256. *Reaction Kinetics and the Walden Inversion. Part V. Action of Silver Salts in Hydroxylic Solvents on α-Bromopropionic Acid, its Methyl Ester, and Sodium Salt.*

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The stereochemical study of the reactions of halides with silver salts in hydroxylic media is here extended to halides with either a formally neutral or an ionic modification of the carboxyl group ($\cdot CO_2Me$, $\cdot CO\cdot NH_2$; or $\cdot CO_2^-$) in attachment to the seat of substitution. The silver salts included silver nitrate in solution and silver oxide in suspension; the halogen compounds were derivatives of α-bromopropionic acid, which was used in the form of its methyl ester, the acid itself or its silver salt, and its sodium salt. However it was shown kinetically that when either the acid or one of its salts is employed the entity substituted is essentially the α-bromopropionate ion, so that effectively we have only two cases to consider, characterised respectively by the attachment of a substituted carboxyl group, and a carboxylate ion group, at the asymmetric centre. It was also proved kinetically that the reagent supplied by silver nitrate is silver ions adsorbed on silver bromide, whilst with silver oxide the attack is by silver ions on both silver bromide and silver oxide.

The optical data relate to the methoxylation of the methyl ester with silver nitrate, and the hydroxylation of the amide with silver carbonate, and of the anion with silver nitrate, carbonate, and oxide. With the ester and amide the predominating orientation was inversion, whilst with the anion it was retention of form; but in all cases there was definite racemisation. Quantitative particulars are given. The results of Parts IV and V resemble those obtained for homogeneous unimolecular substitution (Parts I—III).

The aim of the work here reported is to establish the spatial orientation of the hydroxylation and alkoxylation of α-halogeno-carboxylic acids and their derivatives when these substitutions are carried out by means of silver salts in the presence of aqueous or alcoholic media. As examples of silver salts we have employed silver nitrate in solution and silver oxide in suspension. As halogen compounds we have used derivatives of one of the simplest optically resolvable halogeno-acids, *viz.*, α-bromopropionic acid, which was employed as such or in the form of its methyl ester or silver or sodium salt; but we shall show that when either the acid or one of its salts is used the entity substituted is essentially the α-bromopropionate ion; so that effectively we have to consider only two cases, typified respectively by the attachment of a carbomethoxyl group and a carboxylate ion group to the atom at which substitution occurs. We shall treat these cases separately, as the results are rather distinct. The reactions examined were the methoxylation of the methyl ester by means of silver nitrate in methyl-alcoholic solution; and the hydroxylation of the anion, either by aqueous silver nitrate, or by silver oxide suspended in water or aqueous acetone.

(1) *The Ester* (*and an Amide*).—A kinetic study of the action of silver nitrate in alcoholic solution on methyl bromoacetate and several homologues has been recorded by Senter (J., 1911, **99**, 95). He observed heterogeneous catalysis by silver bromide, although this effect seemed less powerful than in corresponding experiments with the free acids; and his results could be represented in terms of second-order constants which tended to decrease as reaction progressed. Our more restricted experiments with methyl α-bromopropionate and silver nitrate in methyl alcohol as solvent confirm Senter's. With both solutes originally in 0·16*M*-concentration, the period of half-change at 64° was 4·7 hours, and the approximate second-order rate constant 0·0005 sec.$^{-1}$ g.-mol.$^{-1}$ l. Since, even at 100°, the homogeneous reaction of the bromo-ester with methyl alcohol, independently of silver salts, has a first-order rate constant of only 0·00000295 sec.$^{-1}$, corresponding to a half-change period of 67 hours (Part III), this process must be quite negligible in comparison with the reaction of the bromo-ester with silver nitrate. The silver nitrate reaction evidently involves a heterogeneous attack by silver ions on bromo-ester adsorbed on silver bromide; but it is rather more likely here than in some other reactions of silver salts with halides that there is also a homogeneous attack by silver ions, although any rigorous proof of this would be difficult to devise.

The optical effect of the substitution is shown by the following experiment. A methyl-alcoholic solution, originally 0·16*M* with respect to methyl *d*-α-bromopropionate and 0·166*M* with respect to silver nitrate, was kept at 64° for 7 days, a time amply sufficient to complete the decomposition. The product, a mixture of methyl α-methoxypropionate and *methyl α-nitratopropionate*, was separated into its constituents by distillation. The rotations were as follows * :

$$(\alpha_D^{20^\circ} + 31{\cdot}8^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2Me \xrightarrow[\text{in MeOH}]{AgNO_3} \begin{cases} CH_3{\cdot}CH(OMe){\cdot}CO_2Me\ (\alpha_D^{17^\circ} - 36{\cdot}4^\circ) \\ CH_3{\cdot}CH(ONO_2){\cdot}CO_2Me\ (\alpha_D^{17^\circ} - 35{\cdot}9^\circ) \end{cases}$$

As was shown in Part III, an inversion in the sign of rotation on passing from the bromo-ester to the methoxy-ester means an inversion of configuration. The maximal rotatory powers (α_D) of these two esters being 74° and 95° respectively, the retention of activity in the substitution amounts to 89%. Presumably the inverted sign of rotation of the nitrato-ester also signifies an inversion of configuration, but this relationship has not been independently established, nor has the maximal rotatory power of the nitrato-ester been determined.

