ISOTOPIC TRACER INVESTIGATIONS OF MECHANISM AND STRUCTURE IN INORGANIC CHEMISTRY

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Received September 20, 1956

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I. Introduction

The history of the application of isotopic tracers to the study of inorganic chemistry is marked by three distinct periods. Before 1934 only the heavy elements which had radioactive isotopes, for example, lead, bismuth, thallium, and thorium, could be used to "trace" the movement of atoms during reaction. Simple experiments were involved and the utility of the methods was very limited. The discovery of artificial radioactivity in 1934 (124) provided the chemist with radioactive isotopes (or "radioisotopes") of many of the more familiar and useful lighter elements. Because of the low neutron fluxes attainable at this time, only short-lived radioisotopes of low specific activity could normally be produced. These included Cl^{38} ($t_{\frac{1}{2}}$ = 38 min.), Br^{80*} (4.4 hr.), I^{128} (25 min.), S^{35} (87 days), Mn^{56} (2.6 hr.), As^{76} (26 hr.), and P^{32} (14 days). Moreover the difficulties encountered in the accurate assay of the radioactive materials combined with the unreliability of the detection instruments (usually electroscopes and Geiger–Müller tubes) severely limited their general use. While some very important experiments were performed, it is probably true that the research topic was often planned around the isotope. It was fortunate that about this time stable isotopes, notably H^2 (D) and O^{18}, also became available for tracer investitions. These isotopes were relatively easily analyzed and many quantitative experiments were possible. Accordingly so much work was carried out with deuterium that it was worthwhile holding a symposium in 1937 devoted entirely to the chemistry of this isotope (57). Full reviews of the work of this period have been given by Reitz (388) and by Seaborg (415).

Since 1945, the successful operation of nuclear reactors and the continued development of particle accelerators has made possible the attainment of high particle fluxes. Consequently radioisotopes, both short- and long-lived, of nearly all the elements have become commercially available. This, coupled with the production of reliable and sensitive detection equipment, has marked the beginning of the third and most fruitful period. Earlier exploratory and qualitative studies have now given way to quantitative and more detailed investigations. The lack of suitable radioisotopes of the important elements nitrogen and oxygen has been offset by the commercial availability of enriched stable isotopes of these elements and of instruments for their accurate estimation (mass spectrometers, etc.).

Only one textbook has been published in English which deals solely with the applications of radioisotopes to chemical problems (464); it includes a comprehensive literature survey up to January, 1950. Its wide coverage precluded a detailed discussion of any particular topic. A bibliography devoted to isotope separation and isotope exchange and covering a good deal of the published work between 1907 and 1953 is particularly useful (40). Other books have included discussions of exchange and other tracer reactions in inorganic chemistry (114, 174, 279, 317). Haissinsky (209, 210), Edwards (149a), and Amphlett (15) have discussed the subject of isotopic exchange reactions in recent reviews, and in reviews dealing with the mechanism of complex-ion reactions (36, 445) the application of isotopic investigations has been incidentally mentioned.

This review sets out to enumerate the value of tracers in (*a*) the study of the mechanism of inorganic reactions and (*b*) the determination of the structure of inorganic molecules. Particular stress will be placed on their unique value and limitations. Because reviews have been recently published dealing with electron-transfer processes (15, 492) this important application of tracers will not be dealt with specifically, but some examples from this field will be used to illustrate principles involved. Although a few heterogeneous reactions and reactions involving organic molecules may be used as examples to clarify points, the bulk of the discussion will be concerned with homogeneous reactions involving inorganic molecules. Dole (134) has dealt with the chemical applications of oxygen-18, and only work subsequent to 1952 will be incorporated in the extensive tables which form an important part of this review and which are believed to be comprehensive up to March 1957.

