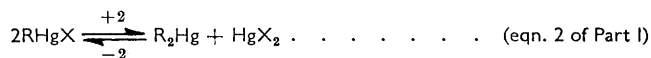


506. *Mechanism of Electrophilic Substitution at a Saturated Carbon Atom. Part II.* Kinetics, Stereochemistry, and Mechanism of the Two-alkyl Mercury-exchange Reaction.*

By H. B. CHARMAN, E. D. HUGHES, and SIR CHRISTOPHER INGOLD.

Mercury exchange between mercuric bromide as substituting agent and optically active di-*s*-butylmercury as substrate, to produce optically active *s*-butylmercuric bromide, proceeds in ethanol with complete retention of configuration. This is the first demonstration that retention of configuration is the preferred stereochemical path of an electrophilic substitution at saturated carbon in the absence of stereospecific influences from neighbouring asymmetric groups. This reaction, alike in ethanol and in acetone, follows the second-order form, $\text{Rate} = k_2[\text{HgX}_2][\text{R}_2\text{Hg}]$. These two results exclude unimolecular electrophilic substitution, S_E1 , but are compatible with either bimolecular electrophilic substitution, S_E2 , or internal electrophilic substitution, S_Ei . The last two mechanisms were distinguished by comparing results of a number of such parallel investigations with different substituting agents. On the one hand, the original agent HgBr_2 was complexed with extra halide ion in LiHgBr_3 , so decreasing the cationic nature of the reagent mercury, but providing loosely held bromide to combine with the mercury expelled from the substrate. A great reduction of rate resulted. On the other hand, the original HgBr_2 was replaced by the increasingly ionic salts $\text{Hg}(\text{OAc})_2$ and $\text{Hg}(\text{NO}_3)_2$. All these substitutions went with total retention of configuration in ethanol, and the last also in ethanol-water; they all had the same second-order kinetics, but their absolute rates increased strongly with increasing ionicity of HgX_2 . It is concluded that the substitutions by salts HgX_2 in the dialkyl R_2Hg , and the reverse reactions of substitution between two molecules RHgX , all proceed by a configuration-retaining, bimolecular, electrophilic mechanism of substitution, S_E2 .

IN Part I * it was shown that three, and only three, mercury-exchange reactions can exist as independent electrophilic substitutions, two of which had not previously been recognised. They have now all been realised, and we shall report their kinetics and stereochemistry. This paper is concerned with the one which was previously recognised, the "two-alkyl" mercury-exchange, as we call it to distinguish it from the others:



This is the longest-known of the "alkyl redistribution" reactions of mercury. In almost all investigated examples, the equilibrium so lies that the main natural direction of reaction is from right to left (-2). However, the reaction can be led from left to right ($+2$) by continuously removing the formed mercuric salt, *e.g.*, by anion exchange with

* Part I, preceding paper.

precipitation, as of mercuric sulphide, or by co-ordination with a strongly complexing ligand, such as ammonia. In this form, the reaction, called "symmetrisation," has been regarded as a special case of alkyl "redistribution." However, the reaction in both directions has been recognised as a form of electrophilic substitution by Winstein, Reutov, and others.

(1) *Previous Stereochemical Work.*—First, as to the reaction in its natural (−2) direction, Wright¹ added the groups OMe and HgOAc to cyclohexene, with the aid of mercuric acetate in methanol, to give the racemic forms of the so-called α- and β-diastereoisomers of 2-methoxycyclohexylmercuric acetate, of which the β-isomer was the more thermodynamically stable; from them, by reduction with hydrazine, he obtained the symmetrisation product di-(2-methoxycyclohexyl)mercury in three forms, of which the most thermodynamically stable was assumed to be the ββ-form; finally, by treatment of this form with mercuric acetate, he obtained the pure β-form of 2-methoxycyclohexylmercuric acetate. Since half the carbon–mercury bonds in the last product are formed by substitution, and the thermodynamically less stable isomers of the di-(2-methoxycyclohexyl)mercury gave, at least in part, the less stable α-acetate, it was concluded that substitution proceeds with retention of configuration. Winstein, Traylor, and Garner² supplemented this finding by converting β-2-methoxycyclohexylmercuric chloride by means of 2-methyl-2-phenylpropylmagnesium chloride into β-2-methoxycyclohexyl-(2-methyl-2-phenylpropyl)mercury, and then, with the aid of mercuric chloride, regenerating β-2-methoxycyclohexylmercuric chloride, along with 2-methyl-2-phenylpropyl (neophyl) chloride. Although, as was shown by isotopic labelling, 48% of the carbon–mercury bonds in the recovered methoxycyclohexylmercuric chloride had been formed with a mercury-for-mercury substitution, that product was still the pure β-isomer.* Winstein and Traylor⁴ showed that di-4-camphylmercury and mercuric chloride give 4-camphylmercuric chloride, and hence that the necessity for a retained configuration does not prevent the occurrence of substitution. Reutov, Beletskaya, and Mardaleishvili⁵ found that a particular diastereoisomer of di-(−)-menthyl mercurybis-α-(phenylacetate) could be converted into the same diastereoisomer of (−)-menthyl α-(bromomercuri)phenylacetate in two ways, namely, by treatment with hydrogen bromide, a reaction in which none of the carbon–mercury bonds eventually appearing in the bromomercuri-product suffers cleavage, and by treatment with mercuric bromide, a reaction in which 50% of the carbon–mercury bonds of the product are formed as a result of mercury exchange. This again points to retention of configuration in the exchange. It is possible so to conduct the reaction with mercuric bromide that some stereoisomeric change results,⁶ but this could be due to interference by the prototropic system in the acetic ester residue.

