743. *Mechanism of Electrophilic Substitution at a Saturated Carbon Atom. Part VII.* Kinetics and Stereochemistry of a One-alkyl Mercury Exchange, which has Bimolecular and Unimolecular Mechanisms, as well as Anion-catalysed Derivative Mechanisms.*

By (the late) E. D. Hughes, C. K. Ingold, and R. M. G. Roberts.

The kinetics of mercury exchange between α-carbethoxybenzylmercuric halides and radiomercuric halides have been examined. Despite a contrary report, we found that the kinetics of the exchange of the bromides in " 70% " aqueous dioxan were those of mechanism S_E2. In dimethylformamide the exchange was too slow, and in dioxan, acetone, and acetonitrile, it was too fast for us to measure; but, in a mixture of dimethylformamide and acetonitrile, it was shown to be autocatalytic, and to proceed by a bromide-ion-catalysed mechanism. In dimethyl sulphoxide, we found, as Reutov has, the kinetics of mechanism S_E1. We optically resolved α-carbethoxybenzylmercuric bromide, and, by a comparison of radiometric and polarimetric rates, showed that mechanism S_E1 proceeds with racemisation. The optical instability of the substrate in acetonitrile suggests that the rapid exchange in this solvent proceeds by mechanism S_E1. We observed also a bromide-ion-catalysed derivative-form of this mechanism, designated $S_E1–2Br^-$, because it is kinetically quadratic in the catalyst. This mechanism also is racemising.

The familiar concept of nucleophilic aliphatic substitution as a family of reactions, admitting considerable varieties of reactant type, while bound together by common mechanistic forms, has been our model in attempting similarly to incorporate electrophilic aliphatic substitutions into a family of reactions, by establishing its particular pattern of mechanisms. As to the methodology, the first step is kinetically to characterise the mechanisms, and the second to determine the stereochemical course of each mechanism so characterised. We emphasise that the second step is dependent on the first, because the steric course of a reaction is a property of its mechanism, not of its stoicheiometry; and so, to describe steric course apart from mechanism, as has often been done, is like finding a lost hat without discovering the owner.

When we undertook the task of characterising mechanisms of electrophilic substitution in its central area of organo-metal substitutions, we turned first to organomercury compounds, because we could command stable optical activity dependent on an asymmetric substitution-centre bearing mercury.[1] More particularly, we started with mercury-for-mercury substitutions, using isotopic labelling as required, and thereby avoiding the problem, which may impend when the expelled element is replaced by a different one, of relating sign of rotation to configuration.[2]

For the purpose of guiding experimental work, one has to have some preconceptions as to what stoicheiometries, and what mechanisms of substitution may occur. In Part I [2a] we set down three expected, stoicheiometrically different forms of electrophilic mercury-for-mercury substitutions, which we called the 1-alkyl, 2-alkyl, and 3-alkyl mercury exchanges. The 2-alkyl exchange was already known, and we examined it with respect to mechanism.[2b] We have since described, and likewise investigated for mechanism, the other two mercury exchanges.[2c,d] †

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* Part VI, ref. 2f.

† We must apologise for having missed this opportunity to mention that Jensen *et al.*[3] determined the steric course of a 2-alkyl mercury exchange contemporaneously with ourselves.[2b] We were thinking then of kinetically controlled stereochemical demonstrations, and Jensen's demonstration was thus not quite in context.

[1] Charman, Hughes, and Ingold, *Chem. and Ind.*, 1958, 1517.

[2] Charman, Hughes, Ingold, Thorpe, and Volger, (a) *J.*, 1959, 2523; (b) *J.*, 1959, 2530; (c) *J.*, 1961, 1121; (d) *J.*, 1961, 1133; (e), *J.*, 1961, 1142; (f), *J.*, 1961, 2359.

[3] Jensen, Whipple, Wedegaertner, and Landgrebe, *J. Amer. Chem. Soc.*, 1959, **81**, 1262.

In Part I we also set down three expected basic mechanisms of electrophilic substitution, which were called the unimolecular (S_E1), bimolecular (S_E2), and internal (S_Ei) mechanisms, and were considered, respectively, to involve dissociative, open associative, and cyclic associative transition states. The second and third of these mechanisms have been well established.[2b-f] We have been searching for the first mechanism, S_E1, which involves the rate-controlling formation of an intermediate carbanion.

(1) *Search for the Unimolecular Mechanism, S_E1.*

Up to 1960 we had employed only mono- and di-alkyl compounds of mercury containing unsubstituted alkyl groups, ranging in complexity from methyl to neopentyl, with s-butyl as the asymmetric representative; and we had failed to observe the kinetics characteristic of the S_E1 mechanism. We therefore began at that time a search for the S_E1 mechanism, by the use of substituted alkyl groups having substituents with electron-absorbing properties calculated to aid formation of the carbanionic intermediate involved in the mechanism, by absorbing some of the anionic charge.

One of the first reactions thus studied, and the one on which our work is now most advanced, is the 1-alkyl mercury exchange between α-carbethoxybenzylmercuric salts and radiomercuric salts. A Paper by Reutov, Beletskaya, and Yin-Tsei had just appeared,[4] reporting that the mercury exchange of the bromides in 70% aqueous dioxan at 50—70° had kinetics indicating a substitution of second order overall, first order in each reactant. While we were examining this reaction in other solvents as mentioned below, a further Paper by Reutov, Solokov, and Beletskaya appeared,[5] which reported that, when some kinetic inconsistencies apparently due to adventitious changes in the solvent were eliminated, the substitution declared itself to be of first order in the bromomercuri-ester and of zeroth order in the mercuric salt, kinetics which are diagnostic of the S_E1 mechanism.

Now we had encountered kinetic inconsistencies in various solvents; but we had traced ours to hydrogen bromide, which was present as an impurity in our radiomercuric bromide, when this was prepared from radiomercuric oxide and hydrogen bromide; and we had found that we could eradicate this disturbance completely by preparing our radiomercuric bromide by a different route (*cf.* Section 6.1). We therefore examined the mercury exchange in " 70% " aqueous dioxan, using radiomercuric bromide which we knew to be kinetically satisfactory. We found that the substitution was of second order overall, first in each reactant (Section 2.2), as Reutov, Beletskaya, and Yin-Tsei had originally reported. This conclusion was supported by the check of reducing the water content of the aqueous dioxan, when the reaction ran faster, instead of slower as would be expected of a rate-controlling ionisation (Section 2.2). The conclusion was further supported by the check of changing the substituting agent from mercuric bromide to mercuric chloride, which reacted at a quite different rate (Section 2.3). The conclusion was again confirmed by a stereochemical check made later, after we had optically resolved the bromomercuri-ester (Section 2.2).

In the hope of throwing some light on the difference between Reutov, Solokov, and Beletskaya's results and ours, we examined the effect of added bromide ion on the exchange between the bromomercuri-ester and mercuric bromide. We found that bromide ion selectively catalysed a demercuration by hydrolysis. The effect on the radiometric measurements was to send back into inorganic form radioactivity which exchange had transferred to the organic solute, and thus to make the exchange appear slower than it is. Obviously if bromide ion were introduced in proportion to mercuric bromide, the kinetic order in mercuric bromide would appear smaller than it is.

Concurrently we, and as it transpired Reutov and his co-workers, were exploring the

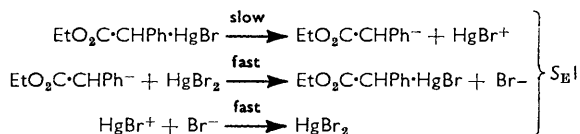[4] Reutov, Beletskaya, and Yin-Tsei, *Izvest. Akad. Nauk S.S.S.R.*, 1960, 43.
[5] Reutov, Sokolov, and Beletskaya, (a) *Doklady Akad. Nauk S.S.S.R.*, 1961, **136**, 631; (b) *Izvest. Akad. Nauk S.S.S.R.*, 1961, 1217.

reaction in other solvents: they have published their findings. They found that the substitution is of second order, first in each reactant, in pyridine,[6] and also in 80% aqueous ethanol.[7] The latter result seemed strange,[9] because the solvent was chosen in view of its expected similarity to 70% aqueous dioxan, in which the substitution was at the time taken to be of first order overall. Our re-examination of the reaction in 70% aqueous dioxan removes this difficulty.