II. ISOTOPIC EXCHANGE REACTIONS

An exchange reaction occurs when atoms of a given element interchange between two or more chemical forms of this element. The term "isotopic exchange reaction" arises since such a process can only be detected by isotopic labelling methods. A typical isotopic exchange may be described by the chemical equation:

$$\mathrm{Fe(phen)_3^{2+} + Fe^{*2+} \rightleftharpoons Fe^{*}(phen)_3^{2+} + Fe^{2+}}$$

This equation expresses the fact that when a solution containing $\mathrm{Fe^{2+}}$ tagged with radioactive iron atoms is mixed with a solution containing $\mathrm{Fe(phen)_3^{2+}}$, radioactive iron atoms will gradually disappear from the $\mathrm{Fe^{2+}}$ species and reappear in the $\mathrm{Fe(phen)_3^{2+}}$ species. This net transfer continues until equal concentrations of radioactive iron atoms exist in the two species and a kinetic isotopic equilibrium will be established. (A discussion of the possible mechanisms by which such a transfer can occur will be given in later sections.) It is important to realize that this continual transfer of iron atoms from one chemical species to another will occur in the absence of tagged iron atoms; the latter are only introduced as an analytical tool to detect and measure the rate of the process.

A knowledge of the rate at which isotopic exchange reactions proceed is extremely important in all tracer investigations. Thus if it is desired to study the mechanism of decomposition of aqueous $\mathrm{O^{18}}$-labelled hydrogen peroxide, the rates of exchange of hydrogen peroxide with the product oxygen and of these separately with solvent water must be known, and for the tracer method to be worthwhile, these exchange rates should preferably be negligible compared to the duration of the experiment. Frequently it may be possible to assume that these exchanges between reactant and product are immeasurably slow, but any such assumptions must be based on experimental studies on analogous exchange systems. Therefore investigations of isotopic exchange reactions not only yield important results in themselves but also form the basis of other tracer studies.

A. KINETICS OF ISOTOPIC EXCHANGE REACTIONS

The general equation for an isotopic exchange reaction may be written

$$AX + BX^* \rightleftharpoons AX^* + BX$$

where * designates the distinguishable (radioactive or stable) isotope. The rate of disappearance of the isotopic species from an initially labelled reactant (BX) or the rate of appearance in an initially unlabelled reactant (AX) is described by a first-order rate law. This law was first derived by McKay (325), but it is fair to point out that earlier investigators had used equivalent, but less general, forms of the first-order law in the exchange of iodide with organic iodides (247) and of arsenious and arsenic acids in the presence of iodide ion (484). Subsequently it has been shown that this first-order exchange law will be applicable irrespective of the actual exchange mechanism, the number of chemically equivalent exchangeable groups, the reactant concentrations, any differences in isotopic reaction rates, and the concentration of the labelling isotope, provided tracer amounts are employed (218). (For radiotracer investigations, this last condition is amply fulfilled but for studies employing macro amounts of deuterium special rate laws must be derived (77).[1]) Then, provided the reaction is conducted in a stable homogeneous phase and the overall concentrations of AX and BX do not change owing to net reaction or dilution, the *rate* R at which X atoms (both labelled and unlabelled) interchange between AX and BX is

$$R = \frac{-2.303}{t} \cdot \frac{ab}{a+b} \log_{10}(1 - F) \qquad (1)$$

a and b signify the total concentrations $(AX + AX^*)$ and $(BX + BX^*)$, respectively. Should AX or BX contain n equivalent exchangeable atoms or groups, the effective concentrations will be n times the ordinary (molar) concentrations. F, the fraction of exchange at time t, is given by:

$$F = \frac{x_t - x_0}{x_\infty - x_0} \qquad (2)$$

where x, for a particular molecular species, represents either specific activity for a radiotracer or percentage isotopic abundance excess (i.e., above normal abundance) for a stable tracer. If the exchange reaction is followed by measuring the rate of appearance of activity in the initially unlabelled species (AX), then x_0 is zero and equation 2 simplifies to:

$$F = \frac{x_t}{x_\infty} \qquad (3)$$

(Norris (352) has set down a number of useful alternative expressions for the fraction of exchange.) The infinite time value x_∞, substantially attained after

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[1] The kinetics of competitive exchange between three species have been recently derived (496).

six to eight exchange half-times have elapsed, is determined from the specific activity of the initially labelled species BX by the material balance:

$$(a + b)x_\infty = b(x_0)_{\mathrm{BX}} \tag{4}$$

isotope effects being neglected for the present (see Section VII,C).

