, merely lifted slightly at the right-hand end in order to be asymptotic to the time-axis instead of to a line just below it.

FIG. 2.



The full-line curve represents the loss of optical activity from a 0·60*N*-methyl-alcoholic solution of methyl α-bromopropionate at 100°. Four effects contribute to produce this curve. The dotted curve shows the fall in the partial rotation of bromo-ester which would be caused by methoxylation only. Taking account of the hydrogen-racemisation in addition, we obtain the broken-line curve. Now, counting in the bromine-racemisation, we derive the chain-line curve, which represents the actual partial rotation due to bromo-ester. Allowance being made finally for the partial rotation of the methoxy-ester, we obtain a curve indistinguishable from the experimental curve.

Part of the fall of rotation due to bromo-ester arises from the disappearance of this substance in the first-order substitution. We know already that the rate constant for this reaction is 0·00000295 sec.$^{-1}$ (half-change 67 hours), and we can draw a curve (the dotted line in Fig. 2) to represent how the fall of rotation would run if this effect acted alone. Fixing attention for the moment on the *initial* rate of fall of rotation, we see that methoxylation accounts for only slightly more than 10% of the observed initial fall.

The remainder of the initial rate of decrease of the partial rotation of the bromo-ester is due to a first-order racemisation of the bromo-ester itself. This is the reaction which depends on the presence of an α-hydrogen atom (prototropy), and we may call it the " hydrogen-racemisation " in order to distinguish it from another racemising process mentioned later. Hydrogen-racemisation acting alone would lead to an exponential fall of rotation, and we can roughly evaluate the rate constant: continuing to neglect the partial rotation of the methoxy-ester, we may take the whole of the difference between the initial slopes of the experimental curve and of the curve calculated for the fall of partial rotation of bromo-ester due to methoxylation as representing the initial rate of hydrogen-racemisation. The rate constant thus obtained is 0·000025 sec.$^{-1}$ (half-change 7·7 hours). This value must be a little too high, but it is obvious that the rate of hydrogen-racemisation alone is about ten times greater than the rate of substitution.

In the alkaline methoxylation of the bromo-ester (Fig. 1) hydrogen-racemisation was very rapid. In the acid reaction now under consideration it is relatively very slow. Its slowness furnishes the opportunity for the incursion of another racemisation process, which is intrinsically rather slow, and was therefore not observed in the presence of the rapid, alkali-catalysed hydrogen-racemisation. This is the racemising attack of bromide ions on the bromo-ester, the bromide ions being, of course, those liberated in the methoxylation. This mode of racemisation depends, not on the presence of α-hydrogen, but on that of α-bromine: the bromide ion displaces the bromine atom with inversion in the well-known way. We can call this process the "bromine-racemisation." Its rate varies with time in a rather complicated way because the supply of one of the reactants (bromide ion) is dependent on a distinct reaction. However, one can see qualitatively what shape the reaction–time curve will have: initially the rate is zero because there are no bromide ions; and finally it is zero because there is no optically active bromo-ester. The rate must therefore pass through a maximum, and the reaction–time curve must be sigmoid with a horizontal asymptote at each extremity.

FIG. 3.

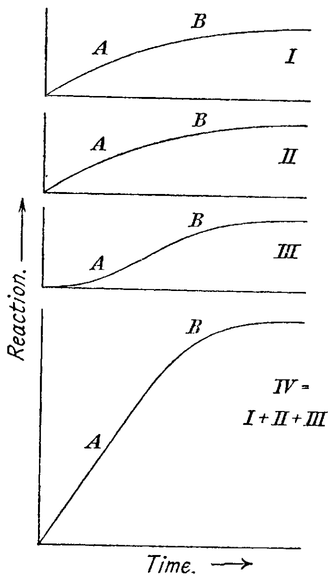


Illustration of the manner in which the substitution and two racemisations combine to produce the "hockey-stick" curve of Fig. 2.

These considerations provide the qualitative explanation of the initial linearity of the observed rotation–time curve and of its rather sharp turn near the time axis. There are three contributory effects—apart from the neglected partial rotation of the methoxy-ester. The first is the methoxylation, the reaction–time curve for which must be everywhere concave to the time axis (Fig. 3, I). The second is the hydrogen-racemisation for which the same statement is true (Fig. 3, II). The third is the bromine-racemisation, the reaction–time curve for which is sigmoid (Fig. 3, III). When these curves are compounded, then in the region marked A the curvature of III opposes the curvatures of I and II, so that the resultant curve is almost straight; whilst in region B the curvature of III reinforces the curvatures of I and II, and the resultant curve exhibits a rather sharp turn in the direction of the time axis (Fig. 3, IV). This curve, in which the ordinates are supposed to represent the amount of reaction, has to be turned upside down for comparison with the "hockey-stick" curve (Fig. 2) in which the ordinates are optical rotations.

Using our approximate value for the rate constant of the hydrogen-racemisation we can plot a curve to represent the way in which the partial rotation of the bromo-ester would fall owing only to the combined action of methoxylation and hydrogen-racemisation. The curve thus obtained will not be accurate because we neglected the partial rotation of the methoxy-ester in calculating the rate constant; nevertheless it must lie only slightly below the accurate curve, which, calculated as described below, is shown by a broken line in Fig. 2. The divergence of our approximate curve from the experimental curve gives an approximate measure of the rate of the bromine-racemisation. Initially, the difference of the ordinates of the two curves increases with the square of the time, *i.e.*, the difference of slope increases linearly with the time. The difference of slope represents the excess rate of loss of optical activity due to the bromine-racemisation. By comparing the time-rate of increase of this excess rate with the known time-rate of increase in the concentration of the attacking bromide ions we can estimate the rate constant. The value obtained is 0·00075 sec.$^{-1}$ g.-mol.$^{-1}$ l.

Having now obtained approximate values of the rate constants of the two racemisation processes, we can calculate approximately the proportion in which optical activity should be retained in the methoxy-ester formed at " infinite " time if no loss of activity occurred during the substitution itself. When we compare the value thus obtained with the percentage retention of activity derived from experiment, we find that the substitution must have been accompanied by a substantially complete inversion.

This approximate result now enables us to refine the whole of the previous calculations by taking into account the fourth factor which contributes to the observed rotation, *viz.*, the hitherto neglected partial rotation of the methoxy-ester. Assuming that each small increment of methoxy-ester has the same proportion of its maximal rotatory power (with inverted sign) as has the bromo-ester from which it was formed, we can calculate for any time the partial rotation of the methoxy-ester which has accumulated up to that time. Subtracting this partial rotation from the observed rotation, we obtain the corrected curve, represented by a chain-line in Fig. 2, for the partial rotation due to bromo-ester. By measuring the initial slope of this curve we obtain a more accurate value for the rate constant of the hydrogen-racemisation, *viz.*, 0·0000225 sec.$^{-1}$. From this value we can calculate a more accurate curve, the broken line in Fig. 2, for the fall in the partial rotation of the bromo-ester due to methoxylation and hydrogen-racemisation. From the divergence between this curve and that for the corrected partial rotation of bromo-ester, we can find a better value, 0·00076 sec.$^{-1}$ g.-mol.$^{-1}$ l., for the rate constant of the bromine-racemisation. Then, using these improved values, we can again calculate the proportion in which optical activity should be retained in a complete methoxylation if the only cause for loss of activity were racemisation prior to substitution. The answer is 7·3%. The observed value was 7·0%. These figures leave no room for any considerable racemisation as an *accompaniment* of the act of substitution, which therefore proceeds with substantially complete inversion.

The above reasoning can be checked by setting up a theoretical equation for the rotation–time curve, as we have done in the Appendix. Into this equation we can insert the values already derived for the rate constants of the methoxylation and two racemisations, and the ratio of rotatory powers characterising the methoxylation. The equation should now represent the observations throughout their whole range; and the test thus indicated is real, because we used only initial rates in order to calculate our rate constants. Actually the " theoretical " curve lies so closely on that obtained experimentally that they cannot be shown separately in Fig. 2.

Reactions III and IV (*Sodium Salt + Sodium Methoxide*).—Continuing the detailed description of the reactions formulated in Scheme A, the connexion of the rotatory powers of the bromo- and the methoxy-ester with those of the bromo- and the methoxy-acid obtainable from them by saponification is as shown by the following observed rotations :

$$(\alpha_D^{21°}\ +28{\cdot}9°)\ CH_3{\cdot}CHBr{\cdot}CO_2Me \longrightarrow CH_3{\cdot}CHBr{\cdot}CO_2H\ (\alpha_D^{18{\cdot}5°}\ +19{\cdot}1°)$$

$$(\alpha_D^{20°}\ -53{\cdot}7°)\ CH_3{\cdot}CH(OMe){\cdot}CO_2Me \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2H\ (\alpha_D^{20°}\ -52{\cdot}8°)$$

In each case the saponification is so rapid that the rotations of the acids can be only slightly if at all affected by racemisation.

The methoxylation of sodium α-bromopropionate (reactions III and IV) proceeds at a speed convenient for measurement at 64°, and we have made this the standard temperature for both the kinetic and the optical observations on the sodium salt. As Senter and Wood have already concluded (J., 1916, **109**, 681), first- and second-order reactions proceed side by side at comparable rates under ordinary conditions of concentration. At higher concentrations of sodium methoxide the second-order process predominates, whilst at lower the first-order reaction assumes control; and we have approximately isolated the separate reactions by suitably choosing the concentrations of the reactants.

A number of second- and first-order velocity constants are summarised in Table I; the details of their determination will be found in the experimental section. In the range of concentration of sodium methoxide 0·5—1·0*M* we obtain good second-order constants. (This does not mean that the reaction is kinetically pure, because the constancy of a velocity constant is not a senstive test for kinetic purity.) The difference between constants for the

$0{\cdot}5M$ and $1{\cdot}0M$ concentrations of methoxide is an effect of ionic strength, as is shown by the constant for the run carried out in the presence of added sodium bromide. The effect is in the right direction for the bimolecular mechanism: a dense ionic atmosphere must favour the condensation of charges of like sign, and therefore the formation of a transition state between two negative ions such as the methoxide and α-bromopropionate ions.

In the range of concentration $M/32$—$M/16$ we obtain good unimolecular constants. (Again, this does not indicate more than an approximate kinetic purity.) For this first-order reaction the effect of ionic strength works in the opposite direction, as is shown by the constant for the run conducted in the presence of added sodium bromide. We expect this; indeed, it is part of the evidence that the second- and first-order reactions have fundamentally different mechanisms. The rate-controlling stage of the first-order reaction is an ionisation, in the transition state of which the anionic charge becomes divided between the carboxylate group and the bromine atom; and, since a dense ionic atmosphere opposes the sub-division of like charges, it must oppose the formation of such a transition state. The first-order constants obtained in the absence of added sodium bromide vary slightly over the range of concentration $M/32$—$M/16$, and the variation is opposite in direction to the ionic-strength effect, which, however, will be small at such concentrations. This observed variation is due to the circumstance that a little of the second-order reaction is present. Without a more extensive investigation of the ionic-strength effect it is impossible accurately to calculate how much of each reaction accompanies the other at the various concentrations, but we estimate that in the presence of $M/1$-sodium methoxide the second-order reaction constitutes about 95% of the whole change, whereas when the initial concentrations are $M/32$ about 90% of the total change proceeds by way of the first-order reaction.

TABLE I.

Reaction Orders and Rate Constants for Methoxylation of Sodium α-Bromopropionate (NaαBP) *by means of Sodium Methoxide in Methyl Alcohol at* 64·0°.

Approx. initial concns.			2nd-Order k (sec.$^{-1}$ g.-mol.$^{-1}$ l.).	Approx. initial concns.			1st-Order k (sec.$^{-1}$).
NaαBP.	NaOMe.	NaBr.		NaαBP.	NaOMe.	NaBr.	
$M/4$	$M/1$	—	$8{\cdot}48 \times 10^{-4}$	$M/32$	$M/32$	—	$5{\cdot}33 \times 10^{-5}$
$M/4$	$M/2$	—	$5{\cdot}20 \times 10^{-4}$	$M/32$	$M/16$	—	$5{\cdot}77 \times 10^{-5}$
$M/4$	$M/2$	$M/2$	$7{\cdot}93 \times 10^{-4}$	$M/16$	$M/16$	—	$5{\cdot}93 \times 10^{-5}$
				$M/32$	$M/32$	$M/2$	$3{\cdot}78 \times 10^{-5}$

The optical effect obtaining in the second-order reaction was ascertained by allowing a solution which was $1{\cdot}01M$ with respect to sodium methoxide and $0{\cdot}252M$ with respect to sodium α-bromopropionate to undergo reaction at 64° for 18·5 hours. The rotations of the α-bromopropionic acid used and of the methoxy-acid obtained were:

$$(\alpha_D^{20^\circ}\ +12{\cdot}9^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2H \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2H\ (\alpha_D^{26^\circ}\ -19{\cdot}8^\circ)\quad . \quad . \quad . \quad (III)$$

Evidently configuration has here been inverted. The rotatory power, $\alpha_D^{20^\circ}$, of optically pure bromo-acid is 49°, whilst that of optically pure methoxy-acid is 93·5°. From these figures it follows that under the conditions specified an optically pure bromo-acid would have given a methoxy-acid with an inverted configuration and with 81% of its full optical activity. Owing to its anionic charge the α-bromopropionate ion does not readily racemise (Wilson, *loc. cit.*), and, of course, the α-methoxypropionate ion must be still more optically stable. Hence we do not expect the figures given for the retention of enantiomeric purity to be appreciably affected by racemisation which is previous or subsequent to the process of substitution. For the same reasons it is unnecessary to correct the experimental result for the incompleteness of conversion.