Considerations of analogy and theory suggest that amides should behave quite similarly to esters with respect to the property we are concerned to investigate; but we have not carried out a similar study with a representative amide because this case is really covered by an experiment performed by E. Fischer (*Ber.*, 1907, **40**, 489). He effected the hydroxylation of *l*-α-bromopropionylglycine by means of silver carbonate and water, and observed an optical effect which we can recognise as indicating a predominating inversion of configuration : the original glycine was prepared from *l*-α-bromopropionic acid and the final glycine hydrolysed to *d*-lactic acid † :

$$l\text{-}CH_3{\cdot}CHBr{\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO_2H \xrightarrow[H_2O]{Ag_2CO_3} d\text{-}CH_3{\cdot}CH(OH){\cdot}CO{\cdot}NH{\cdot}CH_2{\cdot}CO_2H$$

The retention of activity observed by Fischer may be estimated from his data as 73%, but his technique was unsuitable for quantitative work : he converted the lactylglycine into lactic acid, and, for polarimetric examination, isolated crystalline zinc lactate, which, owing to its considerable solubility, was obtained in poor yield, and doubtless with some

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

† This is the lævorotatory acid which gives dextrorotatory salts and esters : Fischer calls it *l*-lactic acid.

preferential separation of either the principal enantiomeride or the racemate. However, there can be no doubt about the qualitative orientational similarity between our alkoxylation of the ester and his hydroxylation of the amide, through the agency of silver salts.

(2) *The Acid and its Salts.*—The kinetics of the hydroxylation of α-halogeno-acids by means of silver nitrate in aqueous solvents have been studied by several authors. Euler (*Ber.*, 1906, **39**, 2726) examined the reaction between chloro- and bromo-acetic acid on the one hand, and aqueous or aqueous-alcoholic silver nitrate on the other; and found that calculated second-order rate constants decreased as substitution progressed, owing, as he deduced, to the circumstance that most of the reaction went through the small proportion of chloro- or bromo-acetate ion, which the liberated nitric acid progressively suppressed. Senter (J., 1910, **97**, 346), studying the reactions of bromoacetic acid and several of its homologues with aqueous silver nitrate, discovered the heterogeneous catalysis by silver bromide, and confirmed Euler's conclusion concerning the greater reactivity of halogeno-anions than of the corresponding undissociated acids. Euler and Ölander (*Z. Elektrochem.*, 1930, **36**, 506) experimented with sodium bromoacetate and aqueous silver nitrate, but even under these conditions bromoacetate ions must become partly replaced by bromoacetic acid molecules, owing to the liberation of nitric acid as reaction proceeds; and no simple kinetic order was found. Finally Kappanna (*Proc. Indian Acad. Sci.*, 1935, **2**, 512), working with sodium α-bromopropionate and aqueous silver nitrate, confirmed Senter's observation of the catalysis by silver bromide, observed a period of induction in the absence of initially added silver bromide, and an accelerated rate up to the point at which the formed silver bromide coagulated.

As it was necessary for the interpretation of our optical experiments to confirm the hypothesis of reaction through the halogeno-anion, we carried out rate measurements of the reaction between α-bromopropionic acid and aqueous silver nitrate in the presence of various concentrations of initially added nitric acid. Lacking a precise reaction order, it is not possible accurately to express ratios of rates numerically; but we show that when the hydrion concentration is increased several-fold, so that the concentration of the bromopropionate ion is decreased correspondingly, the rate decreases by approximately the same factor. For example, when the mean hydrion concentration was increased from 0·143 to 1·08*N* and 2·04*N*, *i.e.*, by factors of 7·5 and 14 respectively, the mean rate, calculated as an approximate second-order constant, became decreased by factors of 7 and 12 respectively. This shows that, even in rather strongly acid solutions (*e.g.*, *N*), the reaction goes almost entirely through the anion.

Summarising, we may conclude that, whether we employ the bromo-acid or one of its salts, the reaction with silver nitrate consists essentially in an attack by silver ions on bromo-anions adsorbed on silver bromide.

The reactions of α-halogeno-acids with suspended silver oxide involve certain differences of behaviour. If the silver salt of the halogeno-acid is at all readily soluble, the rate of hydroxylation by means of silver oxide and water is much greater when the free acid is used than when a salt is employed. This is notably true, as we have shown by qualitative observations, for α-bromopropionic acid and its sodium salt; the difference is opposite in direction to that found when the reagent is silver nitrate. This does not mean that with silver oxide the reaction no longer proceeds through the halogenated anion: it is due merely to the circumstance that the first action of the free bromo-acid on silver oxide is to dissolve some of it, thus building up a much greater concentration of silver ions in solution than would have been produced by the suspended silver oxide in the absence of an acidic substance.