R can be determined from the slope of the $\log_{10}(1 - F)$ against time linear plot or more conveniently by estimating the half-time of exchange, $t_{\frac{1}{2}}$, from this plot (when $F = 0.5$) and substituting in the expression:

$$R = \frac{0.693}{t_{\frac{1}{2}}} \frac{ab}{a + b} \tag{5}$$

The rate of an isotopic exchange reaction is most usually characterized by the half-time and hence by R, which is the total number of exchanges (tracer and nontracer) occurring in unit time and expressed in the concentration units of AX and BX (normally moles per liter). For a given set of reaction conditions R will be a constant. However R is not a rate constant but is dependent on the concentrations of AX and BX, this functional dependence being determined by the detailed mechanism of the exchange process, e.g., in the simplest case of bimolecular second-order exchange

$$R = k_2[\mathrm{AX}][\mathrm{BX}]$$

where k_2 is the rate constant for the exchange reaction.

Since R is estimated from the slope of the semi-log plot of the rate of approach to isotopic equilibrium, it is not essential to know the value of x_0 at $t = 0$. The first experimental value of x_t can be taken as the zero-time sample and the reaction-time scale adjusted accordingly. Furthermore, Guggenheim's modification for first-order reactions is applicable and although this method has only been used once (14) in a published exchange study, it has some advantages. An experimental determination of the specific activity of AX (or BX) at infinite time is avoided (and this might be difficult if marked decomposition occurred), and once again a knowledge of the exact time of commencement of the exchange is unnecessary. Ames and Willard (14) measured the rate of exchange of $S^{35}O_3^{2-}$ with $S_2O_3^{2-}$ and used the expression

$$R = \frac{2.303}{t} \cdot \frac{[SO_3^{2-}][S_2O_3^{2-}]}{[SO_3^{2-}] + [S_2O_3^{2-}]} \log (x_{t+\epsilon} - x_t) \tag{6}$$

where ϵ represented a constant time interval (about two half-lives) and x the specific activity of the $S_2O_3^{2-}$ (initially inactive).

The experimental determination of an exchange rate can therefore be seen to involve the following:

(*a*) *Mixing* AX *and labelled* BX: This is preferably performed by mixing two inactive solutions of AX and BX, allowing them to settle to the required temperature, and injecting a small amount of BX* of relatively high activity to initiate the exchange.

(*b*) *Separating* AX *and* BX *at various times*: Usually this includes at least one early separation in addition to one when exchange has sensibly reached equilibrium. A discussion of the various separation methods available and of their relative advantages has been given by Amphlett (15). These include precipitation, solvent extraction, ion-exchange, diffusion, and electrophoretic methods. As to the question of the optimum times of exchange to use, Davidson and Sullivan (128) have discussed this point. They assume that the errors involved in measuring concentrations and time are usually small compared with the errors in radioassay (both in the statistical counting and in the preparation of samples for counting). Dealing more particularly with the simpler case where the rate is measured by the decrease in activity of that component initially active (BX* in the above equation), they find that the minimum error due to radioassay occurs at a time of reaction about $t = 1.4\ t_{\frac{1}{2}}$ (for BX > AX) and about $t = 1.4\ t_{\frac{1}{2}}$ to $4\ t_{\frac{1}{2}}$ (for AX $\gg$ BX). Jones (270) also considers the fractional error in R as a function of the extent to which the reaction has proceeded and comes to similar conclusions.

