

841. *Mechanism of Electrophilic Substitution at a Saturated Carbon Atom. Part VIII.* Kinetics and Stereochemistry of a Thallium-for-Mercury Substitution. The Unimolecular Mechanism in Thallium-for-Mercury, Mercury-for-Thallium, and Thallium-for-Thallium Substitutions. Appendix: The Dubious Existence of Alkylthallic Salts.*

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The electrophilic substitution of diethylthallic bromide in di-*s*-butylmercury in dimethylformamide has been established as the first metal-for-metal substitution, involving only simple alkyl groups, which is kinetically shown to have the S_E1 mechanism. Quantitative racemisation accompanies the substitution. The substitution is reversible, and, on account of the principle of microscopic reversibility, the kinetic study of mechanism includes one of the substitution by *s*-butylmercuric bromide in *s*-butyldiethylthallium, which also has the S_E1 mechanism. The similar substitution of *s*-butylmercuric nitrate in triethylthallium was examined, and, by a correlation, this more rapid reaction was shown likewise to have the S_E1 mechanism, its first and rate-controlling step being ionisation of the triethylthallium. The principle that the first steps of all unimolecular substitutions in the same substrate are the same, independently of the substituting agent, shows that the fast substitution by diethylthallic bromide in triethylthallium has available the same S_E1 mechanism. This exchange was examined by introducing a label of radioactivity, and it was established that the substitution does employ this mechanism, inasmuch as a comparison of dialkylthallic and alkylmercuric salts as electrophiles shows that the former could not attack a trialkylthallium, by a much larger margin than that by which the latter is known to be unable to do so, before the trialkylthallium ionises.

The Appendix reviews previous attempts to prepare alkylthallic salts, and reports the results of some new attempts by other methods. It is concluded that these salts have not yet been prepared; and that this is so, not because they are not formed in the regulated alkylations and dealkylations of cationic thallium, but because, when not captured by excess of the reagent used to produce them, they decompose spontaneously to thallos salts and products of reaction of the alkyl carbonium ion. A rational connexion is suggested between the instability of alkylthallic salts, the ionicity of dialkylthallic salts, and the nucleophilic reactivity of trialkylthalliums, and, more widely, between these properties of thallium alkyls and those of mercury alkyls at the analogous stages of alkylation.

(1) *First Observations and Influences.*

(1.1) *The Original Plan.*—The study, developed in this Series, of mechanism in aliphatic electrophilic substitution now takes its first step out from the nursery of mercury exchanges into the wider world of generalised metal-for-metal substitutions. The step is only a small one—from mercury to thallium. But we conceive that most metals, many of them only when supplied with suitable ligands, are potential subjects for such studies, which we hope to extend.

Originally, the plan was to investigate thallium exchanges between pairs of compounds, chosen one compound from each of the three types, trialkylthallium, dialkylthallic salts, and alkylthallic salts. Dialkylthallic salts were well known, trialkylthalliums were known, and alkylthallic salts had been described.

Our first discovery was that the report of alkylthallic salts, although detailed, is incorrect; these salts seem never to have been made. In their absence, the main possibility

* Part VII: ref. 3.

for electrophilic thallium exchange among thallium alkyls was that between a dialkylthallic salt and a trialkylthallium. We tried such an exchange, and found that it was instantaneous, denying all hope of kinetic investigation under any conditions that we could devise.

Following these two frustrating observations, we considered theoretically, as outlined below, possible causes of the observed properties of the thallium alkyls, in order, if possible, to attune our approach to them more suitably.

(1.2) *Comparisons of Thallium and Mercury Alkyls.*—Dialkylthallic salts R_2TlX may be compared with alkylmercuric salts $RHgX$; but the former are much more ionising. Thus, compounds R_2TlBr are ionic salts, whereas compounds $RHgBr$ are wholly covalent. In the mercury series, one has to go over to much more weakly co-ordinating anions than bromide, to an anion such as nitrate, in order to find an alkylmercuric salt comparably ionic with a dialkylthallic bromide. The dialkylthallic ion, R_2Tl^+ , is isoelectronic with dialkylmercury, R_2Hg , and, like the latter, is linear.¹ This could account for the greater ease of ionisation in the thallium than in the mercury series. For the ionisation of R_2TlX allows thallium to re-hybridise its bonding orbitals from sp^2 to sp , and so to replace its two metal-carbon bonds in the covalent molecule by two stronger and better separated bonds in the ion R_2Tl^+ . In contrast, the ionisation of $RHgX$ will make no substantial difference to the sp hybridisation in its one metal-carbon bond; and thus the ion RHg^+ will enjoy no corresponding factor of stabilisation.

A trialkylthallium R_3Tl may be compared with a dialkylmercury R_2Hg . But, if the explanation just given is correct, we must expect that the former will ionise, to give R_2Tl^+ and R^- , much more readily than the latter will, to give RHg^+ and R^- . This would allow us to understand why trialkylthalliums are instantly and exothermically hydrolysed by water to form R_2TlOH and RH , whilst dialkylmercurys do not show such high reactivity. This explanation implies that the hydrolysis of a trialkylthallium is a unimolecular electrophilic substitution, S_E1 , initiated by the ready ionisation of the substrate to R_2Tl^+ and R^- , and completed by the attack of water on the formed carbanion R^- ; and it implies that such a mechanism is not so easily available to the much less readily ionising dialkylmercurys. Furthermore, since all unimolecular electrophilic substitutions in the same substrate start with the same ionisation, the wider implication is that a fast unimolecular mechanism S_E1 is available to all electrophilic substitutions of trialkylthalliums, including thallium-for-thallium substitutions; but that no such universally easy route for electrophilic substitution is open to the dialkylmercurys. We know that mechanism S_E1 is far from universal among the substitutions of mercury alkyls; and that, when it is found, it is not particularly fast. We were now contemplating that fast S_E1 mechanisms are universal among the substitutions of trialkylthalliums, and therefore that the fast thallium exchange, which we had observed, was fast because it had that mechanism.

A monoalkylthallic salt, $RTlX_2$, if it existed, would be comparable to HgX_2 . But $RTlX_2$ has a survival problem, which has no counterpart in HgX_2 . By successive ionisations it will form RTl^{2+} , in which, we assume, the double positive charge so withdraws the bond electrons that pressure by the non-bonding electrons weakens the metal-carbon bond; and so the alkyl group is lost. It could be lost in such a way as to divide the double charge between mutually repelling cationic fragments, R^+ and Tl^+ , which are then recovered, the one in simple alkyl compounds, such as alcohols, and the other in thallous salts. These ideas concerning alkylthallic salts receive a certain amount of experimental support, as described in the Appendix (Section 6).