For the investigation of the first-order reaction we used a solution which was $0{\cdot}063M$ with respect to sodium α-bromopropionate and $0{\cdot}077M$ with respect to sodium methoxide, the reaction being allowed to proceed at 64° for 26 hours. The rotations of the bromo-acid used and of the methoxy-acid obtained were:

$$(\alpha_D^{20^\circ}\ +12{\cdot}9^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2H \longrightarrow CH_3{\cdot}CH(OMe){\cdot}CO_2H\ (\alpha_D^{26^\circ}\ +17{\cdot}9^\circ)\quad . \quad . \quad (IV)$$

Here there is a retention of configuration, and it can be calculated that an optically pure bromo-acid would have yielded a methoxy-acid with 73% of its maximal activity. Again we do not expect the result to be influenced by the occurrence of racemisation before or after substitution.

Since the optical effects of the second- and first-order reactions are opposite in sign, it follows that our estimates of the percentage retention of enantiomeric purity are rendered too low by the occurrence along with each reaction of a small proportion of the other. Making the most probable estimates of the amounts of these minor reactions, we judge that the retention of optical purity for the second-order reaction is at least 85% with inversion, whilst for the first-order reaction it is at least 90% with retention of configuration.

Mechanism of Methoxylation.—Before leaving the Scheme A, we should mention that the reason why we have used the experimental terminology, "second-order," "first-order," and not the mechanistic nomenclature, "bimolecular," "unimolecular," is that the two sets of terms are interchangeable only for three of the four reactions. The two second-order reactions (I and III) are obviously nucleophilic, bimolecular substitutions (S_N2). The first-order reaction of the bromopropionate anion (IV) is equally certainly unimolecular (S_N1): its speed is far too great to admit of the supposition that it is a bimolecular ("ψ-unimolecular") reaction with solvent methyl alcohol acting as a base; and besides, we have the evidence of the optical behaviour. On the other hand, the very slow first-order substitution in α-bromopropionic ester (II) could be a bimolecular (ψ-unimolecular) reaction with solvent methyl alcohol, and the optical result indicates that it is: this reaction follows mechanism (S_N2), even although it is kinetically of the first order (cf. Part VI).

(B) *Hydroxylation.*

For the experiments on hydroxylation we have used both α-bromopropionic acid and its anion, water being the solvent; when we wished to substitute the carboxylic acid our practice was to add sufficient sulphuric acid largely to suppress the splitting of the bromo-acid into its ions; in experiments designed to substitute the anion we employed sodium α-bromopropionate and operated in the presence of sufficient sodium hydroxide to ensure that the solution would remain alkaline throughout the reaction.

The following scheme summarises the qualitative observations:

SCHEME B.

Hydrolysis of α-Bromopropionic Acid and Sodium α-Bromopropionate.

$$\begin{tikzcd}
d\text{-CH}_3\cdot\text{CHBr}\cdot\text{CO}_2\text{H} \arrow[r, "\text{First order}"'] \arrow[dd] & l\text{-CH}_3\cdot\text{CH(OH)}\cdot\text{CO}_2\text{H} \arrow[d] & \text{. . . . . (V)} \\
 & l\text{-CH}_3\cdot\text{CH(OH)}\cdot\text{CO}_2^- & \text{. . . . . (VI)} \\
d\text{-CH}_3\cdot\text{CHBr}\cdot\text{CO}_2^- \arrow[ur, "\text{Second order}"'] \arrow[r, "\text{First order}"'] & d\text{-CH}_3\cdot\text{CH(OH)}\cdot\text{CO}_2^- & \text{. . . . . (VII)}
\end{tikzcd}$$

The symbols *d* and *l* signify configuration. The relations with sign of rotation are normal [*d*(+) and *l*(—)] except for free lactic acid; however, all hydroxylation products were examined for rotatory power in the form of ethyl lactate, for which again the relations are normal.

Reactions V (Acid + Water).—As will be shown in detail later, the anion of α-bromopropionic acid undergoes hydrolysis in aqueous solution considerably more rapidly than does the undissociated acid. It is, therefore, difficult completely to isolate the hydrolysis of the undissociated acid; for even in an acidic solution, in which the concentration of the acid is much greater than that of the anion, some hydrolysis of the latter is liable to occur. We investigated the kinetics and optical characteristics of the hydrolysis of α-bromopropionic acid in 0·5*N*-aqueous sulphuric acid. This concentration of mineral acid is sufficient to ensure that the hydrolysis of the undissociated acid shall be the principal reaction, even though some hydrolysis of the anion proceeds simultaneously.

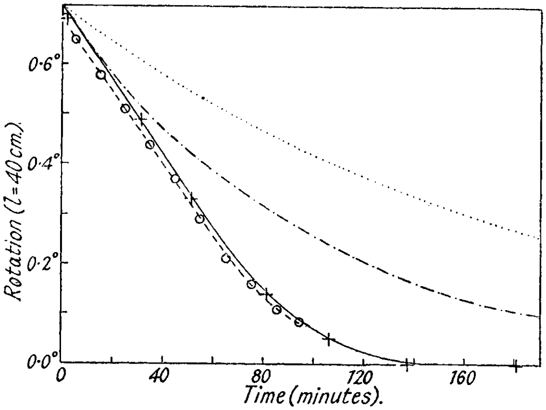
Like the acid methyl alcoholysis of the bromo-ester, the acid hydrolysis of the bromo-acid is very slow, and we were therefore forced to study it at 100°, although we would have preferred to use some lower temperature for which the ionisation constant of the acid is known. At 100° the reaction is experimentally of the first order, the rate constant being 0·000091 sec.$^{-1}$; the period of half-change is 126 minutes.

A solution 0·098*M* with respect to α-bromopropionic acid and 0·53*N* with respect to sulphuric acid was heated for 50 hours at about 91°, a time amply sufficient to complete the substitution. The lactic acid thus produced was converted into ethyl lactate. The following rotations were observed:

$$(\alpha_D^{25^\circ} +19\cdot0^\circ)\ CH_3\cdot CHBr\cdot CO_2H \longrightarrow CH_3\cdot CH(OH)\cdot CO_2Et\ (\alpha_D^{23^\circ} -0\cdot61^\circ) \quad . \quad . \quad (V)$$

Configuration has here been inverted, but with much racemisation. The rotation of optically pure ethyl lactate is $\alpha_D^{19^\circ}$ 11·5° (Wood, Such, and Scarff, J., 1923, **123**, 600), and hence a bromo-acid having 39% of its maximal rotation has yielded an ethyl lactate with 5·3% of its full rotation. Optically pure bromo-acid would under the same conditions have given ethyl lactate with an inverted configuration and 14% of its maximal rotatory power.

FIG. 4.



The full-line curve and the points marked by crosses represent the loss of optical activity from a 0·1*M*-solution of α-bromopropionic acid in 0·53*N*-aqueous sulphuric acid at 100°. (The broken line and circles represent another experiment made with a slightly lower initial concentration of bromo-acid.) The dotted curve indicates the fall of activity which would be produced by hydroxylation if the bromopropionic acid did not racemise. The chain-line curve shows how the activity would vary if hydrogen-racemisation were the only mechanism of racemisation. Allowance being made for the bromine-racemisation, we obtain a curve almost coincident with the experimental curve.

We have to decide how much of the loss of optical activity represented by this figure takes place before, and how much during, substitution: none can occur after substitution, since the product, lactic acid, is optically stable under the experimental conditions. We require to know the rate of racemisation of α-bromopropionic acid under the conditions employed for the hydrolysis, and have therefore studied the variation with time of the rotations of sulphuric acid solutions of α-bromopropionic acid. An aqueous solution, 0·099*M* with respect to α-bromopropionic acid and 0·53*N* with respect to sulphuric acid, was kept at 100°; and from time to time samples were withdrawn for the measurement of their rotation at room temperature. The results are shown by the crosses about the full-line curve of Fig. 4. The broken line and the points marked by circles refer to a duplicate experiment with a slightly lower concentration of bromo-acid. It will be seen that the experimental curve has the " hockey-stick " shape encountered previously, although the present curve does not cross the time-axis.

The reason why the curve runs into the time-axis is simply that the specific rotatory power of lactic acid in aqueous solution is so small that, even although this acid is produced with an appreciable fraction of its maximal activity, it contributes practically nothing at any time to the observed rotation of the solution. It can be calculated from the result of the " isolation " experiment recorded above that, even at " infinite " time, the partial rotation due to lactic acid would be less than 0·01°, which is the error of measurement. Therefore, the curve representing the partial rotation of the bromo-acid may be taken as identical with the experimental curve for the total rotation.

As in the example previously described, the fall of the partial rotation of the bromo-compound arises from three contributing causes. The disappearance of bromo-acid due to hydroxylation would produce an exponential fall of rotation : the known rate constant of this contribution is 0·000091 sec.$^{-1}$ (half-change 126 mins.). The curve showing how the rotation would vary if this effect acted alone is represented by the dotted line in Fig. 4. Fixing attention on the initial stages of reaction, we see that hydroxylation accounts for rather more than half the initial rate of loss of optical activity.

The remainder of the initial rate is due to a first-order racemisation of the bromo-acid itself. This is the reaction which we call " hydrogen-racemisation." In the acid medium we would expect it to be slow, and it is actually somewhat slower than the hydroxylation. From the difference between the *initial* slopes of the experimental rotation–time curve and of the curve which shows how the rotation would fall in the absence of racemisation, we can deduce the rate constant of the hydrogen-racemisation : the value is 0·000083 sec.$^{-1}$ (half-change, 139 mins.).

The hydroxylation and hydrogen-racemisation acting together, but without any third contributory effect, would produce an exponential fall of rotations, the curve for which, drawn from the known rate constants, is shown by a chain-line in Fig. 4. The divergence between this curve and the experimental curve is due to the racemising attack of bromide ions on the bromo-acid, the bromide ions being those liberated in the hydroxylation. This " bromine-racemisation " starts with zero velocity, and its speed then increases, passes through a maximum, and finally decreases again to zero. As explained in the previous instance and illustrated in Fig. 3, it is this special kind of rate-variation which, when combined with the more normal trend of the rates of the substitution and hydrogen-racemisation, leads to the initial straightness of the experimental curve and to the rather sharp turn near the time axis.

We can determine the rate of the bromine-racemisation in either of two ways. For the initial stages of reaction, the divergence between the experimental rotation–time curve and the curve representing the rotations which would be observed in the absence of the bromine-racemisation measures the rate of the bromine-racemisation; and the time-rate of increase of the divergence measures the time-rate of increase of the rate of this process. By comparing this time-rate with the known time-rate of increase of the concentration of the attacking bromide ion, we can find the rate constant : it is 0·0080 sec.$^{-1}$ g.-mol.$^{-1}$ l.

Alternatively, we can employ the theoretical equation, given in the Appendix, for the variation of rotation with time. The equation contains the known rate constants of the hydroxylation and the hydrogen-racemisation, and the required rate constant of the bromine-racemisation; it does not contain a constant representing a ratio of rotatory powers characterising the hydroxylation, because this constant would be required only in order to express the negligible partial rotation of the hydroxylation product. Hence the rate constant for the bromine-racemisation is the only unknown, and a single point on the experimental curve suffices to determine it. Using, *e.g.*, $\alpha = 0{\cdot}15°$ at $t = 80$ mins., we find for the rate constant 0·0080 sec.$^{-1}$ g.-mol.$^{-1}$ l., in agreement with the result given by the other method.

All the rate constants being known, we can plot a curve representing the theoretical course of the change of rotation with time. This curve agrees so closely with that drawn through the experimental points that the two cannot be shown separately in Fig. 4.