(*c*) *Measuring the specific activity* (*or enrichment*) *of the separated reactants* AX *and* BX: This involves standard analytical procedures (see Section III,B). Allowance must be made for any natural decay of the radioisotope during the counting operation. This may be accomplished either by making use of the known half-life of the isotope (285) or preferably, experimentally, by counting samples at various times and from the constructed exponential curves reducing all counting rates to a common time. With a few radioactive isotopes an isomeric transition occurs between a parent and a daughter isotope (e.g., Br^{80*}). In these cases the separated samples should be left for at least six half-lives of the daughter isotope in order for equilibrium to be attained before counting. It is possible to measure exchange reactions involving two radioactive isotopes of the same element. This naturally arises with the actinides which only exist as radioactive isotopes. Thus the Np(V)–Np(VI) exchange was studied using Np^{237} (α, 2.2×10^6 yr.) as the "normal" isotope and Np^{239} (β, 2.33 days) as the tracer isotope. The amounts of Np^{239} in each species could be determined by absorbing the Np^{237} alphas during the counting operation (109).

B. ASSIGNMENT OF RATE CONSTANTS

As in nontracer kinetic studies, the determination of the form of the rate expression is of prime importance in indicating the probable mechanism of isotopic exchange reactions. The functional dependence of the exchange rate R upon reactant concentrations may be deduced by the general methods available in chemical kinetics (179, 288). Perhaps the simplest is to assume the rate expression to be of the general form:

$$R = k_p[\mathrm{AX}]^m[\mathrm{BX}]^n \tag{7}$$

In the special case where it is possible to conduct the investigation at varying, but equal, reactant concentrations ([AX] = [BX] = a), then for a first-order rate expression $t_{\frac{1}{2}}$ (= $\ln 2/2k_1$) will be independent of concentration, for a second-order law $t_{\frac{1}{2}}$ (= $\ln 2/2k_2a$) will be inversely proportional to the concentration, and for the general rate law of the p^{th} order ($p = m + n + \cdots$)

$$t_{\frac{1}{2}} \; \alpha \; \frac{1}{k_p a^{p-1}} \tag{8}$$

This approach was first suggested by Duffield and Calvin (142) in the exchange of copper chelates with copper acetate in pyridine solution. In this case the observed second-order law was then presumed to be first order in each exchanging species. Alternatively, from measured values of R at various reactant concentrations, the rate constant k_p (equation 7) can be calculated directly on the basis of a first, second $\cdots$ order rate law; constancy of k_p then indicates the desired overall rate law. This approach fails however when two concurrent exchange paths of different order are operative; this circumstance frequently arises in exchange reactions in aqueous solution.

A more general, and more satisfactory, method is to study in turn the dependence of R on a single reactant concentration, the other concentrations being maintained constant. Then a plot of log R versus log [AX] should be linear of slope m, and similarly for the other reactant concentrations. Such an approach was adequate for the thermal U(IV)–U(VI) exchange reaction (401) for which

$$R_{25^\circ} = 2.5 \times 10^{-5}[\mathrm{U(IV)}]^2[\mathrm{U(VI)}][\mathrm{H^+}]^{-3}$$

and even for the relatively complex Fe^{3+}–$Fe(EDTA)^-$ exchange system (see Section VI) when the rate expression includes three distinct terms (268). In the latter case the three exchange paths were operative in different pH ranges and the separation of rate terms was unambiguous. However, when more than one concurrent exchange path is important, the rate R is not expressible by an equation of the form of equation 7 and fractional reaction orders are often found. Thus the Br_2–BrO_3^- exchange was found (47) to be described by the law:

$$R_{25^\circ} = 0.023[\mathrm{Br_2}]^{0.3}[\mathrm{BrO_3^-}]^{1.7}[\mathrm{H^+}]^{1.1}$$