(1.3) *The Revised Procedure.*—The foregoing results and interpretations had brought us to the position that the type of thallium exchange which we would have to investigate was that between a dialkylthallic salt and a trialkylthallium; and that, although this reaction appeared to be much too fast to allow of any direct kinetic demonstration, we had obtained an idea to work to in devising an indirect approach to the question of its mechanism.

¹ Powell and Crowfoot, *Z. Krist.*, 1934, **87**, 370.

The approach devised depended on this preconception, and amounted to taking the "small" step, from mercury to thallium exchanges, in a series of smaller steps. We must explain how each step contributes to the overall plan.

The first step was to find a thallium-in-mercury-out substitution of the general type

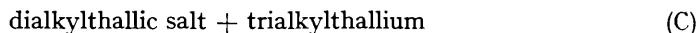


which could be fully investigated by kinetic methods. Our previous experience of electrophilic mercury exchanges suggested that this should be possible. The mechanism of the substitution might have its own inherent interest, as, indeed, proved to be the case. But our main object was to establish and describe this mechanism, whatever it was, so fully that the principle of microscopic reversibility could be applied. This would lead to the second step in our programme, which was rigorously to deduce the mechanism of a mercury-in-thallium-out substitution of the general type



If our provisional ideas were wrong, we could go no further: the overall scheme would break down at this point. But if they were right, we would now have proved that substitution (B) had the unimolecular electrophilic mechanism S_E1 . A qualitative additional check on our preconception could be applied at this stage, because it would follow that, by using, in substitution (B), an alkylmercuric salt comparably ionic with the dialkylthallic salt used in substitution (A), substitution (B) would be found to be instantaneous.

Our next proceeding would be to apply the principle that the first steps, that is, the ionisation steps, of all unimolecular substitutions in the same substrate are the same, independently of the substituting agent. We could use this principle to deduce that a substitution of the form



which employs two of the four reactants of the investigated substitutions (A) and (B), has available a mechanism S_E1 , which has the same high rate, controlled by the ionisation of the trialkylthallium, as has the substitution (B).

Substitution (C) is the thallium exchange, which was the original object of our enquiry. In order to show that it actually uses the mechanism S_E1 , we must exclude the unlikely possibility that this fast mechanism is overlaid by a still faster S_E2 mechanism. If the work had gone as hoped, we would already know that the same S_E1 mechanism, identically rate-controlled, as it applies to substitution (B), is not so overlaid. The only circumstance which could conceivably import into substitution (C), but not into substitution (B), the capacity for such a very fast S_E2 mechanism that it could be competitively successful, would be in case the dialkylthallic salt of substitution (C) were an extremely active bimolecular electrophile, in particular, one much more active than the alkylmercuric salt of substitution (B). So, as a control on this possibility, our fourth and final operation would be kinetically to examine a substitution of the form



which employs the remaining two reactants of the investigated substitutions (A) and (B). Substitution (D) is a mercury exchange, and, from experience, we would expect it to be kinetically measurable. We would then be able, by means of a comparison of the two kinetically examinable reactions (A) and (D), to compare the reactivities of their substituting agents, the dialkylthallic salt and the alkylmercuric salt, towards a common substrate.

This scheme, required by and built on the initial disappointments, has been carried through in just this way, except that we had no need to pursue the fourth step of investigating kinetically the substitution (D). The reason for this was that our study of substitution (A) had shown already that its dialkylthallic reagent is a remarkably poor

performer in an S_E2 mechanism. To such an extent is this so, that our existing experience of mercury exchanges of type (D) provided all the control that we needed.

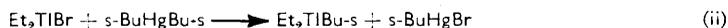
As reactants for substitution (A), we used diethylthallic bromide (because this had been used in radioactive form in our preliminary study of thallium exchange), and di-*s*-butylmercury (because we could have this in optically active form, when we wished).

(2) *Diethylthallic Bromide and Di-s-butylmercury.*

(2.1) *Stoichiometry and Chemical Kinetics.*—From the standpoint of the classification of metal-alkyl interactions, which, without regard to mechanism, labels them as alkyl “redistributions,” two redistributions are possible between the reactants named above. The first would be the alkyl exchange (i), analogous to the reaction labelled (d) in Part I.²



The second would be the alkyl-for-anion exchange (ii), analogous to the reaction designated (e) in Part I:



By an argument set out in Part I, reaction (i) is forbidden as an electrophilic substitution; but reaction (ii) is allowed.

The first need was thus to determine the stoichiometry of any observed reaction. We had to have a solvent with which a trialkylthallium would not react, and in which dialkylthallic salts were soluble; and one of the few that fulfilled these conditions was dimethylformamide, which we accordingly employed. At about 70° in this solvent, a reaction took place. The evidence was that the amount of diethylthallic bromide that could be recovered from a sample of the reaction solution, kept at this temperature, diminished with time over some hours. We checked this result by starting with diethylthallic bromide which had been ¹⁴C-labelled in the ethyl groups. We could then show that the total radioactivity in the separated diethylthallic bromide initially fell in proportion to the quantity of the latter. This meant that the specific activity of the recovered dialkylthallic bromide was initially constant, and therefore that neither ethyl group was leaving the thallium atom. All this pointed to the stoichiometry of reaction (ii). The fact that, at late times, the specific activity of the diethylthallic bromide falls can also be understood on the basis of equation (ii), as arising from alkyl-for-anion exchange between diethylthallic bromide and the formed trialkylthallium.