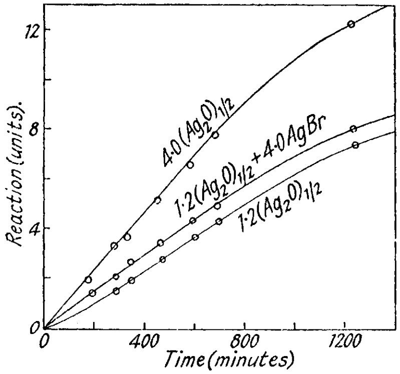
The essentially specific effect of silver oxide is best brought out by following its reaction with a salt of the halogeno-acid. The one previous investigation of this kind, that of Euler and Fahlander (*Z. physikal. Chem.*, 1922, **100**, 171), who used aqueous sodium bromoacetate, showed that the reaction-rate increased with the quantity of suspended silver oxide. Employing sodium α-bromopropionate, we have proved the heterogeneous catalysis by silver bromide, and confirmed the dependence of the rate on the excess of silver oxide. The two effects are illustrated by the reaction–time curves of the figure.

All these phenomena so closely correspond with those observed for alkyl halides that we may surely generalise the conclusion reached in Part IV, *viz.*, that, whether the reagent is a soluble silver salt or a suspension of silver oxide, the attack on the halogen compound is by silver ions adsorbed on silver halide, and also on silver oxide if any is present. The new point which arises is that the anions of α-halogeno-acids are very much more susceptible to attack by silver ions than are the acids themselves. In this respect the silver reaction resembles homogeneous unimolecular substitution (S_N1); and we shall find a further analogy between the two processes in the stereochemical results now to be described.

The following experiment shows the optical effect accompanying the hydroxylation of α-bromopropionic acid by the action of aqueous silver nitrate. A solution, initially 0·10*M* with respect to both *d*-α-bromopropionic acid and nitric acid, and 0·11*M* with respect to silver nitrate, was stirred at 50° for 15 hours, a period more than sufficient to ensure the completion of the reaction, and the lactic acid produced was converted into its ethyl ester. The following rotations were observed :

$$(\alpha_D^{19^\circ} + 9{\cdot}90^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2H \xrightarrow[\text{(and esterification)}]{AgNO_3 + HNO_3 + H_2O} CH_3{\cdot}CH(OH){\cdot}CO_2Et\ (\alpha_D^{19^\circ} + 2{\cdot}02^\circ)$$

As shown in Part III, a retention of the sign of rotation in the hydroxylation and esterification indicates a retention of configuration in the substitution. The maximal rotatory powers of the factor and product being 49° and 11·5° respectively, we can calculate that optical activity is preserved to the extent of 87%.



The action of silver carbonate in aqueous suspension on optically active α-bromopropionic acid was studied by E. Fischer (*loc. cit.*). He observed an optical effect which can be recognised as indicating also a retention of configuration, although with considerably more accompanying racemisation than arises with the use of silver nitrate: roughly estimated, the retention of activity amounted to about 36%. We have studied the action of silver oxide on optically active α-bromopropionic acid, and also on its sodium salt, under various conditions. In all cases configuration was preserved, but the retention of optical activity varied in the different experiments over the range 28—58%. Probably one should expect some such variation owing to the presence of two catalytically active surfaces, the relative efficacies of which are difficult to control and are probably sensitive to the precise conditions of experiment. The following record will serve as an illustration of our procedure. A 0·25*N*-aqueous solution of sodium *d*-α-bromopropionate was stirred with 1·2 equivs. of silver oxide at 0°. After the reaction had been carried to completion the lactic acid was esterified with ethyl alcohol. The observed rotations correspond to a 58% preservation of optical activity.

$$\begin{tikzcd}
(\alpha_D^{18^\circ} + 10{\cdot}18^\circ)\ CH_3{\cdot}CHBr{\cdot}CO_2H \arrow[d] & CH_3{\cdot}CH(OH){\cdot}CO_2Et\ (\alpha_D^{18^\circ} + 1{\cdot}40^\circ) \\
CH_3{\cdot}CHBr{\cdot}CO_2Na \arrow[r, "Ag_2O + H_2O"] & CH_3{\cdot}CH(OH){\cdot}CO_2Na \arrow[u]
\end{tikzcd}$$

(3) *Results.*—Without entering into the details of the remaining experiments, we collect together the essential results in Table I, in which are included the two experiments

by E. Fischer already mentioned. Cols. 1—5 show the materials used, their proportions, the solvent and the temperature; col. 6 indicates the nature of the substitution; cols. 7—9 give the observed rotations; and the final col. the percentage retention of optical purity. The signs in col. 10 indicate whether configuration has been preserved (+) or inverted (—).

TABLE I.

Optical Effects in Reactions between Silver Salts and α-Bromopropionic Acid Derivatives.