As to the left-to-right (+2) exchange, Winstein and Traylor⁴ and Nesmeyanov, Reutov,⁵ and their co-workers have shown that a diastereoisomer of (−)-menthyl α-(bromomercuri)phenylacetate, on treatment with ammonia, yields a form of di-(−)-menthyl mercurybis-α-(phenylacetate), from which hydrogen bromide regenerates only the original diastereoisomer of (−)-menthyl α-(bromomercuri)phenylacetate. In the mercurybis(phenylacetate), 50% of the carbon–mercury bonds are new, and a 50% sample of these new bonds is recovered in the regenerated bromomercuri-compound; evidently the new bonds are formed with retention of configuration.

(2) *The Present Objectives.*—In summary, Section 1 shows that all workers agree that

* These β-forms are described as *cis*, but there is some doubt about this identification,³ which is not essential to the conclusion drawn.

¹ Wright, *Canad. J. Chem.*, 1952, **30**, 268.

² Winstein, Traylor, and Garner, *J. Amer. Chem. Soc.*, 1955, **77**, 3741.

³ Brook and Wright, *Acta Cryst.*, 1951, **4**, 50; Wright, *Ann. New York Acad. Sci.*, 1957, **65**, 436.

⁴ Winstein and Traylor, *J. Amer. Chem. Soc.*, 1956, **78**, 2597.

⁵ Reutov, Beletskaya, and Mardaleishvili, *Doklady Akad. Nauk S.S.S.R.*, 1957, **116**, 617.

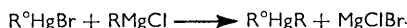
⁶ Nesmeyanov, Reutov, and Poddubnaya, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 1953, 649.

configuration is preserved at mercury-bearing carbon in the two-alkyl exchange reaction. Yet all the examples involve more than one asymmetric carbon atom, so that none of the investigated substitutions is free from internal asymmetric influences, which are often the strong influences of asymmetry coupled in rings. Further, in all the examples, the carbon atom at which substitution occurs is not in a simple alkyl group, but in some substituted or involuted structure, holding various possibilities of special stereochemical effects from neighbouring groups in the structure. Thus, despite the historical unanimity, we are still without any demonstration as to whether substitution with retention of configuration is the preferred stereochemical path of the two-alkyl mercury-exchange in a typical and simple alkyl system, in the absence of all possible stereospecific influences. This is the first gap we now seek to fill. The second, equally obvious in the prior investigations, is that in no case has an observed stereochemical result been associated with a kinetic study such as might link steric course with mechanism.

We studied reaction (2), stereochemically and kinetically, in the thermodynamically natural direction (—2). It is unnecessary to study the mechanism of a reversible reaction experimentally in both directions, for by the principle of microscopic reversibility its mechanism in both directions is known as soon as it is determined for one.

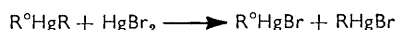
(3) *Stereochemistry of Substitution.*—As R in reaction (2), we used *s*-butyl (see Part I). This is a typical alkyl group, and as simple as can provide an asymmetric seat for the mercury exchange; in particular, it has no asymmetric centre other than that bearing the metal. As X we used three potential anions, namely, bromide, acetate, and nitrate.

The principle of the stereochemical part of these studies can be explained by reference to the example of substitution in di-*s*-butylmercury by mercuric bromide. Optically active *s*-butylmercuric bromide, the specific activity of which we will call θ , was converted by the use of a (necessarily racemic) Grignard reagent prepared from *s*-butyl chloride, into a di-*s*-butylmercury labelled by optical activity in one only of its two alkyl groups:



(The degree sign denotes labelling by optical activity; the asterisk is reserved to indicate labelling by radioactivity, since both will occur in forthcoming Parts.) The original carbon-mercury bonds $R^{\circ}\text{Hg}$ are untouched in this reaction, and accordingly, *in them*, the label suffers no dilution, though an equal number of new and unlabelled carbon-mercury bonds RHg are formed.