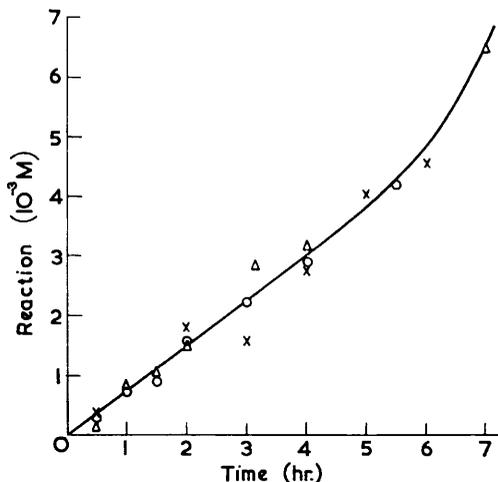
This conclusion was confirmed when we came to devise ways of following the kinetics of the substitution. We could have done it by separation of diethylthallic bromide, and, having employed this substance in radioactive form, following its disappearance radiometrically. But we found two chemical methods, which were more accurate. The first was argentometric, and amounted to following the disappearance of diethylthallic bromide, the only material present which provided immediately titrable bromide ion. The second method was acidometric, and it followed the appearance of trialkylthallium, inasmuch as all trialkylthalliums react instantly and quantitatively with water to give the ionic base, dialkylthallic hydroxide, which could be titrated with acid. We used both these methods, the first almost always, and the second in addition very frequently. They gave the same results, though we got the impression that the argentometric method was a little more accurate than the acidimetric method. The essential equivalence between the radiometric and the two chemical methods is shown by their common plot in the Figure. This equivalence confirms that the reaction had indeed the stoichiometry of equation (ii).

The kinetics of the substitution seemed at first to be very complicated. As is seen in the Figure, an autocatalysis sets in after a certain time. Furthermore, detailed study showed that the earlier part of the reaction-time curve, drawn as straight in the Figure, is only approximately and accidentally so in the runs there illustrated. More generally, the

² Charman, Hughes, and Ingold, *J.*, 1959, 2523.

reaction-time curve is the combined result of an auto-accelerating effect, and an auto-retarding effect, both superposed on the kinetic curve, as, if undisturbed, it would be determined by the molecularity of the substitution.

The auto-retarding effect was easily traced to the formed trialkylthallium. The initial addition of 10% of an equivalent of triethylthallium lowered the initial rate by 60%. Evidently we were dealing with a strongly reversible substitution. The obvious way to circumvent the kinetic effect of its retrogression was to trap the formed trialkylthallium as fast as it was produced. This we could do, making use of its instantaneous hydrolysis by water, if we would make our dimethylformamide solvent very slightly moist. The method worked well. With millimolar amounts of water in the solvent, an initial period of the substitution, roughly the first half-hour at 70°, or the first 7% of reaction, was thus cleared of all kinetic disturbances; for the auto-acceleration came in only after that. This allowed



Three runs in dimethylformamide at 69.7°.

○ Run 15: Initially $[Et_2TlBr] = [s-Bu_2Hg] = 0.0097M$. Disappearance of Et_2TlBr followed by titration with Ag^+ .

△ Run 13: Initially $[Et_2TlBr] = 0.0098$, and $[s-Bu_2Hg] = 0.0097M$. Appearance of $Et_2TlBu-s$ followed by adding water and titrating with acid.

× Run 18: Initially $[Et_2TlBr] = 0.0086$ and $[s-Bu_2Hg] = 0.0097M$. Followed by fall in total radioactivity in separated Et_2TlBr (in the period before alkyl-for-anion exchange with formed trialkylthallium becomes important).

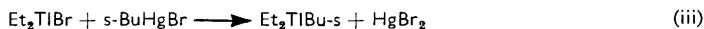
us to infer for the first time, simply from initial rates, the kinetic form of the substitution, and its rate constant, though we confirmed both results afterwards by using much more of the reaction-time curve. We observed at this stage, though we rationalised the observation later, that it is inadvisable to introduce into the dimethylformamide solvent much more than enough water to fulfil its intended purpose.

As to the acceleration, which, in the above conditions, sets in after the first half-hour at 70°, we showed that it was not due to the other product of the substitution, *s*-butylmercuric bromide; for although this has a kinetic effect, as will be mentioned later, the effect is much too small to be made responsible for the observed autocatalysis. Various indications suggested that this might be due to a concurrent radical-chain process, having a well-marked induction period of zero rate, lasting about half-an-hour at 70° in the conditions described above, during which time we were allowed to study our electrophilic substitution. We found that we could lengthen this period of induction by addition of one of the usual radical inhibitors, such as benzoin, or cyclohexene. With the latter, which we soon came to use as a routine, we could extend the induction period to 5–6 hours at 70°, so clearing the first 50% of the electrophilic substitution from all kinetic disturbances. This required a cyclohexene concentration of 0.007M. We limited the inhibitor concentration to that figure, because much higher concentrations seemed to create a new disturbance, perhaps by their engaging in addition reactions, analogous to the well-known additions of methanolic mercuric salts to olefins. In any case, there was no point in trying to clear much more than the first 50% of the electrophilic substitution from all disturbances, because there was another disturbance, as mentioned below, well built into the reaction scheme, which would

not be noticeable during the first 50% of our reaction, but would become a complication in the second 50%.

Our standard concentration of inhibitor, 0.007M, was of the same order of magnitude as the concentration of either reactant for the substitution, and was therefore much larger than would seem necessary for the trapping of a low-concentration intermediate derived solely from either reactant. We suppose that the solvent must be involved in the production of the chain-carrying radicals; and it is easy to invent schemes in which the initiation of radical-chains depends stoichiometrically on the consumption of solvent only. Thus, neglecting differences between different alkyl groups, we could suppose that the reaction between R_2TlX and R_2Hg in $HCO\cdot NR_2$ starts with an ordinary electrophilic substitution to produce some R_3Tl , which is then very slightly homolysed to give $R\cdot$ and $R_2Tl\cdot$, the latter attacking the solvent, with restoration of the consumed R_3Tl , and production of $HCO\cdot NR_2$. We now have two radicals $R\cdot$ and $HCO\cdot NR_2$, either or both of which could start radical-chains involving R_2TlX and R_2Hg ; and the only stoichiometric cost of the starting of these chains is a solvent molecule.

Our routine tests for kinetic disturbances included the initial addition of the other product, *s*-butylmercuric bromide. This appeared to produce a small increase in the rate of substitution by diethylthallic bromide in di-*s*-butylmercury. However, when, in an otherwise similar experiment, the di-*s*-butylmercury was omitted, a slow reaction occurred between the diethylthallic bromide and the *s*-butylmercuric bromide, a reaction which could be followed both by the disappearance of the diethylthallic bromide, and by the appearance of a trialkylthallium. This reaction was fast enough to account for the small apparent increase in the rate of the reaction between diethylthallic bromide and di-*s*-butylmercury, when *s*-butylmercuric bromide was added initially. Evidently this rate increase was only apparent: it just happened that the extra reaction was measured by the same two analytical pointers as measured the original reaction. It was obvious that the extra reaction was (iii):



In the absence of initially added *s*-butylmercuric bromide, reaction (iii) will depend on such *s*-butylmercuric bromide as is formed in the original substitution. Reaction (iii) constitutes a second stage of a serial thallium-for-mercury substitution, of which the first stage is the reaction (ii) (p. 4375), now under investigation.