X in CHMeBrX.	Re-agent.	Equivs. Ag.	Solvent.	Temp.	Entrant group, R.	α_D Halide.	α_D CHMeR CO$_2$Me.	α_D CHMeR CO$_2$Et.	Retention optical purity, %.
CO·OMe	$AgNO_3$	1·04	MeOH	64°	OMe	+31·8°	−36·4°	—	−89
					ONO_2	+31·8	−35·9	—	—
CO·NHA†	Ag_2CO_3	excess	H_2O	room	OH	—	—	—	−73 *
CO·OH	$AgNO_3$	1·1	aq.-HNO_3	50	,,	+ 9·9	—	+2·02	+87
,,	Ag_2CO_3	2·2	H_2O	0	,,	—	—	—	+36 *
,,	Ag_2O	1·2	,,	0	,,	+10·0	—	+1·07	+45
,,	,,	2·1	,,	0	,,	+ 9·8	—	+0·65	+28
,,	,,	10·0	,,	0	,,	+19·5	—	+1·56	+34
,,	,,	2·1	aq.-Me_2CO	0	,,	+10·0	—	+1·24	+53
CO_2Na	,,	1·2	H_2O	0	,,	+10·2	—	+1·40	+58
,,	,,	1·1	aq.-Me_2CO	0	,,	+10·0	—	+1·17	+50

* Experiments by E. Fischer (*loc. cit.*), who isolated the lactic acid incompletely as zinc lactate; wherefore the figures given are subject to the error mentioned on p. 1244.

† A = $CH_2·CO_2H$. Purdie and Williamson (J., 1896, **69**, 837) hydrolysed *d*-α-chloropropionic acid by means of silver oxide and water, and obtained a partly racemised zinc lactate with a retained sign of rotation.

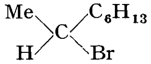
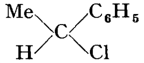
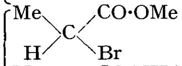
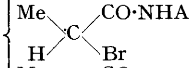
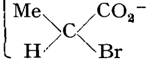
SUMMARY.

(Covering Parts IV and V.)

Recalling the kinetic evidence that, even under more acidic conditions than any used in these experiments with optically active material, practically the whole of the reaction of the free carboxylic acid takes place by way of its anion, we can summarise these results in a more compact form by relating the observed effect to the entity which actually undergoes the substitution. This is done in the lower section of Table II, in the upper part of which we give a similar summary of the results of the preceding paper, in order to bring the whole of the evidence concerning the silver reaction into a single conspectus. The entries in the column headed " reagent " show, in order, the silver ion, the catalytic surface or surfaces on which it attacks the " halide substituted " (col. 2), and the solvent molecule which completes the substitution. The headings of the remaining columns are self-explanatory.

TABLE II.

Optical Effects in the Reactions of Halogen Compounds with Silver Salts.

Paper.	Halide substituted.	Reagent.		Approx. temp.	Entrant group.	Effect on configtn.*	Optical purity, %.
IV		$Ag^+ + AgBr$	$+ H_2O$	35—80°	OH	I + Ra	72
		$Ag^+ + AgBr$	$+ EtOH$	35—80	OEt	,,	94
		$Ag^+ + AgBr + Ag_2O$	$+ H_2O$	80	OH	,,	74
		$Ag^+ + AgBr + Ag_2O$	$+ EtOH$	80	OEt	,,	94
		$Ag^+ + AgCl + Ag_2O$	$+ H_2O$	20—70	OH	,,	3—29
V		$Ag^+ + AgBr$	$+ MeOH$	64	OMe	,,	89
		$Ag^+ + AgBr + Ag_2CO_3$	$+ H_2O$	room	OH	,,	*ca.* 73
		$Ag^+ + AgBr$	$+ H_2O$	50	,,	Re + Ra	87
		$Ag^+ + AgBr + Ag_2CO_3$	$+ H_2O$	0	,,	,,	*ca.* 36
		$Ag^+ + AgBr + Ag_2O$	$+ H_2O$	0	,,	,,	28—58

* I = Inversion; Ra = racemisation; Re = retention.

The principal conclusions to be derived from an inspection of this table would appear to be the following. (1) The reactions of all the halogen compounds with all the silver salts in all the solvents used involve definite racemisation; and if a phenyl group is attached to the seat of substitution the amount of racemisation is particularly great. (2) When, in addition to a hydrogen atom and a methyl group, a hexyl, phenyl, carboxylic ester, or carboxylamide group is attached to the seat of substitution, the predominating orientation is an inversion; but, when the asymmetric atom bears a carboxylate ion group, then the predominating stereochemical effect is retention of the original configuration. The work described in the present paper brings out clearly the contrast between the orienting effect of the non-ionised carboxyl substituents ·CO·OR and ·CO·NHR on the one hand and the ionic substituent $\cdot CO_2^-$ on the other. In Part III we exposed a quite similar contrast between the non-ionised forms ·CO·OR and ·CO·OH, which also lead to predominating inversion, and the ionic group $\cdot CO_2^-$, which again causes retention of configuration, in homogeneous unimolecular substitution (S_N1). This stereochemical parallel constitutes further evidence of an analogy of mechanism, already indicated by the similar effects of structure on the rates of the S_N1-reaction and the silver reaction.

