THE KINETICS OF CHLORINE ATOM EXCHANGE
BETWEEN ANTIMONY TRICHLORIDE AND TRIMETHYLCHLOROSILANE
IN BENZENE AND HEXANE

by

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A Thesis submitted to the Australian National University
for the degree of Doctor of Philosophy.

February, 1959.
I hereby declare that this Thesis describes my own original work, including the choice of subject and planning of experiments. The experimental studies were made in the Radiochemistry Department of the Research School of Physical Sciences, Australian National University, during the tenure of a scholarship awarded by the University, which I gratefully acknowledge.

I am greatly indebted to Dr. R. Mills for his supervision and many helpful discussions and suggestions, and am pleased to acknowledge the helpful advice of Dr. J.R. Richards. My thanks are due to the workshop staff, in particular to Mr. W. Tys, for their patient aid in the construction of apparatus.

Two further studies, one extending the analytical methods described in this Thesis, and one concerned with chemical kinetic aspects of virus-antibody reactions (including the exchange of antibody by processes formally analogous to isotopic exchange reactions), were also undertaken during
the tenure of my scholarship. I am grateful to Dr. Fazekas de St. Groth of the Microbiology Department of this University, for suggesting the problems to me, and for kindly inviting me to collaborate with him. These studies are described in the communications listed below.


I. A Model of Virus-Antibody Interaction.
   By S. Fazekas de St. Groth, G.S. Watson and A.F. Reid

II. A Critical Comparison of Hypotheses.
   By S. Fazekas de St. Groth and A.F. Reid.

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1. **INTRODUCTION**

Silicon - halogen compounds are reactive towards a variety of reagents such as water\(^1\), \(^2\), \(^3\), alcohols\(^2\), phenols\(^4\), amines\(^5\), and organomagnesium halides\(^6\),\(^7\). Typical reactions are discussed by Gilman and Dunn\(^8\) in a review comparing organosilicon and carbon compounds, and by Rochow\(^9\). In addition to their general reactions, which are facilitated by the large covalent radius of silicon, the high electronegativity difference between silicon and the halogens, and the presence of unoccupied \(d\) orbitals in the silicon valence shell, enabling at least temporary formation of a five covalent species\(^10\),\(^11\),\(^12\), silicon-halogen compounds undergo a large number of halogen or 'pseudo-halogen' replacement reactions. These are governed in general by bond energy considerations\(^13\), and usually the halogen of lower atomic weight replaces the one with the higher. Where volatility or solubility relations are favourable, however, the reverse reaction is sometimes observed. Numerous studies with silver salts have been reported\(^13\),\(^14\),\(^15\),\(^16\), and several authors have established 'conversion series' for the action of silver salts\(^13\),\(^14\) and anhydrous halogen acids\(^13\).

Various other compounds are effective in producing halogen exchange, for example ammonium fluoride with silicon-chloride compounds\(^17\), and of particular interest for the work described in this thesis, a large number of halogen replacement reactions are effected by covalent metal halides. While a number of ordinary substitution reactions, and many of the halogen replacement reactions,
proceed by nucleophilic, possibly ionic, and often heterogeneous mechanisms (6.b), those replacements involving covalent metal halides are likely to proceed by covalent mechanisms, and in particular, by co-ordination to the central metal atom of the halide attached to silicon, as discussed below.

It is of interest to discover whether, when a particular halogen replacement reaction occurs, the corresponding isotopic halogen exchange can also occur, and elucidation of isotopic exchange mechanisms should be useful in the general study of silicon-halogen and organosilicon reaction processes. Isotopic exchange reactions have the particular characteristic that the reaction products are chemically identical with the reactants, and hence there is no heat or entropy of reaction to complicate the interpretation or comparisons within a series of activation energies or entropies.

Covalent metal halide halogen substitution reactions on silicon halides which have been reported include the conversion of trimethylchloro- and bromosilanes to trimethylfluoro- and chlorosilanes by the action of antimony trifluoride$^{18}$ and trichloride$^6$ respectively; the action of aluminium iodide on silicon tetrafluoride$^{19}$ and of aluminium halides on organofluorosilanes$^{20}$; and the reactions of the halides of antimony, aluminium, arsenic, and titanium on silicon cyanates and thiocyanates$^{21}$. It was observed that the reaction of
aluminium iodide with triethylfluorosilane does not occur by nucleophilic substitution on silicon, but most probably by electrophilic attack by aluminium iodide on the fluorine of the silicon-fluorine bond. The intermediates suggested are Et₂Si⁺, AlF⁻, but these probably do not actually separate (6.b).

In a study of the kinetics of the reaction of methylmagnesium halides with trimethylhalogenosilanes it was found that halogen replacement as well as methylation occurred when the halogen of the methylmagnesium halide was of lower atomic weight than that of the halogenosilane. Halogen replacement was observed separately for the action of magnesium bromide on trimethyliodosilane. Presumably the exchange mechanism was similar to that of the methylation, which appeared to involve co-ordination of the silane halogen to magnesium, a process which would be expected to allow transfer of either a methyl group or a halogen atom to the central silicon atom.

In the present experimental studies attention is confined, apart from hydrogen chloride, to halogen isotopic exchange reactions of halides of aluminium, antimony and magnesium with trimethylhalogenosilanes.

It is noteworthy that the covalent metal halides mentioned contain central metal atoms with unoccupied valence orbitals, and that in each of the compounds the metal can form further stable bonds, either directly or by co-ordination. Antimony can of course form antimony pentachloride, and antimony trichloride forms a large
number of addition compounds with aromatic and oxygen containing solvents, and with various adducts such as ammonia. Aluminium halides form stable bridged dimers, and magnesium dihalides form stable dietherates. There is also evidence that magnesium halides and alkylmagnesium halides together form bridged structures. It would be of considerable interest to discover whether a general pattern of reaction mechanisms exists involving co-ordination of the halosilane halogen to the central metal atoms (electrophilic attack on the silane halogen), and the study of isotopic halogen exchange reactions with this class of compounds would afford a useful means of elucidating such mechanisms. Although outside the scope of the present studies, it would also be of interest to find whether compounds such as lithium bromide, sodium iodide, and silver cyanide, in appropriate solvents, can effect isotopic halogen exchange with halogenosilanes, and whether the mechanisms would involve simple ionic species, as for example the exchanges between such salts and the alkyl halides in various solvents. That such reactions need not necessarily occur with halogenosilanes is indicated by the fact that lithium bromide and calcium chloride, despite favourable solubility relations, do not effect halogen replacement with triethylfluorosilane, whereas aluminium iodide does. Exchange studies involving the aluminium halides would also be of interest because of the catalytic action of these compounds in a number of organosilicon reactions, intra-molecular rearrangements and intermolecular halogen substitution rearrangements. Antimony trichloride also acts as a catalyst in
several organosilicon reactions\textsuperscript{34} and preparations\textsuperscript{35}.

When the present work was begun, the only reported isotopic exchange reactions of halogenosilanes were a slow exchange between hydrogen chloride and silicon tetrachloride\textsuperscript{36}, and a very slow or negligible exchange between bromine and silicon tetrabromide\textsuperscript{37}. (Exchange of iodine atoms between sodium iodide and iodomethyltrimethylsilane had also been reported\textsuperscript{38}). While the work described in this thesis was in progress, a study of the kinetics of the exchange between hydrogen chloride and silicon tetrachloride was reported\textsuperscript{39}, and exchange was observed between tetramethylammonium chloride and silicon tetrachloride and trimethylchlorosilane\textsuperscript{40}. Antimony tribromide had been shown to exchange bromine atoms with bromine\textsuperscript{41}, but not with bromobenzene\textsuperscript{42} or butyl bromide in a number of solvents\textsuperscript{43}. Antimony atom exchange had been observed between antimony trichloride and tribromide\textsuperscript{44} and during the present work a study of the exchange of antimony atoms between the trichloride and pentachloride was published\textsuperscript{45}.

In preliminary investigations in this work (3.9) chlorine and bromine isotopic exchange were observed between trimethylbromo- and chlorosilanes and the corresponding halides of aluminium, antimony, and magnesium. (Magnesium chloride was omitted). Exchange was also observed between hydrogen chloride and trimethylchlorosilane. Of these systems, antimony trichloride - trimethylchlorosilane was chosen for initial preliminary investigation, since the need for the development of methods of manipulation and separation made
desirable the use of readily purified and stable compounds, as well as a long lived isotope. It was hoped that when these techniques had been developed, the trimethylchlorosilane – aluminium chloride and trimethylbromosilane – magnesium bromide systems could be investigated, but the complexity of the system chosen was greater than had been anticipated.

Apart from its interest as a reactant in the scheme of investigation envisaged above, antimony trichloride seemed a suitable compound for use in exchange studies, as its vapour is monomeric, and the molecule has been shown from electron diffraction and microwave spectral studies to have a symmetrical (pyramidal) structure with all chlorine atoms equivalent. The solid crystals consist of a monomeric molecular lattice in which the chlorine atoms in each molecule are equivalent. Those in a free molecule are therefore certainly chemically equivalent, and in isotopic exchange reactions should exhibit simple exchange behaviour (2.a). Benzene was initially chosen as a solvent because of the high solubility of antimony trichloride in it. Although a crystalline compound 2SbCl₃·C₆H₆ was known to exist from freezing point-composition studies, the form of the diagrams also shows that the compound is extensively dissociated in the liquid phase, although incomplete compound formation does probably persist. Freezing point data also indicates some degree of association of antimony trichloride in benzene solution. It was however expected that, for such equilibria, the rate of turnover of the antimony
trichloride molecules between free and bound states would be rapid, and would ensure that over a finite period of time all the chlorine atoms would have occupied equivalent environments. If this was not the case it should be evident from the exchange curves. (A further discussion on antimony trichloride in benzene is given in Chapter 6).

The first exchange curve obtained (3, figure 8), at rather low reactant concentrations, was apparently linear within a limit of error of ±5% on the values of F, although apparent linearity within such limits need not necessarily mean that the reaction is not complex54. Further curves obtained at higher concentrations were markedly non-linear, and followed no definite pattern (5.d.ii). At this time a paper was published55 which showed from infra-red data that an antimony trichloride-benzene compound persists in the liquid phase in benzene, and referring to viscosity57 and other studies52,58 which also indicate that this is the case.

As indeed the benzene data suggests interactions more complex than would have been expected between antimony trichloride and trimethylchlorosilane, a solvent was sought in which solvent-solute interaction would be minimal. Antimony trichloride complexes with aromatics decrease markedly in stability with withdrawal of electronic charge from the benzene nucleus24: dibromo- and dichlorobenzene do not form complexes at all23. An aliphatic hydrocarbon should not be capable, therefore, of forming a complex with antimony trichloride, and would be expected to have minimal solvating power.
Antimony trichloride was found to be soluble in n-hexane (3.f.iv), a solvent with molecular weight and volatility similar to those of benzene, and a number of exchange curves were obtained under various conditions using this solvent.

Irreversible chemical reactions between antimony trichloride, trimethylchlorosilane, and benzene were not expected, but tests were made to confirm this expectation (5.f).
2. DESIGN OF EXPERIMENTS

(a) Considerations in the Determination of Exchange Rates, Molecularity and Rate Constants

The determination of rate constants and concentration dependence for isotopic exchange reactions has been discussed by Wahl and Bonner\(^{59}\) and in a recent review by Stranks and Wilkins\(^{60}\).

It is evident that the primary experimental requirement is the measurement of the fraction of exchange occurring between reactants during a given time and under specified conditions of concentration and temperature. Reactants, one of which is initially isotopically labelled, and which is of known specific activity in the case of radioactive tracers, are mixed, and after a given time the change in specific activity in the reactants determined. Since it is usual to separate the reactants for this purpose, the investigation of an exchange reaction in most cases devolves on finding methods of mixing the reactants under definite conditions and subsequently separating them (see below).

For a simple isotopic exchange reaction in a stable homogeneous medium where the labelling isotope is present in tracer amounts the relation

\[
\ln (1-F) = -\frac{Rt.(A) + (B)}{(A)(B)} + \ln (1-F_0),
\]

(1)

can be shown to apply independent of the mechanism of exchange\(^{59}\).

In this expression (A) and (B) are the concentrations, in gram atoms per litre, of the species undergoing exchange between the reactants A and B. R is the net rate of exchange, for both active and inactive atoms, for given (A) and (B), and is a function of these latter and the
rate constants of the particular mechanisms by which exchange is proceeding. \( F \) is the fraction of exchange observed after separation at the time \( t \), and \( F_0 \) (the 'zero-time exchange') is the fraction of exchange occurring during separation, mixing, or due to incomplete separation. Thus for a set of experiments in which \( (A), (B), F_0 \) and the temperature are kept constant, a plot of \( \log(1-F) \) versus \( t \) will be linear with slope \( \frac{R}{2.303} \left( \frac{(A)}{(A)} + \frac{(B)}{(B)} \right) \). When the exchange reaction is complex, as for example when the exchanging atoms in one of the reactants are not all equivalent, such a plot is no longer linear, but may often be resolved into linear components.

From the exchange rate and its concentration dependence, rate constants and the molecularity of the reactions can be calculated by the general methods of reaction kinetics \textsuperscript{60} (4.b). The minimum requirement for obtaining the concentration dependence of \( R \) at a given temperature is the determination of \( \log(1-F) \) versus time plots at two different sets of concentrations of the reactants, assuming only one mechanism to be operative. Should more than one mechanism occur, it would be necessary to vary one reactant concentration at a time, all other conditions being kept constant. Although this is the more general method, it also requires a larger number of experiments. However, a minimum coverage for each reactant is obtained in three experiments with the concentrations paired as follows:

\[ a_1, b_1; a_2, b_1; a_1, b_2. \]

This procedure was adopted in the hexane solution experiments.
2. (b) **Separation of Reactants**

i. **Requirements and basis of method**

The separation method must be such that complete exchange is not produced by or during it, and for equation (1) to apply, the amounts of exchange occurring during separation in a series of experiments needs to be very small or else sensibly constant. Separation need not be complete provided one component can be obtained enriched with respect to the other, and the procedure is reproducible. The degree of enrichment can be variable if the residual component can be left pure, as its specific activity can be used in correcting the specific activity of the enriched fraction. (4.a.iii).

In the present reaction system the reactants are very readily hydrolysed by water, and hence aqueous extraction or separation methods are not applicable. The solubility of the reactants in a wide range of solvents makes it difficult to find a solvent extraction method, as the reaction was already proceeding in benzene or hexane solution. Trimethylchlorosilane and the solvents used are, however, readily separated from antimony trichloride by distillation at atmospheric pressure. It was found possible to separate the volatile silane component from the relatively involatile antimony trichloride by rapid controlled evaporation of the former and the solvent from the reaction solution or a sample of it (see 3.e.ii for experimental details), the reaction being carried out in a vacuum apparatus with the thoroughly outgassed solution held under its own vapour pressure. The separated silane fraction contained 0.2% to 15% of the total amount of antimony trichloride initially in the reaction solution (table 2) depending on the initial concentrations.
ii. Theory of separation of volatile components from each other and the involatile component.

Assuming Raoult's law, the rates of evaporation of the components of a solution when the rate of removal of vapour from the space above the liquid is small compared with the rate of transfer across the surface plane will be proportional to their vapour pressures in the pure state and their mole fractions in the solution. However, the number of molecules evaporated in unit time from a pure liquid into a perfect vacuum is shown by kinetic theory to be also inversely proportional to the square root of the molecular weight, and the rate of mass transfer to be thus directly proportional to it. Hence for evaporation into a vapor pressure comparable with that at equilibrium we will have, for two components,

\[
\frac{dN_1}{dt} = \frac{P_1N_2}{(N_1 + N_2)} ,
\]

and similarly for \( \frac{dN_2}{dt} \). Hence

\[
\frac{dN_1}{dN_2} = \frac{P_1N_1}{P_2N_2} .
\]

When the pressure above the surface is small compared with the equilibrium pressure the right hand member of (3) will be multiplied by \( \sqrt{\left( \frac{M_2}{M_1} \right)} \). In the first case the relative volatility, \( r \), of the two components is simply \( \frac{P_1}{P_2} \), and in the second, \( \left( \frac{P_1}{P_2} \right) \sqrt{\left( \frac{M_2}{M_1} \right)} \). In either case, integrating from \( N_0 \) to \( N \),

\[
\left( \frac{N}{N_0} \right)_1 = \left( \frac{N}{N_0} \right)_2^r.
\]

Thus, if the vapour pressure of the volatile reactant is higher than that of the solvent, there will be, for partial separation, an enrichment of the former in the evaporated fraction with respect to the solution, as well as of course with respect to the involatile reactant which remains
largely unevaporated. Since (4) is dimensionless,
\[ \frac{b}{b_0} = \left( \frac{v}{v_0} \right)^x, \]
where \( b \) is the total amount of the volatile component in the solution and \( v \) is the volume of the solvent, taken as that of the solution for dilute solutions. For prediction of the degree of solute-solvent enrichment for partial evaporation it could be assumed that Raoulte's law applied and any change in relative volatilities with cooling of the liquid during evaporation neglected. In fact the degree of enrichment of silane with respect to solvent was found to be somewhat greater than that predicted from Raoult's law (5. b. iv), and therefore even greater than predicted by inclusion of the molecular weight term. The amount of antimony trichloride carried over with the separated silane was much the same whether evaporation was partial (80%) or complete.

If the freezing point of the solution is accessible and reached, then for a dilute solution of a compound miscible in all proportions with the solvent, pure solvent will freeze out until the remaining liquid is at the eutectic composition of the solvent-solute system. This in general will produce considerable enrichment of the volatile solute in the remaining liquid, and hence a relatively increased rate of evaporation of the solute. In such cases a higher recovery of volatile solute from the solution would be obtained than by continued evaporation from the liquid system. This would be an advantage when the solute is less volatile than the solvent.

iii. Exchange during separation.

Since separation is effected by the purely physical process of evaporation, induced exchange during separation should not occur and
and this was found to be nearly the case \(5.b.iii\). Once trimethyl-
chlorosilane and any antimony trichloride carried in the vapour stream
have passed from the reaction solution, any further exchange between
them will not affect the specific activity of the chloride contained in
the separated fraction, and we need only consider the reaction solution.
In general, separation times were short compared with half times of
exchange (less than \(0.1\% -1\%\)), and only a small amount of exchange would
therefore occur during separation. Since this amount fixes the intercept
of the \(\log (1-F)\) versus \(t\) plot, it is, however, useful to determine
its value either by calculation or experiment and thus obtain a fixed
point through which the exchange curve would be expected to pass. It
should then be possible to take a smaller number of measurements, in
which fortuitous variation could otherwise produce a much different
intercept, and an inaccurate slope for the plot. The validity of the
calculation can be checked by performing a set of experiments sufficient
to obtain a curve passing through the calculated point, within the
observed limits of error and also by separating a reaction solution
immediately on mixing, and observing the fraction of exchange, \(F_0\).
This value will be subject to the error of a single experiment, however,
and will be expected to agree with the calculated value only within
this limit.

The amount of antimony trichloride in the solution will remain
approximately constant; it will be assumed that \(R\), the number of ex-
change events per unit time in unit volume, has been obtained as a
function of the concentrations of the reactants and that the variation
of \(h/h_0\) and \(v/v_0\) with time has been obtained by calculation or experi-
ment. The case of the simple bimolecular process will be treated as an example. Considering R as a variable, and T as referring to time during separation, then for unit volume

\[ R_T = \text{const.} \frac{A(B)}{v^2} = \frac{ab}{v^2}. \]  

(6)

For the whole volume,

\[ \text{net} R_T = \text{const.} \frac{ab}{v}. \]

Considering the corresponding expression for \( T = 0 \),

\[ \text{net} \frac{R_T}{R_{To}} = \frac{bv_0}{b_0}v = \frac{(B)}{(B_0)}. \]  

(7)

Assuming that (8) applies, this gives

\[ R_T/R_{To} = \left(\frac{v}{v_0}\right)^r - 1. \]  

(8)

Inserting experimental values of \( b/b_0 \) and \( v/v_0 \) in (7) or calculating on the basis of (8) there can be constructed a graph of relative net rate versus time, or volume remaining. Integrating from \( v = 0 \) to \( v \) will give the ratio of the amount of exchange occurring during separation up to this volume remaining, relative to that which would have occurred in the same time if the system were left undisturbed. The fraction of exchange occurring in the undisturbed system during the time \( T \) can be calculated from the observed half time of exchange. For example, for a constant rate of evaporation, and \( r = 2 \), this ratio calculated on the basis of (8) would have the value \( \frac{1}{2}(1+v/v_0) \).

Hence up to time \( T \) the fraction of exchange occurring during separation would be given by

\[ \log \left(1-F_0\right) = \frac{(1 + v/v_0)T \log (1-F)}{2t}. \]  

(9)

Where \( F \) is the fraction of exchange observed for a reaction time \( t \).
large compared with $T$. If $T$ is taken as the time required for complete separation, then $v/v_0$ vanishes in (9).

iv. **Effect of incomplete separation.**

Provided the separation procedure is reproducible, incomplete separation will have the effect of displacing the exchange curve with respect to the log $(1-F)$ axis, the slope remaining constant. A constant proportion of the involatile component carried over with the separated fraction will lead to a constant percentage increment in the fraction of exchange (which is a measure of the transfer of activity from one compound to the other), which will produce a constant absolute displacement on a logarithmic scale.

The reproducibility of separation is shown in table 1, section 3.e.ii and its effect on the exchange curves in figure 12.

v. **Applicability of the separation method.**

From the above discussion it will be seen that the method of separation could be applied to any reaction system consisting of a volatile and relatively involatile reactant, in either the presence or absence of a solvent. The method could also be applied to reactants of comparable volatility, the degree of enrichment to be expected being predictable from equation 4, 2.b.ii. In such systems the results would probably be much less accurate than when the volatility difference is large. It can be seen from the experimental results (figure 12) that the accuracy is somewhat less in the present reaction studies when the fraction of exchange based on separated silane is uncorrected for antimony trichloride carried over.
(c) **REACTION PROCEDURES**

i. **Maintenance of purity and effect of impurities.**

Since the reactants are readily hydrolysed, experiments must be carried out under anhydrous conditions, especially, since the presence of hydrolysis products might accelerate the exchange reaction. To check whether the precautions taken are adequate, experiments should be made with impurities added and their effect observed. Such experiments are discussed in Chapter 5.

ii. **Concentrations, temperatures and volumes.**

As wide a range of concentrations as is feasible should be employed, and a range of temperatures adequate to determine activation energies. The solution sample volume should be sufficient for accurate analysis of its components, but small enough for convenient and sufficiently rapid separation. The lower concentration limit will be governed by the accuracy of analysis, and too high concentrations should not be used if appreciable variation in the reaction environment is to be avoided. The concentration of antimony trichloride that could be used in hexane is in any case limited by its solubility. The values used, and details of individual experiments, are given in Chapter 5.

iii. **Minimization of error.**

a. **By procedure.**

Apart from making errors as small as possible by care in manipulation and analysis, the effect of errors can be further reduced by proper design of experiments, as indicated below.

The compound present in lower concentration should if possible
be the one initially labelled so that the change in specific activity is greatest. In radio-assay the samples counted and analysed should be independently pipetted to reduce transfer error, and the activities used should be high enough for good counting statistics. The determination of fraction of exchange should preferably be based on the compound not initially labelled, so that it is calculated as the ratio of two specific activities, and the ratios of differences are not involved. Continued sampling experiments will give more precise fractions of exchange (4.a.ii.b) than single sample experiments, in which each F value contains the transfer errors involved in making up the reaction solution sample. When samples are counted for radioactivity at different times, a standard should be counted with them, and, in the case of continued sampling experiments where all samples are counted in one group, the order of counting adopted should place the samples requiring greater counting accuracy nearest to the standard sample (3.h.v).

b. By choice of sampling time.

Davidson and Sullivan\textsuperscript{62} have shown that in determinations of fractions of exchange from the compound initially labelled, the error in R for a given total count passes through a minimum with time of reaction. Two half times (75\% exchange) can be shown to be a best choice for a range of values of (A):(B) from 1 to 0.1, where A is initially labelled. However, in experiments of the present kind, the fraction of exchange can be determined more precisely from the activity of the compound not initially labelled and for a given number of total counts per sample the absolute error increases with F, the percentage
error remaining constant. However, since the count rate increases with \( F \), and of course longer counting times can often be used, the percentage error in \( F \) can be made to decrease with increase in \( F \). Typically, at \( F = 0.20 \) the error was 1.7\%, and at 0.60, 1.3\%. Points on the \( \log(1-F) \) versus time plot need to be sufficiently far from the origin to give an accurate value of the slope, (preferably spaced at even intervals for fitting the curve), but not so far that the absolute error becomes too large.