We did not examine the kinetics of reaction (iii) in any detail; but we did ascertain that its rate, in relevant comparable conditions, is smaller by an order of magnitude than that of reaction (ii). We could thus compute that our measurements of the rate of reaction (ii), even measurements over the longer range, 0—50% of reaction, could not be appreciably affected by substitution (iii). We could further compute that a correction for reaction (iii) would be required, if we should extend, beyond the first 50% of reaction, the range of kinetic observations accepted for the calculation of rate constants. However, as explained already, we had other reasons for not attempting to extend the acceptable range beyond the first 50%.

The various complications having been dealt with, we were able to examine the kinetics of reaction (ii). The two observational ranges, 0—7% in the absence of cyclohexene, and 0—50% in its presence, gave the same kinetic form, and the same rate constant. To our surprise, the reaction was of first order in di-*s*-butylmercury and of zeroth order in diethylthallic bromide. Table 1 contains calculated values of some of the conceivable first- and second-order rate constants. One sees that the only true rate constant is $k_1^{(a)}$. Its value is $3.0 \times 10^{-5} \text{ sec.}^{-1}$ in dimethylformamide at 69.7°. We shall call it $T_{k_1}^{(a)}$, because it is based on titrimetric observations, and is to be compared below with a polarimetric first-order rate constant, $^P k_1^{(a)}$.

These kinetics of substitution, together with the many observations which distinguish

TABLE 1.

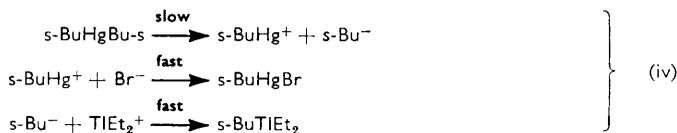
First- and second-order titrimetric rate constants for substitution by diethylthallic bromide in di-*s*-butylmercury in dimethylformamide at 69.7°.

a = initial [*s*-Bu₂Hg]. b = initial [Et₂TlBr].
 $k_1^{(a)}$ = first-order rate constant in *s*-Bu₂Hg (in sec.⁻¹).
 $k_1^{(b)}$ = first-order rate constant in Et₂TlBr (in sec.⁻¹).
 $k_2^{(ab)}$ = rate constant of second-order, first in each reactant (in mole⁻¹ l. sec.⁻¹).

Run	10 ² a	10 ² b	10 ⁵ $k_1^{(a)}$	10 ⁵ $k_1^{(b)}$	(10 ² $k_2^{(ab)}$)
51	0.89	0.38	3.4	7.9	8.9
57	1.29	0.69	2.9	5.4	4.2
60	1.30	0.69	3.1	5.8	4.5
49	1.79	0.76	3.0	7.1	3.9
52	1.79	0.38	2.9	13.5	7.6
58	1.96	0.70	3.3	9.2	4.7
59	1.96	1.74	3.3	3.7	1.9
62	2.64	1.40	2.7	5.1	1.9
50	3.62	0.77	3.0	14.0	3.9
54	4.55	0.78	2.8	16.0	3.7
56	5.48	0.71	2.8	21.8	3.9
74	0.80	0.47	3.4	5.8	7.3
75	0.79	0.46	3.0	5.1	6.5

Mean 3.0 ± 0.2

it from a homolytic process, establish its character as a unimolecular electrophilic substitution S_E1. It is evidently rate-controlled by a preliminary ionisation of the di-*s*-butylmercury:



It is easy now to see why we found it necessary to limit the amount of water added to the dimethylformamide solvent for the suppression of the back reaction to not very much more than was required for that purpose. Much more water would have effected a unimolecular hydrolysis of the di-*s*-butylmercury.

This thallium-in-mercury-out substitution is the first metal-for-metal exchange involving only simple alkyl groups, for which the mechanism S_E1 has been kinetically established. The previous successful search for this mechanism by Reutov, and by ourselves, relied on the introduction of electron-absorbing substituents to secure the preliminary formation of a carbanion from the organomercury compound undergoing substitution (cf. Part VII³).

(2.2) *Polarimetric Kinetics*.—In Part VII it was shown, in the first proved example of a metal-for-metal substitution by an S_E1 mechanism, that its stereochemical concomitant was total racemisation, each molecular act of substitution leading to either enantiomeric form of the product with the same probability. However, the substrate in that substitution, α -carbomethoxybenzylmercuric bromide, and therefore the intermediate α -carbomethoxybenzyl carbanion of mechanism S_E1, contained electron absorbing carbomethoxyl and phenyl groups. These substituents are expected to have two effects. The first, arising from their electro-negativity, is kinetic and is to lengthen the average life of the formed carbanion. The second is stereochemical, and arises from the unsaturated nature of the substituents. Supposing that carbanions in general are not flat in their equilibrium configurations, but are pyramidal with an inversion frequency, like ammonia, the substituents in the α -carbomethoxybenzyl carbanion will, by importing mesomeric character, either partly or wholly flatten the equilibrium configuration. The effect will be to increase any inversion frequency towards, and perhaps to, its upper limit in the frequency of an out-of-plane vibration of a planar structure. In other words, the effect of the substituents will be to decrease the

³ Hughes, Ingold, and Roberts, *J.*, 1964, 3900.

enantiomeric life of the carbanion very substantially, and even perhaps to zero. The combination of these two effects, the lengthening of the kinetic life, and the shortening of the enantiomeric life, could well lead to such a relation between the two lives that total racemisation would accompany the S_N1 substitution, as, indeed, it does.

It will be clear that we cannot assume, simply from the results in Part VII, that all substitutions by mechanism S_N1 will entail total racemisation. In the carbanion of a simple alkyl group, such as *s*-butyl, the average kinetic life would be shorter, and the enantiomeric life longer, than in the case described involving substituents; and the enantiomeric life might conceivably be long enough to permit some preservation of enantiomeric form over the span of the kinetic life. In that case, racemisation would, to say the least, be incomplete.