This dialkylmercury was converted by treatment with mercuric bromide into *s*-butylmercuric bromide:



The stoichiometry shows that the label, if assumed to “stick” to its alkyl group, suffers a two-fold dilution in the total product, the specific activity of which, on the assumption made, should be $\theta/2$. However, the consequences of the label’s not “sticking” require to be examined.

The dialkyl will be attacked with equal probability at R and at R° ; each attack will produce two molecules of product, one having a preserved, and the other an exchanged, carbon-mercury bond. Thus, a quarter of the product will arise from attack on R, to give molecules containing an untouched $R^{\circ}\text{Hg}$ bond: the specific activity of this part of the product will be θ . A second quarter will come out of the same attack by the formation of the new RHg bond: its specific activity will be 0. The third quarter will arise from attack at R° to give molecules with an untouched RHg bond: its specific activity will also be 0. The fourth quarter will be formed by mercury replacement at R° , and its specific activity will depend on the stereochemical course of substitution. If configuration is wholly preserved, the specific activity of this quarter of the product will be θ , and that of the whole product will accordingly be $\frac{1}{4}(\theta + 0 + 0 + \theta) = \theta/2$. If the asymmetric centre is completely racemised by substitution, the activity of the fourth quarter will be 0, and that of the whole product $\frac{1}{4}(\theta + 0 + 0 + 0) = \theta/4$. If configuration is wholly inverted

in the substitution, then the activity of the fourth quarter will be -0 , and that of the whole product $\frac{1}{4}(\theta + 0 + 0 - \theta) = 0$.

Here is a clear distinction. It is the same, if the reagent is mercuric acetate or nitrate, provided that the optical activity of the formed *s*-butylmercuric acetate or nitrate is tested in the corresponding bromide (which, being more sparingly soluble in water, can be produced very easily from either of the other salts by treatment with aqueous potassium bromide).

The results of our experiments on these lines are in Table I. With all these substituting agents, to within observational error, the specific rotation of the *s*-butylmercuric bromide, formed by or through mercury-exchange between these substituting agents and di-*s*-butylmercury was one-half of the specific rotation of the *s*-butylmercuric bromide from which the di-*s*-butylmercury was prepared. This demonstrates substitution with retention of configuration in all these three two-alkyl mercury-exchanges.

Lithium bromide was introduced into experiment S2 for reasons to do with the work

TABLE I. *Optical rotations (in acetone, with $l = 2$) of s-butylmercuric bromide converted into di-s-butylmercury and obtained therefrom by reaction with mercuric salts in ethanol or aqueous ethanol at 0° .*

Rotation of initial BuHgBr: $c = 4.63$; $[\alpha]_D^{20} = -15.2^\circ$.				Final BuHgBr	
No.	[Bu ₂ Hg]	Reagents	Solvent	c	$[\alpha]_D^{20}$
S1	0.1	0.1M-HgBr ₂	EtOH	5.74	-7.6°
S2	0.1	0.1M-HgBr ₂ + 0.3M-LiBr	"	3.56	-7.8
S3	0.1	0.1M-Hg(OAc) ₂	"	4.59	-7.5
S4	0.1	0.1M-Hg(NO ₃) ₂	"	4.76	-7.8
S5	0.075	0.075M-Hg(NO ₃) ₂ + 0.75M-HNO ₃	1 : 1-aq.-EtOH	2.03	-7.2
				Mean:	-7.6
S6	0.075	0.15M-HBr	1 : 1-aq.-EtOH	5.74	-7.6

described in Section 4. In experiment S5, water and nitric acid were introduced to increase ionisation, but limit hydrolysis, of the reagent. This was the only experiment in which a detectable side-reaction occurred: a small amount of mercurous nitrate was formed. Experiment S6 was essentially a blank to ascertain whether the di-*s*-butylmercury was in reality, as had been assumed, optically inactive with respect to one of its two *s*-butyl groups. It might not have been either because (i) the optically active *s*-butylmercuric bromide might have reacted more quickly with one enantiomer of the Grignard reagent than with the other, when rapid racemisation of the Grignard compound would have restored the more extensively consumed form, which eventually would have been found to have reacted in excess, or (ii) the di-*s*-butylmercury, even if truly racemic in one alkyl group when formed, is a mixture of diastereoisomers, which should have different boiling points (we saw signs of this, material of higher rotation having higher b. p.), and therefore might inadvertently have become partly separated when, during preparation, the dialkyl was distilled. In fact, no errors arose from these causes. Experiment S6 so converts di-*s*-butylmercury into *s*-butylmercuric bromide that all the carbon-mercury bonds of the latter are carried in untouched, half coming from the optically active side of the di-*s*-butylmercury and half from its supposedly inactive side. That the latter was inactive is shown because the rotation of the finally formed *s*-butylmercuric bromide was just one-half of that of the original sample used to prepare the di-*s*-butylmercury.