Therefore in the interpretation of exchange data, it is preferable to plot first R versus [AX] (at constant [BX] and vice versa); the shape of the curve will immediately indicate the importance of possible concurrent exchange paths and the probable dependence of R upon reactant concentrations. For example, Rich and Taube (391) found for the $AuCl_4^-$–Cl^{*-} exchange system that a plot of R versus $[Cl^-]$ (at constant $[AuCl_4^-]$) was linear with a positive intercept at $[Cl^-] = 0$. The rate expression was therefore:

$$R = k_1[\mathrm{AuCl_4^-}] + k_2[\mathrm{AuCl_4^-}][\mathrm{Cl^-}]$$

and the two rate constants could be readily deduced from the slopes and intercepts of the plot. This approach is also illustrated by the analysis of the data for the Ce(III)–Ce(IV) exchange reaction (143). The evaluation of rate constants by this method is more accurate than that from a log R versus log (concentration) plot. It will be appreciated that if one rate term were smaller than the main rate term, then the former could be missed in a logarithmic plot.

Having evaluated the rate expression, the normal procedure is then to postulate an exchange mechanism consistent with the kinetics and chemical behavior of the system. Harris and Stranks (220) have adopted an alternative, but completely equivalent, approach in deducing the detailed first-order exchange law for a postulated mechanism and fitting this law to the observed kinetic results. In deducing rate constants, these authors have plotted $0.693/t_{\frac{1}{2}}$ (rather than R) versus concentration. In the common circumstance for which $R = k_1[a] + k_2[a][b]$, then

$$\frac{0.693}{t_{\frac{1}{2}}} = \frac{a+b}{ab}R = k_1\left(\frac{a}{b}+1\right) + k_2(a+b) \tag{9}$$

This method has no advantage over the previous method (R versus concentration) for determining the form of the rate law and in fact the law is not immediately apparent from such graphical plots. However, when significant isotope effects occur in the exchange reaction, these effects can be assigned to definite steps in the exchange mechanism. The approach has been recently improved (241) whereby the detailed exchange law for a postulated mechanism is calculated in the form of equation 1 and R is plotted as a function of reactant concentrations.

C. COMPLICATIONS ACCOMPANYING EXCHANGE REACTIONS

Complications can arise from "zero-time" exchange or from a nonlinearity of the log $(1 - F)$ against time plot (the exchange curve).

1. *Zero-time exchange*

Although extrapolation of the exchange curve to zero time should lead to a value of $F = 0$, it is often found that this is not the case. The explanation for this may be simple. Systematic errors in the estimation of times could lead to zero-time exchange (especially if the exchange is a fast one) (383, 417). Alternatively the separation procedure may not lead to a complete separation. In some cases, a zero-time exchange is observed which can be correlated with a definite phenomenon. For example, although the electron-transfer reaction between Hg(I) and Hg(II) in perchloric acid is known to be extremely fast (486), the addition of cyanide ions to the Hg(II) before mixing with Hg(I) slows down the electron-transfer rate appreciably, although a zero-time exchange is observed. This zero-time exchange varies from 8 to 50 per cent as the $[CN^-]/[Hg(II)]$ ratio decreases from 1.83 to 0.50. With these conditions, Hg^{2+}, $Hg(CN)^+$, and $Hg(CN)_2$ will be present in concentrations governed by the known disproportionation constant (487) for the equilibrium:

$$Hg^{2+} + Hg(CN)_2 \rightleftharpoons 2Hg(CN)^+$$

Isotopic exchange is immediate *only* for the uncomplexed Hg(II) present, since the cyanide-complexed and the uncomplexed Hg(II) are not in labile equilibrium and electron transfer between Hg(I) and Hg(II)–CN complexes is slow. The amount of zero-time exchange can be exactly correlated with the (known) proportion of uncomplexed Hg(II) present (486, 487).

Related to this cause is one arising from extreme differences in the exchangeability of the atoms within a molecule. The exchange of phosphorus pentachloride with chlorine in carbon tetrachloride solution gives a straight-line exchange curve which does not extrapolate to zero exchange at zero time. The amount of the initial very rapid exchange can be shown to correspond in amount to three-fifths of the chlorine of the phosphorus pentachloride. The three equatorial chlorine atoms undergo then a very rapid exchange with chlorine, while the apical chlorine atoms exchange at a slower measurable rate (140).