The matter was for experimental determination by following the polarimetric changes during the S_N1 substitution by diethylthallic bromide in optically active di-*s*-butylmercury. Unlike all the other substitutions that have been kinetically followed with optically active organomercury compounds, this one is non-isotopic: its factors and products are chemically different, and hence a change of rotation is expected to accompany substitution, whatever the mechanism, and whatever its steric course may be. But the rate of change of rotation, and its final value, will give some information. If the rotation falls finally to zero, and, in the period before the onset of the autocatalytic effect, falls according to a first-order rate law, and with the same first-order rate constant as was found titrimetrically for the substitution in the same conditions, the conclusion would be that the substitution is fully racemising. If the rotation changes at any other rate, or to any other end-result, that would mean that the substitution is not fully racemising, and a further research would be needed to determine the relations between the configurations and signs of rotation, before we could decide whether configuration is being predominantly retained or inverted in the substitution.

The polarimetric runs were conducted under the conditions of the titrimetric runs, *viz.*, in dimethylformamide at 69.7°, but with di-*s*-butylmercury having $[\alpha]_D^{20} -14.9^\circ$. Timed samples were withdrawn, chilled, and polarimetrically examined at 20°. It was found that the rotation fell finally to zero. In the period before the onset of autocatalysis, it fell according to a first-order rate law, though after that it fell at an accelerated rate reflecting the titrimetric behaviour of the reaction. Furthermore, the mean, first-order, polarimetric rate constant, ${}^P k_1^{(a)} = 3.1 \times 10^{-5} \text{ sec.}^{-1}$, was identical, to within the experimental error, with the mean titrimetric rate constant ${}^T k_1^{(a)} = 3.0 \times 10^{-5} \text{ sec.}^{-1}$. These results are in Table 2. They show that this unimolecular electrophilic substitution, which involves the simplest of asymmetric alkyl groups, is associated with total racemisation.

TABLE 2.

Substitution by diethylthallic bromide in di-*s*-butylmercury of $[\alpha]_D^{20} -14.9^\circ$ in dimethylformamide at 69.7°: first-order rate constants of accompanying racemisation.

Run	$10^2 a$	$10^2 b$	$10^5 k_1^{(a)}$	$10^5 P k_1^{(a)}$
P1	9.77	1.72	3.7	} 3.1 ± 0.3
P2	9.77	1.72	2.9	
P3	3.20	1.04	2.8	

(2.3) *Products.*—We were not able to isolate diethyl-*s*-butylthallium, because of the low concentration in which it was formed in dry dimethylformamide, and the similarity of its boiling point to that of dimethylformamide. In moist dimethylformamide, the trialkylthallium is decomposed as fast as it is formed. Its main hydrolysis product is diethylthallic hydroxide, as we found by isolating its bromide, the structure of which does not, however, prove that the trialkylthallium was its immediate precursor.

s-Butylmercuric bromide was extracted in an almost pure form, when runs in moist dimethylformamide containing cyclohexene were stopped after 2—3 half-lives.

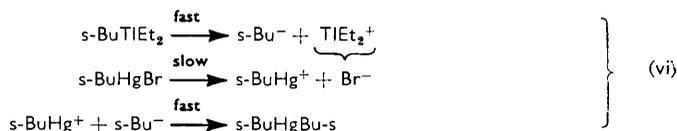
(3) *s*-Butylmercuric Salts and Trialkylthalliums.

(3.1) *s*-Butylmercuric Bromide and Diethyl-*s*-butylthallium.—We have noted that the thallium-in-mercury-out substitution, formulated in equation (ii), is strongly reversed, unless the trialkylthallium is trapped as fast as it is formed. In Sections 2·1 and 2·2 above we presented kinetic and stereochemical evidence that the mechanism of reaction (ii) is of the S_{E1} type, represented in equations (iv).

We are now concerned with the mercury-in-thallium-out reaction (v), which is the reverse of reaction (ii), the compound substituted being a trialkylthallium, and the substituting agent an alkylmercuric salt:



If we apply the principle of microscopic reversibility to the mechanism (iv) of reaction (ii), we shall deduce, except for one detail, that the mechanism of reaction (v) is as shown in equations (vi). Apart from that detail, mechanism (vi) has the same experimental basis, and the same degree of authenticity, as mechanism (iv). The outstanding detail is in the identity of the slow step in mechanism (vi). For convenience, this identification is made in equations (vi), in anticipation of the evidence contained in Section 3.2. Like mechanism (iv), mechanism (vi) is of the S_{E1} type:



The reversal of the first and the slow step of mechanism (iv) constitutes the third step of mechanism (vi); and, as an association, with covalent binding, of two reactive counterions, this step must be fast. The second and third steps of mechanism (iv), which for similar reasons must be fast, on reversal furnish, respectively, the second and first steps of mechanism (vi); and one at least of the latter steps must be slow, or reaction (ii) would not go forward to an observable degree.

It was obvious to presume that the second step of mechanism (vi), the ionisation of *s*-butylmercuric bromide, would be slow, because we knew that anion exchange with this material is usually somewhat slow. For example, had that not been so, we would not have been able to follow the kinetic runs recorded in Section 2.1 by titrating diethylthallic bromide, in the presence of *s*-butylmercuric bromide, with silver nitrate. We also presumed, on the basis of the theoretical considerations advanced in Section 1.2 above, that the first step of mechanism (vi) would be fast. However, these reasonable assumptions needed experimental support.

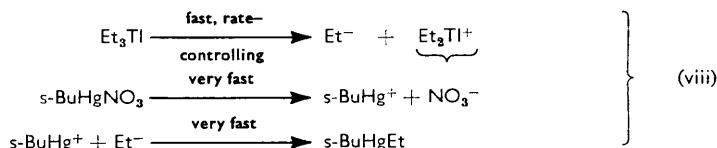
The alternatives were that the second step of mechanism (vi) might be either fast or slow, that if it were slow, the first step might be either fast or slow, and that if the second step were fast, the first would have to be slow. We had the possibility of settling these ambiguities at one stroke by replacing the *s*-butylmercuric bromide in reaction (v) by a pre-ionised *s*-butylmercuric salt. If the second step of reaction (vi) were, as we thought, the only slow step, the change of anion would make the reaction instantaneous. If it did not, the first step of reaction (vi) would thus be shown to be the slow step.

(3.2) *s*-Butylmercuric Nitrate and Triethylthallium.—The substituting agent was *s*-butylmercuric nitrate, an ionic salt. We could not take diethyl-*s*-butylthallium as the compound to be substituted, because it would have been impossible to prepare and preserve this substance in the solvent up to the moment of reaction, without disproportionation among its easily ionising alkyl groups. So we took triethylthallium, the model reaction being that of equation (vii):



This reaction was instantaneous in dimethylformamide at 70°, and, as far as we could tell, instantaneous also at 0°, and at -20°. It followed that the second step of the mechanism represented in equation (vi) is the slow step, and that the first step of that mechanism, like the third step, is fast.