If all material is recovered and counted, the total input counts should be observed. If only a portion of each reactant is recovered and counted, there should still be a balance of specific activities. This would be confirmed if the fractions of exchange based on the activities of the two separated reactants agree within expected experimental error, and also if the final specific activity in either reactant or the totally hydrolysed reaction solution agrees with that calculated from the relation

\[
S_\infty = S_0 \frac{(A)}{(A) + (B)}
\]

where reactant \( A \) initially contains all activity, and \( S_0 \) is determined from independent measurements.
3. EXPERIMENTAL

(a) General

i. General technique.

The separation method was based on vacuum evaporation from an outgassed reaction solution prepared under anhydrous conditions, and for kinetic experiments it was found convenient eventually to purify or prepare all compounds and solutions under vacuum, and, as far as possible, in all-glass apparatus.

ii. Vacuum system.

This was constructed of 'Pyrex' glass, with conventional ground glass stopcocks. A main manifold of 3 cm diameter tubing ran on either side of a rectangular open box frame, and was pumped through a liquid air trap by a fast three stage mercury diffusion pump backed by a mechanical oil pump. The pressure in the manifold was registered by means of a Penning ionization gauge connected to a micro-ammeter and joined to the vacuum manifold through a liquid air trap. The gauge was not calibrated, but indicated the residual gas pressure to approximately $10^{-6}$ mm of mercury. In general the manifold was kept pumped at that indicated pressure. Individual vacuum assemblies were connected to the manifold through liquid air traps to prevent volatile and radioactive wastes from reaching the pumps. An auxiliary glass manifold carrying dry nitrogen was connected through high vacuum stopcocks to each of the individual vacuum lines. All new glass or metal assemblies were flamed out under vacuum as far as possible or else heated in position with dry nitrogen passing through them.
iii. **Miscellaneous Purifications.**

a. **Nitrogen.**

Nitrogen for use in manipulating anhydrous solutions or compounds was freed of all traces of oxygen, moisture and carbon dioxide by passage through liquid sodium-potassium alloy. (Mass spectrometric analysis of nitrogen purified in this way shows no peaks whatever at mass numbers corresponding to these compounds). 

b. **Mercury.**

Mercury purified by distillation in air was further purified by distillation under vacuum at $10^{-5}$ mm Hg, and was usually distilled directly into the apparatus in which it was to be used.

c. **Solvents.**

Benzene and n-hexane were dried by refluxing over liquid sodium-potassium alloy. Analar benzene was simply distilled from the alloy, but 'chemically pure' hexane was fractionated through a 30" packed column, a middle fraction boiling over a $0.2^\circ$ range being taken. 

Reaction solutions were made up from outgassed solvents stored under vacuum over sodium-potassium alloy. The storage vessels connected to the vacuum system through a fine glass sinter to prevent any carry-over of solid material. Stopcocks lubricated with silicone high-vacuum grease were used to close off the vessels, as this grease was found to withstand the solvent vapours for long periods.

iv. **Miscellaneous methods.**

a. **Glassware cleaning.**

Glassware was cleaned when necessary with a mixture of 20% concentrated hydrogen peroxide solution and 80% of concentrated sulphuric acid. This solution removes silicone and hydrocarbon greases, hydrolysed...
antimony compound deposits and most others without dissolving the glass. In stubborn cases 20% hydrofluoric acid solution was used to remove silicone and other deposits.

b. Magnetic stirring.

Magnetic stirrers were made of mild steel cylinders enclosed in glass. (Suitable lengths from nails of various sizes are conveniently used). The stirrers were actuated by a bar-magnet mounted on a pulley on the shaft of a bicycle hub, and driven by a belt from a similar pulley on an axle parallel to the first, both being mounted on the same base plate. The second axle extended through the pulley and connected through a length of heavy rubber tubing to a stirrer motor. This assembly allowed the magnet to be operated under apparatus in a thermostat bath, with the stirrer motor above and to one side.

v. Temperature control

The temperatures of water filled thermostat baths were usually maintained to \( \pm 0.03^\circ C \) (at 20° to 40°), and the thermometers used were calibrated against standard thermometers to give the temperature accurate to \( \pm 0.05^\circ C \).

(b) Preparation of Inactive Compounds

i. Trimethylchlorosilane.

The trimethylchlorosilane used in preliminary experiments to establish exchange was prepared from silicone tetrachloride via trimethylphenylsilane and trimethylbromosilane, by the action of antimony trichloride on the latter. Rate experiments were made with the material prepared by the cleavage of hexamethyldisiloxane when this intermediate became available. Cleavage with aluminium chloride was found more
convenient than cleavage by ammonium chloride in the presence of concentrated sulphuric acid\textsuperscript{65,66} and better than 75\% yield was obtained by the action of a small excess of commercial anhydrous aluminium chloride on hexamethyldisiloxane. These methods are preferable to distillation of the technical material because of the certainty of obtaining only the monochlorinated silane.

The compound was further purified by fractional distillation under dry nitrogen to a boiling range of 0.1\(^\circ\) at 58\(^\circ\)/710 mm, followed by outgassing under vacuum, and several passages through a trap at -78\(^\circ\) to remove any hydrogen chloride, a small initial and final fraction being discarded. (The vapour pressures of the two compounds at this temperature are approximately 10\(^{-1}\) mm and 1500 mm). The process was continued until constant vapour pressure had been obtained and successive fractions of the sample showed the same vapour pressure (72.4 mm at 0\(^\circ\)) to within \(\pm\) 0.1 mm.

ii. Trimethylbromosilane.

This compound was prepared by the direct cleavage with bromine of trimethylphenylsilane\textsuperscript{16}, and also by the action of aluminium bromide in ether solution on hexamethyldisiloxane\textsuperscript{64}. The former intermediate was prepared in 40\% yield from silicone tetrachloride by successive reaction with phenylmagnesium bromide and methylmagnesium bromide\textsuperscript{30,67}. Improved yield (greater than 90\%) was obtained in the first method of preparation by the addition of a small quantity of aluminium powder to produce aluminium bromide, by analogy with the use of aluminium iodide as a catalyst in the preparation of trimethyliodosilane\textsuperscript{30}. The product in either case was fractionally distilled to a boiling range of 0.5\(^\circ\) at 80\(^\circ\)C.
iii. Antimony trichloride.

Commercial antimony trichloride was dried over phosphorous pentoxide in a vacuum dessicator, distilled twice at 50 mm$^4$ pressure in a slow stream of dry nitrogen, and the receiver then connected to a vacuum sublimation assembly.

The compound was finally dried by melting under vacuum, and outgassed at 10$^{-5}$ mm. It was then twice sublimed, with intermittent pumping, to seal-off ampoules containing glass break seals (figure 1). The resulting material melted sharply at 73° and gave an analysis within 0.1% of that required by the formula.

(c) Preparation of Labelled Compounds.

i. Radio-isotopes.

   a. Chlorine-36.

   This isotope was obtained as HCl$^{36}$ in 2 N hydrochloric acid solution from the Radiochemical Centre, Amersham, England.

   b. Bromine-82.

   One or two litres of bromobenzene was exposed to a slow neutron flux obtained by the moderation, with paraffin, of neutrons emitted during the operation of the Australian National University Research School of Physical Sciences' 8 Mev cyclotron. The activity produced was extracted into water, and isotopically diluted by shaking the water with a few ml of bromine. The bromine was separated from the water, and dried by distillation from phosphorous pentoxide.

   ii. HCl$^{36}$ gas.

   HCl$^{36}$ solution was neutralized with dilute sodium hydroxide solution, the solution of NaCl$^{36}$ evaporated to dryness, and HCl$^{36}$
generated by the action of concentrated sulphuric acid on it.

iii. \( \text{AlCl}_3^{36} \).

This compound was prepared essentially by the method of Wallace and Willard\(^6\). Silver chloride was prepared from \( \text{HCl}^{36} \) solution, dried with acetone and a heating lamp, and then by melting under vacuum. Dry aluminium turnings were shaken onto it and the two heated to 450°. A rapid evolution of aluminium chloride occurred. This was sublimed through a seal-off constriction and the residual material sealed off.

iv. \( \text{Me}_3\text{SiCl}^{36} \).

Purified trimethylchlorosilane was transferred under vacuum on to solid \( \text{AlCl}_3^{36} \) and the two left in contact for several hours. The silane was then returned to storage, with, if necessary, one or two passages through a trap at -78° to re-establish constant vapour pressure. It was subsequently found more convenient to equilibrate the silane with \( \text{SbCl}_3^{36} \), which is soluble in trimethylchlorosilane to the extent of 11 moles per cent.

v. Chlorine-36 gas

Chlorine gas containing \( \text{Cl}^{36} \) was prepared in 10 mill-equivalent quantities from \( \text{HCl}^{36} \) stock solution further diluted with one normal hydrochloric acid solution, using the method of Brown, Gillies and Stevens\(^6\), which gives a practically quantitative yield. The hydrochloric acid was run onto a 2-3 fold excess of potassium persulphate in an apparatus flushed with dry helium or argon. The gas was gently bubbled through the mixture, which was heated to 70° to 80°.
The chlorine evolved was dried by passage through concentrated sulphuric acid and frozen out of the carrier gas stream in a trap surrounded by liquid air. The chlorine was outgassed by several cycles of freezing with liquid air, pumping at 10^{-5} \text{ mm}, thawing and freezing, and any water removed by several distillations from a trap at -80^\circ to one cooled in liquid air. A further purification could, if required, be effected by the method of Fye and Beaver\textsuperscript{70}, who used quartz apparatus and stopcocks lubricated with phosphoric acid; in the present work borosilicate glass and silicone stopcock lubricant were used, pre-treated by passage of chlorine vapour followed by pumping at 10^{-6} \text{ mm} to remove any volatile chlorinated products. Oxygen formed by the action of persulphate on hot water was not entirely removed by the above processes. Passage of the chlorine through a trap at the melting point of pentane would, if necessary, be sufficient to achieve this. In the preparation of antimony trichloride under the conditions described below, the only oxychloride likely to be formed is antimonyl chloride\textsuperscript{46} which is much less volatile than antimony trichloride, and in any case decomposes on heating to form antimony trichloride and the involatile antimony trioxide. 

vi. \( \text{SbCl}_3 \)

\( \text{Cl}_3^{36} \) was condensed into one limb of a two-limbed reaction vessel containing spectrographically pure antimony in one limb and containing a break seal for eventual removal of antimony trichloride. The vessel was sealed off and the chlorine brought to -80^\circ, or else the limb was cooled intermittently in liquid air, so that the vapour reacted with antimony at a controlled rate. When reaction was complete the vessel was heated to 200^\circ-300^\circ to ensure disassociation of any penta-
Chloride formed, and complete reaction of traces of chlorine with excess antimony. The trichloride was subsequently sublimed under vacuum into a U-bend connecting to seal-off ampoules and the reaction vessel sealed off. Purifications was effected as for inactive antimony trichloride (3.b.iii), by freezing, pumping, and thawing cycles, followed by two successive sublimations with intermittent pumping. The purified compound was sealed in storage ampoules containing glass break seals. The crystals were well formed and melted sharply at 73 °; analyses for chlorine and antimony gave values agreeing within 0.1% of those required by the formula.

vii. \( \text{MgBr}_{2}^{\text{82}}, \text{SbBr}_{3}^{\text{82}}, \text{AlBr}_{3}^{\text{82}} \).

These compounds were prepared under anhydrous conditions by the action of bromine, containing bromine-82, on the metals, contained under ether or benzene. \( \text{SbBr}_{3}^{\text{82}} \) has also been prepared by heating dry powdered \( \text{NaBr}_{2}^{\text{82}} \) with \( \text{SbBr}_{3}^{\text{44}} \), and by the reaction of \( \text{KBr}_{2}^{\text{82}} \) with \( \text{Sb}_{2}(\text{SO}_{4})_{3}^{\text{42}} \).

(d) Preparation and Manipulation of Reactant Solutions
i. Preparation and sampling of antimony trichloride solution.
   a. Under nitrogen.

Antimony trichloride, either inactive or labelled with chlorine-36 was sealed into a glass tube containing a break seal. This was joined through a seal off constriction to a solution storage and sampling apparatus, as shown in figure 1. The same limb of the apparatus was also joined to a vessel containing outgassed benzene stored over sodium-potassium alloy. The connecting limb contained a glass sinter
to prevent carry over of any solid material. With a short length of pressure tubing closing off the burette exit the apparatus was thoroughly evacuated with careful heating. Antimony trichloride was sublimed under vacuum into the vessel and benzene condensed onto it. The filling limb was then sealed off with the vessel cooled in liquid air. After re-attainment of room temperature the vessel was brought to atmospheric pressure with dry nitrogen. With nitrogen passing out the burette exit a teflon and glass needle valve (see below) was put in place as in the diagram. Application of nitrogen pressure and manipulation of the stopcocks allowed the burette to be filled and the liquid levelled off, excess solution returning to storage. The sample could then be run from the burette with a slight following pressure of nitrogen. The burette was calibrated by weight with dry benzene; the volumes of successive 4.5 ml deliveries agreed within 0.2% and of 2 ml volumes within 0.4%.

Teflon and glass needle valve.

This valve was obtained from the Emil Greiner Company, 26 - 28 North Moore Street, Dept. 221, New York 13, New York, U.S.A.
The split teflon ring supplied with the valve was found insufficient to seal in the connecting tubes, and a neoprene o-ring was used instead.

b. Antimony trichloride solution prepared under vacuum.

In the continued sampling method used for the experiments with hexane solutions, antimony trichloride solution in hexane was prepared in all glass apparatus by essentially the same procedure as above. A 250 ml bulb was connected through a glass sinter to a limb to which were joined, through seal off constrictions, two or three 50 ml storage bulbs,
"A" in figure 3. The connected vessels were dried by being flamed while dry nitrogen was passed through them. The apparatus was then pumped and outgassed, with flaming, to a pressure of less than $10^{-6}$ mm. Antimony trichloride was sublimed under vacuum into the 250 ml bulb, and an appropriate volume of outgassed hexane dried and stored over sodium-potassium alloy was condensed onto it. The vessel was then sealed off, and warmed to dissolve the antimony trichloride. For making up solutions at the highest concentrations used, the filling vessel was equilibrated at a temperature one or two degrees below that at which exchange experiments were to be conducted, and the saturated solution poured through the sinter into the storage bulbs. These were then cooled simultaneously in liquid air, and sealed off. Subsequently they were sealed to the kinetics apparatus as shown in figure 3, care being taken during the glass working to avoid heating too close to the break seal.

Before being connected to the filling vessel, the storage bulbs were thoroughly cleaned, and dried in an air oven. The limb containing the break seal was temporarily sealed off to keep it clean until ready for use.

ii. Trimethylchlorosilane solutions and sampling.

a. Under nitrogen.

In preliminary experiments (set 3, table 5) trimethylchlorosilane solution in anhydrous benzene was made up under nitrogen by much the same procedure and in similar apparatus to that used for antimony trichloride solutions. (3.d.i.). Manipulation of the solution under nitrogen resulted in a substantial change in concentration of a 0.01
molar solution after a number of samples had been withdrawn, and another system of delivering standard samples had to be devised.

b. Vapour delivery.

Both silicone and hydrocarbon greases dissolve the vapour and an apparatus using conventional glass stopcocks lubricated with them gave very erratic deliveries. A vapour delivery apparatus was constructed using cut-offs consisting of steel balls held against ground glass surfaces by mercury. The construction of such cut-offs has been described by Bottomley. The apparatus contained a storage bulb connecting to a manometer, and through a U bend containing a cut-off in each limb to a vapour space. This connected through a further U bend to the vacuum line. The two U bends connected through independent stopcocks to a common mercury reservoir. The use of steel ball-ground glass valves in their place would have been an improvement, but the apparatus worked adequately with the stopcocks if they were only lightly greased. To prevent deposition of liquid silane in the vapour space and inlet it was found necessary to thermostat the space at a higher temperature than the storage space. In operation the apparatus delivered 0.2 m.e. samples with a variation of 0.3%. It was however difficult to maintain and manipulate, and most of the experiments with benzene solutions were made with a delivery apparatus described below.

ii. c. Delivery of trimethylchlorosilane solution under vacuum.

Subsequent to the construction of the vapour delivery apparatus described above, high vacuum brass needle valves were obtained from the Hoke Company, 1485 Dean Street, Englewood, N.J., U.S.A., and
an apparatus for delivering, under vacuum, fixed volumes of a solution of trimethylchlorosilane in benzene was put into use and found completely satisfactory. A glass storage bulb was connected by a metal to glass seal to the brass connecting limb of one valve, and the outlet limb of this valve connected to the inlet of a second one, the outlet of the latter being connected by a further metal to glass seal to the vacuum line. The storage bulb was mounted vertically above the two valves. Before mounting the apparatus in this position the silane solution was prepared by condensing outgassed benzene dried over liquid sodium-potassium alloy into the bulb with the apparatus placed with the bulb lowest. An appropriate amount of purified silane was then condensed onto the benzene, the valves closed, and the solution melted. After shaking to produce homogeneity in the solution, the apparatus was connected to the line with the bulb uppermost. To deliver a sample, the space between the valves was evacuated, the lower valve closed and the other opened. The intermediate space filled completely with solution, and the upper valve was closed. The lower valve was opened, and the solution run into a bulb connecting to the vacuum line. This bulb was then cooled in liquid air to condense all the liquid and vapour from the delivery space and the lower valve closed. The sample was melted, and evaporated into the upper compartment of the reaction vessel.

Calibration by weight of benzene of the 2.5 ml delivery volume enclosed by the valves gave values agreeing within 0.1%, and the amounts of silane delivered (0.3 me.) varied by $\pm$ 0.25%.

Since the dead space in the storage bulb increases as solution is
run from it, the residual solution will be relatively depleted of silane, since the vapour pressure of the latter is higher than that of benzene. This effect would usually be negligible however. For example, for a 0.1 N solution of Me₃SiCl in benzene the mole fraction of the former is approximately 0.01. At 25° the vapour pressure of the pure compound is - 250 mm; hence the number of milliequivalents occupying 1 ml of the vapour space is 0.000127. Removal of 20 ml of solution will cause 0.0025 m.e. of silane to enter the vapour phase, so that provided say 10 ml of solution remains, the change in concentration will be from \((30 \times 0.1000)/30\) to \((10 - .0025)/10\); i.e. from 0.1000 to 0.09998N.

Subsequently the valves were used to close off storage bulbs containing pure trimethylchlorosilane. The compound was found, by separate tests, not to affect the surface of polished and degrease brass or copper; any moisture present is of course converted to anhydrous hydrogen chloride. Antimony trichloride solutions were found to deposit antimony metal on the copper or brass surfaces even under anhydrous conditions.

(e) Exchange Rate Experiments

i. Single sample method.

In this method, used for the experiments with benzene solutions, the whole of the reaction solution (5 ml) was separated at one time. Thus each experiment gives only one value of the fraction of exchange, and a number of experiments must be made to obtain an exchange curve. This limitation was largely imposed by the need to conduct the reaction in a vacuum system, because of the separation
method, and because at first suitable stopcocks for the containment and delivery of volatile liquids under high vacuum conditions were not available.

The reaction vessel consisted of a ground joint apparatus fitted with high vacuum stopcocks as shown in figure 2, the lower compartment containing a magnetic stirrer sealed in glass. The upper and lower compartments were separated by a thin walled glass bulb, which could be broken when desired by a plunger sliding in a double o-ring seal in precision bore glass tubing.²

The neoprene o-rings used in this seal were lightly greased with silicone high vacuum grease, and after an initial outgassing period, movement of the plunger hardly effected a vacuum of $10^{-6}$ mm.

Before use, the reaction vessel was thoroughly cleaned and dried in an air oven, then connected by one ground joint and one pressure tubing connection to the vacuum line containing the trimethylchlorosilane storage assembly. The vessel was finally dried by flaming both under vacuum and filled with dry nitrogen, and evacuated to a pressure of $10^{-6}$ mm. The lower compartment was filled with dry nitrogen, and with a counter current of dry nitrogen passing out the side arm of the stopcock, the tip of the antimony trichloride solution burette (figure 1) was inserted through the bore of the stopcock, and a 2 ml - 5 ml sample of solution delivered into the vessel.

After reconnection of the vessel to the vacuum line, the solution was outgassed by cycles of freezing, pumping and thawing to a residual pressure of less than $10^{-4}$ mm. Trimethylchlorosilane solution stored and delivered under vacuum (3.d.ii.e) was condensed in the upper
compartment, cooled by pouring liquid air on a wrapping of cotton wool. The reaction vessel was then placed in a thermostat bath, and connected through the separation sinter vessel (3.e.iii) to the separation line, figure 4. When temperature equilibrium had been reached, the reaction was started by breaking the glass bulb and allowing the upper solution to drain into the stirred lower solution. After an appropriate time the stopcock closing the upper compartment was opened to allow rapid evaporation of the volatile components of the stirred reaction solution into a liquid air trap (3.e.iii).

The concentrations of the reactants in the reaction solution were calculated from the concentrations and volumes of the reactant solutions (4.a.ii), appropriate corrections being made for the change of benzene density with temperature\(^7\).

The ground joint connecting the two parts of the reaction vessel and the two stopcocks were greased with silicone high vacuum grease, as this is much less soluble in hydro-carbon solvents than hydro-carbon greases. However, the latter were used when not in prolonged contact with solvent vapours, as they are much more readily removed.

**Effect of vapour dead space on concentration and exchange**

The reaction solution volume was usually 5-10 ml, and the total volume of the reaction vessel 80 ml. It can readily be calculated that at the concentrations used, of the order of one per cent of trimethylchlorosilane was in the vapour phase. However, it has been demonstrated\(^7\) that isotopic equilibrium is reached in such circumstances in a few minutes, and as most half times were greater than several hundred minutes, any effect on the fraction of exchange due to a small
fraction of the silane being present as vapour would be negligible.

ii. Reaction kinetics experiments with continued sampling.

The apparatus finally developed, and used for kinetics experiments with hexane solutions, is shown in figure 3. This apparatus depended on the use of a greaseless stopcock obtained from the Springham Company, Harlow, England, and allowed the withdrawal under vacuum of a number of samples of solution without contamination of the remainder. The general method was found to be very satisfactory, although requiring considerable mechanical care in the preparation of reaction solutions, and allowed the reaction to be carried out in all glass apparatus closed off by a small surface of polythene (0.25 cm²). Although slightly soluble in hydrocarbons at elevated temperatures polythene is one of the most inert of plastics, and in the form used, 0.004" sheet, has the desirable property of deforming slightly under pressure to give a high vacuum seal against glass. Teflon sheet was found unsatisfactory as it wrinkled too easily.

With the reaction vessel the opposite way up to that shown in the diagram, a storage bulb, A, containing antimony trichloride solution, was sealed to the bulb B, care being taken not to heat too close to the break seal. Dry nitrogen was then passed through the heated vessel which was connected to the vacuum system, and contained a temporary opening in the limb S. This was then sealed off and the vessel evacuated, with heating, to 10⁻⁶ mm. When it was thoroughly outgassed a small amount of trimethylchlorosilane was condensed into it, to react with any remaining adsorbed reactive layers on the glass. The vessel was again evacuated, an appropriate amount of the silane condensed into it,
and the valve closed. After equilibration of the vessel at the
reaction temperature (with the vessel exit closed with a rubber stopper)
the striker S was dropped on the break seal and solution poured be-
tween A and B until the reactants were thoroughly mixed. The vessel
was then placed in the thermostat bath in the position shown in figure 3,
the base plate of the bath having been, until then, closed off with a
rubber stopper. The upper of the two O-rings shown served as a
temporary water seal until the lower one was fixed in position, and the
two served as a stable, flexible and water tight support, allowing the
vessel to be rotated or moved up and down. The evaporation vessel K
and the separation sinters were put in place and evacuated, the upper
sinter vessel being connected to the separation line (figure 4) through
a length of pressure tubing.

For withdrawal of a sample, the stopcock above the top sinter was
closed, and the valve G slightly opened. The pressure of vapour in
the reaction vessel forced out a stream of solution, which continued to
emerge provided the vessel K was kept at a lower temperature. When
a sufficient sample (6 - 7 ml) had been removed the valve was closed,
and with the stirrer L rotating rapidly, the evaporation vessel was
opened to an evacuated hydrolysis trap containing a measured volume of
hydrolysis solution frozen in liquid air (see below). When evaporation
to dryness was complete, the hydrolysis trap was closed, and the
rest of the space brought to atmospheric pressure with dry nitrogen.
The vessels K and M were replaced with similar ones, after the body
of the valve G had been flushed clean of any residual antimony tri-
chloride with benzene from a hypodermic syringe forced in through a
thin polythene tube and glass jet. Hydrolysis solution was pipetted into K and the dissolved antimony trichloride solution assayed for antimony and radioactivity. The hydrolysis trap was warmed to room temperature, shaken, and the aqueous phase separated into a centrifuge tube for assay for chloride, antimony and radioactivity.