It can also be seen from Table II that, although the quantitative data are very various, the qualitative stereochemical result of substitution with the aid of silver ions is independent, first, of whether the reaction studied is hydroxylation, methoxylation, or ethoxylation, and secondly, of whether the active surface available to the silver ions is silver chloride or bromide, or one of these together with silver carbonate or oxide. This enables us to express the main outcome of the investigation described in both the previous paper and this one in the condensed form adopted in Table III. This table is cast into the same form as Table IV of Part III (this vol., p. 1224), and the two together epitomise the empirical knowledge thus far obtained concerning the relationship between steric course of the replacements of ·Hal by ·OR on the one hand, and the structure of the reagents and mechanism of the reactions on the other. A comparison of the two tables clearly shows the analogy between the homogeneous unimolecular and the heterogeneous mechanisms.

TABLE III.

Steric Course of the Heterogeneous Replacement of ·Hal *by* ·OR.

X in CHMeX·Hal.	Effect on configuration (silver reaction).
C_6H_{13}	Racemisation + inversion
C_6H_5	Large racemisation + inversion
CO·OR, CO·NHR	Racemisation + inversion
CO_2^-	Racemisation + retention

EXPERIMENTAL.

Materials.—The sources of the optically active and racemic halogen compounds were as stated in Part III. Concerning the reagents, the only noteworthy point is that silver oxide was prepared by precipitation from a solution containing a small excess of silver ions. The reason for this is that hydroxide ions are rather strongly adsorbed on silver oxide; so that, when silver oxide is precipitated from a solution containing an excess of alkali, there is danger of its carrying down hydroxide ions, which, by the rule of solubility products, must alter the solubility of the oxide with respect to silver ions, on which its activity as a reagent partly depends. Naturally, oxide required for several comparative kinetic experiments, or for a kinetic experiment and a parallel optical investigation, was prepared in a single batch.

Rate of Reaction of Methyl dl-*α-Bromopropionate with Silver Nitrate in Methyl Alcohol at* 64°.—A solution of methyl α-bromopropionate (7·953 g.) in 0·159*N*-methyl-alcoholic silver nitrate (300 c.c.) was sealed up in portions of 10 c.c. in glass bulbs, which were heated for known times at 64·0°, the silver-ion content being estimated thereafter by titration with ammonium thiocyanate. An estimation made after heating a bulb for 30 minutes was treated as a value corresponding to zero time. Titrations made after " infinite " time showed that the bromo-ester and silver nitrate had been in exactly equivalent proportion: when silver ions were no longer present no bromide ions could be obtained by hydrolysis with sodium hydroxide. In the following table, $a - x$, the concentration of unreacted bromo-ester, is expressed in c.c. of the thiocyanate solution per 10 c.c. sample of the reaction mixture. The value of a, given as

32·40 c.c., is 0·1203*N*, after correction for thermal expansion, the factor for which was taken as 0·94. In order to provide a rough measure of the rate, second-order " constants " (min.$^{-1}$ g.-mol.$^{-1}$ l.) have been calculated, although they have no definite chemical meaning in relation to the heterogeneously catalysed reaction :

t (min.)	0	30	90	102	180	270	310	452	727	870	1188
$a - x$ (c.c.)...	32·40	29·20	24·10	23·50	19·40	16·50	14·90	12·60	9·28	8·15	6·80
10^2k_2	—	3·02	3·18	3·08	3·09	2·96	3·14	2·90	2·85	2·84	2·80

A few estimations of the acidity were made. The values obtained were equivalent to only about 70% of the consumption of silver ions. The difference measures the formation of methyl α-nitratopropionate, simultaneously with the main products, which are methyl α-methoxypropionate and nitric acid. This is shown by the isolation of the nitrato- as well as the methoxy-ester (below).