We can also deduce that the mechanism of the substitution (vii) is as shown in equations (viii). The first step is fast, but is rate-controlling, because its ionic products have at most to associate with counter-ions which are pre-formed. In other words, although the first step is fast, the succeeding steps are faster. This mechanism is also of an S_N1 -type:



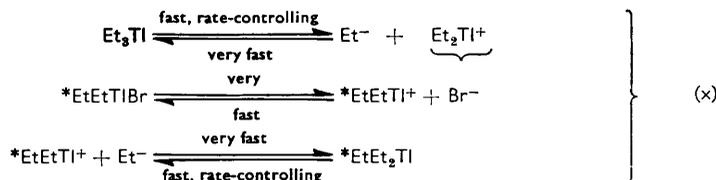
(4) *Diethylthallic Salts and Triethylthallium.*

(4.1) *Diethylthallic Bromide and Triethylthallium.*—This exchange is the electrophilic substitution which we at first hoped kinetically to investigate in a direct way. It was examined, then and later, by providing the diethylthallic bromide with a label of radioactivity due to carbon-14 as represented in equation (ix) (the asterisk signifies the label):



In dry dimethylformamide, with or without added cyclohexene, the exchange reached equilibrium at 70° in less time than the few seconds that we required to separate the chemical species. The same was true, when we repeated these experiments at 0°, and again at -20°.

The work described in Sections 2 and 3 proves that the thallium-for-thallium substitution (ix) has available an S_N1 mechanism, which is shown in equations (x). This mechanism is completely analogous to the mechanism (viii), which has been established for the mercury-for-thallium substitution (vii):



The two mechanisms are identical with respect to their first, and rate-controlling, step. This step, in its rate-control of mechanism (viii), has been shown to be practically instantaneous in dimethylformamide at and below 0°. Nevertheless, this step rate-controls mechanism (viii), and must equally rate-control mechanism (x), because, in the subsequent steps of either mechanism, the ionic products of the first step have either nothing at all to do, or they have only to unite with pre-formed counter-ions. Thus mechanism (x) as a whole provides the practical instantaneity, which we have found to be a property of the thallium exchange (ix).

It remains to be considered whether it is possible that, notwithstanding the availability of this fast S_N1 mechanism, a still faster S_N2 mechanism provides the route actually followed by the exchange. This would imply that diethylthallic bromide attacks triethylthallium in a bimolecular way extremely rapidly, in particular, before the rapidly ionising triethylthallium has time to ionise. Let us examine this possibility.

It was shown in Section 2, that diethylthallic bromide does not bimolecularly attack di-s-butylmercury before the latter ionises in dimethylformamide. It was shown in

Part III⁴ of this series, that, on the contrary, *s*-butylmercuric bromide does bimolecularly attack di-*s*-butylmercury before that substrate ionises in ethanol, and, moreover, attacks it at a rate which is comparable, for our concentrations and temperatures, with the rate at which the substrate ionises in dimethylformamide. It was also shown in Part III, that *s*-butylmercuric nitrate, which is comparably ionising to diethylthallic bromide, bimolecularly attacks the same substrate 10⁴ times faster than does *s*-butylmercuric bromide: this rate must be enormously greater than the rate of ionisation of the substrate. Going back now to the result from Section 2, we see no evidence that diethylthallic bromide is outstandingly *better* as a bimolecular electrophile than *s*-butylmercuric bromide, or, more pertinently, than *s*-butylmercuric nitrate. The evidence is very strongly in the other direction. Yet outstandingly the better is what diethylthallic bromide would have to be in order to rationalise the idea that this substance is engaging in an S_B2 attack on triethylthallium, before the latter has time to ionise. For it is shown in Section 3 that neither *s*-butylmercuric bromide, nor even *s*-butylmercuric nitrate, is able to execute a bimolecular attack on triethylthallium, before this substrate ionises. This completes our case for the actual use of the S_B1 mechanism (x) by the thallium exchange between diethylthallic bromide and triethylthallium.

(4.2) *Diethylthallic Ethyl Sulphide and Triethylthallium*.—We did entertain the idea of bringing mechanism (x) of thallium exchange into a form suitable for direct kinetic investigation, by making the second step rate-controlling, and suitably slow. This was to be done by changing the anion from bromide to one which was sufficiently strongly covalently bonded to thallium to give rates of a convenient magnitude.

We feel sure that it would be possible to do this, but, in our one attempt, we overdid the reduction of ionicity. We prepared the ethyl sulphide, Et₂Tl·SEt. This did not generate ions in any obvious way. It apparently contained a good TlS covalency, because its infrared spectrum yielded a Tl-S stretching frequency, 352 cm.⁻¹, not known before from observation, but in good agreement with the frequency calculated, by Gordy's rule.⁵

The exchange was tried between non-radioactive diethylthallic ethyl sulphide and radioactive triethylthallium, the activity being that of carbon-14. The principle of the test was that, if no exchange occurred, the label distribution would remain as on the left-hand side of equation (xi), and hydrolysis would discharge as ethane one-third of the radioactivity; whereas, if equilibrium were reached, one-half of the material would have the label distribution shown on the right-hand side of equation (xi), and that half was expected to contribute no loss of radioactivity on hydrolysis:



When the materials represented on the left-hand side of the equation were brought together in dry dimethylformamide, the hydrolysis of an immediately taken sample did discharge one-third of the radioactivity. After the dimethylformamide solution had been kept for 16 hours at 69.7°, the hydrolysis of a sample still discharged one-third of the radioactivity. This shows that, even though there must be a small, but rapid equilibrium production of ethyl carbanions from the triethylthallium, the diethylthallic ethylsulphide does not ionise sufficiently easily to trap them.

EXPERIMENTAL

(5.1) *Materials*.—The required dialkylthallic halides, particularly diethylthallic bromide, were prepared in the standard way from thallic chloride and excess of the appropriate Grignard reagent.

Triethylthallium was prepared by interaction of diethylthallic bromide and ethyl-lithium out of contact with air, using Birch's technique.⁶ Our yields were variable, the best 50%. Some separation of metallic thallium always occurred during the reaction, and there were

⁴ Charman, Hughes, Ingold, and Thorpe, *J.*, 1961, 1121.

⁵ Gordy, *J. Chem. Phys.*, 1946, **14**, 305.