The second area explored by both Reutov and his colleagues and ourselves refers to the solvent dimethylformamide. Reutov, Solokov, and Beletskaya found [8] that the mercury exchange between α-carbethoxybenzylmercuric bromide and mercuric bromide at 60—80° had an autocatalytic character, which could be removed, with an increase in the initial rate, on pre-maturing the mercuric bromide in that solvent. They assumed a slow complexing of the solvent with the mercuric salt to give a more active substituting agent. In our exploratory work, we had found that the exchange with pure reactants in pure dimethylformamide at 60° was unobservedly slow, and that in acetone, and also in acetonitrile, it was too fast for kinetic measurement. But we did make some measurements in the 60 : 40 vol. solvent mixture, dimethylformamide : acetonitrile. Here we found an autocatalysis, which was removed, with increases of rate, not only initially, but also throughout reaction, by sufficiently pre-maturing either reactant in the medium (Section 3). We found further that similar results could be obtained, without pre-maturing, by adding small amounts of tetraethylammonium bromide to the reaction solution (Section 3). We formed the impression that the pre-maturing processes might involve slow bromide ionisations from the molecular reactants, so allowing transfers of bromide ions to form more active ionic reactants. But we agree with Reutov that the dimethylformamide is in some way deeply involved.

The most interesting common finding by Reutov and his co-workers,[9] and by us, is that in dimethyl sulphoxide at temperatures between 25 and 60°, the mercury exchange between α-carbethoxybenzylmercuric bromide and mercuric bromide has well-defined first-order kinetics, which, in particular, are of first order in the bromomercuri-ester, and of zeroth in the mercuric salt (Section 4.1). This result identified the unimolecular electrophilic mechanism S_E1, which both groups of workers had been seeking.

$$\left. \begin{array}{l} EtO_2C \cdot CHPh \cdot HgBr \xrightarrow{\text{slow}} EtO_2C \cdot CHPh^- + HgBr^+ \\ EtO_2C \cdot CHPh^- + HgBr_2 \xrightarrow{\text{fast}} EtO_2C \cdot CHPh \cdot HgBr + Br^- \\ HgBr^+ + Br^- \xrightarrow{\text{fast}} HgBr_2 \end{array} \right\} S_E1$$

In agreement with this mechanism, Reutov and his collaborators have shown [9] that electron-attracting substituents in the potentially anionic, α-carbethoxybenzyl portion of the bromomercuri-ester, for instance, a *para*-nitro-group, increases the rate of the mercury exchange, and that the electron repelling *para*-t-butyl substituent decreases the rate of exchange. We have contributed that an increase of electronegativity in the potentially cationic, halogenomercuri-portion of the substrate, as on changing it from a bromo-mercuri- to a chloromercuri-group, decreases the rate of exchange, as it should (Section 4.2).

We have optically resolved the bromomercuri-ester (Section 5.1), and this has allowed us to study the stereochemistry of this unimolecular mercury-for-mercury substitution (Section 5.2), which is quite different from that of all previously described mechanisms of electrophilic mercury-for-mercury substitutions.

We have kinetically and stereochemically characterised another new mechanism, which is a derivative form of unimolecular electrophilic substitution, characterised by a catalysis
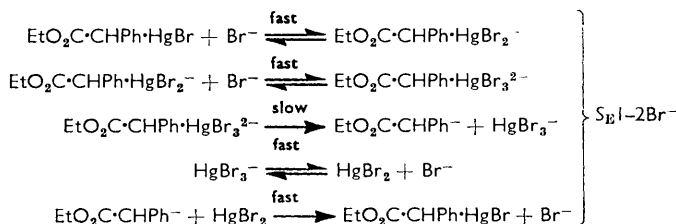
[6] Reutov, Sokolov, and Beletskaya, *Izvest. Akad. Nauk S.S.S.R.*, 1961, 1213.
[7] Reutov, Sokolov, Beletskaya, and Ryabokobylko, *Izvest. Akad. Nauk S.S.S.R.*, 1963, 965.
[8] Reutov, Sokolov, and Beletskaya, *Izvest. Akad. Nauk S.S.S.R.*, 1961, 1561.
[9] Reutov, Praisner, Beletskaya, and Solokov, *Izvest. Akad. Nauk S.S.S.R.*, 1963, 970.

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of the rate-controlling ionisation by anions, in our example, bromide ions.   This type of mechanism may be regarded as a counterpart of the well-known derivative form of unimolecular nucleophilic substitution, which involves catalysis by cations, for example, by silver ions in the solvolyses of some organic halides.   A special feature of the new mechanism is that it involves two bromide ions, wherefore we label it S_E1–$2Br^-$.   It is concluded (Section 5.3) that successive bromide ions are added to the substrate in pre-equilibria, and that the instability necessary for catalysis of the rate-controlling heterolysis arises when a two-fold negative charge has been built up, which can be split in this process to give two mutually repelling anions:

$$
\begin{aligned}
&\text{EtO}_2\text{C·CHPh·HgBr} + \text{Br}^- \overset{\text{fast}}{\rightleftharpoons} \text{EtO}_2\text{C·CHPh·HgBr}_2{}^- \\
&\text{EtO}_2\text{C·CHPh·HgBr}_2{}^- + \text{Br}^- \overset{\text{fast}}{\rightleftharpoons} \text{EtO}_2\text{C·CHPh·HgBr}_3{}^{2-} \\
&\text{EtO}_2\text{C·CHPh·HgBr}_3{}^{2-} \overset{\text{slow}}{\underset{\text{fast}}{\longrightarrow}} \text{EtO}_2\text{C·CHPh}^- + \text{HgBr}_3{}^- \\
&\text{HgBr}_3{}^- \overset{\text{fast}}{\rightleftharpoons} \text{HgBr}_2 + \text{Br}^- \\
&\text{EtO}_2\text{C·CHPh}^- + \text{HgBr}_2 \overset{\text{fast}}{\longrightarrow} \text{EtO}_2\text{C·CHPh·HgBr} + \text{Br}^-
\end{aligned}
\Biggr\} S_E1\text{–}2Br^-
$$

We proceed to describe our several contributions.

(2) *Mercury Exchange between α-Carbethoxybenzylmercuric Salts and Mercuric Salts in " 70% " Aqueous Dioxan.*

(2.1) *Qualitative Comparison of Rates of Exchange, Hydrolysis, and Acidolysis.*—Our solvent was a mixture of 70 vol. of dioxan with 30 vol. of water.   We were not troubled by any lack of constancy in the kinetic properties of this medium, but we did know of the need, when working with aqueous organic solvents generally, to avoid ionising halides as impurities.

The original reason why we were disinclined to accept the report that the exchange of mercury between α-carbethoxybenzylmercuric bromide and mercuric bromide in 70% aqueous dioxan proceeds by the unimolecular mechanism, S_E1, arose from our observations, which we then extended to this medium, on the kinetic importance of halide ions.   We argued that, if the mercury exchange did indeed use mechanism S_E1, then its rate would be that of the ionic separation of the bromomercuri-group from the organic residue; and that the carbanion so formed would be compelled, if the mercuric bromide was omitted, to react with solvent water, whereby a hydrolytic demercuration would ensue, the rate of which would be identical with the rate of exchange of mercury in the presence of mercuric bromide.   Also, if acid were added, in the presence of which the demercuration might be called acidolytic, its rate could never be less than that of the mercury exchange.   Our observations on halide-ion effects were quite inconsistent with these deductions.