Reaction of Methyl d-*α-Bromopropionate with Silver Nitrate in Methyl Alcohol at* 64°.—A solution of the ester (30·06 g.), $\alpha_D^{20°}$ + 31·8°, in a methyl-alcoholic solution of silver nitrate (31·0 g.) was made up to 1100 c.c. with dry methyl alcohol, and kept at 64° for 7 days. Test portions, examined for silver ions and bromo-ester (production of bromide ions by hydrolysis with alkali), showed that the former were present only in small amount, whilst the latter was wholly absent. Another test portion was freed from silver ions with sodium bromide, and examined for acidity by titration with methyl-alcoholic sodium methoxide; the result showed that 36% of the bromo-ester had been converted into nitrato-ester, and the remainder into methoxy-ester (see above). Methyl-alcoholic sodium bromide was added to the main part of the solution to precipitate the excess of silver, and the filtrate from the silver bromide was neutralised with methyl-alcoholic sodium methoxide. The methyl alcohol was removed by distillation through an efficient column, and the salts separated by filtration. Ether was added finally to precipitate the salts, and, after evaporation, the residual esters were fractionated under reduced pressure. Two pure fractions were obtained. The first, methyl α-methoxypropionate, had b. p. 43°/20 mm., and $\alpha_D^{17°}$ − 36·44° (Found : C, 50·65; H, 8·45. Calc. : C, 50·8; H, 8·53%). The second, *methyl α-nitratopropionate*, had b. p. 74·5°/17 mm., $\alpha_D^{17°}$ − 35·90° (Found : N, 9·4. $C_4H_7O_5N$ requires N, 9·4%).

Rate of Reaction of dl-*α-Bromopropionic Acid with Silver Nitrate in Dilute Aqueous Nitric Acid at* 50°.—Three experiments were carried out with the following approximate initial concentrations of reagents :—

No.	HNO_3.	$NaNO_3$.	Bromo-acid.	$AgNO_3$.
11	0·1*N*	—	0·10*M*	0·15*M*
12	1·0*N*	1·0*M*	0·25*M*	0·37*M*
13	2·0*N*	—	0·25*M*	0·37*M*

The details of the preparation of the solutions are as follows. (11) An aqueous solution of the bromo-acid (3·837 g.) was added to a mixture of 0·2000*N*-silver nitrate solution (187·5 c.c.) and 0·6624*N*-aqueous nitric acid (38·00 c.c.). The separate solutions were raised to 50° before being mixed, and the mixture was made up to 250 c.c. at the same temperature. (12) A solution of the bromo-acid (9·50 g.) in water was added to a solution made from silver nitrate (15·95 g.), sodium nitrate (20·5 g.), 2·408*N*-aqueous nitric acid (100 c.c.), and water (50 c.c.). The solution was made up to 250 c.c. at 50° as before. (13) An aqueous solution of the bromo-acid (9·574 g.) was added to a solution of silver nitrate (15·94 g.) in 2·408*N*-aqueous nitric acid (100 c.c.), and the mixture made up to 250 c.c. at 50°.

The results are in Table IV. The values of $b - x$, the concentration of unreacted silver ions, are expressed in c.c. of 0·1000*N*-ammonium thiocyanate solution per 10 c.c. sample. In the same units, the value of b, the initial concentration of silver ions, is given by the first entry under $b - x$, whilst a, the initial concentration of bromo-acid, is represented by the difference between the first and last entries. In order to provide the data for conversion of the concentrations into absolute units, a and b are re-expressed as normalities. As a convenient, if arbitrary, measure of the reaction rate, second-order " constants " (min.$^{-1}$ g.-mol.$^{-1}$ l.) have been calculated. The mean rates are roughly inversely proportional to the mean concentration of hydrogen ions, which in the introduction is computed by adding half the initial concentration of bromo-acid to the initial concentration of nitric acid, in order to allow for extra nitric acid produced in the course of reaction.

Reaction of d-*α-Bromopropionic Acid with Silver Nitrate in Dilute Aqueous Nitric Acid at* 50°.—The conditions were chosen approximately to correspond to expt. 11 (preceding paragraph). A solution of the bromo-acid (16·30 g.), $\alpha_D^{19°}$ + 9·90, in water (264 c.c.) was mixed at

TABLE IV.

Expt. 11 $\left\{\begin{array}{l} a = 0{\cdot}0856N \\ b = 0{\cdot}1378N \end{array}\right.$			Expt. 12 $\left\{\begin{array}{l} a = 0{\cdot}2265N \\ b = 0{\cdot}3595N \end{array}\right.$			Expt. 13 $\left\{\begin{array}{l} a = 0{\cdot}2320N \\ b = 0{\cdot}3640N \end{array}\right.$		
t (min.).	$b - x$.	10^2k_2.	t (min.).	$b - x$.	10^2k_2.	t (min.).	$b - x$.	10^2k_2.
0·00	13·78	—	0·00	35·95	—	0·00	36·40	—
2·83	12·90	31·0	5·53	34·00	4·68	9·58	34·25	2·86
6·95	11·65	32·9	10·47	32·35	4·87	16·67	32·80	3·00
11·75	10·60	33·1	16·95	30·50	5·03	23·75	31·50	3·00
17·42	9·65	33·1	25·0	28·60	4·95	34·92	29·75	2·94
23·55	8·75	35·2	32·0	27·30	4·87	46·2	28·15	2·99
31·25	7·95	36·3	42·4	25·30	5·06	57·5	26·80	3·02
44·17	7·10	36·9	52·2	24·00	5·00	70·0	25·65	2·98
66·5	6·30	37·1	67·7	22·25	5·00	84·7	24·40	2·95
106·7	5·65	37·7	89·0	20·50	4·96	100·0	23·20	2·97
195·6	5·30	—	187·0	16·30	4·96	126·0	21·65	2·96
"∞"	5·22	—	212·0	15·80	4·91	150·0	20·55	2·91
			292·0	14·55	5·14	180·5	19·35	2·92
Mean (Expt. 11)		34·8	"∞"	13·30	—	229·0	17·90	2·95
,, (Expt. 12)		4·95				285·0	16·85	2·88
,, (Expt. 13)		2·95				"∞"	13·20	—