⁶ Birch, *J.*, 1934, 1132.

occasions when, in its final distillation, the triethylthallium decomposed explosively. We found b. p. 46—48°/0.2—0.3 mm. and 50—52°/0.6—0.8 mm. Immediately on preparation, the material was dissolved in the solvent in which it would be required, usually dimethylformamide. Such solutions were stored in the dark at 0°. The concentration of triethylthallium in solution was determined immediately before use by adding water and titrating the formed diethylthallic hydroxide with acid.

The radioactive organothallic compounds were prepared starting from [2-¹⁴C]ethanol, as supplied with 0.1mc. activity by the Radiochemical Centre, Amersham. After suitable dilution (*e.g.*, 5000-fold) with ordinary ethanol, [2-¹⁴C]ethyl bromide was prepared, and from this di[2-¹⁴C]ethylthallic bromide.

Tri[2-¹⁴C]ethylthallium was prepared by means of the fast thallium exchange between diethylthallic bromide and triethylthallium. Solutions of ¹⁴C-labelled diethylthallic bromide (0.12 g.) in dimethylformamide (20 ml.) and ordinary triethylthallium (0.58 g.) in dimethylformamide (20 ml.) were mixed and distilled to dryness at 0.5—2.0 mm. The distillate was a solution of ¹⁴C-labelled triethylthallium, and was made up to 100 ml. with dimethylformamide. Its chemical concentration and radioactivity were determined just before use.

We tried at first to prepare *diethylthallic ethyl sulphide* by treating diethylthallic bromide, or hydroxide, with sodium ethyl sulphide in methanol or aqueous methanol, but obtained thus only impure cream-coloured solids with compositions (C ~ 10%) approximating to that required for thallos ethyl sulphide. The required substance was made by evaporating a solution of triethylthallium (0.58 g.) and ethanethiol (0.5 ml.) in dimethylformamide (20 ml.) to dryness under reduced pressure. The residual yellow solid had m. p. 167—170° (decomp.) (Found: C, 21.4; H, 4.6. C₆H₁₅STl requires C, 22.3; H, 4.6%). We could not crystallise the substance, because it decomposed. An attempt to crystallise it from ethanol gave back a solid substance (C, 11.6; H, 3.5%) apparently similar to the products obtained in the attempted preparations by anion exchange in methanol and aqueous methanol.

s-Butylmercuric bromide was prepared as described in Part I,² and was stored in the dark at 0°. s-Butylmercuric nitrate was prepared as described in Part III,⁴ and was stored in the dark at -80°. Di-s-butylmercury, prepared as described in Part II,⁷ had b. p. 45°/1.3 mm., and was stored in the dark at 0°, usually in solution in dimethylformamide.

Optically active s-butylmercuric bromide was prepared, as described in Part I,² by crystallisation of the (-)-mandelate from acetone, and reconversion into bromide. The triangular scheme of separation, set out in Part I, was pursued only as far as the third row, fractions 3a and 3b of which gave bromide, having $[\alpha]_D^{20}$ (acetone) -17.9 and -15.0°, respectively, *i.e.*, fractions about 70 and 60% resolved. Fraction 3a was converted, by the method noted above, into di-s-butylmercury, which had $[\alpha]_D^{20}$ -14.9° in dimethylformamide, and was used for polarimetric kinetics.

Dimethylformamide was purified as described in Part VII,³ and all other materials were purified by methods which are standard.

(5.2) *Titrimetric Kinetics.*—The reaction between diethylthallic bromide and di-s-butylmercury in dimethylformamide at 69.7° was studied as follows. Each run was conducted in a volumetric flask (50 ml.), and timed samples (5 ml.) were withdrawn. Each sample was run into water (100 ml.) acidified with nitric acid, and was then titrated with standard silver nitrate to a potentiometric end-point, which was sharp and reproducible.

The same reaction was studied as follows. Each timed sample (5 ml.) of the reaction solution was run into water (100 ml.), and the alkali formed was titrated with standard hydrochloric acid, Methyl Red being the indicator. The reaction between s-butylmercuric nitrate and triethylthallium in dimethylformamide was examined by the same analytical method. But for temperatures of 0° and below, the reaction was run on a small scale, and the whole reaction solution was taken for analysis, to give a single reading of reaction progress.

(5.3) *Polarimetric Kinetics.*—The reaction between diethylthallic bromide and optically active di-s-butylmercury, $[\alpha]_D^{20}$ -14.9°, in dimethylformamide at 69.7° was examined as follows. The runs were again conducted in volumetric flasks (50 ml.), and timed samples (4 ml.) were withdrawn. Each was immediately cooled in a stoppered tube at 0°, then allowed to warm for a few minutes towards room temperature, and then transferred to a 2-cm. cell, jacketed to 25°, in the automatic polarimeter. The rotation was read some 15—20 min. later, when the attainment of thermal equilibrium had become sensibly complete.

⁷ Charman, Hughes, and Ingold, *J.*, 1959, 2530.

(5.4) *Radiometric Kinetics*.—The reaction between radioactive diethylthallic bromide and di-*s*-butylmercury in dimethylformamide at 69.7° was studied as follows. The runs were conducted in flasks as before, and timed samples were withdrawn. Each sample (2 ml.) was run into dry ether at -80°. The separated diethylthallic bromide was filtered with suction, washed with pre-cooled ether, and dissolved in dimethylformamide to provide the solution (5 ml.) for radiometric assay.

In the experiments on the exchange between radioactive diethylthallic bromide and triethylthallium, the salt was separated and prepared for radioactive assay in the same manner. However, as these exchanges were conducted at 0° and lower temperatures, the runs were on a small scale, and the whole reaction solution was chemically separated, and radiometrically examined, to give a single reading of reaction progress.

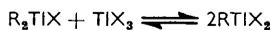
In the experiments with radioactive triethylthallium and diethylthallic ethyl sulphide, the solutions (5 ml. each) of either compound in dimethylformamide were mixed, kept at 69.7° for a determined time, and then treated with water (5 ml.) and dilute hydrochloric acid (1 ml.), and evaporated to dryness under reduced pressure at 80°. The residual solid consisted of the ethyl sulphide, together with diethylthallic chloride, formed from triethylthallium by hydrolytic loss of ethane. In order to measure the loss of radioethane, the solid was dissolved in dimethylformamide (2 ml.), and the solution was radiometrically counted.