In aqueous organic solvents, including " 70% " aqueous dioxan, in the presence of halide ions, α-carbethoxybenzylmercuric halides undergo moderately rapid demercurations by hydrolysis, and, in the additional presence of acid, much more rapid demercurations by acidolysis.   These processes are catalysed by the anions, in some conditions by two anions.   We shall report on their kinetics in a later Paper.   Here we need refer only to the qualitative situation regarding α-carbethoxybenzylmercuric bromide in " 70% " aqueous dioxan, at the temperatures employed for the study of its mercury exchange with mercuric bromide, in the periods of time used to measure this exchange.   In the presence of bromide ions, demercuration by hydrolysis may run concurrently and completely with the exchange.   In the additional presence of acid, a much faster demercuration by acidolysis supervenes.   In the absence of bromide ions, the exchange still goes on at a rate unaltered in order of magnitude; but neither hydrolysis, nor, if acid is present, acidolysis, takes place.   Thus at 60°, with solute concentrations in the centimolar range, and in the presence of ionic

bromide, our exchange runs occupied a few hours, and our hydrolytic demercurations comparable periods, while our acidolysis runs were mostly over in a few minutes. In the absence of ionic bromide, the exchange runs again occupied a few hours, but were unaccompanied by hydrolytic demercuration; and on omitting the mercuric bromide, and adding perchloric acid, no acidolytic demercuration at all could be detected after 24 hours at the temperature. This non-occurrence, when catalytic anions are excluded, of demercurating reactions, which, in the absence of mercuric bromide, should go at least as fast as mercury exchange reaction goes in the presence of mercuric bromide, if mechanism S_E1 were in operation, seems to exclude the possibility that the exchange has this mechanism. This follows because the carbanion intermediate formed in the rate-controlling step of mechanism S_E1, would be rapidly captured by the water in the solvent, if it were not more rapidly captured by added mercuric bromide.

(2.2) *Kinetics of Mercury Exchange between α-Carbethoxybenzylmercuric Bromide and Mercuric Bromide.*—The measurements were of transfers of mercury-203, between initially non-radioactive α-carbethoxybenzylmercuric bromide and initially radioactive mercuric bromide. One has to be able rapidly to separate the chemically distinct species, and this we did by shaking withdrawn samples of the reaction solution with mixtures of chloroform and aqueous sodium bromide. We usually followed the accumulation of radioactivity in the bromomercuri-ester, but sometimes we followed also the disappearance of radioactivity from the mercuric salt: whichever we did made no difference to the answers.

It is well understood that isotopic label-transfer must follow a first-order rate-law, whatever the mechanism of the reaction responsible for the transfer, provided that no non-isotopic change of composition occurs concurrently. At 57·8°, this test for constancy of non-isotopic composition, during the period of the isotopic exchange, was satisfied over about the first 6 hours, long enough to allow at least 75% of the ultimate amount of label-transfer to be followed without disturbance from side-reactions involving stoicheiometric change. However, at later times such a disturbance did encroach, and when it did so, observations were discontinued.

From the measured first-order rate-constants of label-transfer, we deduced the kinetics of substitution in the standard manner.[2c] The first-order rate-constant k_1 of label-transfer x led to an absolute initial rate of transfer $k_1 x_\infty$, where x_∞ is the ultimate amount of transfer, and, in the absence of isotopic discrimination, is equal to $ab/(a + b)$, where a and b are, respectively, the initial concentrations of α-carbethoxyphenylmercuric bromide and mercuric bromide. This initial rate of label transfer is equal to R, the rate of exchange of mercury atoms between the two chemically different species, apart from labels. In order to obtain the rate-constant of substitution, we divide the rate of exchange by the initial value of the concentration product in the rate-equation for the substitution. The validity of the rate-equation is tested by the constancy of the rate-constant of substitution under independent variations of the initial concentrations of the reactants.

In Table 1 we test in this way all the possible first-order and second-order rate-equations for substitution. The rate-equations are

$$dx/dt = k_1^{(a)}(a - x) \qquad dx/dt = k_1^{(b)}(b - x)$$
$$dx/dt = k_2^{(aa)}(a - x)^2 \qquad dx/dt = k_2^{(ab)}(a - x)(b - x) \qquad dx/dt = k_2^{(bb)}(b - x)^2$$

where $\qquad k_1^{(a)} = R/a, \ k_1^{(b)} = R/b, \ k_2^{(aa)} = R/a^2, \ k_2^{(ab)} = R/ab, \ k_2^{(bb)} = R/b^2$

and $$R = k_1 ab \ (a + b)$$

This Table shows that the only rate-constant which satisfies the test of constancy, under variations of both the initial concentrations a and b, is the second-order constant $k_2^{(ab)}$. We conclude that the substitution is of second order, first in each reactant. The second-order rate-constant at 57·8° is $2·8 \times 10^{-3}$ mole^{-1} l. sec.$^{-1}$. The decision between the two second-order mechanisms, S_E2 and S_Ei, has to be more tentative, and is considered below.

Kinetic salt effects, including general, specific, and apparent effects, are very complicated, and many more experiments than we have done would be needed to analyse them quantitatively. Our descriptions of them will therefore be qualitative, and our interpretations tentative. Illustrations, limited to those needed to clarify descriptions of this nature, are in Table 2.

TABLE 1.

Radiometric rates of exchange (R in mole l.$^{-1}$ sec.$^{-1}$), and first-order ($k_1^{(a)}$ and $k_1^{(b)}$ in sec.$^{-1}$) and second-order ($k_2^{(aa)}$, $k_2^{(ab)}$, and $k_2^{(bb)}$ in mole^{-1} l. sec.$^{-1}$) rate-constants of substitution, for mercury exchange between α-carbethoxybenzylmercuric bromide and radiomercuric bromide in " 70% " aqueous dioxan at 57·8°. (Run series RD.)

RD	10^2a	10^2b	10^7R	$10^4k_1^{(a)}$	$10^4k_1^{(b)}$	$10^3k_2^{(aa)}$	$10^3k_2^{(ab)}$	$10^3k_2^{(bb)}$
(i) *Followed by uptake of radioactivity in α-carbethoxybenzylmercuric bromide.*								
23	1·00	3·00	8·0	0·80	0·27	8·0	2·7	0·89
28	2·00	3·00	16·1	0·80	0·54	4·0	2·7	1·6
30	3·00	3·00	26·9	0·90	0·90	3·0	3·0	3·0
26	3·00	2·00	17·1	0·57	0·85	1·9	2·9	4·3
24	3·00	1·00	9·0	0·30	0·90	1·0	3·0	9·0
29	2·00	4·00	20·8	1·04	0·52	5·2	2·6	1·3
27	2·00	2·00	10·9	0·54	0·54	2·7	2·7	2·7
25	4·00	2·00	25·7	0·64	1·28	1·6	3·2	6·4
							Mean 2·8	
(ii) *Followed by loss of radioactivity from mercuric bromide.*								
23	1·00	3·00	7·7	0·77	0·26	7·7	2·6	0·86
24	3·00	1·00	9·0	0·30	0·90	1·0	3·0	9·0
25	4·00	2·00	24·7	0·62	1·23	1·5	3·1	6·2
27	2·00	2·00	11·7	0·58	0·58	2·9	2·9	2·9
28	2·00	3·00	15·6	0·78	0·52	3·9	2·6	1·7
							Mean 2·8	

TABLE 2.

Effects of salts on rates of mercury exchange between α-carbethoxybenzylmercuric bromide and radiomercuric bromide in " 70% " aqueous dioxan at 57·8° (symbols and units as in Table 1.)

RD	10^2a	10^2b	Salt	10^2[Salt]	10^7R	$10^4k_1^{(a)}$	$10^3k_2^{(ab)}$
Table 1	various	various	—	—	various	—	2·8
31	3·00	3·00	$LiClO_4$	3·00	12·0	0·40	1·35
32	3·00	3·00	LiBr	3·00	10·1	0·34	1·14
33	3·00	3·00	,,	10·0	93	3·10	10·3
—	3·00	3·00	,,	10·0	—	1·13 *	—

* Hydrolysis followed by titration of liberated base.

Lithium perchlorate exerts a negative kinetic effect. A negative general salt effect would be expected by analogy with the negative polar cosolvent effect mentioned below. Both can be understood on the hypothesis that the carbethoxyl group and the polarised bond of the departing mercury atom complete a cycle of electrostatic attractions in the bimolecular transition state, so reducing the external electrostatic field.