One other conceivable source of error in the recorded rotations has to be considered, namely, that which would arise from any incompleteness of crystallisation of the formed, partly resolved *s*-butylmercuric bromide. As shown in Part I, Section 6c, the racemic form is a little less soluble than either enantiomer, and therefore an error due to this cause should result in low rotations. However, the rotations in Table I show no evidence of any such systematic error.

(4) *Kinetics of Substitution.*—Two methods of following the kinetics were evolved, both dependent on the quenching of the substitution at known times by an instantaneous irreversible reaction of the surviving inorganic mercuric salt, this reaction producing a colour, or change of colour intensity, which could be measured without uncontrollable disturbances from the organic mercury compounds present. The first was the dithizone method (D in the Tables), which can be used in acetone but not in ethanol; the second was the generally more versatile sulphide method (S). The procedures are described in Sections 6c and 6d.

The reaction of mercuric bromide with di-*s*-butylmercury was followed in acetone by the dithizone method, and in ethanol by the sulphide method. The record of a run is contained in Table 2, which indicates a kinetic course represented by the second-order rate-equation. A number of second-order rate-constants for this substitution, with various initial concentrations of reactants, are collected in Table 3, which shows the rate-constants to be independent of the concentrations of both reactants. Evidently the kinetic equation, $\text{Rate} = k_2[\text{HgBr}_2][\text{Bu}_2\text{Hg}]$, is obeyed.

TABLE 2. *Kinetic course of the reaction of mercuric bromide with di-*s*-butylmercury (Run 24a. Method D. $[\text{HgBr}_2]_0 = [\text{Bu}_2\text{Hg}]_0 = 0.40$ mM in acetone at 25°).*

<i>t</i> (min.)	3.5	4.4	6.4	7.3	8.8	10.8	13.1	
$[\text{HgBr}_2]$ (10^{-4}M) { uncorr. ...	2.80	2.72	2.44	2.32	2.24	2.00	1.92	
corr.* ...	3.40	3.32	3.04	2.92	2.84	2.60	2.52	
k_2 (l. mole ⁻¹ sec. ⁻¹)	2.1	1.9	2.2	2.1	1.9	2.1	1.9	Mean 2.0

* The basis of this correction is explained in Section 6c.

TABLE 3. *Second-order rate-constants of the reaction of mercuric bromide with di-*s*-butylmercury at 25°.*

Solvent (Method)	$[\text{HgBr}_2]_0$ (mM)	$[\text{Bu}_2\text{Hg}]_0$ (mM)	k_2 (l. mole ⁻¹ sec. ⁻¹)	Solvent (Method)	$[\text{HgBr}_2]_0$ (mM)	$[\text{Bu}_2\text{Hg}]_0$ (mM)	k_2 (l. mole ⁻¹ sec. ⁻¹)
Me ₂ CO (D)	0.08	0.08	2.8	Me ₂ CO (D) {	0.40	0.40	2.0
	0.20	0.20	2.3		1.00	1.00	2.2
	0.40	0.20	2.7				
	0.40	0.20	2.8			Mean: 2.4	
	0.40	0.40	2.3				
EtOH (S) ... {				EtOH (S) ... {	2.00	2.00	0.38
					2.00	2.00	0.40

The effect of added lithium bromide on the reaction between mercuric bromide and di-*s*-butylmercury in acetone was next investigated. The specimen run in Table 4, and the rate-constants in Table 5, show that added lithium bromide reduced the rate of mercury-exchange, as expressed by k_2 of $\text{Rate} = k_2[\text{HgBr}_2][\text{Bu}_2\text{Hg}]$. However, as long as the concentration of lithium bromide was well below that of the mercuric bromide, the modified second-order equation, $\text{Rate} = k_2^{\text{Li}}([\text{HgBr}_2] - [\text{LiBr}][\text{Bu}_2\text{Hg}])$ was obeyed, in which the constant k_2^{Li} , starting from identity with k_2 in the absence of lithium bromide, retained the same value when lithium bromide was introduced. This can be understood on the basis that the lithium bromide, when in defect, is almost completely complexed with mercuric bromide to form LiHgBr_3 , and that it withholds from the exchange reaction the equivalent of mercuric bromide thus complexed. However, when the proportion of lithium bromide equals or exceeds that of the mercuric bromide, k_2^{Li} becomes infinite or negative and hence meaningless, whilst a calculated k_2 continues to fall sharply. A more complicated kinetic situation now obtains, which we have not attempted to elucidate quantitatively. Most of the mercuric bromide will now be combined in the complex, just as most of the lithium bromide previously was, and reactivity in the exchange will depend largely on the small residue of mercuric bromide which remains uncombined, and hence on a minor component in the material balance, controlled by the reversible reaction, $\text{LiBr} + \text{HgBr}_2 \rightleftharpoons \text{LiHgBr}_3$, of which we do not know the equilibrium constant. Moreover, in this situation, further thermodynamically-uninvestigated complexing and ionising

equilibria may become relevant. Some of these runs were followed by the dithizone method, and some by the sulphide method because dithizone combines with only that part of the mercuric bromide which is in excess of the lithium bromide, and thus does not react with LiHgBr_3 , whereas sulphide is formed from the total inorganic mercury.