We now have all the data necessary to calculate in what proportion optical activity should be retained in the lactic acid formed by complete hydroxylation of α-bromopropionic acid under the conditions of the " isolation " experiment, if the only cause for loss of activity were the racemisation of the bromo-acid (by both mechanisms) in advance of hydroxylation. The answer is 26%. The observed result was an inversion retaining 14% of the possible optical activity. Hence the hydroxylation acting in the absence of any prior racemisation of the bromo-acid would have inverted configuration with a retention of 54% of the maximal optical activity.

Now we shall show later that hydrolysis of the α-bromopropionate ion in the absence of a large excess of alkali leads to a lactic acid which preserves the original configuration and retains practically the whole of the optical activity. Since in the experiments described above a certain amount of the hydroxylation must have taken place by way of the α-bromopropionate ion, it follows that our figure 54% is a minimum value for the retention of activity characterising the inversion which takes place in the hydroxylation of the undissociated acid. If we knew the proportion in which hydrolysis occurred through the anion we could make a correction, and thus quote a precise value instead of a minimum for the proportion of activity retained with inversion in the hydroxylation of the undissociated acid.

An experimental basis for this correction can be obtained by changing the initial concentration of sulphuric acid, and therefore the proportion of reaction which proceeds through the anion, in known ratio, and measuring the corresponding change in the rate of hydrolysis. If, for instance, we halve the concentration of hydrogen ions, the proportion of α-bromopropionic acid which is ionised will be doubled; and therefore the rate of that part of the reaction which proceeds through the α-bromopropionate ion will also be doubled. The increase of rate will thus be equal to the partial rate of hydrolysis of the bromopropionate ions as it stood before the concentration of hydrogen ions was halved; and the ratio of this partial rate to the observed total rate will give the required proportion of reaction which, under those conditions, took place through the anion. This assumes, first, that the fraction of bromopropionic acid which is ionised under the conditions of the comparative experiments is small, as it certainly would be; and secondly, that the mass law is a good approximation. Practically we have to make the calculation in a slightly more complicated way, because hydrobromic acid is liberated in the course of hydrolysis, so that the concentration of hydrogen ions is not quite constant throughout a determination of reaction rate; however, this circumstance is sufficiently allowed for by calculating with mean, rather than initial, hydrogen-ion concentrations.

Two rate determinations were carried out at the same time in the same thermostat at 100°; in each the initial concentration of α-bromopropionic acid was $M/10$; but in the first the concentration of sulphuric acid was $0{\cdot}491N$, whilst in the second it was $0{\cdot}245N$; so that the *average* concentrations of hydrogen ions were $0{\cdot}541N$ and $0{\cdot}296N$ respectively. This means that in the second experiment the rate of that part of the reaction which proceeds through the anion should have been increased in the ratio $0{\cdot}541/0{\cdot}296$, *i.e.*, by 83%. The observed mean rates were 0·000100 and 0·000119 sec.$^{-1}$. Attributing the increase, 0·000019 sec.$^{-1}$, to the increased proportion of anion, we calculate that in the first experiment the partial rate of the reaction of the bromopropionate ion was 0·000023 sec.$^{-1}$; whilst by difference the partial rate for the bromopropionic acid molecule was 0·000077 sec.$^{-1}$. Hence the proportion of reaction which proceeded through the anion was 23%. In our experiment with optically active material the mean acidity was a little greater than in the first of the above comparative experiments, and, allowing for this, we find that the proportion of anion hydrolysis in the optical experiment must have been 22%. Assuming that this part of the reaction proceeds exclusively with retention of stereochemical form, it follows from the observed optical effect of the total reaction that the proportion in which optical activity is retained in the inversion which characterises the substitution of the undissociated acid is 97%.

Reactions VI and VII (*Sodium Salt + Sodium Hydroxide*).—When sodium α-bromopropionate is hydrolysed in aqueous solution in the presence of at least one equivalent of sodium hydroxide, second- and first-order hydroxylations proceed side by side at comparable rates under the usual conditions of concentration. Senter originally arrived at this conclusion (J., 1909, **95**, 1827); the re-interpretation of his results proposed by Zawidzki (*Rocz. Chem.*, 1926, **6**, 136; *Z. physikal. Chem.*, 1928, **137**, 72) is incorrect. We have approximately isolated the separate reactions by suitably selecting the concentrations of the reactants.

Some rate constants, applying to aqueous solutions at 64°, are given in Table II, which is abstracted from the more detailed record in the experimental section. The isolation of the second-order reaction is rather incomplete: even in the run with $M/1$-sodium hydroxide there is something like 20% of first-order reaction, so that the true second-order constant will be correspondingly lower than that recorded. This effect will be about twice as great in the run with *M*/2-sodium hydroxide, and, as the figures show, the difference between the two disturbances outweighs the ionic-strength effect, and makes the observed constant slightly greater, instead of rather considerably smaller, in the more dilute solution. The isolation of the first-order reaction is more complete, and in the most dilute solutions the amount of accompanying second-order process cannot be more than a few units per cent.

TABLE II.

Reaction Orders and Rate Constants for Hydroxylation of Sodium α-Bromopropionate (NaαBP) *by Means of Aqueous Sodium Hydroxide at* 64·0°.

Approx. initial concns.		2nd-Order k	Approx. initial concns.		1st-Order k
NaαBP.	NaOH.	(sec.$^{-1}$ g.-mol.$^{-1}$ l.).	NaαBP.	NaOH.	(sec.$^{-1}$).
M/4	*M*/1	$6·35 \times 10^{-4}$	*M*/32	*M*/32	$1·18 \times 10^{-4}$
M/4	*M*/2	$6·7 \times 10^{-4}$	*M*/32	*M*/16	$1·19 \times 10^{-4}$
			M/16	*M*/16	*ca.* $1·23 \times 10^{-4}$ *
			M/10	*M*/10	*ca.* $1·3 \times 10^{-4}$ *

* Values fall during run.

The optical effect in the second-order reaction was investigated by allowing a solution, 0·250*M* with respect to sodium α-bromopropionate and 1·00*M* with respect to sodium hydroxide, to undergo reaction at 64° for 3 hours; the lactic acid formed was converted into ethyl lactate. The following rotations were observed :

$$(\alpha_D^{18·5^\circ}\ +19·1^\circ)\ CH_3·CHBr·CO_2H \longrightarrow CH_3·CH(OH)·CO_2Et\ (\alpha_D^{26^\circ}\ -2·26^\circ)\ \ .\ \ .\ \ \text{(VI)}$$

These figures mean that configuration is inverted, and that a bromo-acid with 39% of its maximal rotation has given an ethyl lactate with 20% of its maximal rotation; with optically pure bromo-acid the retention of activity in the ethyl lactate would be 51%. For reasons similar to those given in connexion with the methoxylation of sodium α-bromopropionate, we do not expect any appreciable disturbance from racemisation before or after the substitution, and therefore no correction is necessary for the incompleteness of substitution.

For the optical examination of the first-order reaction we allowed a solution, 0·065*M* with respect both to sodium α-bromopropionate and to sodium hydroxide, to undergo reaction at 64° for 16·25 hours. The rotations were :

$$(\alpha_D^{18·5^\circ}\ +19·1^\circ)\ CH_3·CHBr·CO_2H \longrightarrow CH_3·CH(OH)·CO_2Et\ (\alpha_D^{26^\circ}\ +3·12^\circ)\ \ .\ \ .\ \ \text{(VII)}$$

There is here a retention of configuration, and optically pure bromo-acid would have yielded an ethyl lactate with 70% of its full activity. These figures also should be unaffected by any appreciable racemisation prior to or following the substitution.

When we make the most probable allowances for the minor proportion in which each reaction must accompany the other in these experiments, we find that the retention of optical purity in the second-order process must amount to 80—100% with inversion, whilst for the first-order reaction it must be 85—100% with retention of configuration.

Mechanism of Hydroxylation.—Concerning the interpretation of the Scheme B, the second-order substitution of the anion is obviously bimolecular in mechanism (S_N2), and the first-order substitution of the anion is proved by its high speed and by the optical result to be unimolecular (S_N1). The slow first-order substitution of the undissociated acid might *a priori* be either a unimolecular reaction or a bimolecular (ψ-unimolecular) substitution with solvent water acting as a basic reagent. The optical result indicates that the reaction is actually bimolecular (S_N2), even though it is of the first order (cf. Part VI).

SUMMARY

(Covering Parts I, II, and III).

The principal conclusions reached in this paper are summarised in Table III, in which the results recorded in Parts I and II are included for convenience. The first col. indicates the paper of this series in which the details are to be found. The next four cols., which contain respectively the formula of the compound substituted, the substitution process, the solvent, and the temperature, require no explanation. Under the heading "reagent" is inserted, for the S_N2-reactions, the molecule or ion which enters along with the halogen compound into the bimolecular process; but, for the S_N1-reactions, the entries represent the molecule from which, after the rate-determining step has been accomplished, the substituent is derived. A distinction is made in the next two cols. between reaction order and mechanism: the "order" represents the experimental kinetic result; and a second-order reaction always corresponds to a bimolecular mechanism, whereas a first-order reaction may signalise either a bimolecular or a unimolecular mechanism, according to the criteria given in the preceding detailed discussion. The penultimate col. contains a qualitative statement of the effect of the substitution on configuration (Ra = racemisation; Re = retention; I = inversion), and the last col. the proportionate retention of optical purity associated with the inversion or retention of configuration. Figures such as 96% and 94% may be regarded as scarcely distinguishable in practice from 100%. If the retention of optical purity is p%, the proportion of the major enantiomeride is the greater quantity $\frac{1}{2}(p + 100)$%.

TABLE III.

Relation of Optical Effect to Kinetics and Mechanism of Substitution.

Paper.	Halide subsd.	Subsn. process.	Solvent.	Approx. temp.	Reagent.	Reaction. Order.	Reaction. Mechanism.	Effect on configtn.	Retention of optical purity, %.
I	$\left.\begin{array}{r}C_6H_{13}\\CH_3\\H\end{array}\right\rangle C\cdot Br$	Hydroxylation	60% aq. EtOH	80°	OH^-	2	S_N2	I	96
					H_2O	1	S_N1	Ra + I	66
		Ethoxylation	,,	80	OEt^-	2	S_N2	I	96
					HOEt	1	S_N1	Ra + I	74
		,,	Anhydr. EtOH	80	OEt^-	2	S_N2	I	~100
	$\left.\begin{array}{r}C_6H_{13}\\CH_3\\H\end{array}\right\rangle C\cdot Cl$	,,	,,	80	OEt^-	2	S_N2	,,	~100
II	$\left.\begin{array}{r}C_6H_5\\CH_3\\H\end{array}\right\rangle C\cdot Cl$	Hydroxylation	H_2O	20	H_2O	—	S_N1	Ra + I	17
			60% aq.-Me_2CO	70	H_2O	1	S_N1	,,	5
			80% aq.-Me_2CO	70	H_2O	1	S_N1	,,	2
		Methoxylation	Anhydr. MeOH	70	OMe^-	2	S_N2	I	(high)
			,,	70	HOMe	1	S_N1	Ra + I	(low)
		Ethoxylation	Anhydr. EtOH	70	OEt^-	2	S_N2	I	(high)
			,,	70	HOEt	1	S_N1	Ra + I	(low)
	$\left.\begin{array}{r}C_6H_5\\CH_3\\H\end{array}\right\rangle C\cdot Br$	Hydroxylation	H_2O	20	H_2O	—	S_N1	,,	(low)
III	$\left.\begin{array}{r}CO_2H\\CH_3\\H\end{array}\right\rangle C\cdot Br$	Hydroxylation	Dil. aq.-H_2SO_4	90	H_2O	1	S_N2	I	~100
	$\left.\begin{array}{r}CO_2Me\\CH_3\\H\end{array}\right\rangle C\cdot Br$	Methoxylation	Anhydr. MeOH	25	OMe^-	2	S_N2	,,	~100
				100	HOMe	1	S_N2	,,	~100
	$\left.\begin{array}{r}CO_2^-\\CH_3\\H\end{array}\right\rangle C\cdot Br$	Hydroxylation	H_2O	64	OH^-	2	S_N2	,,	80—100
					H_2O	1	S_N1	Re	90—100
		Methoxylation	Anhydr. MeOH	64	OMe^-	2	S_N2	I	85—100
					HOMe	1	S_N1	Re	90—100

A more condensed statement of the main outcome can be given, because, as Table III clearly shows, the qualitative results are independent of the halogen which is replaced

TABLE IV.

Steric Course of the Homogeneous Replacement of ·Hal by ·OR.

R in CHMeR·Hal.	Effect on configuration. Mechanism S_N2.	Effect on configuration. Mechanism S_N1.
C_6H_{13}	Inversion	Racemisation + inversion
C_6H_5	,,	Large racemisation + inversion
CO_2H, CO_2Me	,,	(Not known)
CO_2^-	,,	Retention

Note.—Racemisation accompanying inversion is increased by dilution of the hydroxylic solvent with a non-hydroxylic solvent.