The counting of β -rays from the carbon-14 was done by adding a measured amount of the solution to a solution of 2,5-diphenyloxazole in toluene, and counting the scintillations in a thermostated counter at -20°, the electrical conditions being adjusted to maximise the signal : background ratio.

(6) Appendix—The Dubious Existence of Alkylthallic Salts.

They have been claimed, and the claim has been denied, as noted in Section 6.1 below. We tried to prepare them by four methods, as outlined in Sections 6.1—6.4. We failed to obtain them, but our results seem to display a certain pattern, as is suggested in Section 6.5.

(6.1) *Reaction of Thallic Halides with Dialkylthallic Halides*.—Melnikov and Gracheva⁸ claimed that alkylthallic halides could be prepared by disproportionation between dialkylthallic halides and thallic halides, in water or aqueous ethanol. They give the stoicheiometry as



and that of a side-reaction as



(though this second equation does not balance). Salts with R = Me, Et, and isopentyl, and with X = Cl and Br, were described, and good analytical figures were given. The salts were said to decompose according to the equation



We had failed to confirm this work, when Sarrach reported⁹ that he could not repeat it. With R = Me and Et, and X = Cl, the only salts that he could obtain, apart from unchanged R_2TlCl , were the lower inorganic chlorides $(TlCl_2)_2$ and $(Tl_2Cl_3)_2$. He also showed by radiochromatography, using ²⁰⁴Tl, that no other thallium compound could be detected thus in the solutions. As to organic products, he obtained methanol and ethanol as their 3,5-dinitrobenzoates, and, in the case R = Et, he detected acetaldehyde. Alkyl chlorides might have been present, but they were not detected.

We first attempted to secure a disproportionation of the type described by Melnikov and Gracheva between di-*s*-butylthallic chloride and thallic chloride in water. We obtained an immediate yellow precipitate of $(TlCl_2)_2$, and some more of the same material on subsequently adding ethyl alcohol. On attempting to use n-propyl alcohol as solvent, we recovered only thallic chloride, $TlCl$. We then tried the reaction between dimethylthallic chloride and thallic chloride, and obtained the products subsequently reported by Sarrach.⁹

⁸ Melnikov and Gracheva, *J. Gen. Chem., U.S.S.R.*, 1935, **5**, 1786.

⁹ Sarrach, *Z. anorg. Chem.*, 1962, **319**, 16.

(6.2) *Reaction of a Thallic Halide with a Dialkylmercury.*—We can monodealkylate a dialkylmercury by means of at least two organometal electrophiles, *viz.*, alkylmercuric salts and dialkylthallic salts. It would seem that such a dealkylation could hardly fail to go when the electrophile was a thallic salt. We would then obtain an alkylthallic salt, if it is stable:



We tried this reaction with di-*s*-butylmercury and thallic chloride in ether, at various temperatures between 0 and -50° . *s*-Butylmercuric chloride was formed. Some 80% or more of the thallium was retrieved as thallic chloride, TlCl , whilst 20%, or lesser quantities down to 5%, was recovered as di-*s*-butylthallic chloride, R_2TlCl . In an attempt to moderate the electrophilic activity of the thallic chloride, this reagent was presented in the form of its pyridine complex, or again as its 2,2'-bipyridyl complex. The reaction now required higher temperatures, such as 40 or 60° ; but the products were substantially the same.

(6.3) *Reaction of a Thallic Halide with an Alkylmagnesium Halide.*—Even more than a dialkylmercury, an alkylmagnesium halide is dealkylated by metal and organometal cationic electrophiles. We use this type of reaction preparatively when we convert thallic chloride with excess of a Grignard reagent into a dialkylthallic salt. We wanted to know what would happen to this reaction, if the Grignard compound were supplied in no more than 1 : 1-equivalence. It seemed to us that the alkylthallic salt could hardly avoid being formed; and then, with no excess of Grignard compound to alkylate it further, we ought to find it, unless it is unstable in some other way:



We tried the reaction between thallic chloride and one equivalent of methylmagnesium chloride in ether at various temperatures below 0° . Very little dimethylthallic chloride was formed in these conditions, certainly not 50% of it. The main products containing thallium were thallium dichloride, $(\text{TlCl}_2)_2$, thallium sesquichloride, $(\text{Tl}_2\text{Cl}_3)_2$, and thallic chloride, TlCl .

(6.4) *Reaction of a Dialkylthallic Halide with Halogen in Pyridine.*—This reaction has been examined by Krause and Grosse,¹⁰ who found that the halogen caused a transfer of both alkyl groups from the dialkylthallic halide to the solvent, pyridine, so to form alkylpyridinium ions, which were isolated as complex thallates, $(\text{PyR})^+(\text{TlX}_4)^-$.

We examined the reaction between dimethylthallic bromide and bromine in pyridine, in the hope of finding a way to restrict dealkylation of the dimethylthallic salt to the removal from it of just one alkyl group:



We could isolate Krause and Grosse's salt $(\text{PyMe})^+(\text{TlBr}_4)^-$ without difficulty under all the conditions tried. But when the proportion of bromine was reduced, we merely recovered a smaller amount of it, and no methylthallic bromide, either as such, or as its complex pyridinium salt, $(\text{PyMe})^+(\text{RTlBr}_3)^-$, could be obtained.

(6.5) *Conclusions.*—These experiments leave us with the impression that the unknown alkylthallic salts, RTlX_2 , are very probably formed in all the reactions by which we and others have tried to obtain them, but that they are unstable. They have their own peculiar mode of decomposition, which, however, may be intercepted by their more rapid reaction with an excess of some highly active reagent used to produce them; and when that happens, we observe either double alkylations of thallium, as by Grignard reagents, or double dealkylations, as by halogens in pyridine. But when such reactions do not occur, the normal decomposition supervenes, which, as explained in Section 1.2, we picture as occurring in the cation RTl^{2+} . The main mode of its decomposition appears to be that in which the double charge becomes divided between mutually repelling cationic fragments. One of them, R^+ , appears as some simple alkyl compound, such as the alcohol, ROH . The other, Tl^+ , will be recovered in thallic salts, TlX , unless thallic salts are present, when salts in some intermediate oxidation state, such as $(\text{TlX}_2)_2$ and $(\text{Tl}_2\text{X}_3)_2$, will be produced. We cannot exclude the possibility that, in some circumstances, the alkyl group in the cation RTl^{2+} may be expelled as the radical R^\cdot , which would give a mixture of organic products, and would leave the ion Tl^{2+} , which would be recovered as a thallothallic salt $(\text{TlX}_2)_2$.