Lithium bromide in somewhat low concentrations exerts a larger negative kinetic effect than lithium perchlorate; but part of the observed effect of the bromide is only apparent, and is due, as explained in Section 1, to bromide-catalysed hydrolysis, which reverses some of the transfer of radioactivity by which the exchange is measured; and partly compensating, or over-compensating this, according to concentration, a bromide-ion catalysis of the exchange is present, which becomes dominating at higher concentrations of lithium bromide. We provisionally assume that 1-anion catalysis is succeeded, as the concentration of lithium bromide is increased, by 2-anion catalysis, on the model worked out for

1-alkyl exchange with simple alkyl groups in Parts V and VI,[2e,f] and that at high concentrations of lithium bromide the 2-anion catalysis dominates all other kinetic effects. But even in these conditions, the bromide-ion catalysed hydrolysis may constitute a considerable fraction of the total change undergone by original bromomercuri-ester. In order to illustrate this, the results of a hydrolysis run, belonging to a research which we are not yet ready to publish, have been added to Table 2. Hydrolysis is followed by titrating the liberated alkali. This run is selected for comparison, because the initial conditions of the exchange run, recorded in the penultimate line of the Table, and of the hydrolysis run, the result of which is in the last line, are the same. By comparing, for these runs, the calculated first-order rate-constants with respect to the bromomercuri-ester, $k_1^{(a)}$, we can gain an idea of the proportions in which original bromomercuri-ester undergoes substitution by mercuric bromide and by water in the conditions.

These interpretations imply that the mercury exchange, in the absence of catalytic anions, goes by the bimolecular mechanism, S_E2, and in the presence of catalysing bromide ions, by one or more of the internal mechanisms $S_E i$.

We examined only cursorily the rate of exchange as a function of the composition of aqueous dioxan solvents, but noted that the kinetic effect of solvent composition is strong, and in the direction that a decrease in water-content increases the rate. In dry dioxan at 57·8°, the rate was too great for us to measure, certainly greater by at least 10^2 times than the rate in " 70% " aqueous dioxan. Consistently with our interpretation of the negative salt effect, we tentatively account for this negative polar cosolvent effect by supposing that the solvation of the initial state by water, presumably mainly at the carbethoxyl group, becomes reduced in the transition state by the electrostatic involvement of the carbethoxyl group with the dipole of the breaking carbon–mercury bond.

In connexion with work done later with another solvent, in which S_E1-type kinetics were observed, we optically resolved α-carbethoxybenzylmercuric bromide in order to find the steric course of an S_E1 substitution, and found that it was one of racemisation. Armed with this information and some of the necessary material, we returned to solvent " 70% " aqueous dioxan, and did the single run recorded in Table 3. This shows that

TABLE 3.

Polarimetric run with α-carbethoxybenzylmercuric bromide, and comparison with the calculated progress of exchange at equal times, in " 70% " aqueous dioxan at 59·2° (Run PD1).

t (hr.)	0	1·25	2·75	4·00	6·00	30·0
$[\alpha]_D^{21}$	−11·8	−11·5	−11·4	−11·4	−10·9	−5·6
% Exchange *	0	53	81	91	97	100

* Calculated with $R = 25 \times 10^{-7}$ mole l.$^{-1}$ sec.$^{-1}$ for $a = b = 0.03M$, corresponding to $k_2^{(ab)} = 2.8 \times 10^{-3}$ mole^{-1} l. sec.$^{-1}$, the mean value (cf. Table 1) for 57·8°, no correction being made for the small difference of temperature.

the optically active substrate does not racemise, as it should, if substitution in this solvent did indeed proceed by mechanism S_E1. The optical rotation remained constant for 6 hours at 59·2°, which is the length of time for which we could, as explained above, follow exchange kinetics at this temperature, without interference from a non-isotopic side-reaction. We see here that that side-reaction leads to loss of optical activity. The absence of racemisation in the period which suffices for most of the exchange, and within which all our measurements on it have been confirmed, provides more evidence against mechanism S_E1, and is consistent with our conclusions favouring mechanism S_E2, in " 70% " aqueous dioxan.

(2.3) *Kinetics of Mercury Exchange between α-Carbethoxybenzylmercuric Bromide and Mercuric Chloride.*—The kinetics of this substitution were studied in order to discover whether or not a change in the substituting agent produced a difference of rate, as it should if mechanism S_E2 were under observation, but should not if mechanism S_E1 were operative. The substitution was followed in " 70% " aqueous dioxan at 57·8°. Because the initial

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substitution could be, and no doubt was, succeeded by substitutions of formed α-carb-ethoxybenzylmercuric chloride, we followed only the first 40% of the label-transfer; but the first-order rate-constants of the transfer, k_1, were good over this range.   We followed the substitution through the accumulation of radioactivity in the compound substituted, and also through the disappearance of radioactivity from the substituting agent.   The results are in Table 4.

In this Table we do not show all possible first- and second-order rate-constants, but only $k_1^{(a)}$ the first-order constant required by mechanism S_E1, and the second-order constant,

TABLE 4.

Radiometric rates of exchange (R in mole l.$^{-1}$ sec.$^{-1}$), and first-order ($k_1^{(a)}$ in sec.$^{-1}$) and second-order ($k_2^{(ab)}$ in mole^{-1} l. sec.$^{-1}$) rate-constants of substitution, for mercury exchange between α-carbethoxybenzylmercuric bromide and radio-mercuric chloride (initial concentrations a and b, respectively), determined by following (A) uptake of radioactivity in the α-carbethoxybenzylmercuric, and (B) loss of radioactivity from the mercuric salt, in " 70% " aqueous dioxan at 57·8° (Run series RD).

			Method A			Method B		
RD	10^2a	10^2b	10^7R	$10^5k_1^{(a)}$	$10^4k_2^{(ab)}$	10^7R	$10^5k_1^{(a)}$	$10^4k_2^{(ab)}$
13	3·00	3·00	2·91	0·97	3·2	3·07	1·02	3·4
14	3·00	4·00	3·09	1·03	2·6	2·86	0·95	2·4
15	3·00	2·00	1·69	0·56	2·8	1·88	0·63	3·1
16	2·00	2·00	1·13	0·56	2·8	1·32	0·66	3·3
17	1·00	4·00	0·89	0·90	2·3	1·33	1·33	3·3
18	4·00	1·00	1·32	0·33	3·3	1·51	0·38	3·8
					Mean 2·8			Mean 3·2

$k_2^{(ab)}$ appropriate to mechanism S_E2.   Only the second-order constant remains invariant under variations of the initial concentrations of both reactants.   Furthermore, this constant $3\cdot0 \times 10^{-4}$ mole l.$^{-1}$ sec.$^{-1}$ at 57·8° is smaller by an order of magnitude than the corresponding rate-constant with mercuric bromide as the substituting agent.

(3) *Mercury Exchange between α-Carbethoxybenzylmercuric Bromide and Mercuric Bromide in* 60 : 40 *vol. Dimethylformamide : acetonitrile.*

We report this portion of our work in outline only, partly because the results are broadly similar to those of Reutov, Sokolov, and Beletskaya [8] for the exchange in pure dimethyl-formamide.   However, our results bring out some additional points.   Actually, we did not detect any reaction in pure dimethylformamide at 60°, but we had observed fast reactions in acetonotrile and in acetone, reactions which were too fast for kinetic measurement even at 25°;   and so we were able to make solvent mixtures which gave exchange rates convenient for kinetic study.   We worked mainly with the mixture named in the heading and at 58·7°.   Runs were followed by uptake of radioactivity in the α-carbethoxybenzyl-mercuric bromide from initially radioactive mercuric bromide.

Reutov, Sokolov, and Beletskaya had observed an autocatalytic reaction, from which the period of induction could be eliminated by pre-maturing the mercuric bromide in the dimethylformamide solvent.   We also found an autocatalytic reaction in our solvent mixture;   and we convinced ourselves that it was not an affair of free-radical chains, because it was not affected by radical inhibitors, such as cyclohexene.   The period of induction was not removed from our reaction when the reactants were pre-matured in the medium at 58·7° for only 15 minutes, but it was removed when either the pre-maturing time for mercuric bromide, or that for α-carbethoxybenzylmercuric bromide, was lengthened to 1·0—1·5 hours.   After such pre-treatments, the label-transfer displayed first-order kinetics, and so a rate of exchange, and the various possible rate constants for

substitution, could be calculated. Further extensions of the pre-maturing periods increased the first-order rate-constants for label-transfer, *e.g.*, by 4—6 times when the pre-maturing periods for both reactants were lengthened to 24 hours; and, of course, the rates of exchange, and all the derived rate constants for substitution were increased by like factors. A selection of figures illustrating these points is given in Table 5.