(chlorine or bromine), and of the group which replaces it (hydroxyl, methoxyl, or ethoxyl). The short summary thus made possible is given in Table IV, which will be understood to refer only to *homogeneous* mechanisms of substitution : there are well-known heterogeneous methods of effecting the replacement of halogen by hydroxyl and alkoxyl, and we have still to present our data concerning the steric course of these (see Parts IV and V).

APPENDIX.

The Polarimetric Rate Equations.

(1) *Equation for the rotation–time curve for methyl α-bromopropionate in methyl-alcoholic sodium methoxide* (*Reaction I*; *see Fig.* 1). The following symbols are defined :

α = Observed rotation = $\alpha_B + \alpha_M$.
α_B = Partial rotation due to bromo-ester.
α_M = ,, ,, ,, ,, methoxy-ester.
θ_B = " Rotatory power " of bromo-ester defined by $\alpha_B = \theta_B c_B$.
θ_M = ,, ,, ,, methoxy-ester ,, ,, $\alpha_M = \theta_M c_M$.
c_B = Concentration of bromo-ester = concentration of methoxide ions.
c_M = Concentration of methoxy-ester.
t = Time from commencement of reaction.
α_0 = Value at zero-time of α = value at zero-time of α_B.
θ_0, c_0 = Values at zero-time of θ_B and c_B.
θ_{B1} = Value at time $t = t_1$ of θ_B.
α_{M2} = Value at time $t = t_2$ of α_M.
$\delta\alpha_{M11}$ = Partial rotation at $t = t_1$ due to small increment of methoxy-ester formed at $t = t_1$.
$\delta\alpha_{M12}$ = Partial rotation at $t = t_2$ due to small increment of methoxy-ester formed at $t = t_1$.
θ'_{M11} = Rotatory power at $t = t_1$ of increment formed at $t = t_1$; defined by $\delta\alpha_{M11} = \theta'_{M11}\delta c_{M1}$.
θ'_{M12} = Rotatory power at $t = t_2$ of increment formed at $t = t_1$; defined by $\delta\alpha_{M12} = \theta'_{M12}\delta c_{M1}$.
δc_{B1} = Increment of concentration of bromo-ester destroyed at $t = t_1$.
δc_{M1} = ,, ,, ,, ,, methoxy-ester formed at $t = t_1$.
δt_1 = Increment of time used in producing the increment of concentration $\delta c_{M1} = -\delta c_{B1}$.
k_{2BH} = Second-order rate constant for catalysed hydrogen-racemisation of bromo-ester.
k_{2MH} = ,, ,, ,, ,, ,, ,, ,, ,, methoxy-ester.
k_{2S} = ,, ,, ,, ,, ,, substitution process.
χ = Constant defined by $\theta'_{M11} = \chi\theta_{B1}$ and assumed independent of time. The constant χ is the required ratio of rotatory powers characteristic of the substitution.

By definition

$$\alpha = \theta_B c_B + \theta_M c_M \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (1)$$

The factors in the first term on the right-hand side can be separately calculated. The differential equation for c_B is

$$-(dc_B/dt) = k_{2S}c_B^2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (2)$$

which on integration gives

$$c_B = c_0(1 + c_0k_{2S}t)^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (3)$$

The differential equation for θ_B is

$$-(d\theta_B/dt) = k_{2BH}\theta_B c_B$$

Substituting for c_B by means of equation (3) and integrating, we find

$$\theta_B = \theta_0(1 + c_0k_{2S}t)^{-k_{2BH}/k_{2S}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \qquad (4)$$

From equations (3) and (4) we have for the first term in α

$$\alpha_B = \theta_B c_B = \alpha_0(1 + c_0k_{2S}t)^{-(k_{2BH}+k_{2S})/k_{2S}} \quad . \quad . \quad . \quad . \quad . \qquad (5)$$

In order to evaluate the second term, we first calculate the partial rotation $\delta\alpha_{\mathrm{M}11}$ of an increment of methoxy-ester freshly formed at time t_1. We have

$$\delta\alpha_{\mathrm{M}11} = \theta'_{\mathrm{M}11}\delta c_{\mathrm{M}1} = \chi\theta_{\mathrm{B}1}(-\delta c_{\mathrm{B}1}) = \chi\theta_{\mathrm{B}1}k_{2\mathrm{S}}c_{\mathrm{B}1}{}^2\delta t_1$$

in which use has been made of equation (2). Substituting for $\theta_{\mathrm{B}1}$ and $c_{\mathrm{B}1}$ with the aid of equations (4) and (3) respectively, we find

$$\delta\alpha_{\mathrm{M}11} = \theta'_{\mathrm{M}11}\delta c_{\mathrm{M}1} = \chi k_{2\mathrm{S}}\theta_0 c_0{}^2(1 + c_0k_{2\mathrm{S}}t_1)^{-(k_{2\mathrm{BH}}+2k_{2\mathrm{S}})/k_{2\mathrm{S}}}\delta t_1 \quad . \quad . \quad . \quad (6)$$

The next step is to obtain the relation between $\theta'_{\mathrm{M}11}$ and $\theta'_{\mathrm{M}12}$, so that we can evaluate the partial rotation $\delta\alpha_{\mathrm{M}12}$ of the same increment at a later time t_2. The differential equation for $\theta'_{\mathrm{M}1t}$ is

$$-(d\theta'_{\mathrm{M}1t}/dt) = k_{2\mathrm{MH}}\theta'_{\mathrm{M}1t}c_{\mathrm{B}}$$

Substituting for c_{B} by means of equation (3) and integrating from t_1 to t_2, we find

$$\frac{\theta'_{\mathrm{M}12}}{\theta'_{\mathrm{M}11}} = \left(\frac{1 + c_0k_{2\mathrm{S}}t_2}{1 + c_0k_{2\mathrm{S}}t_1}\right)^{-k_{2\mathrm{MH}}/k_{2\mathrm{S}}} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (7)$$

Combination of equations (6) and (7) gives

$$\delta\alpha_{\mathrm{M}12} = \theta'_{\mathrm{M}12}\delta c_{\mathrm{M}1} = \chi k_{2\mathrm{S}}\theta_0c_0{}^2(1 + c_0k_{2\mathrm{S}}t_1)^{-(k_{2\mathrm{BH}}-k_{2\mathrm{MH}}+2k_{2\mathrm{S}})/k_{2\mathrm{S}}}(1 + c_0k_{2\mathrm{S}}t_2)^{-k_{2\mathrm{MH}}/k_{2\mathrm{S}}}\delta t_1 \quad (8)$$

The partial rotation due to the whole of the methoxy-ester present at the time t_2 is obtained by integrating the coefficient of δt_1 in equation (8) with respect to dt_1 between the limits $t_1 = 0$ and $t_1 = t_2$:

$$\alpha_{\mathrm{M}2} = \chi k_{2\mathrm{S}}\theta_0c_0{}^2(1 + c_0k_{2\mathrm{S}}t_2)^{-k_{2\mathrm{MH}}/k_{2\mathrm{S}}}\int_{t_1=0}^{t_1=t_2}(1 + c_0k_{2\mathrm{S}}t_1)^{-(k_{2\mathrm{BH}}-k_{2\mathrm{MH}}+2k_{2\mathrm{S}})/k_{2\mathrm{S}}}dt_1$$

Evaluating the integral, and dropping the now unnecessary subscript from t_2, we find

$$\alpha_{\mathrm{M}} = \theta_{\mathrm{M}}c_{\mathrm{M}} = \chi\theta_0c_0\cdot\frac{k_{2\mathrm{S}}}{k_{2\mathrm{BH}} - k_{2\mathrm{MH}} + k_{2\mathrm{S}}}\cdot\left\{(1 + c_0k_{2\mathrm{S}}t)^{-k_{2\mathrm{MH}}/k_{2\mathrm{S}}} - (1 + c_0k_{2\mathrm{S}}t)^{-(k_{2\mathrm{BH}}+k_{2\mathrm{S}})/k_{2\mathrm{S}}}\right\} \quad (9)$$

By adding equations (5) and (9), we obtain the complete expression for α :

$$\alpha = \alpha_0\Big[(1 + c_0k_{2\mathrm{S}}t)^{-(k_{2\mathrm{BH}}+k_{2\mathrm{S}})/k_{2\mathrm{S}}}$$
$$+ \chi\cdot\frac{k_{2\mathrm{S}}}{k_{2\mathrm{BH}} - k_{2\mathrm{MH}} + k_{2\mathrm{S}}}\cdot\left\{(1 + c_0k_{2\mathrm{S}}t)^{-k_{2\mathrm{MH}}/k_{2\mathrm{S}}} - (1 + c_0k_{2\mathrm{S}}t)^{-(k_{2\mathrm{BH}}+k_{2\mathrm{S}})/k_{2\mathrm{S}}}\right\}\Big] \quad . \quad (10)$$

The constants $k_{2\mathrm{MH}}$ and $k_{2\mathrm{S}}$ are independently evaluated. The constants $k_{2\mathrm{BH}}$ and χ have to be obtained by fitting the equation to the experimental results. Note that, since the substitution involves inversion in the sign of rotation, χ is negative.

(2) *Equation for the rotation–time curve for methyl α-bromopropionate in methyl alcohol* (*Reaction II* ; *see Fig.* 2). Here the racemisation of the methoxy-ester may be neglected, but an additional process of racemisation of the bromo-ester, due to the attack of bromide ions, has to be taken into account.

The symbols α, α_{B}, α_{M}, θ_{B}, θ_{M}, t, α_0, θ_0, c_0, are defined as before ; and in addition we set :

c_{B} = Concentration of bromo-ester.
c_{M} = ,, ,, methoxy-ester.
$\delta\alpha_{\mathrm{M}}$ = Partial rotation of small increment of methoxy-ester.
θ'_{M} = Rotatory power ,, ,, ,, ,, ,, , defined by $\delta\alpha_{\mathrm{M}} = \theta'_{\mathrm{M}}\delta c_{\mathrm{M}}$.
δc_{B} = Increment of concentration of bromo-ester.
δc_{M} = ,, ,, ,, ,, methoxy-ester.
δt = ,, ,, time used in producing the increments $\delta c_{\mathrm{M}} = -\delta c_{\mathrm{B}}$.
$k_{1\mathrm{BH}}$ = First-order rate constant for hydrogen-racemisation of bromo-ester.
$k_{2\mathrm{BB}}$ = Second- ,, ,, ,, ,, bromine- ,, ,, ,,
$k_{1\mathrm{S}}$ = First- ,, ,, ,, ,, substitution (methoxylation) process.
χ = Constant defined by $\theta'_{\mathrm{M}} = \chi\theta_{\mathrm{B}}$, where θ'_{M} and θ_{B} refer to the same time; χ is assumed to be independent of time.

Evaluating the separate terms of equation (1) as before, we find for c_B

$$-(dc_B/dt) = k_{1S}c_B \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (11)$$

$$c_B = c_0e^{-k_{1S}t} . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (12)$$

The differential equation for θ_B is

$$\begin{aligned} -(d\theta_B/dt) &= k_{1BH}\theta_B + k_{2BB}\theta_Bc_M \\ &= k_{1BH}\theta_B + k_{2BB}\theta_B(c_0 - c_B) \end{aligned}$$

Substituting for c_B from equation (12) and integrating, we find

$$\theta_B = \theta_0 \exp\left\{-(k_{1BH} + k_{2BB}c_0)t + \frac{k_{2BB}c_0}{k_{1S}}(1 - e^{-k_{1S}t})\right\} \quad . \quad . \quad . \quad (13)$$

Combining equations (12) and (13), we have for the partial rotation of bromo-ester

$$\alpha_B = \alpha_0 \exp\left\{-(k_{1S} + k_{1BH} + k_{2BB}c_0)t + \frac{k_{2BB}c_0}{k_{1S}}(1 - e^{-k_{1S}t})\right\} \quad . \quad . \quad (14)$$

The partial rotation of methoxy-ester, α_M, is an integral from 0 to t of $d\alpha_M$. We have $\delta\alpha_M = \theta'_M\delta c_M$, $\theta'_M = \chi\theta_B$, and $\delta c_M = -\delta c_B$; and using equation (11), we obtain

$$\alpha_M = \int\theta'_Mdc_M = -\chi\int\theta_Bdc_B = \chi k_{1S}\int\theta_Bc_Bdt = \chi k_{1S}\int\alpha_Bdt$$

Taking account of equation (14), we have

$$\alpha_M = \chi\alpha_0k_{1S}\int_0^t \exp\left\{-(k_{1S} + k_{1BH} + k_{2BB}c_0)t + \frac{k_{2BB}c_0}{k_{1S}}(1 - e^{-k_{1S}t})\right\}dt \quad . \quad (15)$$

The exact equation for the rotation–time curve is obtained by addition of equations (14) and (15), but, for application over the range experimentally studied, the following approximate equations are good to within about 1%. In equation (14) we must expand the internal exponential as far as the term in t^3:

$$\alpha_B = \alpha_0 \exp\{-(k_{1S} + k_{1BH})t - \tfrac{1}{2}k_{1S}k_{2BB}c_0t^2(1 - \tfrac{1}{3}k_{1S}t)\} \quad . \quad . \quad . \quad (16)$$

In equation (15) the inner exponential need be expanded only as far as the term in t^2:

$$\begin{aligned} \alpha_M &= \chi\alpha_0k_{1S}\int_0^t \exp\{-(k_{1S} + k_{1BH})t - \tfrac{1}{2}k_{1S}k_{2BB}c_0t^2\}dt \\ &= \chi\alpha_0k_{1S} \exp\left\{\frac{(k_{1S} + k_{1BH})^2}{2k_{1S}k_{2BB}c_0}\right\}\int_0^t \exp\left\{-\tfrac{1}{2}k_{1S}k_{2BB}c_0\left(t + \frac{k_{1S} + k_{1BH}}{k_{1S}k_{2BB}c_0}\right)^2\right\}dt \quad . \quad (17) \end{aligned}$$

The definite integral in (17) is an "error function," the values of which can be found in tables. The approximate equation for the rotation–time curve is the sum of equations (16) and (17).