For analysis of the reaction solution a sample was withdrawn from the reaction vessel into an evacuated volume measuring apparatus (figure 5) with provision for sealing off, and a stopcock and ground joint for connection to a separating funnel. The measuring volume consisted of a 6 ml bulb below a length of graduated precision bore tubing, 4 mm in diameter. When a sample had been sealed into the vessel and brought to temperature equilibrium at 20°, the liquid level in the tubing was read with a cathetometer. The volume obtained was corrected to the temperature at which the reaction was being carried out. (The volumes calculated from liquid levels thus measured were checked with weighed samples of water and found to be accurate to ± 0.01 ml).

The apparatus was then connected to a separating funnel containing a measured volume of hydrolysis solution, and the stopcock opened to allow the aqueous and solvent phases to be shaken together. The aqueous phase was then separated and assayed.

From the total count rate and total chloride the specific activity at infinite time (complete redistribution) was calculated, and from the count rate and the antimony concentration the initial specific activity (when antimony trichloride was initially labelled) was calculated. The antimony value gave the concentration of antimony trichloride in the
reaction solution, and from the difference between the amount of chloride due to antimony trichloride and the total chloride the concentration of trimethylchlorosilane could be calculated. When the silane was initially labelled its specific activity was determined directly, and the observed count rate in a reaction solution sample also used as a measure of the silane concentration.

The fraction of exchange based on trimethylchlorosilane was in general calculated from the ratio of the observed specific activity in a separated sample to that of the totally hydrolysed sample. The fraction of exchange, and hence the observed half-time of exchange, is thus independent of any determination of the actual concentrations employed. An example of the calculation of concentrations and fractions of exchange is given in the section on calculation of results.

iii. Separation procedure and apparatus.

As has been stated, the method of separation employed was evaporation of the volatile solvent and solute from the practically involatile solute, antimony trichloride. It was found that when the solvent was well outgassed and effectively stirred, rapid controlled evaporation to a liquid air trap could be effected with little or no frothing of the liquid, provided that the vapour flow rate was limited by a glass sinter of suitable porosity. The sinter also acted to prevent any carry over of fine spray in the vapour stream. In the development of the method capillary tubing was found unsuitable as a resistance to vapour flow.

The separation vessels are shown in figures 2 and 3. The 3 cm diameter flat bottomed vessels contained a magnetic stirrer sealed in
glass. The vessel connected to a 3 cm diameter glass sinter (either No.2 or No.3), connecting through a stopcock and ground joint (or pressure tubing) to the separation line. For the n-hexane system a further coarse sinter was inserted before the finer one to keep the latter clean of spray (figure 3). Several separation traps could be joined by ground joints to the line (figure 4). The traps were closed with a 6 mm stopcock, and had a cooled area of approximately 100 cm\(^2\). Before separation, hydrolysis solution was pipetted into a trap, frozen in liquid air and the residual gas evacuated. After separation the trap was warmed to room temperature and the sample thus hydrolysed without loss.

The observed rates of evaporation and efficiencies of separation are discussed under experimental results (5,b).

f. Subsidiary Experiments

i. Test for chemical reaction in the exchange system

Trimethylbromo- and chlorosilanes can be converted in good yield to the corresponding chloro- and fluoro- compounds by the action of antimony trichloride and trifluoride respectively\(^6,18\). It is hence unlikely that further reaction occurs between antimony trichloride and trimethylchlorosilane. However antimony trichloride can, under favourable conditions, act as a Freidel-Crafts catalyst\(^76\), and formation of trimethylphenylsilane with elimination of hydrogen chloride is conceivable. It has in fact been shown that under rather severe reaction conditions, trichloro- and dichloromethyl- silanes react with benzene, in the presence of aluminium chloride, to produce trichloro- and dichloromethylphenylsilanes, with elimination of hydrogen\(^31\).
Anhydrous benzene (0.2 moles), trimethylchlorosilane (0.15 moles) and purified antimony trichloride (0.05 moles) were refluxed for 15 hours. Despite small mechanical losses, approximately 90% of the silane was recovered by fractional distillation, and no compound boiling between 56° and 80° was apparent. Most of the benzene was recovered by fractional distillation, and no compound was evident from 80° to 220°, the boiling point of antimony trichloride at atmospheric pressure, on distillation of the residue through a short unpacked column. Trimethylphenylsilane boils at 172°.

That antimony trichloride and trimethylchlorosilane do not react chemically with one another was confirmed by the measurement of the vapour pressure of a saturated solution of the former in the latter (3.4.ii), and was further indicated during exchange experiments by the high recovery (up to 98%) of readily hydrolysable chloride in the separated trimethylchlorosilane fraction; by the recovery of nearly pure antimony trichloride; and by the balance of specific activity in these experiments. The chlorine atom in the chloromethylsilanes for example is only hydrolysed with difficulty.

ii. Vapour pressure of a solution of antimony trichloride in trimethylchlorosilane.

A saturated solution of antimony trichloride in trimethylchlorosilane was prepared under vacuum and its vapour pressure observed with a mercury manometer in which the mercury column rose into an evacuated space. The solution was maintained at 20.0° ± 0.02°, and the vapour pressure did not change over a period of 15 hours. The observed value was 175.5 mm of mercury, and that of the
silane (purified to constant vapour pressure) in the same apparatus was 189.1 mm. Hence the fractional decrease of the vapour pressure was 0.929. The solution was analysed for chloride and antimony, and the mole fraction of trimethylchlorosilane found to be 0.921. Since the vapour pressure of antimony trichloride is less than $10^{-1}$ mm at $20^\circ$, the vapour pressure lowering agrees with that calculated from Raoult's law. This confirms that no reaction occurs between the compounds to produce new chemical entities, but does not exclude addition compound formation between them. If an addition compound had negligible vapour pressure, and all antimony trichloride was present in such a form, the amount of trimethylchlorosilane held in the bound form is such that the mole fraction of the free silane remains little altered over a range of concentrations; the mole fraction values would be, for example, 95/100 for no addition compound, and 90/95 if an addition compound was formed.

iii. Conductance of antimony trichloride in benzene and hexane

The apparent conductances, in a cell with bright platinum electrodes, of solutions of antimony trichloride in anhydrous benzene and hexane were practically identical with that of the solvents over a range of frequencies, and extrapolated to zero conductance. No change of conductance was observed over a period of 24 hours. The use of undried "Analar" benzene had negligible effect on the conductance, as did the addition of trimethylchlorosilane to the benzene solution. The conductance bridge used was a Jones type constructed by Leeds and Northrup, and could be matched, at 2000 cycles per second, to 29,900
ohms within one or two ohms.

The non-conductance of antimony trichloride in benzene and hexane solutions contrasts with its measurable conductance in several other more polar solvents, such as ether, chloroform and aniline, in which there is evidence for ionic complexes.

iv. Solubilities of antimony trichloride in hexane and trimethylchlorosilane.

Saturated solutions of antimony trichloride in hexane at 40° and 20° were approximately 0.08 molar and 0.05 molar respectively. The compound forms a saturated solution in trimethylchlorosilane at eleven moles per cent, at 20°.

(g) Other Exchange Systems

In preliminary experiments isotopic exchange was observed under anhydrous conditions in the following systems:

HCl, AlCl₃, SbCl₅ with Me₂SiCl ;
MgBr₂, AlBr₃, SbBr₅ with Me₂SiBr .

The magnesium bromide exchange was conducted in ether, and the others in benzene; hydrogen chloride was also observed to exchange in the absence of solvent. The compounds were mainly separated by distillation, but magnesium bromide was separated from trimethylbromosilane in ether solution by precipitation with dioxane.

(h) Analyses and Radio-assay

i. Volumetric ware.

Pipettes were treated with a silicone water repellant to give complete drainage. This is particularly useful where solutions are manipulated by syringe, and in any case gives more precise and
convenient delivery than ordinary wet drainage. The pipettes were recalibrated using distilled water. Micro-pipettes delivering 0.1 to 0.5 ml could be used with a variation of less than 0.0005 ml between successive deliveries, and 1 to 5 ml pipettes with less than 0.001 ml. Ten, 12 and 20 ml pipettes gave successive deliveries within 0.003 ml. The liquid level of 10 ml and 25 ml burettes was read with a magnifying eye-piece to ± 0.01 ml.

ii. Preparation of samples for analysis and counting.

a. Manipulation procedure.

Samples were either condensed under vacuum onto frozen hydrolysis solution, or run into a separating funnel and shaken with hydrolysis solution. The separated aqueous phase was run into a dry centrifuge tube and any fine suspension of solvent collected as a surface film by centrifuging. Ten ml of the solution was pipetted into the well of the liquid counter (3, h.v.) for measurement of activity, and then recombined with the solution remaining. Small losses from the 13 ml of hydrolysis solution during extraction, separation and transfer still allowed appropriate volumes to be pipetted independently for the counting and analysis. The mutual solubilities of benzene and water are such that the volume change of 12 ml of water shaken with 4 ml of benzene is less than 0.05%.

b. Hydrolysis solutions.

Dilute solutions of antimony trichloride in benzene can be extracted with a dilute aqueous solution of bicarbonate and tartrate in the molar ratios 3 to 1. With more concentrated solutions
however an undue amount of carbon dioxide was liberated and a precipitate not readily soluble in the aqueous solution was formed. However such a precipitate or the pure solid was found to dissolve directly in 10 N sulphuric acid, and a 3 ml titre of this was used, followed by dilution with 10 ml of tartaric acid solution containing at least sufficient tartrate to be molecually equivalent to the total amount of antimony. Concentrated tartaric acid solution will also dissolve antimony trichloride directly, or extract it from organic solvents without precipitation.

Extraction of the same solution of antimony trichloride in benzene with bicarbonate-tartrate or sulphuric acid followed by antimony determination with iodine or bromate solution respectively, gave results agreeing within 0.2%. In both methods one extraction was found completely to remove all antimony and chloride from the nonaqueous phase. Addition of moderate amounts of tartrate to sulphuric acid solutions had no apparent effect on the concentration at which initial precipitation occurred (8N H₂SO₄) as more dilute acid was used.

To obtain the same counting efficiencies, the same hydrolysis solution was always used for samples of trimethylchlorosilane as for antimony trichloride when their specific activities were to be compared. Complete hydrolysis was readily obtained with 10 N sulphuric acid solution, as with water or dilute bicarbonate solution.

ii. **Chloride determinations**

All chloride determinations were based on the precipitation of silver chloride. In initial experiments the Volhard method was used, and in later ones where higher accuracy for smaller samples was
required, a differential potentiometric method was adopted.

The thiocyanate – ferric ion end point reaction, unlike the silver nitrate – chromate end point, is unaffected by the presence of antimony ions, and can be carried out in acid solution, as must be the potentiometric titration. When acid hydrolysis solutions were used this is an advantage, and in any case the ferric indicator is the more sensitive. When the Volhard method was used, the silver chloride was precipitated in a centrifuge tube, and after centrifuging, a titre of the supernatant was pipetted for titration with thiocyanate. The solution was filtered before the pale orange colour was matched against an end point blank. Duplicate determinations on 0.2 m.e. samples could be made to within 0.2%. For samples less than 0.05 m.e., the agreement was not usually greater than 1%.

In such cases, greater precision could be obtained with the potentiometric method, which has the advantages of greater sensitivity, and of being a direct titration. The method was eventually adopted for all chloride titrations, and in particular, for the experiments in hexane solution. The electrode assembly consisted of a 0.5 mm capillary fitted with a side arm connecting to a syringe for drawing in and expelling solution. A thin silver-chloride electrode was mounted inside, and a lightly plated 20 s.w.g. one wound round the outside. Before titration, the solution, if not already acid, was made one or two normal with sulphuric or nitric acid. Towards the end point the silver nitrate was added in 0.10 ml increments, with flushing of the capillary between additions. A nearly symmetric peak of voltage increment versus volume added was obtained, the end point
being taken as the vertical bisector of the peak less half the volume increment. A potential change of 30 mv/0.1 ml was obtained at the end point for 0.01 N silver nitrate added to 30 ml of tiritant solution (figure 6), and a correspondingly greater change for more concentrated silver nitrate solution. The volumes of silver nitrate solution required for titration of samples containing 0.05 m.e. could be duplicated within 0.5%, and for 0.2 m.e. or larger samples, within 0.1%.

iii. Antimony determination

In the experiments in which antimony trichloride was extracted into bicarbonate-tartrate solution, antimony was determined by titration with dilute iodine solution, as for the micro-potentiometric titration of arsenite. Two micro-equivalents of antimony could be determined with an accuracy of ± 1%, and 0.1 milliequivalent to ± 0.1%.

A conventional potentiometric titration arrangement was used, with a bright platinum electrode and a salt bridge, connecting to a mercury-mercurous chloride reference electrode, dipping into the stirred solution contained in a 50 ml beaker.

When acid hydrolysis solutions were used, antimony was titrated with potassium bromate solution, the end point being determined potentiometrically. (A titration curve is shown in figure 6). This method has the advantage that potassium bromate can be used as a primary standard, and its solutions are stable. Very precise results were obtained with this reagent, duplicate determinations of 0.05 m.e. samples agreeing within 0.1%, and of 2 micro-equivalent samples
within 0.5%.

The 5 ml burette used for micro-titrations was graduated in 0.01 ml divisions, and was calibrated by weight of water delivered. The tip was extended with a length of polythene tubing and an extra burette tip to allow clearance from the stirring and electrode assembly. Iodine solution was made up 0.01 N and standardized against sodium arsenite in sodium bicarbonate buffer solution, and appropriate dilutions made into 2% potassium iodide solution. Potassium bromate solution was made up by weight, and diluted as required.

For titration with iodine, the sample was buffered with bicarbonate, and the solution made one or two percent with respect to potassium iodide. Near the equivalence point, iodine solution was added in 0.03 ml amounts, the potential change at the end point being 120 mv/0.1 ml. for 0.0005 N iodine solution added to 20 ml of titrant solution. For titration with bromate, the titrant solution was made 1.5 N to 2 N in sulphuric acid and 0.1 N to 0.5 N in potassium bromide. The voltage change at the end point was approximately the same as for iodine titrations.

v. Counting procedure

All chlorine-36 activity was counted in solution, using a thin walled glass Geiger tube fitting through a ground joint into a liquid well. The same jacket in the same orientation with respect to the tube was used throughout a set of experiments, the sample consisting of 10 ml of solution pipetted into the well, so that constant counting geometry was obtained. The count rate was found in fact not
to be sensitive to small variations in the liquid level in the well. The efficiency of liquid counting is dependent on the liquid density, so all samples whose activities were to be compared were counted in an aqueous medium of constant composition. The dead times of the tubes used were determined by observation of recovery time on a cathode ray oscilloscope, and a fixed, measured paralysis time approximately twice the dead time, applied in the scaler circuit so that an accurate correction could be made.

For single reaction sample experiments a standard source was counted before and after each pair of counted samples so that the sets of samples could be compared. The standard source consisted of sodium-22 solution in a double walled sealed glass vessel into the thin walled inner well of which the Geiger tube fitted.

For continued sampling experiments, the accuracy of counting of later samples has to be higher than that of earlier ones to reduce the absolute error in the fraction of exchange. This is of course facilitated by the samples having higher activities. To reduce effects due to any variation in counter efficiency those samples requiring highest accuracy were counted nearest to the complete exchange sample, which was used as the standard in any comparison with count rates from other experiments. When, for example, six samples were to be counted, the order would be 1, 3, 5, complete exchange sample, 6, 4, 2.
4. **CALCULATION OF RESULTS**

(a) **Fraction of Exchange**

i. **Definition of fraction of exchange.**

The fraction of isotopic exchange which has occurred under given conditions is conveniently defined as

\[ F = \frac{(S_0 - S_t)}{(S_0 - S_\infty)} \]  

where \( S \) is the specific activity, in convenient units, of one of the reactants. The subscripts refer to zero time, time \( t \) and infinite time. \( S_\infty \) is of course the resultant specific activity on complete redistribution of the activity initially present in either one of the reactants. For convenience and better accuracy, \( S_0 \) is usually zero for one of the reactants.

For this reactant therefore

\[ F = \frac{S_t}{S_\infty} \]  

The definitions (11) and (12) amount to stating that the fraction of isotopic exchange is the ratio of the change in specific activity which has occurred to that which can eventually occur.

ii. **Methods of calculating \( F \)**

a. For single sample experiments

The initial specific activity of the labelled reactants was determined (as an average of several values), and the concentrations of the reactants in the reaction solution calculated from the concentrations and volumes of the reactant solutions. \( S_\infty \) was calculated from the relation for complete redistribution of activity

\[ S_\infty = S_0 \frac{(A)}{(A) + (B)} \]  


assuming all activity initially in reactant A. The value of $S_t$ for the reactants after separation was measured, and if necessary corrected for incomplete separation (4.a.iii). The fraction of exchange was then calculated from (11) or (12).

b. Calculation of $F$ in continued sampling experiments.

The most accurate procedure was to base the determination of $F$ on the reactant not initially labelled. A sample of reaction solution was totally hydrolysed, and its specific activity ($S_{\infty}$) compared directly with that observed in the separated reactant, using (12). The fraction of exchange thus obtained is independent of any measurement of concentration and depends only on the ratio of the two specific activities.

To determine the fraction of exchange from the reactant initially labelled the initial and final specific activities were determined, and (11) used.

iii. Specific activity correction for incomplete separation

The separated sample was hydrolysed and an aliquot counted (5.h.). The counted solution was then analysed for total chloride ion and for antimony. The amounts of chloride due to hydrolysed trimethylchlorosilane, reactant B, and to antimony trichloride, reactant A, were thus found. Let these be $x$ and $y$. Then the specific activity of the $\text{Cl}^-$ sample counted is

$$S_{obs} = \frac{(x S_B + y S_A)}{(x + y)},$$

(13)

where $S_B$, $S_A$, are the specific activities of the chloride in the two
reactants at the time of separation. Hence

\[ S_B = S_{\text{obs}} - \frac{Y}{X} (S_A - S_{\text{obs}}) \]  \hspace{1cm} (14)

This relation was mainly used to correct the trimethylchlorosilane specific activity, \( S_B \), for that of antimony trichloride carried over during separation. The specific activity of the antimony trichloride residual in the reaction vessel could either be observed or calculated from a first approximate value of \( F \) based on trimethylchlorosilane, and successive iterations used in (14) until the value of \( S_B \) became constant.

iv. Mass and activity balance

In many of the experiments fractions of exchange were measured for both reactants. Agreement between the values of \( F \) shows the activity and concentration values to be at least internally consistent and indicates that the half times of reaction observed are valid. In addition, in a number of cases, the final specific activity \( S \) was compared with that calculated from \( S_0 \) by the use of relation (10), when \( S_0 \) had been determined by independent measurements. As remarked in the discussion on the preparation of antimony trichloride (3.b.iii), analysis for antimony based on potassium bromate as standard, and for chloride based on sodium chloride as standard, gave agreement with the molecular formula within 0.1%.

v. Typical calculation

Experiment 4, hexane solution (tables 12 and 13).

a. Total analysis of the reaction solution

6.52 ml of hexane solution were extracted with
13.08 ml of aqueous solution. Aliquots were counted, and analysed for chloride and antimony. In 10.06 ml the following values were found: Total Cl\(^-\), 3.348 me.; Cl\(^-\) in SbCl\(_3\), 0.0738 me.; Counts per minute, 2124. Hence

\[
S_{\infty}, \text{ cpm/me.} = \frac{2124}{3.348} = 634.4
\]

and

\[
S_0, \text{ cpm/me.} = \frac{2124}{0.0738} = 28780
\]

In the hexane reaction solution:

\[
g\text{-atom/litre of Cl}^-\text{ in SbCl}_3 = (A) = 0.01473
\]

\[
g\text{-atom/litre of Cl}^-\text{ in Me}_3\text{SiCl} = (B) = 0.658
\]

For the same preparation of SbCl\(_3\)\(^{36}\) independently analysed for specific activity \(S_0 = 28990\) cpm/me., and hence \(\frac{(A)}{(A) + (B)}\) \(S_0 = 640\) cpm/me., compared with the observed value of 634 cpm/me.

b. Analysis of separated reactants for fraction of exchange, sample number 4

The reactants in a 4 ml sample of reaction solution were separated and each hydrolysed with 13 ml of the same aqueous solution as was used to hydrolyse the total analysis sample. For 10.06 ml of the aqueous solution the following analysis was obtained:

<table>
<thead>
<tr>
<th>Reactant fraction</th>
<th>Total Cl(^-) me.</th>
<th>Cl(^-) in SbCl(_3) me.</th>
<th>Cpm</th>
<th>Cpm/me.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Me(_3)SiCl</td>
<td>2.244</td>
<td>0.00578</td>
<td>1143</td>
<td>509.4</td>
</tr>
<tr>
<td>SbCl(_3)</td>
<td>0.0419</td>
<td>283</td>
<td>6750</td>
<td></td>
</tr>
</tbody>
</table>

Hence from (11) the fraction of exchange calculated from the activities of SbCl\(_3\) is 0.784. For Me\(_3\)SiCl, from (12) and (14),
\[ F = \frac{(509.4 - 16.2)}{634.4} = 0.778. \]

If the specific activity of the residual SbCl\(_3\) had not been measured, the calculation proceeds by the assumption of a first apparent value of \( F \) of \( \frac{509.4}{634.4} \), i.e. \( 0.802 \). The specific activity of the SbCl\(_3\) was then calculated using (11), and used in (13) to make a first correction to \( F \):
\[ F = \frac{(509.4 - 14.7)}{634.4} = 0.780. \]

The next iteration gives \( \frac{(509.4 - 16.3)}{634.4} = 0.778 \).

The agreement between the \( F \) values based on the observed antimony trichloride specific activities and the iteration procedure is shown for experiment 4 in table 12, and the values on which the calculations are based in table 13.

(b) Exchange and Rate Constants

The slope of the plot of \( \log (1-F) \) versus time was used to find the half time of exchange for a particular set of reaction conditions. The value of \( R \) was then calculated from the relation
\[ R = \frac{(A)(E)}{(A) + (B)} \cdot \frac{0.693}{t_{1/2}} \quad (15) \]

For a bimolecular reaction
\[ R = k_2 \frac{(A)(E)}{n_A n_B} \quad (16) \]

where \( n_A \), \( n_B \), are the number of gram atoms of chlorine per molecule of reactants \( A \) and \( B \) respectively. Hence for the half time expressed in seconds
\[ k_2 = \frac{3}{(A) + (B)} \cdot \frac{0.693}{t_2} \]  

in the units litre.mole\(^{-1}\).sec\(^{-1}\), since \(n_A = 3\), \(n_B = 1\).

(c) **Activation Functions**

Activation energies were calculated from the slope of plots of \(\log k_2\) versus \(1/T\); inserting numerical values in the Arrhenius equation gives

\[ E = 4.576 \frac{d \log k}{d 1/T} \]  

Activation entropy was calculated assuming the absolute reaction rate equation in the form

\[ k_2 = \frac{kT}{h} e^{S/R} e^{-E/RT} \]  

and using the relation

\[ F = E - TS \]  

Inserting numerical values in (20), for \(T = 293^\circ K\),

\[ F = 1350 (\log k_2 - 12.78) \text{ Kcals} \]  

where \(k_2\) is in litre.mole\(^{-1}\).sec\(^{-1}\).

(d) **Calculation of Errors**

The limits of error shown in the exchange curves (Chapter 5) were calculated by compounding the individual errors as determined from replicate measurements of the various quantities, or by estimation in the case of statistical counting error. The correction to the trimethylchlorosilane specific activity for antimony trichloride carried over during separation was in general fairly small and accurately determined, and hence error in its determination did not produce much error in the value of \(F\). The error which it does produce can
be calculated generally however, and often serves as a guide in estimating expected error in the design of an experiment.

Using the notation of 4.a.iii, and assuming all activity initially in the antimony trichloride, then from (14)

\[ F = \frac{S_{\text{obs}} - (y/x)(S_A - S_{\text{obs}})}{S} \]  

(22)

Hence in addition to the direct error in F due to error in the determination of \( S_{\text{obs}} \), there will be an error \( dF \) for a given percentage error \( e \) in \( y/x \) of

\[ dF = \frac{(A) + (B)}{100} \cdot \frac{e}{x} \cdot \frac{(y/x)(S_A - S_{\text{obs}})}{S_{A_o}} \]  

(23)

This will be greatest for zero time, when \( S_A = S_{A_o} \), and can be shown to be nearly proportional, at other times, to \( (1-F) \), such that

\[ dF = \frac{(A) + (B)}{100} \cdot \frac{e}{x} \cdot \frac{y}{y}(1-F) \]  

(24)

with the error decreasing as the specific activities of the two reactants become more nearly equal.
5. EXPERIMENTAL RESULTS

(a) Systems Studied and Experiments Performed

i. Exchange systems.