We found that these effects of pre-maturing, *viz.*, of eliminating periods of auto-acceleration, thereby providing good first-order rate-constants of label transfer, and, after that, of increasing the rate-constants of label-transfer, could be produced, without any more pre-maturing of reactants than was incidental to the bringing of their solutions to the

TABLE 5.

Radiometric rates of exchange, and first-order and second-order rate-constants of substitution, in mercury exchange between α-carbethoxybenzylmercuric bromide and radiomercuric bromide in 60 : 40 vol. dimethylformamide–acetonitrile at 58·7° (symbols and units as in Table 1.   Run series RF.)

| RF | 10^2a | 10^2b | [NEt$_4$Br] | Hours pre-matured | | 10^6R | $10^4k_1^{(a)}$ | $10^2k_2^{(ab)}$. |
				RHgBr	HgBr$_2$			
various	various	various	—	0·25	0·25			
49	3·00	3·00	—	0·25	1·5	6·67	2·2	0·74
48	3·00	3·00	—	1·5	0·25	3·63	1·2	0·40
50	6·00	3·00	—	1·0	0·25	8·53	1·4	0·47
51	3·00	3·00	— ·	24·0	24·0	23·3	7·8	2·6
47	3·00	3·00	0·003	0·25	0·25	13·1	4·4	1·45

(In the "various" row, under 10^6R/$10^4k_1^{(a)}$/$10^2k_2^{(ab)}$ columns: ——autocatalytic——)

reaction temperature, by adding small proportions of tetraethylammonium bromide. An illustration of this effect is included in Table 5.

These experiments, and indeed, all that we have so far done with solvent dimethyl-formamide, must be regarded as preliminary. Our speculation (Section 1), that the autocatalytic rates are partly controlled by bromide ionisations, might be difficult rigorously to prove or disprove.* On the other hand, the question of whether the catalysis by bromide ion is of one of the types described in Parts V and VI [2e,f] and in Section 5, below, or is something new, should be easily determinable, though we have not yet found time to do the necessary systematic work.

(4) *Kinetics of Mercury Exchange between α-Carbethoxybenzylmercuric Salts and Mercuric Salts in Dimethylsulphoxide: Mechanism* S$_E$1.

(4.1) *Mercury Exchange of α-Carbethoxybenzylmercuric Bromide with Mercuric Bromide.* —In dimethyl sulphoxide, unlike " 70% " aqueous dioxan, transfers of the label of radio-activity from radiomercuric salts to α-carbethoxybenzylmercuric salts accurately obeyed a first-order rate-law as long as the kinetics could be followed, without any sign of a succeeding change of non-isotopic composition. The ultimate amount of label-transfer, as measured, for instance, after 24 hours at 60°, or after 50 half-lives, was identical with that calculated from the initial conditions. Such label-transfers were followed by uptake of radioactivity into the bromomercuric-ester.

In order to determine the kinetic form of substitution, the rate of label-transfer, and hence the rate of exchange, was measured at 58·9° for a variety of initial concentrations of the reactants, and the various possible first-order and second-order rate-constants of substitution were calculated from the rates of exchange, as shown in Table 6. The only rate-constant, which remained invariant under changes in the initial concentrations of both reactants was the constant $k_1^{(a)}$ of a substitution of first-order with respect to the bromomercuri-ester, and of zeroth order with respect to the mercuric bromide. As the

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* Different opinions have been expressed as to whether mercuric iodide ionises appreciably by iodide–ion transfer in dimethylformamide. From a survey of the evidence, Deacon concludes that it does (*Rev. Pure and Appl. Chem.*, 1963, **13**, 189).

TABLE 6.

Radiometric rates of exchange, and first-order and second-order rates of substitution, for mercury exchange between α-carbethoxybenzylmercuric bromide and radiomercuric bromide in dimethyl sulphoxide at 58·9°. (Symbols and units as in Table 1. Run series RS.)

RS	10^2a	10^2b	10^6R	$10^4k_1{}^{(a)}$	$10^4k_1{}^{(b)}$	$10^3k_2{}^{(aa)}$	$10^3k_2{}^{(ab)}$	$10^3k_2{}^{(bb)}$
10	1·00	6·00	3·54	3·5	0·59	25·4	5·9	0·98
12	2·00	6·00	8·36	4·2	1·39	20·9	7·0	2·3
15	3·00	6·00	12·3	4·1	2·05	13·7	6·8	3·3
14	6·00	3·00	21·1	3·5	7·0	5·8	11·7	23·0
13	6·00	2·00	25·8	4·3	12·9	7·2	21·5	64·0
8	3·00	3·00	11·9	4·0	4·0	13·2	13·2	13·2

reaction is undoubtedly an electrophilic substitution, having none of the properties of a free-radical process, these kinetics diagnose mechanism S_E1, that is, a substitution rate-controlled by the preliminary ionisation of the compound substituted, to form intermediately a carbanionic centre at the seat of substitution, as formulated on p. 3902.

We made an approximate determination of the Arrhenius activation energy, using the mean rate constants in Table 7. The following equation represents these constants:

$$k_1{}^{(a)} = 10^{5·397} \exp(-13{,}400/RT)$$

The measured rate at 30° is in perfect agreement with that found by Reutov *et al.*[9] Our temperatures, 44 and 59°, were higher than any of theirs, and their Arrhenius equation, deduced from data covering only a small temperature range, leads to higher rates at these temperatures than those we found.

TABLE 7.

Temperature dependence of the rate of substitution by mercuric bromide in α-carbethoxybenzylmercuric bromide in dimethyl sulphoxide.

t (°c)	29·5	44·4	58·9
$10^4k_1{}^{(a)}$	0·52	1·43	3·75

(4.2) *Mercury Exchange of α-Carbethoxybenzylmercuric Chloride with Radiomercuric Chloride.*—This exchange was kinetically investigated in order to ascertain the effect of replacing bromine by more electronegative chlorine on the rate of ionisation of the halogeno-mercuri-group, the rate-controlling process in mercury-for-mercury substitution by mechanism S_E1. As Table 8 shows, the substitution of the chloromercuri-ester like that of the bromomercuri-ester, employs the mechanism S_E1 in dimethyl sulphoxide. The unimolecular rate-constant for the chloromercuri-substitution, $2·05 \times 10^{-4}$ sec.$^{-4}$ at 58·8°, is about one-half that for the bromomercuri-substitution in like conditions. This is qualitatively as would be expected from the difference of electronegativity of the halogens. Accidentally but fortunately, this test of mechanism, through the kinetic effect of a polarity difference in substituents, complements that applied by Reutov and his collaborators,[9] who examined the effect of *para*-substituents in the benzene ring on the rate of exchange, and found that increased electronegativity there increased the rate, again as would be expected from the mechanism.

TABLE 8.

Radioactive rates of exchange and first-order and second-order rate-constants of substitution for mercury exchange between α-carbethoxybenzylmercuric chloride and radiomercuric chloride in dimethyl sulphoxide at 58·8°. (Symbols and units as in Table 1. Run series RS.)