(3) *Equation for the rotation–time curve for α-bromopropionic acid in aqueous sulphuric acid (Reaction V; see Fig.* 4). The previous definitions of symbols apply, except that, as they now relate to the bromo-acid and hydroxy-acid instead of the bromo-ester and methoxy-ester, we should replace the subscript M by H. With this change the formulæ of the preceding section hold good; but, since α_H (the old α_M) is experimentally inappreciable, the right-hand side of equation (14) is a sufficiently accurate expression for α.

EXPERIMENTAL.

Methyl d- *and* l-*Lactate*.—The stock of *d*-lactic acid was a crude, dark syrup supplied many years ago by Messrs. Panton Ltd. to Sir William Ramsay. It was dehydrated at 110° under reduced pressure, and then esterified (420 c.c.) by boiling with methyl alcohol (2200 c.c.) for 4 hours under reflux. (It was not necessary to add a mineral acid.) After evaporation of the methyl alcohol, the residue yielded almost optically pure methyl *d*-lactate (240 g.), b. p. 46°/10 mm., $\alpha_D^{20°}$ (l = 20 cm.) +16·07°. Methyl *l*-lactate was prepared from a commercial sample of lactic acid (250 c.c.), which yielded an ester (88 g.) having b. p. 46°/10 mm., $\alpha_D^{20°}$ (l = 20 cm.) −11·5°, together with head and tail fractions of lower rotation.

Methyl d- *and* l- *and* dl-*Bromopropionate*.—The *l*-bromo-ester was prepared from the above methyl *d*-lactate (111 g.) and phosphorus pentabromide (460 g.) (cf. Walker, J., 1895, **67**, 921). A solution of the ester in chloroform (165 c.c.) was added very slowly to a mixture of the pentabromide and chloroform (100 c.c.). After the violent reaction had subsided the mixture was warmed to complete the solution of the pentabromide, cooled, and poured on to ice. When this decomposition, which must be carefully controlled, was complete, the chloroform layer was separated, shaken with thiosulphate, dried by means of sodium sulphate, and evaporated. The ester was distilled, shaken in ethereal solution with an aqueous suspension of calcium carbonate, recovered, and again distilled. It had b. p. 44°/12 mm., $\alpha_D^{20^\circ}$ −68·57°.

The *d*-bromo-ester was prepared by adding methyl *l*-lactate (71 g.) to phosphorus tribromide (184 g.) in the cold, the reaction being conducted at as low a temperature as possible and completed by very slow warming. The mixture was decomposed by means of ice. The ester, isolated in the normal way (58 g.), had b. p. 46°/14 mm., $\alpha_D^{23^\circ}$ 19·74° (Found : Br, 47·4. Calc. : Br, 47·8%). In other experiments, in which the reaction was allowed longer to go in the cold before warming, 76 g. of methyl lactate and 199 g. of phosphorus pentabromide gave 62 g. and 63 g. of methyl *l*-bromopropionate, b. p. 53°/19 mm., $\alpha_D^{21^\circ}$ −28·87 and −29·05° (Found : C, 29·1; H, 4·3; Br, 47·2. Calc.: C, 28·7; H, 4·2; Br, 47·8%).

The *dl*-bromo-ester was prepared by heating α-bromopropionic acid (40 g.) with methyl alcohol (160 g.) in the presence of concentrated sulphuric acid (8 c.c.) under reflux for 4 hours. The ester, 38 g., had b. p. 56·5°/21 mm.

Methyl l-*α-Methoxypropionate.*—This was prepared by Purdie and Walker's method (J., 1899, **75**, 485) from the above methyl *l*-lactate (87·5 g.), methyl iodide (178 g.), and silver oxide (146 g.). The product, collected in ether and distilled, yielded 62 g. of methoxy-ester, b. p. 41—42°/18 mm., and this on further fractionation gave 44 g. of pure material, b. p. 32—33°/12 mm., $\alpha_D^{20^\circ}$ −53·7°.

Course of Hydrolysis of Ethyl α-Chloropropionate and α-Bromopropionate.—Ethyl *dl*-α-chloropropionate (2·505 g.), dissolved in acetone (55 c.c.), was mixed with 0·926*N*-aqueous potassium hydroxide (39·90 c.c.), and the whole was made up to 100 c.c. with acetone, and kept at 30·0°, portions of 5 c.c. being removed for titration with 0·0950*N*-aqueous hydrochloric acid. After 45 and 270 mins. the titres were 16·15 and 11·85 c.c., the latter value representing the disappearance of 1 mol. of potassium hydroxide. At 270 mins., 5 c.c. of the solution were mixed with water and extracted with ether, and the aqueous solution was examined for halide ions, which were absent.

Ethyl *dl*-α-bromopropionate was investigated in a similar way. Almost immediately after the solution of the ester and potassium hydroxide in aqueous acetone had been made up at 30°, a sample withdrawn for titration showed that 1 mol. of potassium hydroxide had been consumed. However, the solution contained no bromide ions.

Course of the Hydrolysis of α-Chloropropionamide.—The amide was prepared by shaking the methyl ester (30 g.) with concentrated aqueous ammonia (30 c.c.) for 12 hours. The solution thus obtained was evaporated in a vacuum over concentrated sulphuric acid, and the residue was sublimed under reduced pressure and crystallised from light petroleum. A solution of the amide (1·343 g., m. p. 82—83°) in water was mixed with 0·926*N*-aqueous potassium hydroxide and made up to 100 c.c. with water. After 3 hours at 30° no halide ion was liberated, although the solution was 0·117*N* with respect to ammonia, this concentration corresponding to an almost complete hydrolysis of the amide group.

Hydrolysis of Methyl d-*α-Bromopropionate.*—The ester (47 g.), $\alpha_D^{23^\circ}$ +19·74°, was shaken with a solution of potassium hydroxide (32 g.) in water (250 c.c.) until it dissolved (a few minutes), and the solution was extracted with ether, acidified with 6*N*-aqueous sulphuric acid, saturated with sodium chloride, and extracted with ether thoroughly. The second extract was dried with sodium sulphate, and the acid which it yielded was distilled (40 g.), b. p. 102—104°/15—16 mm., $\alpha_D^{20^\circ}$ +12·9° (Found : C, 23·9; H, 3·3; Br, 51·8. Calc. : C, 23·5; H, 3·3; Br, 52·2%). In other experiments 62 g. of ester, $\alpha_D^{21^\circ}$ +28·87°, gave 48 g. of acid, b. p. 84°/3 mm., $\alpha_D^{18\cdot5^\circ}$ +19·12°, and 40 g. of ester $\alpha_D^{23^\circ}$ +29·0° gave 36·4 g. of acid, b. p. 78°/1 mm., $\alpha_D^{25^\circ}$ +19·00°.

Hydrolysis of Methyl l-*α-Methoxypropionate.*—A solution of the ester (20 g.), $\alpha_D^{20^\circ}$ −53·7°, and potassium hydroxide (15 g.) in water (100 c.c.) was kept at room temperature for 3 hours, neutralised, concentrated to 75 c.c. in an open basin, acidified with dilute sulphuric, and extracted 15 times with ether. The crude acid (18 g.) on distillation yielded a pure product (11·6 g.), b. p. 106°/20 mm., $\alpha_D^{20^\circ}$ −52·83°.

Rate of Reaction between Sodium Methoxide and Methyl dl-*α-Bromopropionate in Methyl Alcohol at* 25·0°.—The methyl alcohol was dried by means of magnesium.

(i) The methyl-alcoholic sodium methoxide was standardised by titration with 0·4899*N*-

sulphuric acid : 25 c.c. required 25·90 c.c. with methyl-orange as indicator, and 29·95 c.c. with lacmoid, the end-points being rather indefinite; NaOMe = 0·409*N*. A solution of the bromo-ester in methyl alcohol was mixed with 147 c.c. of the sodium methoxide solution, and the whole made up to 250 c.c. at 25·0°. Samples of 10 c.c. were used for each titration with ammonium thiocyanate after addition of silver nitrate. The reading at ∞_1 was obtained after heating at 25° for 24 hours and then at 64° for 4·5 hours, and that at ∞_2 after adding an equal volume of sodium methoxide solution and heating at 64° for 1 hour.

(ii) Owing to the unsatisfactory nature of the end-points obtained in the titration of sodium methoxide in the presence of water, the titrations in this experiment were carried out by using a solution of hydrogen chloride in anhydrous methyl alcohol. This was standardised against silver nitrate. A solution of the bromo-ester (10·00 g.) in methyl alcohol was mixed with 181 c.c. of 0·662*N*-methyl-alcoholic sodium methoxide, and made up to 250 c.c. with methyl alcohol at 25°. The initial concentration of sodium methoxide was found by adding 10·00 c.c. of the reaction solution to 25·00 c.c. of 0·2317*N*-hydrogen chloride in methyl alcohol, and titrating with 0·2290*N*-sodium methoxide with the addition of solid methyl-orange as indicator : required 4·80 c.c.

The results of expts. (i) and (ii) are typical of those on which we rely for the statements in the introduction concerning the kinetics of this reaction. In Table IVA, a is the initial concentration of sodium methoxide and b that of the bromo-ester; and the bromide-ion concentration and $a - x$ and $b - x$ are expressed in c.c. of 0·1120*N*-bromide per 10 c.c. of solution. The rate constants k_2 are in min.$^{-1}$ g.-mol.$^{-1}$ l.

TABLE IVA.

Expt. (i).

t (min.).	[Br$^-$].	$a - x$.	$b - x$.	10^2k_2.
0·0	0·50	19·45	20·12	—
10·1	1·57	18·38	19·05	2·43
20·0	2·55	17·40	18·07	2·61
30·1	3·23	16·72	17·39	2·46
45·0	4·25	15·70	16·37	2·39
60·0	5·05	14·90	15·57	2·20
75·1	5·90	14·05	14·72	2·29
100·0	7·05	12·90	13·57	2·21
140·0	8·55	11·40	12·07	2·21
173·5	9·50	10·45	11·12	2·18
210·0	10·40	9·55	10·22	2·16
272·0	11·60	8·35	9·02	2·12
350·0	12·70	7·25	7·92	2·08
422·0	13·52	6·43	7·10	1·99
480·0	14·05	5·90	6·57	1·98
540·0	14·50	5·45	6·12	2·03
“ ∞_1 ”	19·95	0·00	0·67	—
“ ∞_2 ”	20·62	—	0·00	—

(a = 0·2178*N*; b = 0·2253*N*.)

Expt. (ii).

t (min.).	[Br$^-$].	$(a - x)$.	$(b - x)$.	10^2k_2.
0·0	0·77	41·90	19·29	—
6·0	2·12	40·55	17·94	2·61
10·5	3·11	39·56	16·95	2·68
16·0	4·07	38·60	15·99	2·60
21·5	5·10	37·57	14·96	2·66
29·0	6·19	36·48	13·87	2·61
36·0	7·16	35·51	12·90	2·60
45·2	8·27	34·40	11·79	2·58
56·0	9·44	33·23	10·62	2·58
69·2	10·67	32·00	9·39	2·57
85·2	11·83	30·84	8·23	2·53
113·0	13·53	29·14	6·53	2·52
130·0	14·27	28·40	5·79	2·48
150·0	15·10	27·57	4·96	2·47
182·7	16·12	26·55	3·94	2·44
215·5	16·79	25·88	3·27	2·37
“ ∞ ”	20·06	22·61	0·00	—

(a = 0·4692*N*; b = 0·2160*N*.)
($a - b$ = 0·2532*N*.)