Isotopic halogen exchange was observed between trimethylbromosilane and, severally, aluminium bromide, antimony tribromide and magnesium bromide, and between trimethylchlorosilane and, severally, aluminium chloride, antimony trichloride, and hydrogen chloride (3g).

The system trimethylchlorosilane - antimony trichloride was chosen for detailed study, as discussed in the introduction.

ii. Trimethylchlorosilane with antimony trichloride.

Benzene was initially chosen as solvent, and exchange experiments made using it. The first set of quantitative data (set 3, table 6, figure 8) gave a linear exchange curve within the estimated experimental error (±5% on the value of F). Further experiments at higher concentrations at both 40° and 25° gave complex exchange curves (figures 7 and 8) with complex concentration dependences, and after several sets had been performed with no particular clarification of the results, a change was made to hexane as solvent (see introduction). A number of experiments were however made in benzene solution to test whether the complexity of the results might have been due to extraneous effects. In particular the effect of hydrogen chloride, the most likely exchange impurity, was of interest because separate experiments had shown that this compound exchanged chlorine atoms with trimethylchlorosilane, and could possibly, therefore, accelerate the exchange between the latter and antimony trichloride.
Table 1
Exchange reaction conditions in benzene solution

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>Concentrations moles/litre</th>
<th>Set</th>
<th>Table</th>
<th>Figure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Me₃SiCl</td>
<td>SbCl₅</td>
<td></td>
<td></td>
</tr>
<tr>
<td>25</td>
<td>0.018</td>
<td>0.0158</td>
<td>3 *</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>0.112</td>
<td>0.0218</td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>0.112</td>
<td>0.269</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>0.0395</td>
<td>0.0953</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>40</td>
<td>0.0392</td>
<td>0.00367</td>
<td>1 **</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>0.1096</td>
<td>0.0214</td>
<td>2</td>
<td>5</td>
</tr>
</tbody>
</table>

* Me₃SiCl solution stored under nitrogen (3.d.ii.a) changed concentration as sampling proceeded (table 6).

** A large scatter of points about a smooth curve was observed in this set of experiments, possibly due to initial difficulties of technique and analysis (6.a.ii).

Individual experiments were carried out in the dark (table 4), in the presence of ultra-violet light (table 4), in the presence of moisture, which would produce hydrogen chloride by hydrolysis of trimethylchlorosilane (tables 4 and 8), and in the presence of antimony pentachloride, a possible trace impurity in antimony tri-chloride. The antimony pentachloride also contained traces of chlorine.

Light had no apparent effect on the exchange, and the other impurities, while producing measurable effects, do not markedly alter the exchange rate even when present in finite concentrations. It was similarly found in a study of the exchange of chlorine atoms between
phosphorus tri- and pentachlorides\textsuperscript{36}, that hydrogen chloride, while altering the exchange rate to some extent, does not have a marked effect on it.

Experiments were made in hexane solution over a range of temperatures, and over a range of concentrations such that that of each reactant was varied while that of the other was kept more or less constant (2.a), this procedure being followed twice over the temperature range. The exchange curves obtained were all complex, but similar, and had initial slopes which gave bimolecular rate constants (table 16; 5.c.iii).

An experiment was made with a few per cent of added benzene to test whether a complex between it and antimony trichloride might persist in hexane solution and effect the exchange rate (table 11). No effect on the exchange rate or behaviour was in fact observed.

Equilibration, in hexane solution, of triraethylchlorosilane with a molar excess of antimony trichloride before addition of a small amount of $\text{SbCl}_3^{36}$ gave a markedly greater initial slope than that calculated for direct mixing (table 11; figure 9; 5.d.iii), and a linear exchange curve to more than 90\% exchange.

b. Subsidiary experiments.

In addition to the exchange experiments a number of other experiments and observations were made with the two compounds, as discussed in 3.f.i,ii, and iii. Tests were made for chemical reaction between the exchange reactants, for any abnormality in the vapour pressure of a solution of antimony trichloride in trimethylchlorosilane, and the conductance of antimony trichloride measured in anhydrous
benzene and hexane, in undried benzene, and in anhydrous benzene to which trimethylchlorosilane had been added.

(b) Observation on the Separation Method

i. General

Typically, at 40°, 5 ml of benzene were evaporated to dryness in 60 seconds, and even for 12 ml of solution initially at 25°, all but a small fraction of a millilitre evaporated without solidification. Less than 0.3% of the antimony trichloride contained in 5 ml of one molar solution was carried over when the solution was evaporated to dryness, and usually 1% to 2% over a range of concentrations. When stirring was not good, as much as 5% of the antimony trichloride was carried over.

Relatively more antimony trichloride was carried over from hexane solution (Table 2). In these separations the evaporation vessel was not in the thermostat bath, and the solution cooled rapidly as evaporation proceeded, with precipitation of solid antimony trichloride. This rapid cooling had the advantage of quenching the reaction so that the subsequent time required to completely evaporate the solution to dryness becomes unimportant as a source of variation in the amount of zero time exchange. It was necessary to warm the vessel with a heating lamp to keep the temperature above 0°C and accomplish evaporation in a reasonably short time, usually four or five minutes for 5 ml of solution.

ii. Efficiency and reproducibility of separation.

The amounts of antimony trichloride carried over with the silane fraction during separation are shown in table 2. For given
initial conditions, the variation in the percentage carried over is not large, and the plots shown in figure 12 show that the uncorrected fractions of exchange fall on a smooth curve below the corrected values. The amount of antimony trichloride carried over was found to be much the same whether evaporation was partial (80%) or complete. As would be expected, the time taken to evaporate a given volume of solution under given conditions was found to be sensibly constant. Perhaps surprisingly, the percentage of antimony trichloride carried over falls off markedly with increase in initial concentration.

Table 2
Efficiency of evaporation separation.

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>SbCl₃ Molarity and Volume</th>
<th>Average % carried over</th>
<th>Number of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>In benzene *</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>0.04 M 7.06 ml</td>
<td>3.5 ± 1.3</td>
<td>6</td>
</tr>
<tr>
<td>40</td>
<td>0.03 M 4.7 ml</td>
<td>1.2 ± 0.8</td>
<td>8 (lowest 0.15)</td>
</tr>
<tr>
<td>25</td>
<td>0.03 M 4.7 ml</td>
<td>2.5 ± 0.5</td>
<td>4</td>
</tr>
<tr>
<td>25</td>
<td>0.27 M 7.06 ml</td>
<td>0.27 ± 0.06</td>
<td>4</td>
</tr>
<tr>
<td>In hexane **</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>40</td>
<td>0.005 M 7 ml</td>
<td>15.8 ± 1.8</td>
<td>6</td>
</tr>
<tr>
<td>30</td>
<td>0.005 M 6 ml</td>
<td>14.9 ± 2.1</td>
<td>4</td>
</tr>
</tbody>
</table>
Table 2 (continued)

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>SbCl₃ Molarity and volume</th>
<th>Average % carried over</th>
<th>Number of observations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hexane ** (continued)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>0.005 M</td>
<td>15.2 ± 1.7</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>7 ml</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20°</td>
<td>0.035 M</td>
<td>5.0 ± 0.8</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>6 ml</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* A 3 cm diameter No.3 sinter at 40° and a No.2 at 25°.

** A 3 cm diameter No.3 sinter preceded by a 2.5 cm No.1 sinter at each temperature.

iii. Zero time exchange.

Experiments in benzene solution in which the reactants were separated shortly after mixing gave a measured zero time fraction of exchange of approximately 0.02, (tables 4, 5 and 6). In hexane solution back extrapolation of the exchange curves gave 0.01 to 0.02 over the range of experiments, provided that correction was made for antimony trichloride carried over in the separated silane. When this correction was not made, zero time exchange was usually of the order of 0.08 to 0.10, with the observed points falling on a smooth curve below the corrected curve (figure 12).

Predicted zero time (2.b.iii) exchange varied from 0.001 \((t_{1/2} = 100 \text{ hours})\) to 0.01 \((t_{1/2} = 10 \text{ hours})\). However the observed zero time exchange of 0.01 to 0.02 was practically independent of the half time of reaction, and must therefore have been produced.
by the separation. For shorter half times, say one hour, the predicted value would be 0.10, and the prediction would be of greater use.

**iv. Relative volatilities of trimethylchlorosilane and benzene.**

The relative rates of evaporation of solvent and solute can be predicted from Raoulte's law, (2.b.ii), and the predictions were checked approximately at 40° for Me₂SiCl - benzene, by evaporating from the same initial amounts of solution for varying times and determining the amounts of solute and solvent carried over.

**Table 3**

Relative volatilities for Me₂SiCl - benzene at 40°.

<table>
<thead>
<tr>
<th>Time (secs.)</th>
<th>v/v₀</th>
<th>a/a₀</th>
<th>r&lt;sub&gt;obs&lt;/sub&gt;</th>
<th>r&lt;sub&gt;predicted&lt;/sub&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>45</td>
<td>0.71</td>
<td>0.35</td>
<td>3.0</td>
<td>2.2 (40°)</td>
</tr>
<tr>
<td>60</td>
<td>0.55</td>
<td>0.21</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>85</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

v is the solvent volume, a the amount of solute remaining in the remaining solution, and r the relative volatility (2.b.ii). The initial volume of benzene solution was 7 ml, 0.04 molar in trimethylchlorosilane. It can be seen that the enrichment of the separated fraction with respect to silane is somewhat greater than that predicted from Raoulte's law, and therefore still greater than that predicted by inclusion of the molecular weight term (2.b.ii).
(c) **Exchange Rate Data**

1. **Exchange in benzene solution.**

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time (Hours)</th>
<th>Fraction of Exchange</th>
</tr>
</thead>
<tbody>
<tr>
<td>13</td>
<td>0.002</td>
<td>0.03 ± 0.015</td>
</tr>
<tr>
<td>8</td>
<td>1.47</td>
<td>0.39</td>
</tr>
<tr>
<td>14</td>
<td>2.43 *</td>
<td>0.52</td>
</tr>
<tr>
<td>9</td>
<td>2.50</td>
<td>0.38</td>
</tr>
<tr>
<td>12</td>
<td>2.55</td>
<td>0.76</td>
</tr>
<tr>
<td>10</td>
<td>8.3</td>
<td>0.75</td>
</tr>
<tr>
<td>11</td>
<td>13.7</td>
<td>0.74</td>
</tr>
</tbody>
</table>

*140 mins., Me₃SiCl = 0.0420 M
SbCl₃ = 0.00351 M

The experimental scatter in this set is higher than was usually observed subsequently, possibly due to initial difficulties of technique, and of analysis.
Table 5
Exchange in benzene solution at 40.0°, set 2, (Figure 7).

Benzene solution volume: 4.79 ml

Molarities: \( \text{Me}_2\text{SiCl} \) \( 0.1096 \pm 0.5\%
\( \text{SbCl}_3 \) \( 0.0643 \pm 1\%

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time</th>
<th>Fraction of Exchange</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Hours</td>
<td>( \text{SbCl}_3 )</td>
<td>( \text{Me}_2\text{SiCl} )</td>
</tr>
<tr>
<td>21</td>
<td>0.05</td>
<td>0.01 ± 0.02</td>
<td>0.02 ± 0.01</td>
</tr>
<tr>
<td>18</td>
<td>2.05</td>
<td>0.49</td>
<td>0.45</td>
</tr>
<tr>
<td>22</td>
<td>2.12</td>
<td>0.40</td>
<td>0.37</td>
</tr>
<tr>
<td>15</td>
<td>3.25</td>
<td>0.59</td>
<td>0.58</td>
</tr>
<tr>
<td>17</td>
<td>5.25</td>
<td>0.65</td>
<td>0.64</td>
</tr>
<tr>
<td>16</td>
<td>7.2</td>
<td>0.74</td>
<td>0.73</td>
</tr>
<tr>
<td>20</td>
<td>12.0</td>
<td>-</td>
<td>0.82</td>
</tr>
<tr>
<td>19</td>
<td>17.8</td>
<td>0.84</td>
<td>0.82</td>
</tr>
<tr>
<td>23</td>
<td>40.6</td>
<td>-</td>
<td>0.95</td>
</tr>
</tbody>
</table>

* Irradiated with 110 watt Hg-Quartz U.V. lamp.
** In the presence of water vapour from 50 ml of laboratory air.
*** In the absence of light.
Table 6

Exchange in benzene solution at 25.3°, Set 3, (Figure 8).

Benzene solution volume: 4.38 ml

Molarities: $\text{Me}_2\text{SiCl}_3$ initially: 0.0195 ± 1%
finally: 0.0160

$\text{SbCl}_3$ 0.0158 ± 0.4%

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time Hours</th>
<th>Fraction of Exchange $\text{SbCl}_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.05</td>
<td>0.024 ± 0.015</td>
</tr>
<tr>
<td>2</td>
<td>0.35</td>
<td>0.35</td>
</tr>
<tr>
<td>3</td>
<td>1.00</td>
<td>0.52</td>
</tr>
<tr>
<td>6</td>
<td>1.50</td>
<td>0.61</td>
</tr>
<tr>
<td>4</td>
<td>2.10</td>
<td>0.80</td>
</tr>
<tr>
<td>5</td>
<td>3.00</td>
<td>0.91</td>
</tr>
</tbody>
</table>

* Calculated allowing for variation in $S_\infty$ with drift in $\text{Me}_2\text{SiCl}_3$ concentration.

$\text{Me}_2\text{SiCl}_3$ solution was stored and manipulated under nitrogen, and changed concentration as a number of samples were withdrawn.

This set of experiments were the first quantitative ones performed.


Table 7

Exchange in benzene solution at 25.0°C, Sets 4 and 5, (Figure 8).

Benzene solution volume: 4.70 ml

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time (Hours)</th>
<th>Fraction of Exchange</th>
<th>Molarities:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>SbCl&lt;sub&gt;3&lt;/sub&gt;</td>
<td>Me&lt;sub&gt;3&lt;/sub&gt;SiCl</td>
</tr>
<tr>
<td>Set 4. Molarities:</td>
<td></td>
<td></td>
<td>Me&lt;sub&gt;3&lt;/sub&gt;SiCl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.112 ± 0.5%</td>
<td>0.112 ± 0.5%</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0218 ± 1%</td>
<td>0.269 ± 0.5%</td>
</tr>
<tr>
<td>27</td>
<td>5.2</td>
<td>0.37</td>
<td>0.36</td>
</tr>
<tr>
<td>24</td>
<td>12.7</td>
<td>0.57</td>
<td>0.54</td>
</tr>
<tr>
<td>28</td>
<td>15.0</td>
<td>0.72</td>
<td>0.69</td>
</tr>
<tr>
<td>26</td>
<td>20.0</td>
<td>0.92</td>
<td>0.88</td>
</tr>
<tr>
<td>25</td>
<td>26.8</td>
<td>0.93</td>
<td>0.93</td>
</tr>
<tr>
<td>Set 5. Molarities:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.112 ± 0.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.269 ± 0.5%</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>6.0</td>
<td></td>
<td>0.25</td>
</tr>
<tr>
<td>30</td>
<td>10.1</td>
<td></td>
<td>0.54</td>
</tr>
<tr>
<td>32</td>
<td>15.5</td>
<td></td>
<td>0.68</td>
</tr>
<tr>
<td>31</td>
<td>20.3</td>
<td></td>
<td>0.96</td>
</tr>
</tbody>
</table>
Table 8

Exchange in benzene solution at 25.0°, Set 6, (Figure 8).

As in Set 5, 2.09 ml of SbCl₃ solution were delivered into the lower reaction compartment and outgassed; an additional 8.6 ml of benzene were then condensed under vacuum onto the sample. Trimethylchlorosilane solution (2.65 ml) was condensed as usual in the upper compartment, to give on mixing, 13.3 ml of reaction solution.

Molarities: Me₃SiCl 0.0395
SbCl₃ 0.0953

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time Hours</th>
<th>Fraction of Exchange Me₃SiCl</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>8.75</td>
<td>0.13</td>
</tr>
<tr>
<td>35</td>
<td>45.0</td>
<td>0.98 *</td>
</tr>
</tbody>
</table>

(* Calculated from experiment 34 : F = 0.35)
Table 9

Exchange in benzene solution, with added impurities at 25.0°.

These experiments were performed with slightly hydrolysed antimony trichloride solution originally used for the experiments in sets 5 and 6, the amounts of solution and trimethylchlorosilane being also the same as in those sets.

Experiment 36. Sufficient water vapour to hydrolyse 5% of the trimethylchlorosilane was condensed in the upper compartment of the reaction vessel. (Compare experiment 17, set 2.)

Experiment 37. Concentrations and conditions as in set 5, no impurity added.

Experiment 38. Approximately 0.002 milli-moles of antimony pentachloride containing traces of chlorine were condensed with the antimony trichloride sample.

<table>
<thead>
<tr>
<th>Experiment Number</th>
<th>Time Hours</th>
<th>Fraction of Observed Exchange Expected from Set 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>36</td>
<td>12.7</td>
<td>0.85</td>
</tr>
<tr>
<td>37</td>
<td>13.0</td>
<td>0.8</td>
</tr>
<tr>
<td>38</td>
<td>7.0</td>
<td>0.6</td>
</tr>
</tbody>
</table>
## ii. Exchange Rate Data for Hexane Solution Experiments.

### Table 10

Exchange in hexane solution at 40° (Figure 9).

<table>
<thead>
<tr>
<th>Experiment</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molarities: Me₃SiCl₅</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SbCl₅</td>
<td>0.35</td>
<td>0.406</td>
</tr>
<tr>
<td></td>
<td>0.057</td>
<td>0.00522</td>
</tr>
<tr>
<td>Time F</td>
<td>Time F</td>
<td></td>
</tr>
<tr>
<td>Hours Me₃SiCl</td>
<td>Hours Me₃SiCl</td>
<td></td>
</tr>
<tr>
<td>0.60</td>
<td>0.032</td>
<td>4.2</td>
</tr>
<tr>
<td>1.05</td>
<td>0.061</td>
<td>8.0</td>
</tr>
<tr>
<td>1.75</td>
<td>0.086</td>
<td>11.7</td>
</tr>
<tr>
<td>2.51</td>
<td>0.145</td>
<td>15.1</td>
</tr>
<tr>
<td>3.85</td>
<td>0.185</td>
<td>20.0</td>
</tr>
<tr>
<td>6.11</td>
<td>0.322</td>
<td>27.2</td>
</tr>
</tbody>
</table>

\[ t_{\frac{1}{2}} : 11.5 \quad 13.5 \]

\[ k_2 \cdot 10^5 \text{, litre.moles}^{-1}.\text{sec}^{-1} \]

9.7 \quad 10.2
Table 11

Exchange in hexane solution at 40° (Figure 9).

<table>
<thead>
<tr>
<th>Experiment</th>
<th>5</th>
<th>9</th>
<th>10**</th>
</tr>
</thead>
<tbody>
<tr>
<td>M : Me₃SiCl</td>
<td>0.0193*</td>
<td>0.737</td>
<td>0.0364</td>
</tr>
<tr>
<td>SbCl₃</td>
<td>0.0535</td>
<td>0.0357*</td>
<td>0.0747*</td>
</tr>
<tr>
<td>Time hrs.</td>
<td>F</td>
<td>Time hrs.</td>
<td>F</td>
</tr>
<tr>
<td>SbCl₃</td>
<td></td>
<td>Me₃SiCl</td>
<td></td>
</tr>
<tr>
<td>17.3</td>
<td>0.254</td>
<td>3.4</td>
<td>0.288</td>
</tr>
<tr>
<td>28.6</td>
<td>0.381</td>
<td>8.0</td>
<td>0.622</td>
</tr>
<tr>
<td>48.5</td>
<td>0.704</td>
<td>10.5</td>
<td>0.756</td>
</tr>
<tr>
<td>66.3</td>
<td>0.906</td>
<td>17.0</td>
<td>0.92</td>
</tr>
<tr>
<td>78.1</td>
<td>0.93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t₁/₂</td>
<td>41</td>
<td>8.0</td>
<td>3.5</td>
</tr>
<tr>
<td>k₂.10⁵, litre.moles⁻¹.sec⁻¹</td>
<td></td>
<td>7.5</td>
<td>8.7</td>
</tr>
</tbody>
</table>

* Initially labelled with chlorine-36.
** Uncorrected for SbCl₃ in Me₃SiCl fraction.

Experiment 5. Mass balance: S₀ = 30,050 cpm/me.; S₀ calc. and obs. = 3293 and 3233 cpm/me. respectively.

Experiment 9. The solution contained two moles per cent of benzene, a two fold excess over that required for formation of 2SbCl₃.C₆H₆, and was equilibrated at 40° for 17 hours before mixing with Me₃SiCl.

Experiment 10. Me₃SiCl and a molar excess of SbCl₃ in 50 ml of hexane were equilibrated at 40° for 36 hours, before mixing with 4 ml of hexane containing SbCl₃⁷³ at the same concentration and having a sufficiently high specific activity that although only 14% of the total activity was eventually transferred to the silane fraction the count rates observed were from 1000 cpm to 2000 cpm.
Table 12

Exchange in hexane at 30°, experiment 4 (Figures 10 and 12).

Molarities: $\text{Me}_3\text{SiCl}$, 0.644; $\text{SbCl}_3^{36}$, 0.00484.

<table>
<thead>
<tr>
<th>Sample No.</th>
<th>Time hrs.</th>
<th>Fraction of $\text{SbCl}_3$ Corrected</th>
<th>Exchange $\text{Me}_3\text{SiCl}$ Iterated Uncorrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13.25</td>
<td>0.236</td>
<td>0.194</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.186</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.323</td>
</tr>
<tr>
<td>2</td>
<td>25.0</td>
<td>0.390</td>
<td>0.387</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.387</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.491</td>
</tr>
<tr>
<td>3</td>
<td>41.0</td>
<td>0.582</td>
<td>0.583</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.584</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.646</td>
</tr>
<tr>
<td>4</td>
<td>62.1</td>
<td>0.784</td>
<td>0.778</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.778</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>0.802</td>
</tr>
</tbody>
</table>

$t_\frac{1}{2}$: 28 hrs., $k_2$ $10^5$ litre.moles$^{-1}$sec$^{-1}$, $3.2$

Calculations for sample 4 are discussed in 4.a.v.
Table 13

Values obtained in experiment 4.

The observations refer to 10.06 ml of hydrolysis solution, and amounts are in milli-equivalents.

<table>
<thead>
<tr>
<th>No.</th>
<th>Me₂SiCl₃ fraction</th>
<th>SbCl₃ fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>cpm</td>
<td>Cl⁻</td>
</tr>
<tr>
<td>1</td>
<td>1062</td>
<td>5.187</td>
</tr>
<tr>
<td>2</td>
<td>1359</td>
<td>4.364</td>
</tr>
<tr>
<td>3</td>
<td>1009</td>
<td>2.460</td>
</tr>
<tr>
<td>4</td>
<td>1143</td>
<td>2.244</td>
</tr>
</tbody>
</table>


<table>
<thead>
<tr>
<th>cpm</th>
<th>Cl⁻</th>
<th>SbCl₃</th>
<th>S₀</th>
<th>S₀</th>
<th>Obs.</th>
<th>Calc.</th>
</tr>
</thead>
<tbody>
<tr>
<td>2124</td>
<td>3.349</td>
<td>0.0738</td>
<td>28990</td>
<td>640</td>
<td>634</td>
<td></td>
</tr>
</tbody>
</table>

The values recorded in table 13 are typical of those obtained throughout the experiments with hexane solutions.
Table 14

Exchange in hexane solution at 30° (Figure 10).