RS	10^2a	10^2b	10^6R	$10^4k_1{}^{(a)}$	$10^2k_2{}^{(ab)}$
33	3·00	3·00	5·75	1·9	64
34	6·00	3·00	12·6	2·1	7·0
35	3·00	1·00	6·95	2·3	23·1
36	3·00	6·00	5·75	1·9	3·2

Mean 2·05

(5) *Steric Course of Mercury Exchange Reactions of α-Carbethoxybenzylmercuric bromide in Dimethylsulphoxide.*

(5.1) *Optical Resolution of α-Carboxybenzylmercuric Salts.*—The method used was based on that of the earlier resolution [1,2a] of s-butylmercuric salts; but modifications were found necessary, to which we were guided by the kinetic studies described above. Thus a trial showed that the previous method of converting the organomercuric bromide with potassium hydroxide into the organomercuric hydroxide, and then adding optically active mandelic acid, in order to obtain the organomercuric mandelate, did not work in the α-carbethoxybenzyl series; and an obvious explanation was that the liberated bromide ions were catalysing solvolytic demercuration. Therefore in the next attempt, free bromide ions were avoided by decomposing α-carbethoxybenzylmercuric bromide with optically active silver mandelate. This method worked well, and the resulting $(\pm)$-α-carbethoxybenzylmercuric $(-)$mandelate had $[\alpha]_D^{20}$ $-47\cdot2°$ in acetone ($c = 1\cdot5\%$ w/v) and m. p. $102°$.

Separation of the diastereoisomers was effected by crystallisation from a mixture of dichloromethane and *n*-hexane. After eight crystallisations a limiting rotation, $[\alpha]_D^{20}$ $-59\cdot8°$ in acetone ($c = 0\cdot5\%$ w/v) was reached. This $(-)$α-carbethoxybenzylmercuric $(-)$mandelate had m. p. $115°$.

Its conversion into bromide by anion exchange had to side-step the difficulty of the catalysis by bromide ion of a racemising mercury exchange. Trial showed that addition to the active mandelate of lithium bromide in acetone, either at room temperature, or even at $-80°$, precipitated lithium mandelate, but left in solution fully racemised α-carbethoxybenzylmercuric bromide. This racemisation was presumably associated with an anion-catalysed derivative-form of unimolecular mercury exchange. It was therefore an obvious next step to go over to the slowest solvent for exchange that we knew, *viz.*, dimethylformamide, in which, when pure, no observable exchange occurred, and when mixed with the very fast solvent, acetonitrile, exchange did occur, but was only mildly catalysed by bromide ions. The anion exchange was accordingly effected with tetraethyl-ammonium bromide in pure dimethylformamide at $0°$, and the α-carbethoxybenzylmercuric bromide was precipitated by addition of water. The mandelate of maximum rotation, $[\alpha]_D^{20}$ $-59\cdot8°$, thus gave bromide with $[\alpha]_D^{21}$ $-13\cdot9°$ in acetone, $c = 1\cdot0\%$ w/v. We did not determine whether any racemisation at all accompanied this conversion, but the rotation shows that such could only be of small amount, and hence, if not negligible, could easily be made so by reducing the conversion temperature. Our concern was only to obtain material suitable for our intended polarimetric studies.

The optical rotation of the bromomercuri-ester was quite unchanged after 29 hours at room temperature in acetone. We set this finding beside another two already mentioned. One is the result just noted that the bromomercuri-ester was produced in racemic form even at $-80°$ from the optically resolved mandelatomercuri-ester by anion exchange with sodium bromide in acetone. The other (Section 3) is that the bromomercuri-ester undergoes mercury exchange with radiomercuric bromide too rapidly for kinetic measurement at $25°$ in acetone. These three observations point to two conclusions regarding the available mechanisms of mercury exchange in acetone. The first is that the very rapid mercury exchange in acetone cannot go by mechanism S_E1, which we show (Section 5.2) to be racemising: presumably it goes by mechanism S_E2. For comparison, it is recalled that we have provisionally concluded (Section 2.2) on other grounds that the very rapid exchange in dry dioxan goes by mechanism S_E2. The other conclusion is that, although mechanism S_E1 is not competitive in acetone in the absence of catalysts, added bromide ions can make successfully competitive a bromide-ion-catalysed mechanism, which is racemising. Since both the known bromide-ion-catalysed modifications of mechanism S_E2 preserve configuration,[2e] the racemising mechanism in acetone is presumably a

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derivative form of mechanism S_E1, probably the racemising mechanism S_E1-2Br^-, demonstrated below (Section 5·3).

The bromomercuri-ester undergoes immediate racemisation at room temperature in acetonitrile. We set this finding beside another (Section 3), *viz.*, that the bromomercuri-ester exchanges mercury with radiomercuric bromide too rapidly to allow kinetic measurements at 25° in acetonitrile. These two findings suggest that the fast mercury exchange in acetonitrile takes place by mechanism S_E1, which we kinetically establish in the slower, but still good ionising solvent, dimethyl sulphoxide (Section 4.1).

(5.2) *Steric Course of Mercury Exchange of α-Carbethoxybenzylmercuric Bromide by Mechanism* S_E1: *Comparison of Kinetics of Substitution and Racemisation.*—In order to ascertain the steric course of mercury-for-mercury substitution in the bromomercuri-ester by mercuric bromide in dimethyl sulphoxide, we must first discover whether any racemisation of the bromomercuri-ester occurs under the conditions in which it undergoes substitution. If so, we have to determine the kinetic form of racemisation, particularly with respect to the dependence of its specific rate on the initial concentration of the reactants for substitution. If the kinetic forms of racemisation and substitution correspond, we have to compare the absolute rates of these processes in like conditions. A racemisation rate which is equal to zero, or to the substitution rate, or to twice the substitution rate, would indicate molecular acts of substitution associated with retention of configuration, or racemisation, or inversion of configuration, respectively.

These questions are all answered in Table 9. Racemisation of the bromomercuri-ester does accompany its substitution with mercuric bromide. The racemisation, like the

TABLE 9.

First-order rate-constants ($k_1^{(a)}$ in sec.$^{-1}$) for the racemisation of $(-)$-α-carbethoxybenzylmercuric bromide (initial rotation $[\alpha]_D^{21}$ $-11\cdot8$ in acetone; c $1\cdot0\%$ w/v), alone and in the presence of mercuric bromide, in dimethyl sulphoxide at 59·2°. (Symbols and units as in Table 1. Run series PS.)

PS	10^2a	10^2b	$10^4k_1^{(a)}$	PS	10^2a	10^2b	$10^4k_1^{(a)}$
1	3·00	—	3·8	5	3·06	15·00	3·1
6	3·00	1·00	3·4	8	4·00	1·00	3·1
3	3·00	3·00	3·7	7	5·00	1·00	3·6
2	3·00	6·00	3·2				—
						Mean	3·4

substitution, is of first order in the bromomercuri-ester, and of zeroth order in mercuric bromide. The first-order rate-constant of racemisation is approximately equal to that of the mercury-for-mercury substitution in the same conditions. Actually, our rate-constant for racemisation, $3\cdot4 \times 10^{-4}$ sec.$^{-1}$, in dimethyl sulphoxide at 59°, is slightly smaller than the corresponding figure for substitution, $3\cdot75 \times 10^{-4}$ sec.$^{-1}$, but we are unwilling at present to attribute significance to the difference, because our experimental accuracy, and our ability to detect small kinetic disturbances, may be lower than we had supposed. On this basis, we conclude that mechanism S_E1 is here associated with racemisation, in the sense that each molecular act of its rate-controlling ionisation yields a carbanion liable with equal probability to give either enantiomeric substitution product.

The rate of racemisation of the bromomercuri-ester is the same when the mercuric bromide is omitted altogether. This fact, together with the kinetic evidence of the mechanism of substitution, and the kinetic correspondence between substitution and racemisation, means that, in the absence of an added substituting agent, racemisation still measures mercury-for-mercury substitution in the substrate, the rate being that at which the substrate prepares itself by ionisation to receive the replacing mercury atom, independently of the source of the latter. In the absence of mercuric bromide, the source must be another molecule of α-carbethoxybenzylmercuric bromide. These considerations allow us to reduce the study of kinetic salt effects on the unimolecular mercury exchange to a

study of such effects on its rate-controlling step of ionisation, as measured by the associated racemisation.

(5.3) *Kinetic Salt Effects, and Kinetics of Bromide-ion Catalysis of the Racemisation associated with Unimolecular Substitution of α-Carbethoxybenzylmercuric Bromide in Dimethyl Sulphoxide. The Mechanism S_E1–$2Br^-$.*—It is difficult to recognise ion-atmospheric effects in the observed kinetic salt effects on this reaction in dimethyl sulphoxide. The observed effects appear to be dominantly specific, and, in some cases to depend on both ions of the salt. The effects may be either retarding or accelerating, as exemplified in Table 10.