Action of Sodium Methoxide on Methyl l-*α-Bromopropionate in Methyl Alcohol at* 25°.—A solution of the bromo-ester (19·952 g.), $\alpha_D^{20°}$ −53·2°, in methyl alcohol was added to 1·692*N*-methyl-alcoholic sodium methoxide (70·6 c.c.), and the whole was made up to 250 c.c., and heated at 25·0° for 19·0 hours. After neutralisation with methyl-alcoholic hydrogen chloride, the bulk of the solvent was removed with the use of a column, and the methoxy-ester (6·0 g.) was isolated by many extractions with ether after the addition of water. It had b. p. 31°/10 mm., 129°/760 mm., $\alpha_D^{20°}$ (l = 2·5 cm.) +0·49° (Found : C, 50·5; H, 8·8. Calc. : C, 50·8; H, 8·5%).

Action of Sodium Methoxide on Methyl d-*α-Bromopropionate in Methyl Alcohol at* 25°.—A solution of the bromo-ester (38·56 g.), $\alpha_D^{21°}$ +32·17°, in 0·3200*N*-methyl-alcoholic sodium methoxide (722 c.c.) was mixed with methyl alcohol (200 c.c.), and kept at 25·0° for 70·0 hours. The methoxy-ester (10·4 g.) had b. p. 52°/40 mm., 129—130°/760 mm., $\alpha_D^{21°}$ −1·06°. There was no indication of the formation of methyl acrylate, and, in particular, the methyl alcohol removed by distillation did not respond to a test with bromine for the presence of an olefin.

Racemisation of Methyl α-Bromopropionate in Methyl-alcoholic Sodium Methoxide at 25·0°.—A solution (i) of the bromo-ester (4·2456 g.), $\alpha_D^{23°}$ +19·74°, in methyl alcohol was made up to 25 c.c. at 25°. A solution (ii) of 1·047*N*-methyl-alcoholic sodium methoxide (24·30 c.c.) was made up to 25 c.c. at 25°. A solution (iii) prepared from (i) (10 c.c.) and methyl alcohol (10 c.c.) was examined polarimetrically. A solution (iv) prepared from (i) (10 c.c.) and (ii) (10 c.c.) was well shaken, quickly put into the jacketed polarimeter tube at 25°, and examined polarimetrically at known times. In Table V the time of the first reading on (iv) is treated as the time zero, but the time of commencement of the reaction is estimated from the reading on (iii) as 54 seconds earlier. As shown in the introduction, more than 95% of the change of rotatory power is due to the second-order racemisation of the bromo-ester, for which the rate constant is 0·888 min.$^{-1}$ g.-mol.$^{-1}$ l. (see Fig. 1, p. 1211).

TABLE V.

($\alpha_D^{25^\circ}$ refers to l = 20 cm.)

	Time,			Time,			Time,		
	min.	sec.	$\alpha_D^{25^\circ}$.	min.	sec.	$\alpha_D^{25^\circ}$.	min.	sec.	$\alpha_D^{25^\circ}$.
Soln. (iii)	—	—	+2·12°	3	17	+0·25°	9	4	−0·08°
Soln. (iv)	0	0	+1·45	3	44	+0·20	9	59	−0·06
	0	29	+1·14	4	19	+0·14	11	7	−0·07
	0	48	+0·94	5	0	+0·08	12	10	−0·07
	1	15	+0·76	5	41	+0·04	20	0	−0·07
	1	33	+0·61	6	9	+0·03	30	0	−0·08
	2	2	+0·50	7	16	±0·00	150	0	−0·10
	2	40	+0·34	8	12	−0·03			

Racemisation of Methyl α-Methoxypropionate in Methyl-alcoholic Sodium Methoxide at 24·7°.—The ester (2·9719 g. at 25°), $\alpha_D^{20^\circ}$ −53·7°, was mixed with 1·692*N*-methyl-alcoholic sodium methoxide (14·90 c.c. at 25°), and the mixture made up to 25 c.c. with methyl alcohol at 25°. After being kept for 15 min. in the thermostat, the solution was transferred to the jacketed polarimeter tube (24·7° throughout the run). The readings of rotation are in Table VI. The logarithms of the rotations give a rectilinear plot against the time. The first-order rate constant is 4·85 × 10^{-4} min.$^{-1}$, and, as the sodium methoxide is 1·007*N*, this corresponds to a second-order rate constant 4·82 × 10^{-4} min.$^{-1}$ g.-mol.$^{-1}$ l.

TABLE VI.

($\alpha_D^{25^\circ}$ refers to l = 20 cm.)

t, min.	$\alpha_D^{25^\circ}$.	t, min.	$\alpha_D^{25^\circ}$.	t, min.	$\alpha_D^{25^\circ}$.	t, min.	$\alpha_D^{25^\circ}$.
0	−8·27°	275	−7·11°	536	−6·21°	1665	−3·61°
23	−8·15	305	−6·98	566	−6·10	1752	−3·47
37	−8·09	320	−6·92	1376	−4·14	1823	−3·36
54	−8·01	416	−6·61	1448	−4·01	1895	−3·22
67	−7·95	446	−6·51	1508	−3·90	1958	−3·14
155	−7·52	473	−6·41	1605	−3·73	2000	−3·07
215	−7·30						

Rate of Reaction between Methyl dl-*α-Bromopropionate and Methyl Alcohol at* 100°.—A solution of the bromo-ester (16·0 g.) was made up to 160 c.c. in dry methyl alcohol, and portions of 10 c.c. were sealed up in glass bulbs, which were heated in pairs for known lengths of time at 100°. The course of the reaction was followed by determining the amount of bromo-ester remaining after various time intervals. The determination was made by pouring the contents of each of a pair of bulbs, which had been heated for the same known time, into water (100 c.c.) to which 2*N*-aqueous sodium hydroxide (7 c.c.) had previously been added. This treatment produces a practically instantaneous hydrolysis of bromo-ester to bromo-acid without causing further detachment of the bromine atom. The two solutions were then extracted with ether in order to remove any methyl bromide, and the concentration of bromide ions in one of them was determined by titration with silver nitrate and ammonium thiocyanate. The other was treated with a further 7 c.c. of 2*N*-aqueous sodium hydroxide and boiled for 30 minutes, in order to hydrolyse all the bromopropionic acid to lactic acid; then the bromide ion present in this solution was determined. The difference between the two amounts of bromide ion represented the amount of bromo-ester which remained undecomposed when the two bulbs were removed from the thermostat. The method was checked by blank experiments and shown to be reliable.

The results are in Table VII. The concentrations of bromide ion are in c.c. of 0·1*N*-silver per 10 c.c. of solution. The mean first-order rate constant is 2·95 × 10^{-6} sec.$^{-1}$.

TABLE VII.

Time (hours).	Bromide ion.			10^6k_1 (sec.$^{-1}$).	Time (hours).	Bromide ion.			10^6k_1 (sec.$^{-1}$).
	(1).	(2).	(2) − (1).			(1).	(2).	(2) − (1).	
0·00	0·00	60·1	60·1	—	65·00	3·16	34·5	31·3	2·79
23·25	1·14	47·4	46·3	3·11	87·50	5·12	29·4	24·3	2·88
39·00	1·98	41·1	39·1	3·01					

Reaction of Methyl d-α-*Bromopropionate with Methyl Alcohol at* 100°.—(i) A solution of the ester (10 g.), having $\alpha_{\mathrm{D}}^{23^\circ}$ +29·0°, in methyl alcohol was made up to 100 c.c., and heated in sealed tubes at 100° for 25 hours. The methyl alcohol was removed by distillation, poured into 4 vols. of water, and extracted with ether. The residue from this extract was added to the main ester residue, and the whole was distilled at 20 mm. After several distillations the material was divided into a yellow head-fraction (0·7 g.), which proved to be impure methyl α-methoxypropionate containing residual methyl α-bromopropionate, and a main fraction (4·8 g.) consisting essentially of methyl α-bromopropionate. The crude methoxy-ester was lævorotatory : $\alpha_{\mathrm{D}}^{23^\circ}$ −0·67°. The bromo-ester was dextrorotatory, but much racemised : $\alpha_{\mathrm{D}}^{22^\circ}$ +1·00°.

(ii) A solution of the ester (20 g.), having $\alpha_{\mathrm{D}}^{20^\circ}$ +29·6°, in methyl alcohol was made up to 200 c.c., and heated in sealed tubes at 100° for 230 hours. When the tubes were opened, volatile products, presumably mainly methyl ether, boiled away, and the remaining solvent was then removed by distillation from a water-bath. The residue was taken up in ether, dried, and after removal of the solvent, distilled. The main fraction, b. p. 80°/5 mm., had $\alpha_{\mathrm{D}}^{21^\circ}$ −2·60°, but after several distillations the rotation rose to $\alpha_{\mathrm{D}}^{20^\circ}$ −2·72°, and then remained constant when in the final distillation a central cut was made. Analysis showed this product to consist of α-methoxypropionic acid containing 7% of residual α-bromopropionic acid (Found : C, 44·3; H, 7·3; Br, 3·77. Calc. for a mixture of 92·95% by weight of α-methoxypropionic acid and 7·05% of α-bromopropionic acid : C, 44·5; H, 7·4; Br, 3·77%).

Racemisation of Methyl d-α-*Bromopropionate in Methyl-alcoholic Solution at* 100°.—A solution of the bromo-ester (25 g.), having $\alpha_{\mathrm{D}}^{20^\circ}$ +29·6°, in methyl alcohol was made up to 250 c.c. Portions of this solution were enclosed in glass bulbs, and heated at 100° for various known times. The rotations of the contents of the bulbs were then measured at 20°. The results given in Table VIII are plotted in Fig. 2 (p. 1215). It is shown in the introduction that nearly the whole of the fall of rotatory power is due to racemisation of the bromo-ester by two mechanisms operating simultaneously.

TABLE VIII.

Time (hrs.)	0·00	1·70	2·30	3·63	4·23	5·25	7·00	9·25	13·00	14·50
$\alpha_{\mathrm{D}}^{20^\circ}$	+1·86°	+1·55°	+1·42°	+1·20°	+1·02°	+0·82°	+0·56°	+0·25°	+0·02	−0·01

Rate of Reaction between Sodium Methoxide and Sodium dl-α-*Bromopropionate in Methyl Alcohol at* 64·0°.—The methyl alcohol was dried by means of magnesium, and the α-bromopropionic acid was dried over phosphoric oxide in a vacuum. The following is a representative selection from our experiments (cf. Table IX, in which second-order rate constants, k_2, are in min.$^{-1}$ g.-mol.$^{-1}$ l. and first-order constants, k_1, in min.$^{-1}$).

(i) The acid (9·83 g.) was added to 1·69*N*-methyl-alcoholic sodium methoxide (190 c.c.), and the solution was made up to 250 c.c. at room temperature, and enclosed in 10 c.c. portions in sealed bulbs. In order to obtain the initial concentration (a) of sodium methoxide, a bulb was shaken for 1 minute in the thermostat at 64°, and its contents then titrated with 0·4899*N*-sulphuric acid : required 19·95, 20·00 c.c., and hence a = 0·9197. The other bulbs were used to estimate the concentration of bromide ions formed after different times at 64·0° ; the estimation was performed by titration with silver nitrate and ammonium thiocyanate. The initial concentration of sodium α-bromopropionate (b) was given by the final, less the initial, concentration of bromide; b = 0·2007. All concentrations are corrected for thermal expansion, the factor used being 0·94. Rate constants are in min.$^{-1}$ g.-mol.$^{-1}$ l.

(ii) A solution of the acid (9·640 g.) in 1·078*N*-methyl-alcoholic sodium methoxide (175 c.c.) was made up to 250 c.c. with dry methyl alcohol. The initial concentrations were a = 0·4650 and b = 0·2192. The estimations were performed as in expt. (i). The final concentration of sodium methoxide should be $a - b$ = 0·2458. A direct determination by titration (10 c.c.) with 0·4899*N*-sulphuric acid (required 5·55 c.c.) gave the value 0·2464*N*. The concentrations are corrected for expansion.

(iii) The acid (9·9470 g.) was added to a methyl-alcoholic solution (229 c.c.) which was 0·852*N* with respect to sodium methoxide, and contained 15·9 g. of sodium bromide per 270 c.c. The initial concentrations, measured as usual after shaking the bulbs for 1 minute in the thermostat, were a = 0·4604, b = 0·2281, $[\mathrm{NaBr}]_{\mathrm{initial}}$ = 0·5038. The concentrations are corrected.