<table>
<thead>
<tr>
<th>Experiment</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molarities:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Me₃SiCl</td>
<td>0.0141</td>
<td>0.0238</td>
</tr>
<tr>
<td>SbCl₅</td>
<td>0.0542</td>
<td>0.0495</td>
</tr>
<tr>
<td>Time (hrs.)</td>
<td>F</td>
<td>Time (hrs.)</td>
</tr>
<tr>
<td></td>
<td>SbCl₅</td>
<td></td>
</tr>
<tr>
<td>13.0</td>
<td>0.054</td>
<td>38.3</td>
</tr>
<tr>
<td>48.0</td>
<td>0.267</td>
<td>62.3</td>
</tr>
<tr>
<td>93.0</td>
<td>0.756</td>
<td>117.5</td>
</tr>
<tr>
<td>162</td>
<td>0.951</td>
<td>200</td>
</tr>
<tr>
<td>t₁/₂ : 120 hrs., k_2 * 10^5, litre.moles⁻¹.sec⁻¹, 2.8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Mass balance for experiments 6 and 7, Table 14.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>29490</td>
<td>2353</td>
<td>2356</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>29430</td>
<td>4105</td>
<td>4120</td>
<td></td>
</tr>
</tbody>
</table>

Experiment 6 was curtailed because of mechanical failure of the greaseless stopcock on the reaction vessel, and in experiment 7 the exchange curve appeared to curve downward somewhat earlier than usual. However, the sums of the gram-atom concentrations were almost the same, 0.1765 and 0.1707 respectively, and the initial slopes of the two exchange curves were the same within an experimental error of approximately ± 8%.
Table 15

Exchange in hexane solution at 20° (Figures 11 and 12).

<table>
<thead>
<tr>
<th>Experiment</th>
<th>3</th>
<th>8</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>,</td>
<td></td>
</tr>
<tr>
<td>Me₃SiCl</td>
<td>0.621</td>
<td>0.376</td>
</tr>
<tr>
<td>SbCl₃</td>
<td>0.00504</td>
<td>0.0354</td>
</tr>
<tr>
<td>Time F</td>
<td>F</td>
<td>F</td>
</tr>
<tr>
<td>hrs. SbCl₃</td>
<td>Me₃SiCl</td>
<td>SbCl₃</td>
</tr>
<tr>
<td>12.5</td>
<td>0.134</td>
<td>14.8</td>
</tr>
<tr>
<td>33.0</td>
<td>0.341</td>
<td>37.9</td>
</tr>
<tr>
<td>58.5</td>
<td>0.477</td>
<td>0.470</td>
</tr>
<tr>
<td>69.0</td>
<td>0.518</td>
<td>0.485</td>
</tr>
<tr>
<td>88.3</td>
<td>0.631</td>
<td>134.3</td>
</tr>
<tr>
<td>131.0</td>
<td>0.892</td>
<td>163.3</td>
</tr>
</tbody>
</table>

\[
t_\frac{1}{2} : 62
\]

\[
k_2 \cdot 10^5, \text{litre.moles}^{-1}.\text{sec}^{-1}
\]

1.5

1.0

iii. Molecularity of Reaction in Hexane Solution.

Although the exchange curves obtained in hexane solution all showed downward curvature, if initial slopes are taken the reaction obeys a second order rate law with reasonable accuracy over the range of temperatures and concentrations employed.

### Table 16
Exchange in hexane solution

<table>
<thead>
<tr>
<th>Temp. °C</th>
<th>Expt. No.</th>
<th>Concentrations, moles/litre</th>
<th>$t_\frac{1}{2}$ hours</th>
<th>$k_2 \cdot 10^5$ 1.mol$^{-1}$sec$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>40°</td>
<td>1</td>
<td>0.35 0.057</td>
<td>11.5</td>
<td>9.7</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.406 0.00522</td>
<td>13.5</td>
<td>10.2</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>0.0198 0.0535</td>
<td>41</td>
<td>7.5</td>
</tr>
<tr>
<td></td>
<td>9 **</td>
<td>0.737 0.0357</td>
<td>8.0</td>
<td>8.7</td>
</tr>
<tr>
<td></td>
<td>10 ***</td>
<td>0.0364 0.0747</td>
<td>3.5</td>
<td>63</td>
</tr>
<tr>
<td>30°</td>
<td>4</td>
<td>0.644 0.00484</td>
<td>28</td>
<td>3.2</td>
</tr>
<tr>
<td></td>
<td>6, 7</td>
<td>0.0141 0.0542</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0238 0.0495</td>
<td>120</td>
<td>2.8</td>
</tr>
<tr>
<td>20°</td>
<td>3</td>
<td>0.621 0.00504</td>
<td>62</td>
<td>1.5</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>0.376 0.0354</td>
<td>118</td>
<td>1.2</td>
</tr>
</tbody>
</table>

* Half times are based on the initial slopes of the curves.

** In the presence of benzene (table 10).

*** Pre-equilibration of inactive SbCl$_3$ with Me$_3$SiCl before addition of SbCl$_3^{36}$ (table 11).

A plot of log $k$ versus $1/T$ (figure 13) is linear and gives an activation energy for the reaction of $18.6 \pm 1.1$ Kcals. The
activation free energy calculated for 20°C is 23.8 Kcals, and the activation entropy $18 \pm 4$ cals/degree. The rate law for the initial reaction is

$$R = 2.2 \times 10^8 e^{-18,600/RT} (\text{Me}_3\text{SiCl})(\text{SbCl}_3).$$

(d) Observations on the Exchange Rate Data

i. Validity of exchange rate data

Although the exchange curves obtained with both benzene and hexane as solvents are complex, there are a number of consistencies in the data which makes it most unlikely that the results are due to artifacts and not to the inherent behaviour of the systems. In set 2, table 4 (figure 7) the different experiments were performed in random order, but still fall on a smooth curve, with agreement between the fractions of exchange determined from each of the separated reactants. Similarly for the other results in benzene solution, although the experimental scatter is somewhat higher in the other sets. The exchange curves extrapolate back through zero (or close to it) and experiments in which separation was almost immediate show almost zero exchange.

In the hexane solution experiments the order in which points on the exchange curves were obtained was necessarily temporal, but the experimental points give a good fit to smooth curves passing through the log(1-F) axis near to the origin, and with good agreement between the fractions of exchange determined from the two reactants (tables 12, 14 and 15; figures 11 and 12). In addition, of course, the initial slopes of the curves give consistent second order rate constants, which fit a linear Arrhenius plot (figure 13).
The relatively small effects of added impurities (moisture, and therefore hydrogen chloride, and antimony pentachloride), show that traces of these impurities would not affect the exchange rates, and the tests for chemical reaction in the exchange system (3.f.i and ii) show that the exchange data is not complex for that reason, although the formation of an addition complex between the reactants or between benzene and antimony trichloride is not precluded.

ii. Behaviour of the Me₃SiCl - SbCl₃ system in benzene solution.

The first set of data (set 3, table 6) was obtained using lower concentrations than in the other sets, and a less refined technique (3.d.ii.a ; 3.e.i), though one which ought to have been reasonably adequate. The exchange curve was apparently linear (figure 8). At 40° the exchange curves obtained with higher concentrations were concave upward to the extent that the rate towards the end of reaction was of the order of ten times slower than initially. At 25° however, the curves were concave downwards, with a rather large scatter of points about a smooth curve. This scatter was several times greater than that calculated according to the discussion in 4.d, and than that observed in the hexane solution studies. In set 5, the experiments were made with an antimony trichloride concentration more than ten times that used in the experiments in set 4, the silane concentration being the same in each set. The two exchange curves are, however, practically coincident, and because of the scatter of points are shown so in figure 8.
The experiments in sets 2 and 4 were performed with the same reactant solutions, and hence may be compared to obtain an activation energy for the exchange process, as any concentration dependence terms will cancel in the comparison of rates provided the initial slopes of the exchange curves can be assumed to refer to the same exchange process.

**Table 17**

Exchange in benzene solution (Figures 7 and 8).

<table>
<thead>
<tr>
<th>Set</th>
<th>Temp. °C</th>
<th>Concentration moles/litre</th>
<th>$t_\frac{1}{2}$ hours.</th>
<th>$&quot;k_2&quot;, 10^5$ l.moles$^{-1}$sec$^{-1}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>40</td>
<td>0.110</td>
<td>0.0214</td>
<td>2.0</td>
</tr>
<tr>
<td>4</td>
<td>25</td>
<td>0.112</td>
<td>0.0218</td>
<td>14.5</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>0.112</td>
<td>0.269</td>
<td>14.5</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>0.0395</td>
<td>0.0953</td>
<td>47.5</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>0.018</td>
<td>0.0158</td>
<td>1.0</td>
</tr>
</tbody>
</table>

The apparent activation energy from sets 2 and 4 is 25 Kcals.

For these experiments the exchange rates are approximately fifteen times greater than for the corresponding concentrations in hexane, but in set 5, as noted above, a ten fold increase of antimony trichloride concentration over that used in set 4 does not alter the initial exchange rate. However, direct dilution of the reaction solution for the experiments in set 6 (table 8), so that both reactant concentrations are altered in the same ratio, alters the initial rate of ex-
change as would have been predicted for a bimolecular reaction.

The fact that smooth curves with good fit of individual points were obtained under similar conditions in hexane solution, and that in it the initial rates were bimolecular, and all rates increased with increased time of contact of the reactants, indicates that the behaviour of the exchange system is anomalous in benzene, presumably because of the interaction of one or both of the reactants with this solvent.

iii. Pre-equilibration experiment in hexane solution.

The data for this experiment are presented in table 11, and the exchange curve in figure 9. Addition of a small, labelled amount of the compound already in excess allows the observation of the exchange behaviour of the excess with any complex (assumed 1:1 for the design of this experiment) formed between the two reactants. The inactive compounds were equilibrated in hexane solution at the reaction temperature (40°) for two half times based on the calculated initial slope for the concentrations used, and were previously in contact for one half time. If one of the reactants had been initially labelled this would have been sufficient time for the exchange to have gone more than 90% to completion. The exchange rate was much faster (7 times) than that calculated for immediate mixing, and the uncorrected exchange curve appeared linear to more than 90% of exchange. The zero time intercept is uncertain in the absence of corrections, but can be calculated (2.a.iv) from the expected amount of antimony trichloride carried over in the silane fraction to be of the order of $F_0 = 0.2$, which is the intercept for the linear plot. Possibly for
longer equilibration times the rate would be faster, but the apparent linearity of the plot and the fact that its slope is near that of the maximum final slopes of the other plots indicates that the rate observed is near to the maximum which could be attained on longer equilibration.

iv. Addition of benzene to exchange system in hexane solution.

This experiment (9, table 11) was conducted at 40°. The hexane solution of antimony trichloride contained two moles per cent of benzene, a two fold excess over that required for formation of $2\text{SbCl}_3\cdot\text{C}_6\text{H}_6$, and was equilibrated at 40° for 17 hours before mixing with trimethylchlorosilane. The calculated half time of exchange in the absence of benzene was nine hours, and that observed (based on the initial slope of the exchange curve) was eight hours. The exchange curve was of the same form as the others at the same temperature, and so the presence of benzene, at least for the equilibration time used, did not affect the exchange behaviour of the system.

( The rate constant from experiment 9 is, in the units of table 16, $k_2 = 8.7$; for the other experiments at 40° listed in that table, the values were 9.7, 10.2 and 7.5 ).

(e) Experimental Errors

As stated in 4.d errors in the observed values of $F$ were estimated by compounding the observed errors in the individual measurements, determined by replication. The error in $F$ due to error in the correction to the specific activity of the separated silane fraction (4.a.iii) was estimated in this way, or by the use
of equation (24).

For typical experiments in hexane solution, \( (A) = 0.15 \) and 
\( (B) = 0.50 \), while 15\% of the antimony trichloride was carried over 
with the evaporated silane. From (24) the error in \( F = 0.500 \) 
due to an error of \( \pm 2\% \) in the value of \( y/x \) in that equation, 
would be expected to be \( \pm 0.0005 \), or \( \pm 0.1\% \).

In general, count rates were 2000 cpm to 4000 cpm, and could 
hence readily be measured with an expected statistical error of 
\( \pm 0.7\% \) to \( \pm 0.3\% \). Since, at least in the hexane solution experi­
ments, most chloride and antimony titrations (except in the micro-
equivalent range) were performed with an agreement between duplicates 
of 0.1\%, the expected error in a value of \( F \) calculated from the 
ratio of two specific activities, allowing for the \( \pm 0.1\% \) error 
calculated above, would be approximately \( \pm 1.5\% \). This is typical 
of the limits of error shown in the exchange curves. In these, the 
diameter of the circles locating the experimental points gives the 
limit of error for \( F = 0.50 \).
6. **DISCUSSION**

(a) **Experimental Results**

i. **Reaction in hexane solution.**

The data shows that the reactants antimony trichloride and trimethylchlorosilane exchange chlorine atoms, at least initially, by a comparatively slow bimolecular process, and that on continued contact a species is produced which allows a more rapid exchange. That this species is not the product of an irreversible chemical reaction is shown by the experiments described in 3.f, in which the reactants were recovered or shown to form a solution with normal vapour pressure, and that the progressively increased rate of the reaction is unlikely to be due to the catalytic effect of traces of impurities was shown in the experiments in which finite amounts of impurities were added without producing a marked alteration in the exchange rates. The validity of the exchange data is discussed in 5.e, and the observed behaviour is almost certainly due to the characteristics of the system and not to artifacts. While it is perhaps difficult to envisage a reversibly formed addition compound between the two reactants of sufficient stability to produce a finite difference in the exchange behaviour and yet able to be dissociated by the evaporation of the reaction solution, formation of such a compound seems the only likely explanation of the observed data.

Addition compounds of volatile substances do often have finite or even high vapour pressure; for example the crystalline addition compounds of antimony trichloride with benzene$^{52}$ and dioxane$^{25}$ and
the addition compounds of silicon tetrahalides and halogenosilanes with trimethylamine\textsuperscript{10}. (SiHF\textsubscript{3}\textcdot NMe\textsubscript{3} has $P_{\text{diss.}} = 24 \text{ mm at } 0^\circ$). It is of considerable interest that a comparatively stable compound PhSiCl\textsubscript{3}\textcdot SbCl\textsubscript{3} has been isolated\textsuperscript{87}, (m.p. $-30^\circ$), and that in it, addition almost certainly occurs between the $\text{-SiCl}_3$ group and antimony trichloride, rather than between the latter and the benzene nucleus, which is strongly de-activated by the $\text{-SiCl}_3$ group.

The fact that in the present system pre-equilibration of the reactants gave an exchange curve (figure 9) apparently linear, and an exchange rate as higher or higher than that observed from the limiting slopes of the fastest exchanges observed in direct mixing experiments, confirms that contact of the reactants produces a relatively stable species allowing faster exchange than that occurring when they are first mixed.

The exchange behaviour of the present system is similar in some respects to that of the complex exchange of antimony atoms between Sb(V) and Sb(III) chlorides in strong hydrochloric acid solution\textsuperscript{89}, in which it was shown that the Sb(V) entity is SbCl\textsubscript{6}\textsuperscript{2-}, for which there is independent evidence, and its rate of formation is, under certain conditions, the governing factor in the exchange. (Antimony trichloride exists in hydrochloric acid solution largely as the ionic complex SbCl\textsubscript{4}\textsuperscript{-}, although in the studies discussed, SbCl\textsubscript{3} itself appears to be the Sb(III) exchanging species). When labelled Sb(V) was added to equilibrated mixtures in 6M HCl, the half time of exchange was 49 hours; when it was added directly in 12M HCl (and therefore, from the known equilibrium constants, was present entirely

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as \( \text{SbCl}_6^- \), the half time of exchange was 12 minutes.

While the present work establishes that a more rapid exchange path exists after equilibration of the reactants, a separate study would need to be made to determine its concentration dependence and molecularity. Sets of experiments at various concentrations would have to be performed, and checks made that equilibration times were sufficient. The effect of adding the labelling isotope in the reactant already in excess, or vice versa, would have to be determined, and it is difficult to surmise in the absence of such experiments what is the mechanism of the more rapid exchange. It is possible that intramolecular rearrangement in an addition compound is more rapid than direct exchange between the free reactants, and it might be expected that the most favourable exchange configuration is similar to that resulting in presumed addition compound formation. That this is not necessarily the case is shown by the observation that the transition complex most probably responsible for the effect of antimony trichloride on the hydrolysis of antimony pentachloride in hydrochloric acid solution is not the same as that presumed to be involved in antimony atom exchange\(^{89}\). Whatever form the species responsible for the faster exchange takes, experiment 10 shows that it is such as to allow of an increased rate of exchange between trimethylchlorosilane equilibrated with excess antimony trichloride, and added \( \text{SbCl}_3^{36} \). The most obvious form of addition compound between trimethylchlorosilane and antimony trichloride is one in which the chlorine atom of the silane is co-ordinated to antimony on the opposite side to the pyramidally disposed chlorine atoms. Such a structure
would presumably involve at least partial disposition of the antimony bonding orbitals to a tetrahedral configuration such as must obtain in the SbCl$_4^-$ ion. Supposing that intramolecular rearrangement in such an addition compound produces more rapid exchange than between the free reactants, it is conceivable that there is also a rapid chlorine exchange between the SbCl$_3^{36}$ added and the chlorine atoms of the bound antimony trichloride. A likely transition state structure in the SbCl$_6^-$ - SbCl$_3^{36}$ exchange (assuming these species) is shown to be

$$\text{Cl}_3\text{Sb-Cl-SbCl}_3^-$$

(I)

this exchange, as discussed above, being rapid. A similar, uncharged, transition state involving Sb(III) only, is equally feasible in the present system for exchange of SbCl$_3^{36}$ with the equilibrated reactants:

$$\text{Me}_3\text{SiCl: Sb-Cl: SbCl}_3^-$$

(II)

and would be consistent with the experimental observations. Configurations similar to (I) are suggested for antimony atom exchange between antimony tri- and pentachlorides in carbon tetrachloride.$^{45}$

No effect on the exchange behaviour was observed when benzene in two fold excess of that required for the formation of 2SbCl$_3$.C$_6$H$_6$
was equilibrated with antimony trichloride in hexane before addition of an excess of trimethylchlorosilane (experiment 9). It is possible that a longer equilibration time might have led to compound formation between antimony trichloride and the benzene, as freezing point studies indicate that such a compound exists in carbon disulphide solution\(^5\). However ether added to antimony trichloride in benzene gave no indication in the freezing point behaviour of the system of the existence of a compound between the first two\(^9\), although electrolysis studies have shown that some form of ionic complex exists between antimony trichloride and ether in the latter as solvent\(^7\).

ii. Reaction in benzene solution.

As noted (5.a.ii), the results obtained in this solvent were complex, both in individual experiments and in the concentration dependences observed, whereas in hexane all exchange curves, although non-linear, were similar, and initial slopes gave a bimolecular rate dependence. This increased complexity compared with the hexane system can only be ascribed to the formation of relatively stable compounds between the solvent and one or both of the reactants, but presumably with antimony trichloride, as a large amount of evidence exists for its interaction or compound formation with a variety of solvents (including benzene) as discussed in the introduction and below. Little evidence exists for such compounds with trimethylchlorosilane, which in many respects would be expected to behave like an alkyl halide in its solvent interactions. In a freezing point composition study of trimethylchlorosilane in ether no evidence was
found for compound formation, though weak compound formation was indicated for dimethyldichlorosilane\textsuperscript{91}. The ultraviolet spectra of pyridine and p-toluidine in triethylfluorosilane and a variety of organosilicon compounds\textsuperscript{12} gives no evidence of compound formation, although there are a number of addition compounds known between silicon tetrahalides and halogenosilanes with bases, notably trimethylamine\textsuperscript{10,12}, and a compound exists between silicon tetrabromide and dioxane\textsuperscript{92}.

As stated in the introduction, antimony trichloride forms a large number of crystalline addition compounds with aromatic compounds\textsuperscript{22,24}, some of which persist, as is shown by conductance studies, in the solvents at relatively high temperatures\textsuperscript{80}, or are unchanged on melting\textsuperscript{93}. Viscosity\textsuperscript{57} and infra-red\textsuperscript{55} data show that some kind of partially dissociated compound persists in liquid benzene; this is, of course, most likely to be the compound stable in the crystalline form, \(2\text{SbCl}_3\cdot\text{C}_6\text{H}_6\). This compound has been shown by dissociation pressure measurements\textsuperscript{56} to have an energy of formation of 12 Kcals, although the large positive entropy of formation associated with such a compound would reduce its free energy of formation in liquid benzene. It has been shown that the compound persists in carbon disulphide solution, and that under certain conditions of concentration, antimony trichloride can act as a Freidel-Crafts catalyst in aromatic solutions, including benzene, a role which demands that the antimony trichloride molecule be free and not bound up in an addition compound\textsuperscript{76}. Under most conditions it is inactive, presumably due to at least partial persistence of the addition compound in liquid benzene. It is of interest that
the structure of the benzene - antimony trichloride complex, as indicated by the infra-red data\textsuperscript{56}, is probably not monomeric, but that the antimony atoms lie out of the plane of the benzene molecules, a likely structure being

\[ \text{Cl}_3\text{Sb} \quad \text{Cl}_3\text{Sb} \quad \text{Cl}_3\text{Sb} \quad \text{Cl}_3\text{Sb} \]

This allows the formation of polymeric chains of varying lengths, and constitutes, most probably, partial persistence of the crystalline lattice structure in the liquid phase.

Taking the present data at its face value, it would appear that at low concentration (0.01 M) the reactants are relatively free, and reaction rapid. As the antimony trichloride concentration increases, complex formation occurring between antimony trichloride and benzene slows the reaction; between sets 4 and 5, with a 10 fold antimony trichloride concentration increase, the rate remains much the same, although direct dilution of the reaction solution used in set 5 slows the initial rate as calculated for a bimolecular reaction (table 17), but with increased exchange rate with time of contact of reactants, presumably as the diluted complex dissociates or an antimony trichloride-trimethylchlorosilane species forms, or both. Superimposed on this concentration dependence pattern, as least at 25\textdegree, is an increased exchange rate with time of contact for given initial concentrations, similar to that observed in hexane solution, but possibly in benzene due also to disociation of an antimony trichloride complex.
on dilution. At 40° the results are anomalous in that exchange slows as time of contact increases, until at 70% exchange it is approximately a tenth of the initial rate. This is the normal behaviour of an exchange system in which the exchanging atoms or groups exist, from the beginning of the exchange reaction, in more than one stable environment in one of the reactants. This behaviour is most probably due to antimony trichloride-benzene compound formation, as the antimony trichloride-trimethylchlorosilane species cannot form until after the reactants are mixed, and from the behaviour of the system in hexane, formation of the latter species leads to faster exchange. These sets (1 and 2) of experiments at 40° indicate that a substantial fraction (of the order of 20% to 30%) of the antimony trichloride in benzene solution is present as a compound with solvent molecules, and that this compound is substantially undissociated during more than 12 hours. The complicated concentration dependence of the exchange rate at 25° confirms the existence of such a compound, but the form of the exchange curves indicates that at this temperature benzene compound formation is displaced in favour of that with trimethylchlorosilane.

The results are, however, certainly complicated by such effects as re-establishment of equilibria after freezing of solutions for outgassing (3.e.i.), and on mixing of antimony trichloride solutions in benzene. Such effects are probably responsible for the rather erratic behaviour of the system (tables 4 to 8) indicated by the scatter of points in figure 3. To establish the real behaviour of the system in benzene the experiments would have to be very
differently designed; for example the antimony trichloride-benzene solution would have to be equilibrated at the reaction temperature before mixing with pure trimethylchlorosilane, and equilibration of silane, antimony trichloride and benzene performed before the addition of a small further amount of labelled silane or antimony trichloride. Until the hexane system is thoroughly elucidated the benzene system is probably not worth further study, and in any case the effect of benzene-antimony trichloride compound formation on the exchange behaviour of the latter would be better studied with exchange reactants unlikely themselves to form addition compounds with antimony trichloride, and which would exchange at faster rates than in the present system, so that exchange between free and bound antimony trichloride species could be distinguished.

Since benzene is a solvent of by no means negligible nucleophilic power, the activation energy of 25 Kcals calculated for the reaction in benzene (5.d.ii) compares reasonably with the value of 18.6 Kcals observed for hexane solution. Displacement of benzene molecules oriented by the polar molecules Me₃SiCl and SbCl₃ would be expected to add significantly to the energy required for reaction in benzene as compared with hexane.

(b) Possible exchange mechanisms is hexane solution.

It would appear that the most likely exchange process for the direct exchange at least, involves some form of transition state complex between the undissociated molecules. If the limiting process in the exchange was the formation of an addition compound between the reactants, the initial rates of exchange ought to depend on the
product of the reactant concentrations, and not their sum, as was observed. However it is possible that a configuration allowing exchange is the one which leads, but not necessarily with the same efficiency, to the formation of the addition compound.

The non-conductance of antimony trichloride in benzene and hexane solutions, and that of trimethylchlorosilane in ordinary solvents [94], shows that there are no finite concentrations of ions in the reaction solutions, although reaction processes involving the transitory formation of ionic species are not entirely excluded on these grounds. However the bimolecular rate dependence over the range of concentrations studied excludes ionic disociation as a rate forming step in the reaction process.