TABLE 10.

Effects of various salts on the first-order rate-constants of racemisation of (−)-α-carb-ethoxybenzylmercuric bromide (initial rotation $[\alpha]_D^{21}$ −11·8 in acetone; $c = 1·0\%$ w/v) in dimethyl sulphoxide at 59·2°. (Symbols and units as in Table 9. Run series PS.)

PS	10^2a	Salt	[Salt]	$10^4k_1^{(a)}$	PS	10^2a	Salt	[Salt]	$10^4k_1^{(a)}$
Table 9	various	—	—	3·40	19	3·00	$LiNO_3$	0·0300	5·05
18	3·00	$KClO_4$	0·0300	2·45	10	3·00	NEt_4Br	0·0085	4·40
17	3·00	$LiClO_4$	0·0300	0·95					

The accelerative effect of tetraethylammonium bromide had been examined in some detail. It disclosed itself as a catalysis, wholly quadratic in the catalyst. Any tendency that the catalysis might have shown to shade off into a linear form near the lower end of the investigated range of concentrations of the catalyst was not detected by our measurements. Thus the measured rates could be represented as sums of the uncatalysed rate and the rates added by the quadratic catalysis. This is shown in Table 11. The equation here being applied is

$$-(d\alpha/dt)/\alpha = k_1^{s(a)} = k_1^{(a)} + k_3^{(ass)}s^2$$

where $k_1^{s(a)}$ is the first-order rate-constant at any catalyst concentration s, and $k_1^{(a)}$ is the rate-constant in the absence of the catalyst, whilst $k_3^{(ass)}$ is the third-order rate-constant of the catalytic part of the process.

TABLE 11.

Effect of tetraethylammonium bromide (concentration s) on the first-order rate-constants ($k_1^{s(a)}$ in sec.$^{-1}$) of racemisation of (−)-α-carbethoxybenzylmercuric bromide (concentration a; initial rotation $[\alpha]_D^{21}$ −11·8° in acetone; $c = 1·0\%$ w/v) in dimethyl sulphoxide at 29·5°, and calculated catalytic rate-constants ($k_3^{(ass)}$ in mole^{-2} l.^{2} sec.$^{-1}$) for quadratic catalysis by the saline bromide. (Run series PS.)

PS	10^2a	10^2s	$10^4k_1^{s(a)}$	$k_3^{(ass)}$	PS	10^2a	10^2s	$10^4k_1^{s(a)}$	$k_3^{(ass)}$
Table 7	various	—	0·52 *	—	29	4·00	1·60	6·92	2·50
27	4·00	0·75	1·65	1·90	30	4·00	1·80	8·26	2·39
22	4·00	1·00	2·58	2·06	23	4·00	2·00	8·85	2·08
25	4·00	1·25	3·49	1·90					—
24	4·00	1·50	4·76	1·89				Mean	2·11

* Determined radiometrically.

The quadratic form of the catalysis shows that two bromide ions have been supplied to the transition state of the catalysed rate-controlling heterolysis, which leads to the carbanion, through which optical activity is lost, and mercury exchange takes place. We thus have a "2-anion catalysis," to use the nomenclature of Part V,[2e] but now of unimolecular electrophilic substitution; and, in accordance with a system of notation which has been found to bring out useful analogies, we label this mechanism S_E1–$2Br^-$, just as we label silver–ion-catalysed unimolecular nucleophilic substitution S_N1–Ag^+, designating the catalyst separately, but omitting it from the numerically expressed molecularity.

As to the manner in which the two bromide ions are assembled in the catalytic transition state, our knowledge of complex mercuric and alkylmercuric halides, including what has

been added thereto in previous Papers of this Series, leads us to assume that the bromide ions are taken up successively by the bromomercuri-ester, RHgBr, in pre-equilibrium, to form first $RHgBr_2^-$, and then $RHgBr_3^{2-}$, each in low stationary concentration, as indeed, chemical analogies apart, the kinetics themselves would require. The value of either of these complex anions as a catalytic intermediate depends jointly on its stationary concentration and its internal instability with respect to the carbanion-forming heterolysis. One can understand that the doubly charged anion would be particularly prone to undergo that process, in which the charge is divided between the separating anions. As we must assume that the formation constant of the doubly charged anion is very small indeed, the observed catalytic constant, 2.1 mole^{-2} l.^{2} sec.$^{-1}$ at 29.5°, must be considered to express a very high specific rate of reaction of this anion. The kinetics of the catalysis would be equally consistent with the idea that $RHgBr^{2-}$ is not a metastable intermediate, but it is a transition state, in which R^- is being lost while the second Br^- is being added. But the implication would still be that the doubly charged structure cannot survive. Thus we rationalise the mechanism S_E1–2Br$^-$, formulated on p. 3903, the steric course of which, as of its parent mechanism S_E1, is that of racemisation.

<div align="center">EXPERIMENTAL</div>

(6.1) *Materials.*—Ethyl α-bromophenylacetate was prepared by refluxing ethyl phenyl-acetate (92 g.), N-bromosuccinimide (100 g.), and benzoyl peroxide (0·1 g.) in carbon tetra-chloride (400 ml.) for 6 hr., filtering off the succinimide, and distilling the carbon tetrachloride, and then the bromo-ester at 99—100°/1·0—1·2 mm. (yield 85%).

Ethyl α-bromomercuriphenylacetate (α carbethoxybenzylmercuric bromide) was obtained by shaking the above bromo-ester (150 g.) with finely divided mercury (480 g.) for 30 min., and, after a further 2 hr., extracting with hot chloroform (3 × 200 ml.), distilling off that solvent, and washing the residue with carbon tetrachloride (yield 64%). Crystallised from methanol it had m. p. 132° (Found: C, 27·2; H, 2·5; Hg, 45·0. Calc. for $C_{10}H_{11}BrHgO_2$: C, 27·1; H, 2·5; Hg, 45·2%).

Ethyl α-mandelatomercuriphenylacetate (α-carbethoxybenzylmercuric mandelate) was made from the bromomercuri-ester (9·2 g.) by refluxing with suspended silver mandelate (6·5 g.) in acetonitrile for 2 hr., filtering off the silver bromide, and evaporating the solvent. The *mandelatomercuri-ester* crystallised from acetone (yield 75%) had m. p. 114° (Found: C, 42·1; H, 3·6. $C_{18}H_{18}O_5Hg$ requires C, 42·0; H, 3·6%).

Ethyl α-chloromercuriphenylacetate (α-carbethoxybenzylmercuric chloride) was prepared from the above mandelate-compound (11·4 g.) and lithium chloride (0·94 g.) in acetone (200 ml.). After the lithium mandelate had been filtered off, the solution was concentrated to yield the *chloromercuri-ester*, which, crystallised from acetone, had m. p. 127—128° (yield 62%) (Found: C, 29·9; H, 3·0. $C_{10}H_{11}O_2HgCl$ requires C, 30·1; H, 2·8%).

The radioactive source was an aqueous solution of mercuric chloride containing 1·9 mg./ml., with a specific activity approaching 1 mc./mg., due to mercury-203. It was diluted about 50,000-fold with ordinary mercuric chloride to give a working stock of radiomercuric chloride, which was crystallised from water, and then from ethanol. From a solution of this, radio-mercuric oxide was precipitated with sodium hydroxide, and converted into radiomercuric nitrate with nitric acid. Radiomercuric bromide was precipitated by sodium bromide from a solution of the nitrate, and was purified by crystallisation from ethanol (Found: Hg, 56·2. Calc. for $HgBr_2$: Hg, 56·7%).

The ordinary salts, and most of the solvents employed in this work were purified by com-pletely standard methods, not needing description. Dimethylformamide was distilled with benzene to remove water, and after subsequent drying with magnesium sulphate, was fraction-ated through a packed and jacketted column under reduced pressure.[10] It has b. p. 55°/25 mm. Dimethyl sulphoxide was passed through a column packed with molecular sieves (grade 4A), and was then fractionated twice through a long, packed, and jacketted column under reduced pressure.[11] It had b. p. 49°/8 mm.