(iv) The acid (1·2042 g.) and 0·2*N*-methyl-alcoholic sodium methoxide (79 c.c.) were together made up to 250 c.c. with dry methyl alcohol. The initial concentrations, determined as usual, were a = 0·0300, b = 0·0309. The reaction was followed by determination of both bromide ions and alkalinity. The concentrations in Table IX are expressed in c.c. of 0·02500*N*-bromide, or 0·0268*N*-alkali per 10 c.c. of solution. All concentrations in this experiment are uncorrected for thermal expansion, since the rate constants are now dimensionless with respect to concentration.

(v) A solution of the acid (1·2014 g.) in 0·2*N*-methyl-alcoholic sodium methoxide (118 c.c.) was made up to 250 c.c. with anhydrous methyl alcohol. The initial concentrations were $a = 0·0577$ and $b = 0·0309$. The reaction was followed by determination of both bromide ions and alkalinity. In Table IX, $a - x$ is expressed in c.c. of 0·0268*N*-alkali, and $b - x$ in c.c. of 0·02500*N*-bromide, per 10 c.c. of solution. Concentrations are uncorrected for expansion.

TABLE IX.

Expt. (i).

t (min.).	$[\mathrm{Br}^-]$.	$a - x$.	$b - x$.	10^2k_2.
0·0	0·0404	—	—	—
1·5	0·0541	0·9060	0·1870	5·16
4·0	0·0747	0·8854	0·1664	5·19
7·0	0·0974	0·8627	0·1437	5·35
10·0	0·1143	0·8458	0·1268	5·22
14·0	0·1362	0·8239	0·1049	5·09
20·0	0·1591	0·8010	0·0820	5·25
29·0	0·1845	0·7756	0·0566	5·25
45·0	0·2071	0·7530	0·0340	4·87
62·0	0·2236	0·7365	0·0175	4·97
77·0	0·2316	0·7285	0·0095	5·09
"∞"	0·2411	0·7190	—	—

Expt. (ii).

t (min.).	$[\mathrm{Br}^-]$.	$a - x$.	$b - x$.	10^2k_2.
0	0·0160	—	—	—
5	0·0307	0·4503	0·2045	3·02
10	0·0460	0·4350	0·1892	3·26
15	0·0608	0·4202	0·1744	3·45
20	0·0698	0·4112	0·1654	3·22
30	0·0888	0·3922	0·1464	3·16
45	0·1114	0·3696	0·1238	3·09
65	0·1355	0·3455	0·0997	3·07
90	0·1575	0·3235	0·0777	3·05
120	0·1792	0·3018	0·0560	3·16
150	0·1924	0·2886	0·0428	3·14
190	0·2051	0·2759	0·0301	3·13
230	0·2135	0·2675	0·0217	3·09
280	0·2208	0·2602	0·0144	3·09
"∞"	0·2352	0·2458	—	—

Expt. (iii).

t (min.).	$[\mathrm{Br}^-]$.	$a - x$.	$b - x$.	10^2k_2.
0	0·5038	—	—	—
10	0·5522	0·4120	0·1797	5·47
16	0·5719	0·3923	0·1600	5·23
23	0·5898	0·3744	0·1421	4·99
31	0·6104	0·3538	0·1215	5·08
40	0·6243	0·3399	0·1076	4·82
50	0·6421	0·3221	0·0898	4·95
63	0·6553	0·3089	0·0766	4·73
79	0·6696	0·2946	0·0623	4·64
96	0·6826	0·2816	0·0493	4·67
121	0·6953	0·2689	0·0366	4·60
146	0·7076	0·2566	0·0243	4·88
176	0·7129	0·2513	0·0190	4·60
211	0·7213	0·2429	0·0106	4·96
"∞"	0·7319	0·2323	—	—

Expt. (iv).

t (min.).	$b - x$.	10^3k_1.	$a - x$.	10^3k_1.
0	12·35	—	11·18	—
30	11·12	3·50	10·18	3·13
70	9·65	3·53	8·63	3·70
118	8·38	3·29	7·08	3·87
170	7·17	3·20	6·13	3·53
230	5·90	3·21	4·48	3·98
310	4·64	3·16	3·53	3·72
430	3·17	3·16	2·43	3·55
600	2·12	2·94	—	—

Expt. (v).

t (min.).	$b - x$.	10^3k_1.	$a - x$.	10^3k_1.
0	12·35	—	21·52	—
30	10·96	3·98	19·90	4·61
65	9·83	3·51	19·00	3·45
110	8·33	3·58	17·30	3·73
165	6·86	3·56	16·40	3·18
235	5·50	3·44	14·55	3·45
310	4·31	3·40	13·45	3·33
430	2·92	3·35	11·40	3·83
600	1·77	3·24	—	—

Expt. (vi).

t (min.).	$[\mathrm{Br}^-]$.	$b - x$.	10^3k_1.
0	0·13	12·31	—
42	1·85	10·59	3·59
64	2·71	9·73	3·67
85	3·37	9·07	3·59
112	4·06	8·38	3·43
140	4·94	7·50	3·53
150	5·11	7·33	3·46
173	5·55	6·89	3·36
204	6·36	6·08	3·46
245	7·01	5·43	3·34
295	7·85	4·59	3·34
356	8·63	3·81	3·30
420	9·27	3·17	3·23
505	9·98	2·46	3·19
"∞"	12·44	—	—

Expt. (vii).

	α.		β.	
t (min.).	$a - x$.	10^3k_1.	$a - x$.	10^3k_1.
0	11·50	—	11·44	—
30	—	—	10·57	2·64
30·5	10·15	4·01	—	—
50	9·90	3·00	10·15	2·40
75	9·37	2·73	9·63	2·24
05	8·10	3·34	9·15	2·13
145	6·90	3·52	8·35	2·17
198	5·72	3·53	7·15	2·37
240	4·90	3·55	6·85	2·14
295	4·00	3·58	5·55	2·45
363	3·30	3·44	5·00	2·28
490	2·30	3·29	4·25	2·02

(vi) A solution of the acid (2·4030 g.) in 0·3992*N*-sodium methoxide (79 c.c.) was made up to 250 c.c. The initial concentrations were $a = 0·0584$, $b = 0·0616$. The concentrations are uncorrected, and, in Table IX, are in c.c. of 0·0500*N*-bromide ion per 10 c.c. of solution.

(vii) A solution, containing the acid (2·4034 g.) and 0·1*N*-sodium methoxide (330 c.c.), and made up to 500 c.c., was divided into two equal portions. The first (α) was studied in the usual way, and the second (β) after additions of 12·9 g. of sodium bromide. The initial concentrations were for (α) $a = 0{\cdot}0309$ and for (β) $a = 0{\cdot}0306$ and $[\mathrm{NaBr}]_{\text{initial}} = ca.\ 0{\cdot}50N$. The concentrations are uncorrected, and, in Table IX, are in c.c. of 0·0268*N*-alkali per 10 c.c. of solution.

Action of Concentrated (N) *Sodium Methoxide on Sodium* d-*α-Bromopropionate in Methyl Alcohol at* 64°.—A solution of the acid (9·65 g.), $\alpha_D^{20^\circ}$ +12·9°, in 1·39*N*-methyl-alcoholic sodium methoxide (226 c.c.) was made up to 250 c.c. with dry methyl alcohol, heated at 64° for 18·5 hours, neutralised with methyl-alcoholic sulphuric acid and evaporated on the steam-bath. Water (75 c.c.) was then added, and the whole evaporated to 35 c.c., acidified with 18 c.c. of dilute sulphuric acid (50% by vol.), and extracted many times with ether. The methoxy-acid (4·9 g.), b. p. 103—104°/22 mm., had $\alpha_D^{26^\circ}$ (l = 2·5 cm.) −4·95° (Found: C, 45·7; H, 7·9. Calc.: C, 46·1; H, 7·7%).

Action of Dilute (N/16) *Sodium Methoxide on Sodium* d-*α-Bromopropionate in Methyl Alcohol at* 64°.—A solution of the bromo-acid (9·696 g.), $\alpha_D^{20^\circ}$ +12·9°, in 0·1725*N*-methyl-alcoholic sodium methoxide (810 c.c.) was made up to 1000 c.c. with dry methyl alcohol, heated at 64° for 26 hours, neutralised with methyl-alcoholic hydrogen chloride, and evaporated to dryness. The residue was dissolved in 15 c.c. of 6*N*-aqueous sulphuric acid, and extracted thoroughly with ether. The methoxy-acid (5·0 g.), b. p. 110°/30 mm., had $\alpha_D^{26^\circ}$ (l = 2·5 cm.) +4·47° (Found: C, 45·5; H, 7·9%).

Rate of Reaction of α-Bromopropionic Acid in Aqueous Sulphuric Acid at 100°.—The acid (3·808 g.) was made up to 250 c.c. with 0·4899*N*-aqueous sulphuric acid, and portions of 10 c.c. were enclosed in bulbs which were heated in a boiling water-bath for known lengths of time before estimation of the bromide ion. The initial estimation was made 10 minutes after putting a bulb into the bath, and the reading was treated as corresponding to zero time. The values of $b - x$ in Table X are in c.c. of 0·0508*N*-bromide ion per 10 c.c. of solution. The constants are in min.$^{-1}$.

TABLE X.

t (min.).	$b - x$.	10^3k_1.	t (min.).	$b - x$.	10^3k_1.	t (min.).	$b - x$.	10^3k_1.
0	18·27	—	70	12·59	5·32	175	7·04	5·45
10·1	17·29	5·45	85	11·59	5·36	200	5·99	5·58
20	16·39	5·42	100	10·64	5·41	230	5·11	5·54
30	15·49	5·49	110	10·01	5·47	260	4·38	5·49
41	14·54	5·57	130	8·84	5·58	295	3·71	5·42
55	13·46	5·55	150	7·94	5·55		Mean	5·48

Reaction of d-*α-Bromopropionic Acid with Aqueous Sulphuric Acid.*—The acid (15·00 g.), $\alpha_D^{25^\circ}$ +19·00°, was made up to 1000 c.c. with 0·534*N*-aqueous sulphuric acid, and the solution heated at 88—94° for 50 hours. The neutralised solution was evaporated under reduced pressure until a considerable amount of salt had separated, and then filtered, the salts being washed with absolute ethyl alcohol. The washings, combined with the filtrate, were evaporated to dryness, and the residue was further evaporated with additions of dry ethyl alcohol, and warmed under reduced pressure, in order to complete the removal of water. The dried residue was then heated under reflux for 3 hours with anhydrous ethyl alcohol (140 c.c.) and concentrated sulphuric acid (7 g.). The solution was neutralised with ethyl-alcoholic sodium ethoxide, and evaporated to remove alcohol, the crystalline salts being separated by filtration. The residue was distilled completely at 20 mm., and the ethyl lactate again distilled. It had b. p. 64°/22 mm. (4·5 g.), and $\alpha_D^{23^\circ}$ −0·61° (Found: C, 50·4; H, 8·7. Calc.: C, 50·8; H, 8·5%).

Rate of Racemisation of d-*α-Bromopropionic Acid in Aqueous Sulphuric Acid.*—(i) A solution of the acid (7·612 g.), having $\alpha_D^{25^\circ}$ +19·0°, in 0·535*N*-aqueous sulphuric acid was made up to 500 c.c. Portions of 40 c.c. were enclosed in glass bulbs, heated for known times at 100°, then chilled and examined for rotatory power. The observed rotations are in Table XI, in which they are compared with the rotations calculated from the theoretical equation (see Appendix).

(ii) Another experiment with the same acid (7·162 g.) was carried out in the same way (all other concentrations and quantities being unchanged) in order to investigate more carefully the earlier part of the reaction. The rotations are in the right-hand part of Table XI.

These results are plotted in Fig. 4. It was shown by special experiments that, within the range of concentration with which we are here concerned, the rotation of a solution of *d*-α-bromopropionic acid in 0·53*N*-aqueous sulphuric acid is accurately proportional to the concentration of the optically active acid. The rotatory power of lactic acid in the sulphuric acid medium

TABLE XI.

($\alpha_{\mathrm{D}}^{22^\circ}$ refers to l = 40 cm.)