TABLE 4. *Kinetic course of the reaction between mercuric bromide and di-s-butylmercury in the presence of lithium bromide (Run 35. Method S. $[\text{HgBr}_2]_0 = [\text{Bu}_2\text{Hg}]_0 = [\text{LiBr}]_0 = 4.0$ mM in acetone at 25°).*

t (min.)	19.5	39.0	61.0	82.0	101.0	120.0	140.0
$[\text{HgBr}_2]$ (mM)	2.9	2.6	1.6	1.25	1.05	1.00	0.90
k_2 (l. mole ⁻¹ sec. ⁻¹)	0.08	0.06	0.10	0.11	0.12	0.10	0.10
	Mean $k_2 = 0.10$ l. mole ⁻¹ sec. ⁻¹ .						

Change of the substituting agent from mercuric bromide to mercuric acetate gives much faster reactions. They were studied by the sulphide method in the more retarding solvent, ethanol, at 0°; even then the times of half-change were a very few minutes. However, it was established that the reactions obey the second-order rate-equation, Rate =

TABLE 5. *Second-order rate-constants of the reaction of mercuric bromide with di-s-butylmercury in the presence of lithium bromide in acetone at 25°.*

Method	$[\text{LiBr}]_0$ (mM)	$[\text{HgBr}_2]$ (mM)	$[\text{Bu}_2\text{Hg}]_0$ (mM)	k_2 (l. mole ⁻¹ sec. ⁻¹)	k_2^{Li} (l. mole ⁻¹ sec. ⁻¹)
D	0.0	0.4	0.4	2.4	2.4
"	0.2	0.4	0.4	0.9	2.2
"	0.4	0.8	0.4	1.0	2.2
"	0.5	1.0	1.0	1.0	2.3
S	4.0	4.0	4.0	0.10	—
"	8.0	4.0	4.0	0.045	—

$k_2[\text{Hg}(\text{OAc})_2][\text{Bu}_2\text{Hg}]$, as shown by the sample run recorded in Table 6 and the collection of second-order rate-constants in Table 7. Correction of these constants for the thermal volume-change reduces them by 2%; the mean, thus corrected, is 5.3 l. mole⁻¹ sec.⁻¹.

TABLE 6. *Kinetic course of the reaction of mercuric acetate with di-s-butylmercury (Run 43. Method S. $[\text{Hg}(\text{OAc})_2]_0 = 0.20$ mM, $[\text{Bu}_2\text{Hg}]_0 = 1.00$ mM, in ethanol at 0°).*

t (min.)	0.58	1.58	2.25	3.08	3.75	4.75	5.75
$[\text{Hg}(\text{OAc})_2]$ (10 ⁻⁴ M)	1.76	1.16	0.87	0.72	0.58	0.53	0.34
k_2 (l. mole ⁻¹ sec. ⁻¹)	4.4	6.1	6.4	6.0	5.8	5.1	5.8
	Mean $k_2 = 5.7$ l. mole ⁻¹ sec. ⁻¹						

TABLE 7. *Rate-constants of the reaction of mercuric acetate with di-s-butylmercury in ethanol at 0° (Method S).*

$[\text{Hg}(\text{OAc})_2]_0$ (mM)	$[\text{Bu}_2\text{Hg}]_0$ (mM)	k_2 (l. mole ⁻¹ sec. ⁻¹)	$[\text{Hg}(\text{OAc})]_0$ (mM)	$[\text{Bu}_2\text{Hg}]_0$ (mM)	k_2 (l. mole ⁻¹ sec. ⁻¹)
0.2	0.2	5.0	0.2	1.0	5.7
0.2	0.4	4.5	0.2	2.0	5.9
0.4	0.4	5.7			Mean: 5.4

Change of the substituting agent to mercuric nitrate gave still faster reactions; it was necessary to reduce the temperature below -45° in order to measure kinetics. Two runs were conducted in ethanol at -46.6°; they gave results corresponding to the second-order equation Rate = $k_2[\text{Hg}(\text{NO}_3)_2][\text{Bu}_2\text{Hg}]$, as is shown for one of them in Table 8, in which also the rate-constants of both runs, corrected by 7% for the thermal volume-change, are noted.