[10] Thomas and Rochow, *J. Amer. Chem. Soc.*, 1957, **79**, 1843.
[11] Cram, Kingsberg, and Rickbourn, *J. Amer. Chem. Soc.*, 1961, **83**, 3695.

(6.2) *Optical Resolution.*—Ethyl α-(−)mandelato-(±)-mercuriphenylacetate was prepared from the bromomercuri-ester and silver (−)mandelate by the method already given (Section 6·1). Crystallised from ether, this material had m. p. 102°, and $[\alpha]_D^{21}$ −47·2 in acetone, $c =$ 1·50% w/v.

It was separated into its diasteroisomeric components by crystallisation from the 60 : 40 vol. solvent mixture dichloromethane : n-hexane, according to the system which was previously used to separate s-butylmercuric mandelate, and is represented by the triangular diagram in Part I.[2a] The progress of separation was followed in the present case through the rotation, taken in acetone, of the mandelate-compound itself, and not, as before, through the rotation of the bromo-compound, formed by replacement of the mandelato-group by bromine, the reason being that the separation of diastereoisomers of the mandelatomercuri-ester was completed before we knew how to accomplish replacement of the mandelato-group. In the third-row fractions, 3a—3c, of the triangular scheme,[2a] and still more in the fourth row fractions, 4a—4d, rotations were well spread on both sides of the original value, the numerically highest negative rotations belonging to the least soluble fractions, 3a and 4a, of their respective rows. The systematic separation was then further pursued, with preference for the less soluble fractions on the left-hand side of the triangular scheme as far as the tenth row. The rotations, taken in acetone, with $c \sim 1·5\%$ w/v, of the successively least soluble fractions, *na* were as in Table 12. The figures show that at the eighth crystallisation the resolution was complete with respect to the less soluble diastereoisomer, which had m. p. 115°, and $[\alpha]_D^{20}$ −59·8° in acetone, $c = 0·5\%$ w/v.

TABLE 12.

Separation of ethyl (−)-mandelato-(±)mercuriphenylacetate by crystallisation from 40 : 60 dichloromethane : n-hexane. Rotations of successive least-soluble fractions.

No. n of crystallisations ...	0	1	2	3	4	5	6	7	8	9	10
$-[\alpha]_D^{21}$ of fraction *na* ...	47·2°	49·2°	51·9°	53·0°	54·3°	56·7°	58·2°	59·4°	59·8°	59·7°	59·9°

The conversion of the mandelatomercuri-ester into the bromomercuri-ester by anion exchange in dimethylformamide was first tried with a sample from fraction 4a. A solution of this material (2 g.) in dimethylformamide (5 ml.) and one of tetraethylammonium bromide (0·8 g.) in dimethylformamide (10 ml.) were mixed, and water was immediately added. The precipitated ethyl (−)bromomercuriphenylacetate was filtered with suction, and dried in a vacuum over magnesium perchlorate. It had $[\alpha]_D^{21}$ −6·9° in acetone (Found: Hg, 44·9. Calc. for $C_{10}H_{11}BrHgO_2$, Hg, 45·2%). The fully resolved mandelatomercuri-ester, having $[\alpha]_D^{21}$ −59·8° in acetone, was similarly converted, except that the dimethylformamide solutions, and the water, were pre-cooled to 0°. The resulting bromomercuri-ester had $[\alpha]_D^{21}$ −13·9° in acetone ($c = 1·00\%$ w/v).

(6.3) *Radiometric Kinetics.*—Separation of the chemically distinct species was effected by adding the sample (10·86 ml.) of the exchanging solution to a cooled mixture of chloroform (10 ml.) and 10% aqueous sodium bromide (10 ml.). On shaking, the inorganic mercury went into the aqueous layer, and the organic mercury into the chloroform layer. The separation was quantitative when the solvent for the exchange was " 70% " aqueous dioxan, or dimethyl sulphoxide. But when it was dimethylformamide, acetonitrile, or acetone, or a mixture of dimethylformamide and acetonitrile, a few units per cent. of inorganic mercury got into the chloroform layer, from which it was removed by a single wash with 2% aqueous sodium bromide. These separations, established by special tests, became our practice in the work on kinetics. An example of a radiometric run is given in Table 13.

TABLE 13.

Run RF 48. Ethyl α-bromomercuriphenylacetate and radiomercuric bromide, each 0·03M, in 60 : 40 vol. dimethylformamide–acetonitrile at 58·7°.

Time (hr.)	Count per 1000 sec.*	% Label transfer	10^6R (R in mole l.$^{-1}$ sec.$^{-1}$)	Time (hr.)	Count per 1000 sec.*	% Label transfer	10^6R (R in mole l.$^{-1}$ sec.$^{-1}$)
0·25	290	19·3	3·6	1·25	1019	67·8	3·8
0·50	463	30·9	3·1	1·50	1122	74·8	3·8
0·75	712	47·4	3·6	29·0	1502	100	—
1·00	918	61·2	3·9				

* In the chloroform extract.

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[1964] *Substitution at a Saturated Carbon Atom. Part VII.* 3915

(6.4) *Polarimetric Kinetics.*—The measurements were made with a Bendix-Ericsson automatic polarimeter, the green line of a mercury arc being the source of light. The procedure varied according to the nature of the run.

The uncatalysed runs at 59·2° were started by mixing solutions, which had been rapidly brought to that temperature, of (−)ethyl α-bromomercuriphenylacetate and radiomercuric bromide in dimethyl sulphoxide and making up to volume (25 ml.) with that solvent. After timed intervals at 59·2°, samples (3 ml.) were withdrawn, and cooled in ice. They were subsequently warmed at 25° for 15 min., and then their rotation was measured at that temperature in a 2-cm. jacketted cell. The zero of the instrument was adjusted before each reading, the pure solvent being used for this standardisation.

The catalysed runs at 29·5° were performed in the jacketted cell of the polarimeter. Solutions, which had been brought to 29·5°, of (−)ethyl bromomercuriphenylacetate and tetraethylammonium bromide in dimethyl sulphoxide were mixed, made up to volume (5 ml.) with solvent, and transferred to the 2-cm. cell, which had been adjusted to, and was kept throughout at 29·5°. Readings of rotation were taken at timed intervals, the time of the first reading being treated as the time zero. The zero of the instrument was adjusted for the solvent. A sample run is recorded in Table 14.

TABLE 14.

Run PS 22.   (−)Ethyl α-bromomercuriphenylacetate, 0·0400M, and tetraethylammonium bromide, 0·0100M, in dimethyl sulphoxide at 29·5°.

Time (min.)	$[\alpha]$ *	% Racemisn.	$10^4 k_1{}^{(a)}$ ($k_1{}^{(a)}$ in sec.$^{-1}$)	Time (min.)	$[\alpha]$ *	% Racemisn.	$10^4 k_1{}^{(a)}$ ($k_1{}^{(a)}$ in sec.$^{-1}$)
0	−9·20°	0·0	—	60	−3·54°	61·5	2·64
30	−5·95	35·3	2·42	70	−3·11	66·3	2·59
45	−4·68	49·1	2·51	80	−2·69	70·8	2·56
50	−4·24	53·9	2·58				

* At 29·5° for mercury line 5461 Å.

(6.5) *Radio-counting Techniques.*—Mercury-203 has a half-life of 45·8 days, and emits both γ and β rays. Two techniques were employed, and in both only γ rays were measured. Counts on the same kinetic run were made on the same day, in order to avoid the need for a correction for radioactive decay.

During the earlier period of this work (1960—1961), we used the conventional Geiger–Muller counter for liquid samples. The maximum counting rate was about 6 per second. The recording efficiency of this method was only of the order of 0·1%.

We subsequently changed to the use of a scintillating crystal of thallium-activated sodium iodide, which, on receiving γ rays, emits protons. These were collected and counted by a photomultiplier, and recorded on an autoscalar. The recording efficiency is much larger than before, counts up to 400 per second representing the previous intrinsic activities. It was found convenient further to dilute the radioactive source material. The liquid sample was contained in an annular polythene holder, shaped to fit over the crystal.

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