In the exchange of antimony ions between antimony trichloride and antimony pentachloride in carbon tetrachloride [45], and in hydrochloric acid solution [89], covalent mechanisms with respect to antimony trichloride have been demonstrated, and antimony trichloride acts as a catalyst in numerous reactions (See Chemical Abstracts) where presumably the particular dimensions and co-ordinating power of the molecule constitute its catalytic properties. Antimony of course forms a large number of covalent organo-antimony compounds, and the formation of aromatic antimony compounds via reaction of antimony trichloride with diazonium or hydrazine compounds, for example, has been shown to proceed by preliminary co-ordination of the halogen of the diazonium compound to antimony [95].

All reported mechanisms of substitution on silicon occur either by means of direct nucleophilic substitution on silicon in the un-
disociated molecule, as in the reaction of tri-isopropylchlorosilane with alcohols and water\textsuperscript{1}, and the alkali-catalysed cleavage of benzyltrimethylsilanes\textsuperscript{96}, or by electrophilic attack on the atom or group attached to silicon which is being replaced, as in the reactions of trimethylhalogenosilanes with methylmagnesium halides\textsuperscript{6}, the reaction of triethylfluorosilane with aluminium iodide\textsuperscript{20} (see introduction) and the reaction of trialkylsilanes with iodine\textsuperscript{97}, or both, as in the reaction of trialkylsilanes with silver perchlorate in various solvents\textsuperscript{98}, and the acidic hydrolysis of organosilicon hydrides\textsuperscript{99}. No mechanism appears to have been substantiated in which positively charged organosilicon ions are reaction intermediates, and it is likely that where such entities are suggested, that at most partial charge separation occurs in the activated complex, since the energies required for such ionizations in solvents of low polarity are exorbitant\textsuperscript{68}.

By comparison the reactions, and in particular the isotopic exchange reactions, of the corresponding carbon halogen compounds (for example tertiary butyl bromide, the carbon analogue of trimethylbromosilane) often occur by mechanisms contributed to by a first order dissociation process. In the isotopic exchange of bromine atoms between lithium bromide and tertiary butyl bromide\textsuperscript{26}, the contributions of first and second order processes are about equal.

While the behavior of the antimony trichloride - trimethylchlorosilane exchange in hexane is fully consistent with a covalent mechanism involving co-ordination of the halogen of the silane to antimony, as suggested in the introduction and in accord with the kinds of mechanisms discussed above, (6.a.i), similar studies would have to be made with
other triorgano- or substituted triorganohalogenosilanes, and the variation of rate and activation energy compared from compound to compound.

The most likely mechanism of exchange is a concerted rearrangement involving a 4-centre transition state of the form

\[ \text{Me}_3\text{Si} \cdots \text{Cl} \]
\[ \text{Cl} \cdots \text{SbCl}_2 \]

which allows tetrahedral disposition of the chlorine atoms about antimony, and involves 5-co-ordination to silicon during the rearrangement. Compensation of charge and numbers of electrons would mean that the effect of a chloromethyl group, say, replacing a methyl group would have no marked effect on the process, as for the corresponding mechanism in the trimethylhalogenosilane-methylmagnesium halide reaction\(^6\), which was also substantiated by reactions with phenyldimethylchlorosilane and p-tolylidimethylchlorosilane. Such tests would distinguish the proposed mechanism from one involving direct nucleophilic attack on silicon. If the compound formed between the present reactants is as suggested in formula II, 6.a.i, then labelled trimethylchlorosilane added in further small amounts to an equilibrated equimolar solution of the reactants in hexane, would be expected to exchange chlorine atoms only very slowly with antimony trichloride, as the co-ordinating positions of the latter molecules would already be occupied.
The order of reaction after pre-equilibration of the unlabelled reactants should also give a useful indication of the kind of interaction occurring between the reactants, and therefore the likely reaction path. Immediate possibilities to check would be whether the reaction was "bimolecular" with respect to the assumed addition compound and excess of antimony trichloride, and whether, as could well be the case, the reaction was first order with respect to the addition compound in the presence of excess trimethylchlorosilane. A "bimolecular" rate for the latter circumstance would almost certainly be different from that for excess antimony trichloride.

(c) Suggested Further Studies

Experiments to elucidate the present mechanism have been suggested in the discussion above, and would mainly comprise investigation of the exchange after equilibration of the inactive reactants, and the use of various substituents in place of methyl groups in trimethylchlorosilane.

It would be of interest to determine the freezing point-composition diagram for antimony trichloride-trimethylchlorosilane, to find whether compound formation occurred under such circumstances; these experiments would have to be made under pressure, as the melting point of antimony trichloride is 73° and the boiling point of trimethylchlorosilane is 57°.

The systems discussed in the introduction remain of interest, and probably the two most rewarding studies would be those of the exchange of bromine atoms between magnesium bromide and trimethylbromosilane, and of chlorine atoms between aluminium chloride and
trimethylchlorosilane.

The methods developed in the present studies are directly applicable to such systems, and as discussed in 2.b.v., the separation method is applicable to any liquid phase reaction system comprised of a volatile and an involatile reactant in the presence or absence of a solvent. The reaction need not necessarily be an isotopic exchange, provided it is not too rapid; for example the kinetics of the reaction between magnesium bromide and trimethyliodosilane could be followed by separating the reactants using the evaporation method, and determining the amounts of iodide and bromide present in the magnesium and organosilane fractions, (although this particular reaction could probably be more readily studied using dioxane precipitation of the magnesium halides).
7. SUMMARY

Isotopic halogen atom exchange has been found to occur between trimethylbromosilane and trimethylchlorosilane and the corresponding halides of aluminium, antimony and magnesium, in benzene or ether solution, and between trimethylchlorosilane and the reactants aluminium chloride, antimony trichloride, and hydrogen chloride in the absence of a solvent. The kinetics of the exchange between antimony trichloride and trimethylchlorosilane in benzene and hexane were studied over a range of temperatures and concentrations, and found to be initially bimolecular in hexane, and probably so in benzene also. The kinetics are complicated in hexane by the formation of a species allowing more rapid exchange with increasing contact time of the reactants, and further complicated in benzene by interaction of antimony trichloride with the solvent. The data are consistent with formation of an addition compound between the reactants which allows faster internal exchange than occurs between the free reactants, and exchanges rapidly with free antimony trichloride by a mechanism similar to that proposed for antimony atom exchange between antimony trichloride and pentachloride.

The reactant separation developed, rapid evaporation from a stirred, outgassed solution held under its own vapour pressure, is of general applicability to reaction systems containing a volatile and involatile reactant.
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The diameter of the circles locating the experimental points in the exchange curves show the estimated limits of error for $F = 0.50$. 
Figure 1

**SbCl₃ SOLUTION STORAGE AND DELIVERY**

A  Glass enclosed striker for adjacent break seal

B  Storage volume

C  Self-levelling burette

D  Seal-off constriction, connecting also to benzene storage vessel

E  Three-way stopcock

F  Nitrogen inlet

G  Pressure release exit
Figure 1

SbCl₃ SOLUTION STORAGE AND DELIVERY
Figure 2

SINGLE SAMPLE REACTION VESSEL

A  Glass plunger
B  Precision bore tubing, 11 mm
C  Sliding O-ring seal
D  Connection to separation line
E  Upper solution compartment
F  Thin glass bulb
G  Reaction compartment
H  Magnetic stirrer
Figure 2

SINGLE SAMPLE REACTION VESSEL
Figure 3

REACTION AND SEPARATION VESSELS

A  SbCl₃ solution storage bulb, 50 ml

B  Mixing and reaction bulb

C  Guard tube

G  Greaseless glass stopcock.
   (Racking mechanism for moving neoprene
diaphragm is not shown)

J  Thermostat bath base, with O-ring seals

K  Evaporation compartment

L  Magnetic stirrer

M  Coarse glass sinter

N  Fine glass sinter

P  Pressure tubing connection to separation line

S  Glass enclosed striker for adjacent break seal
Figure 3
REACTION AND SEPARATION VESSELS

Neoprene
Polythene

A
B
C
S
G
J
K
L
M
P
N
Figure 4

SEPARATION LINE

N Nitrogen inlet

S Glass sinter

V To vacuum manifold via a liquid air trap

Figure 5

TOTAL ANALYSIS SAMPLE VESSEL

A Seal off constriction

B Graduated 4 mm precision bore tubing

C Six ml sample volume
Figure 4 SEPARATION LINE

Figure 5 TOTAL ANALYSIS
SAMPLE VESSEL
Figure 6. Potentiometric titration curves.
Figure 7. Exchange in benzene at 40°.

Data from Table 5.
Figure 8. Exchange in benzene at $25^\circ$.

Data from Tables 6, 7, 8.
Figure 9. Exchange in hexane at 40°.

Data from Tables 10, 11.
Figure 10. Exchange in hexane at 30°.

Data from Tables 12, 14.
Figure 11. Exchange in hexane at 20°.

Data from Table 15.
Figure 12. Exchange in hexane at 30° and 20° (Tables 12, 15) showing corrected and uncorrected curves (2.b.iv; 4.a.iii; 5.b.ii).
Figure 13. Temperature dependence of bimolecular rate constants for exchange in hexane (Table 16).
A. F. Reid:
Micro-Potentiometric Determination of Periodate by Arsenite-Iodine Titration
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Micro-Potentiometric Determination of Periodate by Arsenite-Iodine Titration

By A. F. Reid

(Received September 3, 1957)

Periodate oxidations find wide application to the estimation of α-glycol and similar groups. A recent survey including methods of periodate estimation has been given by Dyer. Periodate solutions in the M/100 concentration range can readily be standardized by the method of Fleury and Lange, or modifications of it, in which periodate in sodium bicarbonate solution is reduced to iodate with excess arsenite, potassium iodide being added to catalyse the reaction. The excess arsenite is titrated with standard iodine solution, starch being used as an indicator. Burmaster has used the method to determine amounts of periodate down to 2.5 micromoles, in a study of the oxidation of α-glycerophosphate. Alternatively, potassium iodide may be added to the buffered periodate and the liberated iodine titrated with arsenite. This method gives accurate results in the M/100 region (Hartman) and has been used by Long and Maguire for the estimation of fractions of a ml of 0.01 M periodate. Dyer, however, does not recommend this method for general application because of the oxidising properties of iodine in bicarbonate solution, and because the slow release of iodine at low periodate concentrations might lead to loss of iodine from the aqueous solutions. This slow reaction precludes the use of the method in kinetic studies of short duration, and also the potentiometric titration of periodate with potassium iodide. By following the iodine-arsenite titration potentiometrically the Fleury-Lange procedure can be extended to the estimation of 0.5 micromoles of periodate with 1% precision, and 0.05 micromoles within 3%, as indicated in Table I. Since it is the difference in the amounts of periodate in a sample and a control which is used to estimate the amount of oxidation occurring in the sample, it is the precision of the periodate determinations under replicate conditions which will fix the accuracy of this estimation, and systematic errors should cancel.

Table I. Periodate Determinations

<table>
<thead>
<tr>
<th>Concentrations*</th>
<th>KIO₄ μmoles</th>
<th>% Differences</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>KIO₄ stock</td>
<td>I₂ μequiv./ml</td>
</tr>
<tr>
<td>10</td>
<td>0.66</td>
<td>5.00</td>
</tr>
<tr>
<td>10</td>
<td>0.14</td>
<td>1.96</td>
</tr>
<tr>
<td>10</td>
<td>0.14</td>
<td>0.985</td>
</tr>
<tr>
<td>**</td>
<td>0.66</td>
<td>1.20</td>
</tr>
<tr>
<td>1</td>
<td>0.62</td>
<td>3.03</td>
</tr>
<tr>
<td>1</td>
<td>0.63</td>
<td>3.03***</td>
</tr>
<tr>
<td>1</td>
<td>0.63</td>
<td>1.04</td>
</tr>
<tr>
<td>1</td>
<td>0.12</td>
<td>0.502</td>
</tr>
<tr>
<td>1</td>
<td>0.12</td>
<td>0.197</td>
</tr>
<tr>
<td>0.17</td>
<td>0.67</td>
<td>0.170</td>
</tr>
<tr>
<td>0.17</td>
<td>0.02</td>
<td>0.033</td>
</tr>
<tr>
<td>0.1</td>
<td>0.02</td>
<td>0.00096</td>
</tr>
</tbody>
</table>

* Approximate values only.
** 0.5 ml taken from a solution containing 5 ml of 0.01 M KIO₄, 10 ml of NaHCO₃, 5 ml of 0.025 N arsenite and 1 ml of 20% KI.
*** Double the amount of NaHCO₃ and KI used for these samples as compared with the previous pair.

Below one micromole it was not possible to avoid systematic errors apparently mainly due to loss of periodate. Higher losses occurred when aliquots of periodate were taken from diluted solutions rather than from M/100 stock solution, and use of ordinary distilled water increased this loss. Since the oxidation potential of the periodate-iodate couple in acid or alkaline media is considerably higher than that of the arsenate-arsenite couple, it can be calculated that the amount of periodate which has not reacted in the presence of excess arsenite should
be negligible at the concentrations used in the present work. It appears that the low values for the periodate determinations are not due to incomplete reaction since a number of the duplicates were left in the dark for periods of up to forty minutes before titration with iodine. The high precision of the arsenite-iodine titrations together with the above considerations make it highly probable that the low values obtained are due to systematic loss. While all periodate solutions were kept in dark bottles and stored in the dark, transfers and dilutions were made, with minimum delay, in ordinary light, avoiding direct sunlight.

Titration of arsenite with iodine at various appropriate dilutions was found to give iodine titres within 0.4% of those required (4 ml) down to 0.0001 N, provided that the titrant solutions contained 1% potassium iodide at the equivalence point. The presence of up to 20 micromoles of potassium iodate did not affect the titre required. Since it was desired to determine periodate in an in vitro biological system titrations were made in the presence of a biological diluent containing small amounts of inorganic salts, glucose, gelatine, chloramphenicol and phenol red. Approximately 0.1 ml of 0.00013 N iodine solution was consumed by 1 ml of the diluent, but otherwise the end point remained unaltered.

### Table II. Arsenite-Iodine Titrations in Sodium Bicarbonate Solution

<table>
<thead>
<tr>
<th>Dilution factor</th>
<th>Iodine Normality</th>
<th>Arsenite Normality</th>
<th>ml I₂ for 1.000 ml of arsenite</th>
<th>Potential change at equivalence</th>
<th>Expect</th>
<th>Observe</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.01673</td>
<td>1</td>
<td>0.0278</td>
<td>8.28</td>
<td>8.26*</td>
<td>8.25*</td>
</tr>
<tr>
<td>25</td>
<td>0.000670</td>
<td>5</td>
<td>0.00556</td>
<td>4.14</td>
<td>4.13</td>
<td>4.12</td>
</tr>
<tr>
<td>125</td>
<td>0.000134</td>
<td>10</td>
<td>0.00278</td>
<td>4.14</td>
<td>4.15</td>
<td>4.16**</td>
</tr>
<tr>
<td>750</td>
<td>0.0000022</td>
<td>50</td>
<td>0.000556</td>
<td>4.14</td>
<td>4.16**</td>
<td>4.16**</td>
</tr>
</tbody>
</table>

* 5 ml added by calibrated pipette.
** In the presence of 20 μmole of iodate.

### Experimental

A conventional potentiometric titration arrangement was used, with a bright platinum electrode and a salt bridge, connecting to a mercury-mercurous chloride reference electrode, dipping into the stirred solution contained in a 20-ml beaker. The 5-ml burette used was graduated in 0.01 ml divisions. All pipettes were treated with a silicone water repellant to give complete drainage. 0.1-ml to 0.5-ml pipettes thus treated could be used to give successive deliveries within 0.0005 ml, and 1-ml to 10-ml pipettes to within 0.1%.

Sodium arsenite in bicarbonate buffer was used as primary standard, and 0.01 N iodine solution and 0.01 M potassium periodate in 0.9% sodium chloride solution were standardized against it. When the latter solution was stored in the dark, its concentration did not change within 0.2% over periods of a week, in accordance with the observations of Head and Hughes. The solutions listed were diluted with 0.2 M sodium bicarbonate, 1% potassium iodide, and 0.9% sodium chloride solutions respectively. For the results given in Table II, all solutions were made up with conductivity water.

Aliquots of periodate were pipetted into 1 or 2 ml of 1 M bicarbonate solution in the titration vessel, followed by appropriate amounts of arsenite and 20% potassium iodide solutions in that order. The concentrations of bicarbonate and iodide at the equivalence point were kept at least 0.2 M and 1% respectively. Where the amount of iodine solution required for excess arsenite was more than 5 ml, an appropriate amount was added by pipette. The dilute iodine solutions used were standardized within a few hours of use, and stored in the dark. The concentration of 0.0001 N iodine solutions did not change by more than 0.5% in this time, the precaution being taken of refilling the burette between determinations with solution freshly poured from a large volume (300–400 ml) kept in a tightly stoppered bottle.

It was found essential to have the platinum electrode thoroughly clean. Before each titration it was washed, and then dipped at red heat into fresh aqua regia, being finally washed in distilled water.

### Summary

The Fleury-Lange method for the estimation of periodate can be extended to samples containing less than 0.05 micromoles by potentiometric titration of the excess arsenite with dilute iodine solution. Iodine solutions down to 0.0001 N can be titrated with 0.4% accuracy.

### Zusammenfassung

Die Methode von Fleury und Lange zur Bestimmung von Perjodat kann auf Proben, die weniger als 0,05 Mikromol enthalten, durch potentiometrische Titration des überschüssigen Arsenits mit einer verd. Jodlösung erweitert werden. Bis 0,0001-n Jodlösungen lassen sich mit 0,4% Genauigkeit titrieren.
Résumé

La méthode de Fleury et Lange pour l’estimation du periodate peut être étendue aux échantillons contenant moins de 0,05 micromoles par le titrage potentiométrique de l’excès d’arséniure avec une solution d’iode diluée. Des solutions d’iode jusqu’à 0,0001 N peuvent être titrées avec une précision de 0,4%.

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THE NEUTRALIZATION OF ANIMAL VIRUSES
I. A MODEL OF VIRUS-ANTIBODY INTERACTION

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Received for publication September 17, 1957

In their recent paper, Dulbecco, Vogt and Strickland (1) have advanced a new theory to account for the kinetics of virus-antibody interaction. The novelty of the theory lies in its rejection of the view, commonly held since the classical studies of Burnet, Keogh and Lush (2), that dissociation of antigen-antibody complexes is of practical importance; and in postulating a "persistent fraction" of virus which cannot be neutralized by antibody.

The former runs counter to experience with other viruses and their antibodies, adequately interpreted in statistico-kinetic terms, that is, by assuming a dissociable virus-antibody complex. The latter would suggest, among other things, that infection by these viruses (Western equine encephalitis and poliomyelitis) can be neither prevented nor stopped by immunological means—a conclusion difficult to reconcile with the fact that neither disease is invariably fatal, that both leave behind lifelong immunity, and that vaccination has been signally successful in preventing them.

Since, after all, prevention of disease is still a legitimate subject for immunologic inquiry, we propose to reinvestigate the processes leading to neutralization of viral infectivity. The first paper of the series, normative, will develop a model and, taking into account the peculiarities of assay techniques, translate it into operational terms. The second, polemic, will use the data of Dulbecco et al. to decide between the two hypotheses. The rest, experimental, will present new evidence on the neutralization process and new methods to study some of its details.

1. THE INTERACTION OF VIRUS AND ANTIBODY

1.1. General assumptions

1.1.1. The conditions of virus-antibody interaction. Consider the system $V$ virus particles and $A$ antibody molecules per unit volume. Antibody is specifically directed against the antigenic sites on the virus surface, but to combine the 2 particles they have to collide first. The number of collisions is given by the Trautz equation (3),

$$v_{zA} = V A (r_r + r_A)^2 \sqrt{8 \kappa T \left( \frac{1}{m_v} + \frac{1}{m_A} \right)}$$

where $v_{zA}$ is the number of collisions/cm$^3$/sec between the 2 types of particles, $V$ and $A$ are their concentrations, $r$ and $m$ the radius and mass of the respective particle indicated by the subscript, $k$ is the Boltzmann constant, and $T$ the temperature in K$^\circ$.

Of these collisions only a fraction $f$ will be sterically correct, i.e., occur between the specific combining area (site) of the virus and a properly orientated antibody molecule. Thus the product $v_{zA} \cdot f$ will give the number of collisions that could lead to union. However only those combinations possessing energy $\geq \varepsilon$ will form a virus-antibody complex.

1 We choose here to discuss the process in terms of the collision theory, $f$ being the frequency (or steric) factor as usually understood in that theory. In absolute rate theory the concept $f$ is replaced by that of entropy of activation, the entropy term entering the rate equation in the form $e^{S/k}$, analogous to that for energy of activation. $S$ is now the measure of the restriction of configuration, including localization of bond energies, occurring when the reacting molecular complex passes through its most restricted form.

For a reaction involving large molecules which form simple addition complexes the main contribution to the entropy term will come from the loss of translational and rotational degrees of freedom, and hence steric orientation considerations are a good approximation to the more sophisticated theory. In either case, the rate equation parameters have to be determined empirically from the variation of reaction rate with temperature and concentration.
1.12. Association of virus and antibody. Whereas collisions occur between virus and antibody, the reaction proper concerns the antigenic sites, here assumed to be $s$ in number per virus particle. Thus, while the number of virus particles remains constant, the number of free sites and free antibody molecules will each decrease by one for each effective collision. After $y$ antigen-antibody complexes have been formed the concentration of free antibody will be $(A - y)$, the concentration of colliding virus remains constant, we may write

$$\frac{dy}{dt} = \frac{k_y}{s} (sV - y)(A - y) - k_y y.$$  

(1.12a)

As an example, consider the dissociation of antigen-antibody complexes. From the Maxwell-Boltzmann distribution the concentration of these molecules equals $y e^{-\frac{y}{kT}}$. Hence the rate of decrease in the number of bound molecules is

$$\frac{dy}{dt} = a y e^{-\frac{y}{kT}}.$$  

(1.13a)

as the energy term remains constant unless the temperature changes. Thus dissociation will be kinetically of the first order.

1.2. The basic model

1.21. Equilibrium of the virus-antibody system. If in a system both association and dissociation are operating under the mechanisms defined in 1.12 and 1.13, the rate of change in the number of virus-antibody complexes per unit volume is their net effect. It is therefore given by

$$\frac{dy}{dt} = \frac{k_y}{s} (sV - y)(A - y) - k_y y.$$  

(1.12a)

At equilibrium, that is, when the rate of association and dissociation is the same, there will be no overall change in the fraction combined. If $y$ is the number of bound antibody molecules at equilibrium, then, putting $dy/dt = 0$ in 1.12a, it is seen that

$$k_y = \frac{y}{s} (sV - y)(A - y).$$  

(1.21b)

1.22. Kinetics of virus-antibody interaction. The approach to the equilibrium state is governed by 1.21a. Experiments are usually so arranged that initially (at time zero) there is only free virus and free antibody in the system, i.e., $y(t_0) = 0$. More generally let the concentration of antigen-antibody complex be $y(t_0) = 0$ at time $t_0$, so that then the concentration of free sites is $(sV - y(t_0))$, and of free antibody is $(A - y(t_0))$. To obtain the concentration of antibody bound at sites to a later time $t$, Equation 1.21a has to be integrated over the time interval $(t_0, t)$, during which time the concentration of bound antibody changes from $y(t_0)$ to $y(t)$. Thus,

$$\int_{t_0}^{t} \frac{dy}{dt} dt = \int_{t_0}^{t} \frac{k_y}{s} (sV - y)(A - y) dt.$$  

(1.22a)

To bring the left side of 1.22a into a form that can be integrated, the integral is first factorized and then expressed in partial fractions, giving

$$\int_{t_0}^{t} \frac{dy}{(sV - y)(A - y)} = \int_{t_0}^{t} \frac{1}{sV + A + \frac{1}{K}} dy.$$  

(1.22b)

where $a$ and $b$ are the roots of the quadratic equation obtained by putting the denominator in 1.22b equal to zero, i.e.,

$$a, b = \frac{1}{2} \left( sV + A + \frac{1}{K} \right) \pm \sqrt{\left( sV + A + \frac{1}{K} \right)^2 - 4saV}.$$  

(1.22c)

This also leads to the concentration of antigen-antibody complex in the equilibrium state, $y_e$, which is given by the smaller root.