We may summarise these results. First, the three mercuric salts, HgBr_2 , $\text{Hg}(\text{OAc})_2$, and $\text{Hg}(\text{NO}_3)_2$, react with di-s-butylmercury to give the appropriate s-butylmercuric salt,

always in accord with the second-order equation. Secondly, the potentially anionic mercury of the complex LiHgBr_3 has little or no reactivity towards di-*s*-butylmercury in

TABLE 8. Kinetic course of the reaction of mercuric nitrate with di-*s*-butylmercury (Run 51. Method S. $[\text{Bu}_2\text{Hg}]_0 = [\text{Hg}(\text{NO}_3)_2]_0 = 0.40$ mM, in ethanol at -46.6°).

t (min.)	1.50	2.25	3.50	5.75	7.75	11.5	
$[\text{Hg}(\text{NO}_3)_2]$ (10^{-4}M)	3.01	2.62	2.39	1.92	1.60	1.24	
k_2 (l. mole $^{-1}$ sec. $^{-1}$)	9.1	9.8	8.0	7.9	8.1	8.0	Mean 8.5

Mean rate-constants corrected for thermal contraction:

$$\left. \begin{array}{l} \text{Run 51, mean } k_2 \text{ (corr.)} = 7.9 \\ \text{Run 57, ,, ,, ,,} = 7.3 \end{array} \right\} \text{Mean: } 7.6 \text{ l. mole}^{-1} \text{ sec.}^{-1}$$

our conditions. Thirdly, the reactivities of the mercuric salts HgBr_2 , $\text{Hg}(\text{OAc})_2$, and $\text{Hg}(\text{NO}_3)_2$ towards di-*s*-butylmercury increase in that order, as is shown by the following mean rate-constants (l. mole $^{-1}$ sec. $^{-1}$) of reaction in ethanol at the temperatures noted: HgBr_2 , 0.39 at 25° ; $\text{Hg}(\text{OAc})_2$, 5.3 at 0° ; $\text{Hg}(\text{NO}_3)_2$, 7.6 at -46.6° . The overall reactivity sequence is, thus, $\text{LiHgBr}_3 < \text{HgBr}_2 < \text{Hg}(\text{OAc})_2 < \text{Hg}(\text{NO}_3)_2$.

(5) *Mechanism of Substitution.*—The complete retention of configuration, and the second-order kinetic form of the substitution with mercuric bromide showed that the unimolecular electrophilic mechanism $S_{\text{E}}1$ could not be operative. However, the bimolecular electrophilic mechanism $S_{\text{E}}2$ admits retention of configuration, and the internal electrophilic mechanism $S_{\text{E}}i$ requires it; both these mechanisms require second-order kinetics (see the preliminary discussion of mechanisms in Part I, Section 2). We thus had to devise kinetic distinctions between mechanisms $S_{\text{E}}2$ and $S_{\text{E}}i$; the rest of the work described was devoted to this end.

The first distinction applied was based on the consideration that mechanism $S_{\text{E}}2$ describes a purely electrophilic attack on carbon by the cationic or potentially cationic mercury of the substituting agent, whilst mechanism $S_{\text{E}}i$ involves a collaborating nucleophilic attack on the expelled mercury by some potentially anionic component in the reagent. If, therefore, in the reagent HgBr_2 , the mercury is complexed with an extra bromide ion, as in LiHgBr_3 , with weakening of its cationic status and some acquisition of negative charge, rate by mechanism $S_{\text{E}}2$ must be strongly reduced. On the other hand, the collaborating nucleophilic attack required in mechanism $S_{\text{E}}i$ would be favoured by the structure of this complex, which contains an extra bromide ion, eager to have its own exclusive mercury, and very easily made available to combine and go off with the expelled mercury atom; therefore the effect of the complexing on mechanism $S_{\text{E}}i$ is unlikely to be to reduce rate strongly, and might well be to increase it. As we have seen, the complexing strongly retards the mercury exchange.