50° with an aqueous 0·2000*N*-solution of silver nitrate (640 c.c.) and an aqueous 0·6624*N*-solution of nitric acid (161 c.c.). The mixture was stirred for 15 hours at 50°. The silver bromide was removed by filtration, and the excess of silver ion eliminated by the use of hydrochloric acid. The filtrate was neutralised with 2*N*-aqueous sodium hydroxide, made very slightly acidic, and evaporated to a small bulk. After the inorganic salts had been filtered off, 18*N*-sulphuric acid was added (15 c.c.), and the solution thoroughly extracted with ether, which dissolved the lactic acid and a certain amount of nitric acid. The ethereal extract was re-extracted with just sufficient dilute sodium hydroxide to make a neutral solution, which was evaporated and freed from sodium nitrate by the addition of dry ethyl alcohol. The sodium lactate was finally esterified by heating under reflux for 3 hours with ethyl alcohol (150 c.c.) and concentrated sulphuric acid (7 c.c.). Evaporation with additions of benzene, and extraction with ether after the addition of water, yielded ethyl lactate, which, on two distillations, gave a central fraction (3·80 g.) having b. p. 56°/15 mm., $\alpha_{D}^{19^\circ}$ + 2·02°.

Reaction of d-*α-Bromopropionic Acid with Aqueous Suspensions of Silver Oxide at* 0°.—Three experiments were carried out with 1·2, 2·1, and 10·0 equivs. of silver oxide, the bromo-acid being in each case in approximately *N*/4-solution.

(Expt. 21) A solution of the acid (16·1 g.), $\alpha_{D}^{21^\circ}$ + 10·05°, in water (320 c.c.) was stirred for 1 hour at 0° with a suspension of silver oxide (corresponding to 21·5 g. of silver nitrate) in water (100 c.c.). The mixture was kept for 2 days, and then filtered after the addition of excess of hydrochloric acid. Measured proportions of the filtrate were taken for tests. In one, the ionic halogen was estimated, and in a second, the total halogen (hydrolysis with sodium hydroxide, followed by titration with silver nitrate). The results showed that the bromo-acid has been substituted to the extent of 96·3%, and this was accepted as being sufficiently near to a complete reaction. The main solution was neutralised and evaporated to dryness, and the residue esterified as usual with ethyl alcohol. The fully rectified ethyl lactate (4·95 g.) had b. p. 56°/15 mm., $\alpha_{D}^{19^\circ}$ + 1·07°.

(Expt. 22) The acid had $\alpha_{D}^{19^\circ}$ + 9·82. The quantities were the same as before except that the silver oxide corresponded to 37·5 g. of silver nitrate. The mixture was stirred at 0° for 24 hours, reaction then being complete to within 3%. The rectified ethyl lactate had b. p. 56°/15 mm., $\alpha_{D}^{19^\circ}$ + 0·65°.

(Expt. 24) A solution of the acid (15·32 g.), $\alpha_{D}^{20^\circ}$ + 19·50°, in water (50 c.c.) was stirred at 0° for 30 mins. with a suspension in water (150 c.c.) of silver oxide prepared from 170 g. of silver nitrate. The mixture was kept overnight, and then worked up for ethyl lactate. The rectified ester (3 g.) had b. p. 53°/14 mm., $\alpha_{D}^{20^\circ}$ + 1·56°. A parallel experiment (no. 23) with the *dl*-acid had shown that under these conditions the reaction is completed to within 3%.

Reaction of d-*α-Bromopropionic Acid with an Aqueous-acetone Suspension of Silver Oxide at* 0°.—The acid (15·33 g.), $\alpha_{D}^{20^\circ}$ + 10·04°, was made up to 50 c.c. with a solution of water (5 c.c.) in acetone (95 c.c.). Silver oxide, prepared from 35·7 g. of silver nitrate, and well washed with water and then with acetone, was suspended in the remainder of the aqueous acetone. The materials were then mixed, stirred at 0° for 2 hours, and kept for 2 days. The product was worked up as usual for ethyl lactate. The rectified ester (3·9 g.) had b. p. 56·5°/15 mm., $\alpha_{D}^{20^\circ}$ + 1·24°.