(i).						(ii).			
t (min.).	$\alpha_{\mathrm{D}}^{22^\circ}$.	α (calc.).	t (min.).	$\alpha_{\mathrm{D}}^{22^\circ}$.	α (calc.).	t (min.).	$\alpha_{\mathrm{D}}^{25^\circ}$.	t (min.).	$\alpha_{\mathrm{D}}^{25^\circ}$.
1	+0·69°	+0·71°	137	+0·01°	+0·02°	5	+0·65°	55	+0·29°
31	+0·49	+0·47	181	±0·00	+0·01	15	+0·58	65	+0·21
51	+0·33	+0·32	226	±0·00	+0·00	25	+0·51	75	+0·16
81	+0·14	+0·15	266	±0·00	+0·00	35	+0·44	85	+0·11
106	+0·05	+0·06				45	+0·37	95	+0·09

was determined by making up a solution of recrystallised *l*-lactic acid (2·098 g.) in 0·535*N*-aqueous sulphuric acid to 250 c.c. and measuring the rotation: $\alpha_{\mathrm{D}}^{20^\circ}$ (l = 40 cm.) = +0·05°. From this figure we can deduce that the lactic acid formed in the experiments recorded in Table XI would not make an appreciable contribution to the rotations.

Effect of Hydrogen-ion Concentration on Rate of Reaction of α-Bromopropionic Acid in Aqueous Sulphuric Acid.—Two experiments with different initial concentrations of sulphuric acid were carried out simultaneously, a boiling water-bath being used as thermostat. This was done in order to eliminate any influence on the rate difference, arising from the effect of varying atmospheric pressure on the exact temperature of the bath. In expt. (i) a solution of α-bromopropionic acid (9·502 g.) in water was made up to 50 c.c., and 20 c.c. of this were made up to 250 c.c. with 0·5345*N*-aqueous sulphuric acid. The sulphuric acid concentration was therefore 0·491*N*, and that of the bromopropionic acid 0·0993*M*. Portions of 10 c.c. were sealed up in separate bulbs, and heated in the bath for the times indicated in Table XII. The values of $b - x$ are expressed in c.c. of 0·03948*N*-ammonium thiocyanate per 10 c.c. sample; and the rate constants k_1 are in min.$^{-1}$. An initial estimation made 10 minutes after putting the bulbs into the bath was treated as corresponding to zero time. In expt. (ii) a solution of α-bromopropionic acid (4·857 g.) in water was made up to 25 c.c., and 20 c.c. of this were diluted to 250 c.c. with 0·2672*N*-aqueous sulphuric acid. The sulphuric and α-bromopropionic acid concentrations were thus 0·245*N* and 0·1013*M* respectively. The reaction was followed in the manner described, with the results recorded in Table XII.

TABLE XII.

Expt. (i).			Expt. (ii).		
t (min.).	$b - x$.	10^3k_1 (min.$^{-1}$).	t (min.).	$b - x$.	10^3k_1 (min.$^{-1}$).
0·0	24·85	—	0·0	24·80	—
10·0	23·25	6·65	10·0	22·85	(8·17)
25·0	21·20	6·35	21·0	21·20	7·45
31·0	20·50	6·20	30·0	19·70	7·68
51·0	18·38	5·90	40·0	18·45	7·38
75·8	15·70	6·07	58·0	16·23	7·29
90·0	14·65	5·88	70·0	15·00	7·18
97·0	14·05	5·88	90·0	13·18	7·04
127·0	12·05	5·70	122·0	10·50	7·04
187·0	8·29	5·85	160·0	8·10	7·00
212·2	7·25	5·80	220·0	5·57	6·79
270·0	5·52	5·57	300·0	3·25	6·77
		Mean 5·99			Mean 7·18

Rate of Reaction between Sodium Hydroxide and Sodium α-Bromopropionate in Aqueous Solution at 64·0°.—Six experiments are here recorded, covering the range of concentration investigated. In Table XIII, second-order rate constants (k_2) are in min.$^{-1}$ g.-mol.$^{-1}$ l., and first-order constants (k_1) in min.$^{-1}$.

(i) α-Bromopropionic acid (9·8489 g.) and 1·971*N*-aqueous sodium hydroxide (164 c.c.) were made up to 250 c.c. at 64·0°, all materials being previously brought to this temperature. After 7 minutes in the thermostat, titrations were commenced, 10 c.c. being withdrawn for each estimation of bromide ion. The concentration of sodium hydroxide at the starting time (a) was measured by titration with sulphuric acid; the corresponding concentration of sodium α-bromopropionate (b) is taken as the difference between the initial and the " infinity " value of bromide ion.

(ii) α-Bromopropionic acid (9·8405 g.), water (142 c.c.) and 1·971*N*-aqueous sodium hydroxide (98 c.c.) were together made up to 250 c.c. at 64·0°, the method being otherwise as under (i).

(iii) A solution of the acid (1·2042 g.) in water (180 c.c.) was mixed with 0·2597*N*-aqueous sodium hydroxide (67 c.c.) and made up to 250 c.c. at 64·0°. The withdrawal of samples for estimation of bromide ion was commenced 5 minutes later. The concentrations of free sodium hydroxide at zero and " infinite " time, estimated by titration with sulphuric acid, were 0·0348N and 0·0056N respectively. The corresponding concentrations of bromide ion were 0·0014N and 0·0310N respectively. In Table XIII, the values of $b - x$ are expressed in c.c. of thiocyanate equivalent to 10 c.c. of the solution; the value of b, given as 18·41 c.c., corresponds to 0·0310 — 0·0014 = 0·0296N.

(iv) A solution of the acid (1·2042 g.) in 0·2597N-aqueous sodium hydroxide (100 c.c.) was made up to 250 c.c. at 64°. The estimations were performed as under (iii) except that the titrations with sulphuric acid were omitted.

TABLE XIII.

Expt. (i).

t (min.).	[Br$^-$].	$a - x$.	$b - x$.	10^2k_2.
0·00	0·0757	0·9552	0·1799	—
1·65	0·0867	0·9442	0·1689	4·05
2·27	0·0903	0·9406	0·1653	3·94
3·27	0·0953	0·9356	0·1603	3·74
4·50	0·1030	0·9279	0·1526	3·90
6·17	0·1108	0·9201	0·1448	3·75
8·25	0·1215	0·9094	0·1341	3·83
10·40	0·1312	0·8997	0·1244	3·84
12·95	0·1403	0·8906	0·1153	3·74
15·7	0·1515	0·8794	0·1041	3·82
19·5	0·1638	0·8671	0·0918	3·81
24·6	0·1782	0·8527	0·0774	3·83
31·9	0·1942	0·8367	0·0614	3·81
43·6	0·2130	0·8179	0·0426	3·80
55·2	0·2260	0·8049	0·0296	3·82
69·3	0·2371	0·7938	0·0185	3·89
92·4	0·2460	0·7849	0·0096	3·80
" ∞ "	0·2556	0·7753	—	—

Expt. (ii).

t (min.).	[Br$^-$].	$a - x$.	$b - x$.	10^2k_2.
0·00	0·0378	0·4650	0·2239	—
8·75	0·0706	0·4322	0·1911	4·04
15·27	0·0906	0·4122	0·1711	4·11
21·30	0·1066	0·3962	0·1551	4·03
26·25	0·1175	0·3853	0·1442	3·98
33·75	0·1338	0·3690	0·1279	4·04
46·1	0·1542	0·3486	0·1075	4·01
61·0	0·1748	0·3290	0·0869	4·08
80·3	0·1929	0·3099	0·0688	4·00
96·0	0·2115	0·2913	0·0502	4·43
141·3	0·2282	0·2746	0·0335	4·03
187·0	0·2429	0·2599	0·0188	4·21
" ∞ "	0·2617	0·2411	—	—

Expt. (iii).

t (min.).	[Br$^-$].	$b - x$.	10^3k_1.
0·0	0·56	11·84	—
12·0	1·43	10·97	6·37
20·7	2·15	10·25	6·98
30·6	2·90	9·50	7·20
40·8	3·60	8·80	7·28
51·2	4·22	8·18	7·22
62·3	4·80	7·60	7·12
78·3	5·60	6·80	7·09
132·5	7·75	4·65	7·06
152·5	8·32	4·08	6·99
171·5	8·80	3·60	6·94
208·5	9·45	2·95	6·68
253·0	10·33	2·07	6·90
" ∞ "	12·40	—	—

Expt. (iv).

t (min.).	[Br$^-$].	$b - x$.	10^3k_1.
0·0	0·63	12·21	—
12·6	1·67	11·17	7·07
21·7	2·32	10·52	6·87
30·6	3·00	9·84	7·05
41·0	3·70	9·14	7·06
50·4	4·42	8·42	7·37
62·1	5·02	7·82	7·18
75·3	5·76	7·08	7·24
89·1	6·39	6·45	7·16
106·3	7·10	5·74	7·10
180·0	9·37	3·47	6·99
210·0	9·86	2·98	6·72
266·0	10·72	2·12	6·58
" ∞ "	12·84	—	—

Expt. (v).

t (min.).	[Br$^-$].	$b - x$.	10^3k_1.
0·0	0·64	11·80	—
11·7	1·60	10·84	7·26
21·0	2·37	10·07	7·56
31·0	3·13	9·31	7·65
41·0	3·80	8·64	7·61
50·0	4·40	8·04	7·67
62·0	5·03	7·41	7·51
74·5	5·65	6·79	7·42
90·0	6·40	6·04	7·46
110·4	7·22	5·22	7·39
131·0	7·95	4·49	7·38
187·0	9·43	3·01	7·31
222·4	10·05	2·39	7·18
260·5	10·55	1·89	7·03
300·4	11·10	1·30	7·34
" ∞ "	12·44	—	—

Expt. (vi).

t (min.).	[Br$^-$].	$b - x$.	10^3k_1.
0·0	1·27	18·41	—
10·8	2·95	16·73	8·85
20·0	4·27	15·41	8·89
29·0	5·40	14·28	8·75
40·0	6·68	13·00	8·70
49·0	7·57	12·11	8·55
61·0	8·65	11·03	8·40
77·0	10·10	9·58	8·48
96·0	11·37	8·31	8·29
142·0	13·75	5·93	7·98
171·0	14·85	4·73	7·95
206·0	15·97	3·71	7·78
246·0	16·90	2·78	7·69
299·0	17·70	1·98	7·46
360·0	18·35	1·33	7·30
" ∞ "	19·68	—	—

(v) The acid (2·4062 g.) and 0·259*N*-aqueous sodium hydroxide (133 c.c.) were together made up to 250 c.c. at 64°. The estimations were carried out as under (iii). The initial and the final concentration of sodium hydroxide, as determined by titration with sulphuric acid, were 0·0678*N* and 0·0095*N*, and those of bromide ion were 0·0032*N* and 0·0628*N*. In the table the value of *b*, given as 11·80 c.c., corresponds to 0·0596*N*.

(vi) The acid (3·832 g.) and 0·2597*N*-aqueous sodium hydroxide were together made up to 250 c.c. at 64°, and the estimations were performed as under (iii). The initial and the final concentration of sodium hydroxide as estimated by titration with acid were 0·1080*N* and 0·0161*N*; the corresponding concentrations of bromide ion were 0·00641*N* and 0·0995*N*. The value of *b*, given as 18·41 c.c., is thus 0·0931*N*.

Action of Concentrated (N) *Sodium Hydroxide on Sodium* d-*α-Bromopropionate in Water at* 64°.—The acid (15·01 g.), $\alpha_D^{18\cdot5^\circ}$ +19·12°, was added to water (133 c.c.) and 1·971*N*-aqueous sodium hydroxide (250 c.c.) at 64°. After 3 hours at this temperature, the mixture was neutralised with 6*N*-aqueous sulphuric acid, and evaporated to dryness under reduced pressure. The residue was re-evaporated with the addition of absolute ethyl alcohol, and heated in a vacuum for 10 minutes. It was then heated under reflux for 4 hours with dry ethyl alcohol (140 c.c.) and concentrated sulphuric acid (7 g.). The cooled product was filtered, and the salts washed with dry ethyl alcohol. The combined filtrate and washings were neutralised with ethyl-alcoholic sodium ethoxide and evaporated, the salts being removed from time to time by filtration, and, in the last stages, by precipitation with ether and filtration. The residue of ethyl lactate, after two distillations, had b. p. 66°/23 mm., $\alpha_D^{26^\circ}$ −2·26° (Found : C, 50·7; H, 8·8. Calc. : C, 50·8; H, 8·5%).

Action of Dilute (M/16) *Sodium Hydroxide on Sodium* d-*α-Bromopropionate in Water at* 64°.—A solution of the acid (15·01 g.), $\alpha_D^{18\cdot5^\circ}$ +19·12°, in water (740 c.c.) was mixed with 0·2597*N*-aqueous sodium hydroxide (755 c.c.) and kept at 64° for 16·25 hours. It was then neutralised with 0·5*N*-aqueous sulphuric acid, and evaporated to dryness, and the residue dehydrated, and esterified with ethyl alcohol as described above. The ethyl lactate had b. p. 64°/21 mm., $\alpha_D^{26^\circ}$ +3·12° (Found : C, 50·4; H, 8·7%).

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