Carrying out the integrations, we obtain

$$\frac{1}{b - a} \left( \ln y(t) - b - \ln y(t_0) - a \right)$$  

(1.22f)

or

$$\frac{y(t) - a}{y(t) - b} - \frac{y(t_0) - a}{y(t_0) - b} = \exp \left( \frac{b - a}{b - a} (t - t_0) \right).$$  

(1.22g)

and hence

$$b(y(t) - a) - a(b - y(t))$$  

(1.22h)

It may be seen that $y_e = y(t_e)$.  

1.3. Alterations of the basic system

Any quantitative change in the above system, either when in equilibrium or in an intermediate state, will result in a new equilibrium which will be approached at a new rate. The possible ways of altering isochoric and isothermic systems (i.e., where molar volume and temperature are not varied) will be dealt with below, always by giving the initial conditions first, then defining the equilibrium state, and finally the kinetics of the reaction leading to it.

1.31. Effect of dilution. The simplest case: the absolute amount of reagents remains constant but their concentration is altered by a factor $\delta$. In practice this factor is usually $<1$; however, it could be $>1$, i.e., the system would then be concentrated. The initial concentrations at time $t_0$ are $[sV, A, y(t_0)]$. By substituting these in 1.21b, the new equilibrium value of $y(t_e)$ satisfies

$$K = \frac{y(t_e)}{y(t_0)}.$$  

(1.31a)

By similarly substituting into Equation 1.22b we can determine the intermediate state at time $t$

$$\left( \beta y(t) - a \right) + \alpha \left( \beta - b y(t) \right)$$  

(1.31b)

The constants $\alpha$ and $\beta$ are the roots of 1.31a regarded as a quadratic equation in $y$.  

1.32. Effect of competition. By adding further quantities of one or more of the components to the system, the established equilibrium can be shifted. If these new additions are of the same kind as those brought together first, the rate constants and hence the equilibrium constant $K$ will remain unaltered, and such a system shall be called isocompetitive. If the added reagents are of a different kind but show the same kinetics of interation, two similar equilibria must be simultaneously satisfied, and such a system is homocompetitive. Heterocompetitive systems, in which reactions proceed by different routes are not known for virus-antibody interactions, and will not be dealt with.

1.33. Inooperation. Suppose that 2 systems are combined at time $t_0$. If the systems are represented by $[V_1, A_1, y_1(t)]$ and $[V_2, A_2, y_2(t)]$, then after they are mixed together the total virus present is $V_1 + V_2 = V$, the total antibody is $A_1 + A_2 = A$ for which $y_1(t_0) + y_2(t_0)$ are initially bound to virus. Let $y(t_0), y(t)$ be the concentration of occupied sites at some later time $t$, and write $x(t) = y_2(t) + y_1(t)$. When the system has reached equilibrium ($t = t_e$), the concentration of bound antibody will have changed from $x(t_0)$ to $x(t_e)$, the smaller root of the equation

$$K = \frac{y(t_e)}{y(t_0)}.$$  

(1.32a)

The kinetics cannot be described by simple substitution into one of the equations derived above since we have two simultaneous reactions.
The constants 

\[ 2 \text{ roots of } 1.321d, \text{ solved for } \]

Hence

\[ \beta \]

by the same methods which were used for 1.22a, we find

\[ \frac{1}{\beta - \alpha} \ln \frac{z(t) - \beta}{z(t) - \alpha} = \frac{k_s}{s} t, \]

or

\[ \frac{z(t) - \beta}{z(t) - \alpha} = \exp \left( \frac{k_s}{s} t \right). \]

Hence

\[ \beta z(t) - \alpha + \alpha z(t) = \frac{(\beta - \alpha) k_s}{s} t. \]

The solution for \( y_2 \) from the second equation of 1.321b is analogous.

1.322. Homocompetition. As in the incomplete system, at the time of adding the new reagents (t = 0) we have \( \{V_1, A_1, y(t_0)\} \) of the original components, and \( \{V_s, A_s, y(t_0)\} \) of the new components. However, the original equilibrium is characterized by the constant

\[ K_1 = \frac{k_0}{s} k_1, \]

and the added system by

\[ K_2 = \frac{k_0}{s} k_2. \]

In the final state (t = \( \infty \)) these equilibria must be satisfied simultaneously, so that we have

\[ y_1 = \left( \frac{y_1}{y_1} \right) \frac{(K_1 + A_1) y_1 - (y_1 + K_1 A_1)}{(y_1 + K_1 A_1)}, \]

\[ y_2 = \left( \frac{y_2}{y_2} \right) \frac{(K_2 + A_2) y_2 - (y_2 + K_2 A_2)}{(y_2 + K_2 A_2)}. \]

By rearranging and expressing the total concentrations as in 1.321 (viz., \( A_1 + A_2 = A \tau \)), we have

\[ y_1 = \frac{y_1 + K_1 A_1}{y_1 + K_1 A_1}, \]

\[ y_2 = \frac{y_2 + K_2 A_2}{y_2 + K_2 A_2}. \]

and then by adding these two equations and rearranging in powers of \( x \), the cubic equation 1.322c is obtained,

\[ x^3 - \left[ 2A + x + \frac{1}{K_1} + \frac{1}{K_2} \right] x^2 + \left[ \frac{1}{K_1} + \frac{1}{K_2} \right] x - A = 0. \]

where we have written \( A \tau = a_1 V_1 + a_2 V_2 \).

If numerical solution shows that the values of \( x \) at \( t = 0 \) and \( t = \infty \) are close, the Bodenstein treatment can be used to find \( y_1 \) and \( y_2 \) for any required point in time. Equation 1.331h applies here too; in this case, of course, not only the parameters but also the constants will be different when calculating \( y_1 \) and \( y_2 \).

2. THE CONDITIONS OF ASSAY

At the present level of knowledge, none of the components in the reactions discussed above can be tested directly by physical methods. It is by their biological properties that infective virus and antibody can be detected. This forced choice of assay is a source of uncertainty, since the mechanism of infectivity and its prevention is scarcely understood. As a consequence, in the following sections several alternatives will be considered side by side, and it is only by experiment that the inapplicable can be rejected.

2.1. Neutralization of infectivity

As the basic example take the system of \( V \) virus particles and \( A \) antibody molecules of which at equilibrium \( y \) are combined with antigenic sites on the viruses. Let the distribution of antibody be at random; in particular, this is to mean that the chance of an antibody molecule reacting with an antigenic site is independent of what is happening at any other sites.

2.11. Suppose that all sites are equivalent, and that the virus loses its infectivity when at least \( r (r \leq s) \) of its \( s \) sites is occupied.

At equilibrium \( y \) of a\( V \) sites are occupied, thus the average chance of any site being occupied is \( y/V \). Hence, from the binomial distribution, the probability of \( r \) out of \( s \) sites being occupied is

\[ P_r = \frac{s!}{r!} \left( \frac{y}{V} \right)^r \left( 1 - \frac{y}{V} \right)^{s-r}. \]

Thus out of \( V \) particles/system \( P_r \) will be neutralized and \( V(1 - P_r) \) remain infective. (The values of \( P_r \) and \( P_r \) can be found in the appropriate statistical tables.) When \( s \) tends to infinity this binomial distribution tends to the Poisson distribution with mean \( y/V \), so that 2.11b becomes

\[ P_r = \sum \frac{s!}{r!} \left( \frac{y}{V} \right)^r e^{-y/V}. \]

Two special cases need be considered. a) When \( r = 1 \), a single molecule of antibody will neutralize the virus, and the probability that a virus is rendered noninfective is given by

\[ P_1 = 1 - P(0) = \left[ 1 - e^{-y/V} \right] \approx 1 - e^{-y/V}; \]

b) When \( r = s \), all sites have to be filled for the virus to be neutralized, so that the probability of neutralization is given by

\[ P_s = P(s) = \left( \frac{y}{V} \right)^s. \]

2.12. The sites are not assumed to be equivalent: there is a number, \( \epsilon \), of critical sites on each particle through which neutralization can be
effected, while the remaining \((s - c)\) sites bind antibody just as effectively but do not play any part in the neutralization process. The distribution of antibody is random over all sites, and if \(r\) of the critical sites are occupied \((r < c)\), the virus loses its infectivity.

The chance of any site being occupied is \(y/sV\). When there is a large number of sites of which a given fraction \(c/s\) are critical sites, the binomial distribution becomes a Poisson distribution with mean \(cy/sV\), so that 2.12b becomes

\[
P_s = \sum_{r=0}^{\infty} \frac{(cy/sV)^r}{r!}.
\]

The two special cases are analogous to those in 2.11. a) When \(r = 1\)

\[
P_1 = \sum_{i=0}^{s} p_i \left( \frac{y}{sV} \right)^i e^{-y/sV}.
\]

b) When \(r = s\)

\[
P_s = \sum_{i=0}^{s} p_i \left( \frac{y}{sV} \right)^i.
\]

2.14. The number of sites per particle varies, but all have a fixed number, \(c\), of critical sites. Therefore

\[
P(r) = \sum_{i=c}^{s} p_i \left( \frac{y}{sV} \right)^i e^{-y/sV}.
\]

The special cases lead to a)

\[
P_1 = 1 - \sum_{i=0}^{s} p_i \left( \frac{y}{sV} \right)^i e^{-y/sV};
\]

b) When \(r = c\)

\[
P_c = \left( \frac{y}{sV} \right)^c.
\]

2.15. Both the number of sites \(i\) and the number of critical sites \(j\) vary from particle to particle \((0 \leq i \leq s; 0 \leq j \leq i)\). This is the general form, and all the above may be regarded as specially restricted cases of it. Here \(s = \sum_{i=0}^{s} i p_i\) is the mean number of sites where \(p_i\) is the proportion of viruses with \(i\) sites of which \(j\) are critical. Hence

\[
P_i = \sum_{j=0}^{i} p_j \left( \frac{y}{sV} \right)^j e^{-y/sV};
\]

and hence

\[
P_c = \sum_{j=0}^{c} p_j \left( \frac{y}{sV} \right)^j.
\]

2.16. Up till now the distinction between critical and noncritical sites was absolute. Finally let us consider the case where such a distinction does not exist, but a molecule of antibody adsorbed to site \(j\) has the probability \(p_i\) of neutralizing the infectivity of virus through that particular spot. This probability \((0 \leq p_i \leq 1)\) is distributed with the density function \(f(p)\), and has a mean of \(p = \int_0^1 f(p) dp\). The attachment of antibody molecules to any site occurs at random, and is thus governed by the formulae of 2.11. On this model the fraction of virus remaining infective is the expectation

\[
E(P(0) + P(1)(1 - p)) + P(2)(1 - p)(1 - p) + \cdots
\]

b) When \(r = c\)

\[
P_c = \left( \frac{y}{sV} \right)^c.
\]

The fraction neutralized is

\[
P_r = 1 - e^{-y/sV}.
\]

A result analogous to 2.11d since \(p(V)\) will be the mean number of neutralizing antibody-virus unions.

Two special cases are of interest here. a) The probability of neutralization is the same for all sites \((0 \leq p_i = p \leq 1)\). The surviving fraction will be the sum

\[
P(0) + P(1)(1 - p) + P(2)(1 - p)^2 + \cdots
\]

b) The probability is constant for all sites of any one particle, but varies from virus to virus. The surviving fraction here is

\[
\int_0^1 f(p) \left( \frac{sV - y}{sV} \right)^j dp - \int_0^1 e^{-y/sV} f(p) dp.
\]

2.17. The virus population is inhomogeneous: it contains \(V_i\) infective and \(V_n\) noninfective particles/cell, i.e., \(V = V_i + V_n\). Noninfective particles bind antibody in the same way as do infective ones, although the neutralization test concerns the latter only.

Hence the chance of any site being occupied is \(y/sV\), and the calculation of \(P_c\) goes through as in the sections above. The surviving fraction however will be \(V_i(1 - P_c)\) and not \(V(1 - P_c)\).

2.2. Technique

2.21. Types of assay. The fraction of virus that remains infective is \((1 - P_c)\), where the value of \(P_c\) depends on the equilibrium conditions defined in Sections 2.1 and 2.3, as well as on the model of neutralization adopted (Section 2.11). This is the surviving fraction in the test tube where the reagents were originally brought together. However, the number of survivors can be determined only in a system of infectible cells.

An assay is direct if each infective unit of virus causes a distinct lesion in the host tissue. Counting of pocks on membranes or plaques on monolayer tissue cultures makes up this group. In an indirect assay the response shows a continuous gradation, and is usually not linearly related to the dose of virus. It may be read in absolute units (such as survival time or diameter of lesions), or on an arbitrary scale (such as degrees of lung consolidation, paralysis, etc.). Both the direct and indirect methods are quantitative. If the response is all or nothing (such as death or survival; presence or absence of lesions, haemagglutinin, a certain pH, etc.), the assay is quantal.

The accuracy of a single test decreases in the above order. Yet, since the ease of performance and evaluation usually falls in the reverse order, the choice between a few direct tests or a larger set of quantal assays becomes a matter of convenience.

2.22. Preparation of the inoculum. Since with each of these techniques the information is concentrated in a narrow range of the dose-response curve, the reaction mixture of virus and antibody has to be diluted by an appropriate factor, \(\delta\), before inoculation of the host tissue.

In direct assays, 2 conflicting principles govern the choice of this dilution factor. The first tends to increase it, thereby ensuring that pocks or plaques appear in countable numbers and each of them originates from a single infective unit. The second tends to decrease the dilution factor.
in order to reduce the variance of counts which equals the mean number plated, the distribution being Poissonian. The usual compromise is struck at dilution giving about 200 plaques or plaques—a number easily counted and carrying an error of about ±22%. In indirect assays the steepest part of the dose-response curve is chosen, and the accuracy obtainable is a function of this curve. In quantal assays the optimal set of dilutions covers the range between 0 and 0.1 infective units to give maximum information. The accuracy can never be greater than ±d/z/2, where d is the dilution step and n the number of replicates per dilution.

Generally, then, in any one test the aim is to set the dilution factor at 

\[ d = \sqrt[2]{V (1 - P)} \]

where the numerator is a constant, the optimal number of infective units characteristic of the type of assay used, and the denominator is the number of surviving particles in that particular test. As a consequence of this dilution the concentration of free virus will have increased by the time the test sample is ready for inoculation. If sufficient time is allowed, a new equilibrium will have been established, as can be worked out by the use of 1.31a; if time was not sufficient, the system will be in a transitional state, as described by 1.31b. In either case a grave systematic error is introduced by ignoring the dilution effect, and equating observed survival with that obtained in the reaction mixture.

2.23. Inoculation of susceptible cells. After the reaction mixture has been suitably diluted, a known fraction of the final dilution is brought into contact with a system of infectible cells. If the inoculum is made in large volumes of diluent to wash away excess reagents. The concentration of free antibody is certainly lowered by several orders of magnitude, but it is entirely unknown how much of the virus is removed at the same time. It is reasonable to assume that the bulk of non-neutralized virus will stay on the cells, and some indeed may have already entered the cells. It is equally reasonable to assume that virus particles which have bound sufficient antibody to show no infectivity, will still have some of their surface uncovered, and thus some chance of being bound by cells. Those more completely covered by antibody will adsorb only if their affinity to cells is much higher than to antibody; otherwise they will be washed away during flooding of the system. What happens in terms of the model developed above is, so to speak, an asymmetric dilution of an equilibrium system. The concentration of antibody is greatly reduced, less so the concentration of neutralized virus. The latter change is selective, and may be imagined as the irregular truncation of a binomial distribution—all terms above a certain level are reduced or vanish. What is left is a population inhomogeneous in its biological behavior: part infective, part neutralized. The complexity of the situation would not include analysis of the loss of infectivity, but the lack of information about the quantitative conditions which does so. Yet, the trend is obvious: since a term in the denominator of 1.21b (the concentration of free antibody) has been reduced out of all proportion to the other terms, the concentration of antigen-antibody complexes must drop to re-establish the equilibrium. This dissociation will be roughly proportional to the concentration of neutralized sites, as the other term of the denominator (free virus) may be regarded as invariable.

2.23. The multiplication process. An ideal assay would measure the instantaneous state of an antibody-virus system. Unfortunately, even the best available method fails far short of this requirement in the case of animal viruses. Some particles will start multiplication early, some later; and whereas in a direct assay the earliest foci of infection may become recognizable in 24 hr, their number increases considerably during the next days. Accordingly, such tests are read after a period about twice as long as it takes for the earliest signs of infection to appear. In some indirect assays the period of observation may extend several weeks. This delay in reading the results in turn gives opportunity for some particles, which were neutralized at the moment of inoculation, to dissociate and boost themselves back to re-exist. The chance of the reverse reaction to occur is remote, since all factors discussed up till now effectively shift the neutralization equilibrium in the direction of more free virus.

The only factor which could counter the appearance of lesions in direct tests, and of the critical signs in indirect and quantal assays, is the continued presence of free antibody in the medium bathing the cells. This would be the case if the step of flooding the system were omitted from the assay. Here a certain fraction of the yield from infected cells would be neutralized before it could enter a second cell. If this were the only route of spread, the rate of growth of the infectious foci would be slowed down, but not stopped. If the virus could get from an infected cell into contiguous cells without entering the medium, the presence of antibody should not influence the rate at which lesions or other signs of infection appear.

2.3. Errors of evaluation

The final reading of lesions does not complete the assay; the results have to be made to refer to the original sample assayed. This is done by allowing for chance and systematic errors.

2.32. Chance errors cause the scatter of readings in replicate tests, and are readily dealt with by standard statistical methods. Since such errors occur at random, their effect is to blur the final result which is thus given as a confidence interval bracketing the true value, rather than a single value.

2.33. Systematic errors may be as many in number as there are steps in the assay procedure. Their effect is to displace the final reading along the scale on which it is measured, i.e., they are directional as opposed to the randomness of chance errors. In the widest sense of the term, the dilution factor is such a systematic error, and is routinely corrected for by multiplying the actual counts or the conventional end point by its reciprocal.

2.331. A fundamental error can be introduced by adopting the incorrect model for the mechanism of neutralization. Yet, by varying the dose of virus and antibody, the surviving fraction postulated by the different models is so different that there is usually no difficulty in deciding which is correct.

2.332. The effect of dilution is a dissociation of formed virus-antibody complexes. It depends as much on the dilution factor as on the original concentrations of the reagents and on the equilibrium constant K (see 1.31a). This dissociation is a fairly rapid process and, since its initial rate is of pseudo-first order, it can be calculated from the dissociation constant K. In some of the virus-antibody systems which have been sufficiently studied to allow such calculation, a halftime of about 5 min can be obtained. Thus in the usual time taken for diluting and injecting the inoculum, the reaction will have gone a long way towards the new equilibrium. As a consequence spuriously high survival rates will be observed, higher by a constant fraction in the range of low antibody to virus ratios, and higher by a certain amount where antibody is in great excess, i.e., when the concentration of non-saturated sites becomes negligible.

Exact allowance cannot be made for this effect, unless time is given for nearly complete equilibration. If the new equilibrium is not reached, the dilution effect leaves the assay with a systematic error of unknown magnitude.

2.333. The additional dilution that comes about with the act of inoculation is additive to the effect just discussed. If the set of susceptible cells is not washed subsequently, this stage of the assay will introduce no further error.

If the system is flooded, free antibody will be removed, as well as a certain unknown fraction of neutralized virus. On the whole the effect is much the same as that of dilution: incompletely neutralized virus will be reactivated roughly in proportion to the fraction of sites occupied, while fully neutralized (saturated) virus will show a constant level of reactivation. The quantitative aspects will remain unknown until the washed-away portion has been analysed.

2.334. The technique which includes washing of the host cells has, during the stage of viral multiplication, an error similar in kind but lower in order to those characterizing the stage of dilution and inoculation. This is due to some neutralized virus becoming free during the long period of incubation (see 2.24).

Where antibody is left in the medium surrounding the infected tissue, the consequences will be as envisaged in the second half of Section 2.24.
Part of the progeny virus will be neutralized, and thus the rate of multiplication may be reduced considerably in its early stages and less so later. Unless allowance is made for this slowing down, the surviving fraction will be underestimated. If sufficient time is given, all particles that started multiplying will eventually give rise to the expected symptoms as, according to 1.31a, an amount of antibody that could not completely neutralize the initial dose of virus will not neutralize a dose constantly increasing. If spread from cell to cell bypasses the medium, the presence of antibody has no effect, and the lesions will appear at the usual time.

SUMMARY

The statistical-kinetic theory of reactions is applied to the system of virus and its specific antibody. The mathematical model defines, without any additional assumptions whatever, the rate at which virus-antibody unions are formed and broken, as well as the equilibrium state of the system. Equations covering the effects of dilution, of altering the concentration of any component, and of competition set up between similar reagents are derived and solved explicitly.

Based on this model, the biological action of antibodies is considered in the form of several equally likely alternatives. Choice of the appropriate mechanism of neutralization must rest on experiment.

The methods available for the study of the neutralization of infectivity are shown to carry various systematic errors. The nature and magnitude of these is discussed, and means are proposed by which they can be either avoided or accounted for quantitatively.

REFERENCES

II. A Critical Comparison of Hypotheses

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Received for publication September 17, 1957

The careful and comprehensive study of the neutralization of Western equine encephalitis (WEE) and poliomyelitis-1 (PI) viruses on monolayer tissue cultures led Dulbecco, Vogt and Strickland (1) to the conclusions a) that the combination of virus and antibody was, for all practical purposes, irreversible; b) that a single molecule of antibody will neutralize a virus particle, the "antibody equivalent" being uniquely defined in terms of the virus concentration; and c) that characteristics of the neutralization process are independent of the cell system used in the assay. Since, however, a fixed fraction of the viruses was found to remain infective whatever the amount of antibody added, and some of the bound antibody could be removed by and transferred to subsequently added live or dead virus, two restricting assumptions had to be incorporated into the theory: first, that each virus preparation contains a fixed fraction of non-neutralizable virus, and second, that antibody is transferred from neutralized to non-neutralized particles when the two collide in the course of their thermal movement.

The basic tenets of this model, which we shall call the "nondissociation hypothesis," or HN for short, have been stated formally by Dulbecco et al. (1); the contending alternative, the "dissociation hypothesis," or HD, has been developed in the first paper of this series (2). These two will now be compared and their implications checked against the published data of Dulbecco et al. It will be shown that whereas the dissociation hypothesis both accounts for all observations and predicts certain trends not explicitly recognized in the original paper, the nondissociation hypothesis is found to be internally inconsistent, its implications at variance with experimental facts, the first of the restricting postulates superfluous, and the second inadequate.

3.1. Interpretative equivalence of the models

To establish the dissociation hypothesis on an equal footing with that of Dulbecco et al., it has to be shown first that it will represent their data equally well.

3.11. Basic experiments. Generally, the experiments were of 2 kinds: a) survival of virus at different intervals after exposure to excess antibody ("kinetic curves"), and b) the survival of virus after completed interaction with varying amounts of antibody ("multiplicity curves"). Both log survival curves had the same shape—a steep, nearly linear initial slope turning fairly suddenly parallel to the abscissa. It is this flattening which forced Dulbecco et al. to postulate a "persistent fraction," i.e., non-neutralizable virus.

3.12. Common assumptions. The fact, on the other hand, that the slope of both the kinetic and multiplicity curves is greatest at their origin led, in agreement with Dulbecco et al., to the conclusion that a single molecule of antibody bound to the right spot will neutralize the infectivity of a virus particle. This simplifies all models of neutralization (see Sect. 2.1) by restricting them to the boundary cases where \( r = 1 \).

Whether all sites are equivalent (i.e., \( s = c \)), or only a fraction of them is "critical" (i.e., \( s > c \)) could be decided only if unbiased multiplicity curves were available. Since, as will be shown below, this is not the case, assumptions have to be made at this point. Considering the more general case, namely that there are critical and noncritical sites, \( s \) will be set to equal the number of antibody molecules that a virus particle can accommodate on its surface. If this is an overestimate, it will have the effect of decreasing the value of the steric factor, \( f \), in 1.12a. As this latter value is determined experimentally as the ratio of observed and theoretical reaction rates, no error is introduced into the calculations as
long as the 2 values occur, as indeed they do, in the form of their ratio, $f/s$.

No arbitrary value will be given to $c$, the number of critical sites per virus particle, as this is one of the unknowns to be determined by the study of virus-antibody interaction. Further, unless forced by evidence to the contrary, the value of $c$ will be regarded constant.

The virus population is known to be inhomogeneous. The value given by Dulbecco et al. is accepted, i.e., 13 noninfective particles for each infective WEE virus ($V = 14V_r$).

3.13. Kinetic curves. This type of test is concerned with the rate of the neutralization process. Predictions by the two hypotheses are given in Equation 4.1 and 1.22 for HN and HD respectively. Since all published experiments were done at large excess of antibody over virus, the simplification proposed by Dulbecco et al. obtains to both hypotheses, and the reactions will have pseudomonomolecular kinetics in the range studied. The simplified equations are of the same form, and vary pari passu when different models of neutralization are considered. As such equations can be made identical by equating their constants, it is obvious that if one of them fits a set of data, so does the other.