Rate of Reaction of Sodium dl-α-*Bromopropionate with Aqueous Suspensions of Silver Oxide at* 0°.—Three experiments were performed with the following approximate initial conditions :

No.	Na salt.	Ag_2O, equivs.	AgBr, equivs.
31	*N*/4	1·2	—
32	*N*/4	1·2	4·0
33	*N*/4	4·0	—

An aqueous solution of bromo-acid (38·4 g.) was almost neutralised with aqueous sodium hydroxide, and the mixture, kept very faintly acid to ensure absence of hydroxide ions, was made up to 1 l. Of this solution, 250 c.c. were used for each experiment. Silver oxide was prepared from 68 g. of silver nitrate by the addition of a slight excess of barium hydroxide and then a slight excess of silver nitrate, again to avoid hydroxide ions. The washed sludge weighed 89 g., and of this 16·7, 16·7, and 55·3 g. respectively were taken for the three experiments. The silver bromide, required for one experiment, was prepared immediately before use from silver nitrate (42·3 g.) and sodium bromide.

The reaction mixtures were all stirred mechanically at 0°, and at known times samples, each of about 12 c.c., were removed and filtered; and 10 c.c. of each filtrate were hydrolysed by boiling for 10 mins. with 2*N*-aqueous sodium hydroxide (10 c.c.). The hydrolysis solutions were diluted, and the bromide ion was estimated by titration with silver nitrate and ammonium thiocyanate. The progress of reaction, *x*, is expressed in Table V in c.c. of 0·1000*N*-ammonium thiocyanate for 10 c.c. of the reaction solution.

TABLE V.

Expt. 31.				Expt. 32.				Expt. 33.			
t (min.).	*x* (c.c.).	*t* (min.).	*x* (c.c.).	*t* (min.).	*x* (c.c.).	*t* (min.).	*x* (c.c.).	*t* (min.).	*x* (c.c.).	*t* (min.).	*x*. (c.c.).
290	1·50	1500	9·18	186	1·38	1436	9·50	179	1·90	1487	14·20
350	1·90	1697	10·25	287	2·07	1694	10·25	279	3·30	1684	15·30
473	2·75	1918	11·55	344	2·65	1913	11·55	335	3·63	1906	17·00
602	3·65	2860	16·67	467	3·40	2859	15·80	457	5·15	2854	19·72
698	4·30	3270	18·35	596	4·30	3270	17·60	586	6·60	3264	20·65
1246	7·37	4340	20·55	694	4·90	4340	20·30	686	7·75	4335	21·45
1390	8·90			1240	8·00			1229	12·25		

Reaction of Sodium d-α-*Bromopropionic Acid with an Aqueous Suspension of Silver Oxide at* 0°.—A solution of the acid (15·90 g.), $\alpha_D^{18°}$ + 10·18°, in water was neutralised with 1·971*N*-aqueous sodium hydroxide (52·5 c.c.), and then made faintly acid. Silver oxide was prepared from silver nitrate (21·2 g.) in the presence of a small excess of silver ions, and suspended in water (113 c.c.). The materials were mixed at 0°, stirred mechanically for 92 hours, after which tests, such as have already been described, showed that reaction had proceeded to the extent of 94%. The product was worked up for ethyl lactate, the rectified specimen of which (4·9 g.) had b. p. 55°/13 mm., $\alpha_D^{19°}$ + 1·40°.

Rate of Reaction of Sodium dl-α-*Bromopropionate with an Aqueous-acetone Suspension of Silver Oxide at* 0°.—A solution of sodium α-bromopropionate (10·90 g.) in water (50 c.c.) was made up to 250 c.c. with acetone. Silver nitrate, prepared as usual from 9·4 g. of silver nitrate, was added at 0° to 200 c.c. of the solution of the sodium salt, and the suspension was stirred mechanically. Satisfactory results could not be obtained by filtration of the silver oxide and analysis of the filtrate, owing to the evaporation of the acetone during filtration; and therefore the following method was adopted. Each day the stirring was stopped for 1 hour, and 10 c.c. of the clear, supernatant solution were then removed. The sample was hydrolysed with sodium hydroxide, and the bromide ion determined. In each case 25 c.c. of 0·1001*N*-silver nitrate were added, the excess of silver ion being titrated with 0·09989*N*-ammonium thiocyanate. The excess of silver ion is expressed below in c.c. of thiocyanate solution per 10 c.c. sample. The last two readings correspond respectively to 94·5 and 98·0% of reaction :

Time (days)	0	1	2	3	5	6
Excess Ag^+	1·00	4·05	10·20	17·40	23·65	24·55

Reaction of Sodium d-α-*Bromopropionate with an Aqueous-acetone Suspension of Silver Oxide at* 0°.—The acid, $\alpha_D^{20°}$ + 10·0°, was converted into sodium salt by precipitation with sodium ethoxide in a mixture of ether and ethyl alcohol. A solution of the salt (17·27 g.) in water (79 c.c.) was made up to 395 c.c. with acetone, and stirred mechanically for 6 days at 0° with silver oxide prepared from 18·7 g. of silver nitrate. The ethyl lactate isolated as usual had b. p. 57·5°/17 mm., $\alpha_D^{19^\circ}$ + 1·17°.

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