The complementary distinction which we have used depends on the consideration that the reactivity of simple mercuric salts HgX_2 as substituting agents in mechanism $S_{\text{E}}2$ must increase with the ionicity of their constitution, and with their ease of ionic dissociation, right up to the limit of the completely free ion Hg^{2+} , whereas, since, in substitution by mechanism $S_{\text{E}}i$, the elements of a cyclic transition state have to be kept together, rate by this mechanism must fall with increasing ease of dissociation, indeed to a zero second-order rate in the limit in which the mercuric salt is completely dissociated. As a series of salts of increasing ionicity, we investigated HgBr_2 , $\text{Hg}(\text{OAc})_2$, and $\text{Hg}(\text{NO}_3)_2$. The reactions of all three with di-*s*-butylmercury in ethanol, and of the third in aqueous ethanol, proceed with quantitative retention of configuration and second-order kinetic form. Thus they form a single class, relevant to our problem of distinguishing between mechanisms $S_{\text{E}}2$ and $S_{\text{E}}i$. The distinction is provided by the observation that the absolute rates increase strongly with increasing ionicity along the series, HgBr_2 , $\text{Hg}(\text{OAc})_2$, $\text{Hg}(\text{NO}_3)_2$. [If it had been necessary, we should have added $\text{Hg}(\text{ClO}_4)_2$.] This points to the incursion of mechanism $S_{\text{E}}2$ in the series and leaves only the doubt as to whether mechanism $S_{\text{E}}2$ or

S_{E1} is dominant at its less reactive end, before the rate increase can be shown to have set in (*i.e.*, $HgBr_2$).

This doubt is removed when we consider the complementarity of our two criteria. The first can be regarded as a backward extension of the second, the effect of thus joining them being to enlarge our reagent series $LiHgBr_3$, $HgBr_2$, $Hg(OAc)_2$, $Hg(NO_3)_2$, in order of increasing positivity of mercury. Along this enlarged series the absolute rate of substitution strongly increases, and, as before, we assume mechanism S_{E2} in order to account for the increase. Thus the doubt about mechanism attaching to the starting point of the series moves back to $LiHgBr_3$ (about whose reaction anyway we know less than about those of the other substituting agents).

Thus, for the reactions of mercuric bromide, acetate, and nitrate, severally, with di-*s*-butylmercury in ethanol, the mechanism of mercury exchange is uniformly that of bimolecular electrophilic substitution S_{E2} . In this mechanism, stereochemical configuration is fully preserved. The same conclusions will apply to the corresponding retrograde reactions ("symmetrisation") in the same conditions.

EXPERIMENTAL

(6a) *Materials*.—The preparation and resolution of *s*-butylmercuric bromide are described in Part I, Section 6. Di-*s*-butylmercury was prepared by gradual addition of a solution of racemic or optically active *s*-butylmercuric bromide (10 g.) in ether (50 ml.) to the Grignard reagent from *s*-butyl chloride (4 g.). After 2 hr., 0.5% aqueous sulphuric acid was added, and the ether layer was dried ($MgSO_4$) and evaporated. The di-*s*-butylmercury, distilled through a 15 cm. vacuum-jacketed column, had b. p. (racemic form) $46^\circ/1.7$ mm., n_D^{25} 1.5118; yield 6 g. (68%). The recorded properties⁷ are b. p. $44.5^\circ/1.3$ mm., n_D^{25} 1.5110. The compound decomposed in light, with formation of a black precipitate, and was stored in the dark at -80° . If necessary it was redistilled before use.

(6b) *Products*.—A solution (5 ml.) in ethanol of optically active di-*s*-butylmercury (0.15M) was added to a solution (2.5 ml.) of the substituting agent (0.3M). When the latter was mercuric bromide in ethanol, the product was separated by adding water (10 ml.), and, after 1 hr. at 0° , was collected, washed successively with 5% aqueous potassium bromide (3×3 ml.), water (3×5 ml.), and methanol (2×2 ml.), and crystallised from pentane; yield 85%. When the reagent was mercuric acetate or nitrate in ethanol (2.5 ml.), or mercuric nitrate in aqueous 1.5N-nitric acid (5 ml.), the product was precipitated by adding 5% aqueous potassium bromide (10 ml.), and the above procedure for isolation was followed. In the reaction involving nitric acid a small amount of mercurous bromide was isolated. One of the reagents used was 0.3N-aqueous hydrobromic acid (5 ml.); the product was isolated as in the other cases.

(6c) *Kinetics by the Dithizone Method*.^{8a}—A standard solution of purified dithizone in carbon tetrachloride was tested for the effect of di-*s*-butylmercury, *s*-butylmercuric bromide, and acetone, on the constancy of the amount of it taken up by mercuric bromide in acetone, as indicated by the reduction in its light absorption at 620 m μ (Unicam spectrophotometer). The effects of time and light on the absorption were also noted. Mercuric bromide in acetone alone gave a reading unaffected by time, light, or acetone; the absorption was reduced by *s*-butylmercuric bromide, both in the absence and in the presence of mercuric bromide, though not by much if all solutions were kept in the dark; di-*s*-butylmercury alone did not affect the absorption, but in the presence of mercuric bromide caused a small (*e.g.*, 5%) downward drift for the first 10 min. only

In order to compensate for these effects, calibration graphs were prepared, corresponding to the successive compositions obtaining during a run. A synthetic sample was added to the dithizone, the solution was kept in the dark for 10 min., then the absorption reading was taken. Table 9 contains the data for the graph used in following run 24a (Table 2) and such other runs in acetone (Table 3) as had equal initial concentrations. (A separate graph was necessary for each initial ratio of reactants. All these graphs were essentially linear.)