3.14. Multiplicity curves. Experiments of this kind test for residual infectivity in mixtures of virus and antibody brought together for periods deemed long enough to allow complete interaction. Theoretical expectations of HN can be derived from Equation 7, which describes the reaction between antibody and the neutralizable fraction of virus; to this has to be added the "persistent fraction" which at higher ratios of antibody to virus becomes noticeable, and dominant at large excess of antibody.

The dissociation hypothesis predicts the course of multiplicity curves in 1.22e. It is a corollary of HD that a certain fraction of virus neutralized at any point of this curve can be reactivated during assay. Since the technique mostly involved large dilutions and always flooding away excess antibody, free antibody left in the system becomes negligible. A certain fraction of virus, free, partially or completely coated with antibody, will stay bound to cells, as envisaged in 2.23 and experimentally demonstrated for WEE virus by Dulbecco et al. (their Table 13). Dissociation of combined antibody will then occur by a first order process, at least initially, and a constant fraction of occupied sites will become free during a standard assay. The observed multiplicity of neutralization (i.e., the mean number of critical sites occupied) will thus be lower by a fraction, $\rho$, than it was in the reaction tube. Clearly, this relation holds equally in the range of saturation where all sites are occupied before assay, and a number of critical sites, $\omega c$, will remain so at its completion. Formally, using now the usual notation of $V_r$ for the initial concentration of infective virus and $V$ for its final concentration, the surviving fraction of virus is given by

$$\frac{V}{V_r} = e^{-\rho/cV_r},$$

and

$$\frac{V}{V_r} = e^{-\rho/cV_r},$$

(3.14a)

where $(\rho/cV_r)$ corresponds to the multiplicity of neutralization, $m$, in the notation of Dulbecco et al.

If the Poissonian limit in 2.12d is an inadequate approximation, the binomial formula must be used, and this will give

$$\frac{V}{V_r} = 1 - \frac{\rho}{sV_r},$$

and

$$\frac{V}{V_r} = 1 - \frac{\rho}{sV_r},$$

(3.14b)

Thus at infinite excess of antibody the observed multiplicity curves will level out at $\exp(-\rho/cV_r)$ (3.14a), and at $(1 - \rho)^c/sV_r$ (3.14b). The difference from this asymptote becomes too small to be distinguished experimentally once the virus is at least $\frac{1}{2}$ saturated with antibody ($\rho/sV_r > 0.7$).

3.15. Interpretation of the basic experiments. To demonstrate graphically the equivalence of the two models, the example of PI virus is chosen, since it complies with the nondissociation hypothesis more closely than does WEE virus, and its multiplicity curves are more completely determined. The expected multiplicity curve will be calculated from 1.22e, but to do this numerical values have to be assumed for the parameters. Taking $9.3 \times 10^4$ molecules of antibody/cm$^3$ of serum (3) and finding from Table 10 that a dilution of $3.10^{-3}$ is equivalent to the saturation level ($c = 12$), we obtain $9.3 \times 10^4 \times 3.10^{-3} = 9.8 \times 10^3$, for $V_r$, the total number of sites. The concentration of bound antibody, $y$, can be derived from the first entries of Table 10. Since no free antibody was detectable, $y$ will be taken to equal $A$, and $(A - y)$ cannot be greater than the error of plaque counts, about 0.3 m, that is, $\leq 2.5 \times 10^{-4}$ of undiluted serum. Thus

$$K = \frac{2 \times 10^{-4} \times 1.93 \times 10^{15}}{0.6 \times 10^{-2} - 2 \times 10^{-4} \times 10^{15}} \geq 1.4 \times 10^{-11}$$

Since this is a limiting minimum, we shall assume $K = 10^{-11}$. (The correctness of these figures is irrelevant to the argument, as long as the set is consistent. Different values for $s$, $V_r$, or $A$ would only be affected by a corresponding change in $K$.)

From 1.22e the values of $y$ for different values of $A$ can now be calculated, and by entering them in 3.14a and 3.14b the true $V/V_r$ ratios are obtained. Both these curves are shown in Figure 11, and it is evident that the Poissonian limit, 3.14a, is a good approximation to the binomial (3.14b) only as long as either $e$ is large ($e \sim \omega$) or the multiplicity of neutralization, $y/sV_r$, is much smaller than unity. These curves run well below the experimentally determined survival curve which is seen to level out at $5 \times 10^{-4}$. Since in this region the $y/sV_r$ ratio differs insignificantly from 1, the second part of equations 3.14a and 3.14b becomes $5 \times 10^{-4} = \exp[-pc] = (1 - \rho)^c/sV_r$, giving directly $\rho = 0.44$ and $\rho = 0.36$. By use of the reactivation factors, the survival values to be expected at the end of the assay can be computed for the whole course of the curve, and these are found to coincide with the experimentally observed curve.

Taking the initial slope of the observed curve to define a scale of "antibody equivalents," the true multiplicity curve for HN is calculated, and allowing of a "persistent fraction" of $5 \times 10^{-4}$, the observed curve expected on this hypothesis. This, again, is indistinguishable from the experimental survival curve from the survival values to be expected at the end of the assay can be computed for the whole course of the curve, and these are found to coincide with the experimentally observed curve.

The reactivation factor. As determined above, $\rho$ is a proportionality factor and chosen to give the best fit of the theoretical curve to the experimental points. There is, however a way of arriving at the same result in a less arbitrary manner.

When excess antibody is used and the kinetic curve is initially of pseudofirst order, the surviving fraction in $V/V_r$ is $\sim (k_d/s) \times (cA/sV_r)$. From the rate of neutralization of PI virus (Fig. 3) the mean value obtained for $k_d/s$ is $2.23 \times 10^{-14}$. Taking $K = 10^{-11}$, this yields $k_d = 3.23 \times 10^{-8}$/sec (cf. 1.13a). Now, suppose dissociation during the first 6 hr of the assay occurs into virtually infinite dilution of antibody:

$$k_d = \ln \frac{\text{number of sites occupied at } t}{\text{number of sites occupied at } t = \text{ln } s}.$$
This gives $p = 0.498$ in, probably fortuitous, agreement with the earlier derived $p = 0.44$. Yet, it shows that the partly assumed values for the above constants are organized into an internally consistent scheme which adequately describes the observed phenomena. The absolute values of the parameters, however, cannot be determined from the present data, since to do this we must know $c$, $s$, $V_0$, and $A$, and the first two remain unknown, as in the published experiment they are always confounded with either the rate constant or the dilution error.

Similar calculations on the system WEE virus and horse serum yield $k_d/s = 3.54 \times 10^{-14}$, $K \geq 10^{-4}$, and hence $k_d \leq 3.54 \times 10^{-4}$. The product of the reaction factor and the number of critical sites comes to 5.8, which, assuming $c = 15$ with Dubbecco et al., would make $p = 0.28$.

3.2. Crucial tests

Since either model seems to account for the general properties of both the kinetic and multiplicity curves, comparison at this level cannot discriminate between the two. Examining their detailed implications, on the other hand, is bound to reveal points at which their predictions are contradictory, that is, regions for critical testing. These are, essentially, the systematic errors of the two restrictive assumptions required only by the model of Dubbecco et al. As the reference material is deliberately restricted to their observations, only such differences will be considered as can be checked directly against the published data.

Both hypotheses envisage, rightly or wrongly, the same mechanism for the neutralization process, so that this part of the assay cannot be used to differentiate between the two.

3.2.1. Effect of dilution. Predictions concerning the next stage (preparatory dilution) are fundamentally different. HN allows of no change here and, indeed, this is the basis of all their calculations. HN allows of no change here and, indeed, this is the basis of all their calculations.

The issue can be decided on the experimental material of Tables 1, 2, 3, 4, and Figure 1—these contain all the tests in which WEE virus and horse antiserum were brought together at multiplicities of 10 or more. The only difference between entries is that in some instances high concentrations of virus were used, and the reaction mixtures had to be diluted before plating; in others low concentrations of virus were used, and here the mixtures were plated without preliminary dilution. These two groups shall be compared now.

Since the difference between diluted and undiluted platings is highly significant, this analysis yields an unequivocal answer: the results are as predicted by HD, and incompatible with HN.

Table 3.21

<table>
<thead>
<tr>
<th>Table 1—entry 1</th>
<th>Table 1—entry 2</th>
<th>Table 1—entry 3</th>
<th>Table 1—entry 4</th>
<th>Table 1—entry 5</th>
<th>Table 1—entry 6</th>
<th>Table 1—entry 7</th>
<th>Table 1—entry 8</th>
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<td>2.128</td>
<td>Mean</td>
<td>2.128</td>
</tr>
<tr>
<td>Standard error</td>
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<td>Standard error</td>
<td>0.222</td>
<td>Standard error</td>
<td>0.054</td>
<td>Standard error</td>
<td>0.054</td>
<td>Standard error</td>
<td>0.054</td>
<td>Standard error</td>
<td>0.054</td>
</tr>
</tbody>
</table>

**Table 3.21**

Comparison of the surviving fractions of WEE virus when virus-antibody mixtures are assayed with or without preliminary dilution. Data of Dubbecco et al. (1).

Whereas the survival fraction of virus is $V/V_0 = \exp(-m/n)$, according to Equation 7 of Dubbecco et al. and, in theory, this formula should hold to good approximation in the range of $m/n \leq 0.4$. Our Equation 2.12b is of the same form, and the two can be made identical by equating the constants ($i.e., n = s/0$). The difference of the hypotheses lies in the definition of $m$, the multiplicity of neutralization. In the nondissociation hypothesis $m = A/V_0$, $i.e., the "input multiplicity", as defined on page 194 of their paper; in the dissociation hypothesis $m = y/V_0$, $i.e., the "equilibrium multiplicity", as defined by our Equation 2.12b. This difference shall serve as our next test criterion.

Written in logarithmic form Equation 7 of Dubbecco et al. reads $\ln(V/V_0) = -A/V_0$. By dividing both sides by $A/V_0$ we obtain

$$\frac{V}{A/V_0} = \frac{1}{n}$$

that is, the logarithm of the observed surviving fraction divided by the input multiplicity should give a constant, as long as the average saturation is $<0.4$, as stipulated by Dubbecco et al. The same treatment of the HD formula yields not a constant but a linear equation in $y/A$:

$$\frac{V}{A} \ln \frac{V}{V_0} = \frac{y}{A} = \frac{y}{A}$$

Dilution and plating errors, nonexistent according to HN, would have a double effect. First, the constant of 3.22b would be multiplied by the activation factor $p$—this does not affect the shape of the curve; second, the multiplicity would be underestimated by the same factor $p$, and thus the observed points would lie closer to saturation. In this area the simplified multiplicity formula does not hold, and the curve will gradually flatten. Since Equation 1.21b gives a hyperbolic $(y, A)$ plot, the flattening over this range can be taken as approximately exponential. As a result, the regression of $(\frac{V}{A/V_0} \ln \frac{V}{V_0})$ on $(\frac{y}{A})$ will bend towards the abscissa as $y/A$ increases. More specifically, the logarithm of these two quantities should plot as a straight line whose slope is less than unity. Such a plot is given for both WEE and P1. Figure 3.22 contains all the 29 tests on the former and horse serum at observed multipli-
plicities of ≤6, and all 11 on the latter and rabbit serum at multiplicities of ≤4.8.

3.21. The nondissociation model demands \( V/F_0 \) to be constant. In statistical terms this means that the variance of tests done at different multiplicities should not be significantly greater than the variance of replicate tests. The found variance ratio of 22.15 (5 and 20 degrees of freedom) for WEE is significant well below the 0.001 level, and thus incompatible with the hypothesis of Dulbecco et al.

3.22. The same conclusion may be drawn from the calculated correlation coefficient of \( +0.798 \) \((P < 0.001)\). This test is more informative insofar as it not only dismisses HN (which allows no correlation), but supports HD (which demands strong positive correlation). Furthermore, as this test does not depend on replication for its error term, it can be applied to PI virus too. The trend here is the same: \( r = +0.800 \) \((P < 0.001)\).

3.23. The validity of HD can be examined by further testing its predictions. The deviations from linearity were found nonsignificant for both WEE and PI viruses, in agreement with the assumption of Dulbecco et al.

3.3. Critique of the assumptions

3.31. The “persistent fraction.” As has been shown, the dissociation hypothesis accounts for the shape of both the kinetic and multiplicity curves without any reference to a “persistent fraction” of non-neutralizable virus. This renders its assumption only superfluous; that it is also unjustifiable on theoretical as well as practical grounds will be clear from the following points.

3.321. Although it is stated in the description of the experiment and again in the discussion that a constant fraction of antibody is removed at each collision, or, in other words, that not all collisions are successful but only those which happen to hit an adsorbed antibody molecule, no term accounting for this appears in the equation. In its original form the equation does not cover this contingency and Smoluchowski, quite explicit on this point, postulates (page 136 of his paper) that the rate would have to be multiplied by \( m/n \), in the notation of Dulbecco et al. This gives initially 0.27 for the first and 0.10 for the last entry of Table 12, and finally 0.15 and 0.07 respectively.

3.322. Although it has been demonstrated earlier in their paper that the binding of antibody to WEE virus required an activation energy of \( (P = 0.002) \), this point is made not so much to prove that the surviving fraction may depend on a certain measure on the host cell used in the assay, but to show how sensitive the \( V/F_0 \) plot is to even minimal variation in \( V \). To this we shall return later.

3.323. Postincubation errors. The plateau and multiplication errors (discussed in 3.232 and 3.244, respectively) cannot be used for crucial testing, as the only data available are 5 entries of Table 1, and although the differences are striking, the 2 effects are here confounded. Since these 2 errors are opposed to each other and we have no information about their magnitude, not even the direction of the shift can be predicted when both are operative.
6000 cal/mole, such a factor does not appear in the equation, if reckoned with, it would reduce the number of successful collisions by $e^{-6000/T}$ that is, by a factor of $5.7 \times 10^{-10}$.

Taken together, these errors lower the figure given by Dulbecco et al. by (0.25 to 0.05) $0.5 \times (0.27 to 0.10) \times 5.7 \times 10^{-4} = 9.6 \times 10^{-7}$ to $1.4 \times 10^{-7}$, i.e., over a millionfold. Obviously, the number of collisions would be far from sufficient, even if the underlying model were acceptable. However, as can be shown readily, even this is not the case.

3.32. If an antibody bearing particle collides with an empty one, antibody can be transferred to the latter. This postulate should be true irrespective of which of the partners was u.v.-killed and which infective, and thus the model implies transfer in both directions. Hence, kinetically, the process should be a second order exchange reaction, whereas the Smoluchowski equation, in the form used, defines a unidirectional zero order process. Smoluchowski himself was quite aware of this, and his kinetic formula (page 142 et seq. of his paper) are of the orthodox form, with the reciprocal of the collision number appearing in the second order rate constant.

3.34. The correct formula for HN would be exactly analogous to that describing bimolecular isotope exchange reactions, with here the "label" antibody molecule exchanged between sites rather than a labelled atom or group exchanged between molecules. For such a process (see e.g. Wahl and Bonner, (4))

$$Rt = -\frac{V_1 V_2}{V_1 + V_2} \ln \left(1 - \frac{q_1 - q_2}{q_1 + q_2}\right)$$

where $R$ is the number of effective collisions in unit volume per unit time; $V_1$ and $V_2$ the concentrations of virus particles of the two kinds; and $q$ the fraction of sites occupied on $V_1$ at times indicated by the subscripts (i.e., $q_2 = q_1/V_1$).

Since it can be reasonably assumed that the activation energy of transfer is not less than that of neutralization, and that the steric factor is the same for the two processes, the value of $R$ is

$$R = -\frac{V_1 V_2 (q_2 + q_1)}{V_1 + V_2} \ln \left(1 - \frac{q_1 - q_2}{q_1 + q_2}\right)$$

by analogy to the derivation used in 1.11.

Calculated by this formula, the exchange of antibody would proceed at a rate several orders of magnitude lower than observed by Dulbecco et al., and redistribution would take about 350 hr instead of the less than 2 hr found experimentally.

3.4. Re-evaluation of the discriminatory tests of Dulbecco, Vogt and Strickland

In a critical comparison of two hypotheses it is usually sufficient to show, as has been done above, that one of them is compatible with the experimental evidence, and the other is not. In the present case a further task remains, namely, to find out why the tests designed by Dulbecco et al. to discriminate between the alternatives led to the wrong conclusions.

3.41. "Dissociation in the neutralization tube." This experiment (Table 3) employed observed multiplicities ("antibody equivalents") ranging from 4,000 to 200,000, i.e., worked at extremes of saturation. According to HD there should be no difference in observed survival here, as the dilution error is proportional to the number of occupied sites, and not to the number of free sites, as Dulbecco et al. seem to imply.

An informative test would cover the range of multiplicities over which the change of occupied sites changes significantly; such have been collected above (3.22) and are in agreement with dissociation.

3.42. "Dissociation during the adsorption period." Again, the test (Table 4) was conducted at multiplicities ranging from 600 to 60,000, and the same objections are called for as in the previous paragraph.

The valid tests (collected in 3.21, 3.22, 3.23 and 3.24) uniformly demonstrate what we called dilution and plating errors, and thus support HD.

3.43. "Presence of free antibody in a mixture of virus and antibody." In this test (Table 5) a nominal multiplicity of 6 was used. Yet, it is difficult to take this figure at its face value. Not only because statements of multiplicity are rather haphazard throughout the paper (to quote one instance only, Table 6, in which the first 3 experiments show the same multiplicity, notwithstanding a threefold variation in $A/V_2$; and the last 2 experiments, reproduced also in Table 12, which have different multiplicities in the 2 Tables, although the experimental data are identical), but mainly because the same combination of virus and antisera gives observed multiplicities

3.44. "Reactivation of neutralised virus upon dilution." All the tests (Table 6), were done on virus preparations ranging from $3.5 \times 10^{4}$ to $10^{9}$ plaque forming units, and these had to be diluted by a factor of the order of 10,000 to give countable plaques at the rate of survival observed.

The final dilution was reached in the normal course of the assay, in the other after interruption for 2 hr at some intermediate stage. Excess antibody was washed away after plating. Since reactivation is an invariable feature of the standard assay of Dulbecco et al. (see 3.21, 3.22, 3.23, and 3.24), no further effect can be expected from allowing some extra time during the dilution procedure.

To test for the dilution effect adequately such doses of virus should be used that can be plated, as controls, also without dilution. Although such critical experiments have not been published, significant reactivation can be demonstrated by contrasting the plateaus done with or without preparatory dilution (3.21).

The next 4 sections call for no special comment. The first, on the heritability of the "persistent fraction" of virus, is negative in character and, although this is what should be expected on HD, the results are not incompatible with HN. The other 3 (on inhibitors, cofactors, and strain differences) are not crucial for either hypothesis.

3.45. The section on the absorption of antibody (Table 10), on the other hand, is instructive in several ways. First, it may serve as an example of how sensitive the results are to even minute variations in the control group. Dulbecco et al. find 0.18 as final survival for the control group of WEB virus. This corresponds to a multiplicity of 1.715 (their value of 1.77 is incorrect, and even this trilling change is enough to reduce the estimate of critical sites from 14.9 to 13.21). Now, the observed survival, being a ratio of two independent determinations, carries the error of $\pm 22\sqrt{2}/5\%$, i.e., $\pm 9\%$. The consequence of shifting the observed value over the modest range of only one standard deviation in either direction are seen in Table 3.45.

If we take 0.12 instead of 0.18, the "absorbed antibody equivalents" show significant trend; at the other end patently impossible results are obtained, and the trend is reversed. The same treatment of the data with P1 virus yields the im.

TABLE 3.45

<table>
<thead>
<tr>
<th>Group</th>
<th>Absorbed Antibody Equivalents</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>17.6 14.1 13.6</td>
</tr>
<tr>
<td>B</td>
<td>24.1 17.0 16.1</td>
</tr>
<tr>
<td>C</td>
<td>28.5 14.6 12.3</td>
</tr>
<tr>
<td>D</td>
<td>35.1 14.0 10.8</td>
</tr>
<tr>
<td>Control*</td>
<td>(0.12) (0.18) (0.27)</td>
</tr>
</tbody>
</table>

* The values in this row show the final virus survival. The central column gives the values calculated by Dulbecco et al. on the left, and the correct ones on the right.
possible negative absorption at the low end, has no point where the amount absorbed could be regarded constant, and gives a highly significant increase with increasing multiplicity at the other end. (It should be remembered that the range chosen covers about 1/2 only of the distribution, and thus one out of three observations would fall even beyond these values.) In the light of these considerations it should be clear that the chosen technique is quite unsuited to the determination of the average number of critical sites, let alone the claim made in the discussion that the values thus obtained are absolute.

On the positive side, this set of experiments contains perhaps the most powerful proof of dissociation of formed virus-antibody complexes. It will be noted that the reagents are the same as used in Figures 5 and 6, the difference being that in Table 10 uncombined antibody was titrated back, whereas in the figures unneutralized virus was assayed. In the case of WEE, where the reaction mixtures were centrifuged to remove free virus, the observed multiplicities are uniformly higher by 296% in the reaction mixture than at the end of a standard assay (Fig. 5). In the case of P1, where removal of virus was deemed unnecessary, the two multiplicities are of course identical. This combination of measurements on WEE virus amounts to a direct determination of the reactivation factor, \( p \), and gives the value of 0.34 for rabbit serum. Thus, the direct determination of the reactivation factor, \( p \), is specifically possible with HIN and, as has been shown in 3.32, even with the auxiliary assumption it does not account for the findings. What remains to be shown is that \( p \) does.

Unfortunately, Dulbecco et al. omitted to give the quantities of virus and antibody used in these experiments. Furthermore, the second column of Table 11 is incorrect, since it equates results obtained with rabbit serum to horse serum, a procedure against which the \( p \) is specifically warned in the footnote of page 172. Thus all one can do is to assume, as is likely, that undiluted virus was used, and work out the corresponding serum concentrations from the data of other experiments. This would give 5 \( \times 10^9 \) pfu/ml of WEE virus, 9.6 \( \times 10^{-3} \) of horse serum for the first entry of Table 11, and correspondingly lower concentrations of serum for the others. With these values the size of the antibody pool can be estimated for \( t_a \) (time of addition of fresh virus) and \( t_b \) (time of final equilibrium). These values are the roots of 1.22a and 1.321d respectively, and are tabulated under the headings \( B_a \) and \( B_b \) in Table 3.46, for 3 different values of the equilibrium constant, \( K \).

Evidently, even the greatest difference (with \( K = 10^{-11} \)) is negligible in terms of experimental error, and thus the Bodenstein treatment is applicable. The last column of Table 3.46 gives the time required for half of the redistribution to be completed; this time is less than an hour in all cases considered. In the experiments at least 2 half times of reaction (2 hrs) were allowed, and the observed redistribution is between 75 and 100%. Hence the dissociation hypothesis is adequate to account for the empirical facts.

3.37. Redistribution of adsorbed antibody. Once more, these experiments (Table 12) contradict the nondissociation model, even after assuming removal of antibody by direct collision, the fallacies of which assumption have been laid bare in 3.32. The dissociation model, on the other hand, accounts readily for the observations since, by taking as high a value as \( 10^{-11} \) for the equilibrium constant and envisaging only first order dissociation, the time required for 1.4-fold reactivation is about 17 min; with lower values of \( K \), the time required for a given degree of reactivation, will be even less. More accurate calculations are impeded by our ignorance of the rate constants characterizing the reactivating agent; as long as these remain unknown equation 1.32; cannot be solved, and the above values have to be taken as limiting maximum rates.

**SUMMARY**

The experimental data of Dulbecco, Vogt and Strickland are used to discriminate between two hypotheses on the mechanism by which the infectivity of viruses is neutralized.

The orthodox hypothesis of dissociation, as developed by Fazekas de St.Groth, Watson and Reid (2) and the nondissociation hypothesis of Dulbecco et al. (1) are found to accord equally well for the trivial features of the neutralization process.

At the quantitative level however, the nondissociation hypothesis becomes incompatible with the experimental evidence on several counts; what it postulates as constants are seen to vary systematically; and its basic assumptions prove to be either inadequate or unnecessary. The dissociation hypothesis is not contradicted at any point by the same evidence.

Finally, it is shown that the discriminatory tests listed in support of the nondissociation hypothesis by Dulbecco et al. are, for the most part, inconclusive as their results are confounded with the systematic errors of the assay technique; the remainder directly contradicts their hypothesis. The dissociation hypothesis fits this further set of data too.

**REFERENCES**