⁷ Winstein and Traylor, *J. Amer. Chem. Soc.*, 1955, **77**, 3747.

⁸ Snell and Snell, "Colorimetric Methods of Analysis," Van Nostrand Co., Inc., New York, 1949, Vol. II, (a) p. 70; (b) p. 75.

The concentrations of "standard" dithizone solutions do not remain constant.^{8a} However, such variation in our experiments affected only the axial intercepts, not the slopes, of our calibration graphs because the latter were linear and the concentration of mercuric bromide

TABLE 9. *Data for the construction of a calibration curve for use in the dithizone method of following kinetic runs.*

[HgBr ₂] (10 ⁻⁴ M)	4.0	3.6	3.2	2.8	2.4	1.6	0.8
[Bu ₂ Hg] (10 ⁻⁴ M)	4.0	3.6	3.2	2.8	2.4	1.6	0.8
[BuHgBr] (10 ⁻⁴ M)	0.0	0.8	1.6	2.4	3.2	4.8	6.4
Reading	0.168	0.202	0.230	0.267	0.303	0.382	0.452

Note: The concentrations refer to the synthetic mixtures before their addition to the dithizone solution.

C_{Hg} is theoretically connected with that of the dithizone C_{Di} , and the absorption reading A , by the linear relation $C_{\text{Hg}} = a\{C_{\text{Di}} - (A/\epsilon)\}$, where ϵ is the extinction coefficient of dithizone and a is a constant. Obviously, a change in C_{Di} will not affect the proportionality constant $-a/\epsilon$. Because the concentrations of our dithizone solutions were not the same at the time of construction of a calibration graph as when used to follow a run which the graph was to help us interpret, the apparent concentrations C_{Hg} applying to the run, as read from the graph, were all subject to a constant correction. This was so determined as to give the correct initial value of C_{Hg} when the readings were extrapolated to zero time. An illustration of this procedure is included in Table 2.

The rate-constants are included in Table 5 of a number of kinetic runs, followed by the dithizone method, of the reaction with di-*s*-butylmercury of mercuric bromide in the presence of lithium bromide in acetone. Only that part of the concentration of mercuric bromide which was in excess of the lithium bromide was estimated by the dithizone method. In these experiments, the calibration plots were curved, and therefore the calibration for a run had to be prepared immediately before the run, in order that the concentration of the dithizone solution should be similar for both.

(6d) *Kinetics by the Sulphide Method.*^{8b}—The estimation of inorganic mercury(II) in aqueous solution absorptiometrically as sulphide, produced as a clear colloid, was adapted for use in the presence of organic mercury compounds and organic solvents in two ways.

In the first, a solution of hydrogen sulphide in boiled-out distilled water (20 ml.) was added to ethanol (50 ml.) and 5% aqueous gum arabic (2 ml.). This solution was added to samples providing a concentration of inorganic mercury of 8×10^{-4} M or less, and absorption readings were taken after 20 min. on a Spekker spectrophotometer with a yellow filter (maximum transmission, 580 m μ). A calibration curve was first constructed; this was used to interpret readings taken during a run. This technique was applied to each of the runs marked S in Tables 4 and 5. The method was somewhat crude in this application, our calibration plots being curved.

In the second, and, where applicable, more satisfactory method, more dilute mercury solutions were used, the gum arabic was omitted, and the proportion of ethanol in the solvent was increased. To a solution (1 ml.) of hydrogen sulphide, prepared by diluting a saturated aqueous solution (25 ml.) with boiled-out distilled water (75 ml.), a synthetic or kinetic mercury solution in ethanol (5 ml.) was added, and, after 35 min., the absorption was measured. The calibration curves were now linear, the concentration of inorganic mercury being directly proportional to the absorption reading. This method was applied to the runs in Tables 6, 7, and 8.

The low temperature, -46.6° , used with mercuric nitrate was maintained by means of a mixture of liquid and frozen acetonitrile in a Dewar flask, in which ethanol (46 ml.), a 0.01M-solution in ethanol of mercuric nitrate, and a 0.01M-solution in ethanol of di-*s*-butylmercury were separately cooled for 1.5 hr. 2 ml. of the mercuric nitrate solution were then added to the ethanol, and reaction was started by the addition of 2 ml. of the solution of di-*s*-butylmercury. The withdrawn samples (5 ml.) were run into the hydrogen sulphide solution (0.5 ml. in Run 51, and 1.0 ml. in run 57). A jacketed pipette was used, the temperature of the inner tube of which was controlled by surrounding it with ethanol cooled with solid carbon dioxide.