In the exchange studies of the ferric ethylenediaminetetraacetate complex, $Fe(EDTA)^-$, with labelled ferric perchlorate in acid solution, a small zero-time exchange is observed. The partial dissociation of the ferric complex in acid will lead to the production of inactive ferric ions:

$$Fe(EDTA)^- \rightleftharpoons Fe^{3+} + EDTA^{4-}$$

The active ferric ions added will then be diluted by these inactive ferric ions. Addition of hydroxyl ions (as the separation method) will precipitate, *even at zero time*, ferric hydroxide of a lower specific activity than that initially added. Since this decrease in activity is a measure of the amount of dissociated inactive ferric ions (a variation of the isotopic dilution method), the extent of the zero-time exchange can be related fairly easily with the dissociation constant of the $Fe(EDTA)^-$ complex (112, 268).

Zero-time exchange may be induced by the separation procedure ("separation-induced" exchange). Prestwood and Wahl (385) have deduced that provided this effect is reproducible at each exchange time, the *slope* of the exchange curve will still be a true measure of the exchange rate. They illustrated this conclusion by considering the Tl(I)–Tl(III) exchange. Depending on whether, in the separation procedure, Tl(I) was precipitated as the bromide, chromate, or chloroplatinite or Tl(III) was precipitated as the hydroxide, 10 per cent, 5 per cent, 5 per cent, or 50 per cent zero-time exchanges, respectively, were observed. Nevertheless the slopes of the exchange curves were identical. Therefore, provided a first-order law is obeyed, which means that the separation-induced or incomplete separation effects are reproducible, an amount of zero-time exchange presents no difficulties.

These small separation-induced exchanges are possibly due, in the case of the Tl(I)–Tl(III) system at least, to the transient formation of labile species which undergo partial exchange before actual precipitation is complete. The precipitant for separation of thallous chromate includes a high concentration of cyanide ion (to complex the Tl^{3+}) and it is significant that large amounts of cyanide ion do catalyze the Tl(I)–Tl(III) exchange (372). Since chloride ion is also a very effective catalyst, it would be informative to correlate the induced exchange occurring on precipitation of bromide ion with a possible catalytic exchange effect of bromide ion.

Unfortunately, definite examples are known where the separation method induces *complete* exchange and, naturally, this is a much more serious matter.

The exchange of nickel perchlorate with both bis-N,N-di-n-propyl- and bis-N,N'-diisoamyldithiocarbamate nickel in acetone is extremely slow. The separation procedure used involves the addition of water to precipitate the complex. If, instead of water, concentrated aqueous ammonia is added to facilitate this precipitation, then complete exchange is observed within the 5-min. separation time. Apparently ammonia adds on to the nickel complex and in weakening the binding increases the exchange lability (see Section VI). The ammonia also affects the form of the Ni_{aq}^{2+}, converting it into $Ni(NH_3)_x^{2+}$. One of the earliest exchanges studied was that between plumbous and plumbic acetates in glacial acetic acid (237). Complete exchange was observed after the mixture had been heated for 10 min. at 80°C., water added, and lead dioxide precipitated on boiling. Similar results were recently obtained by Evans, Huston, and Norris (154), but they draw attention to the work of Zinth and Rauch (491), who showed that the two lead atoms in the oxide $Pb_2O_3 \cdot 3H_2O$ are not equivalent. When this oxide was dissolved in strong base to give a mixture of plumbite and plumbate and the plumbate separated off as barium plumbate, no exchange was observed.

$$HPb^*O_2^- + PbO_3^{2-} \rightarrow Pb_2^*O_3 \xrightarrow{OH^-} Pb^*O_2^{2-} + PbO_4^{4-}$$

but when it was dissolved in acid with lead dioxide precipitating, complete exchange occurred,

$$Pb_2^*O_3 + 2H^+ \rightarrow Pb^*O_2 + Pb^{*2+} + H_2O$$

so that a separation involving the precipitation of lead dioxide seems highly likely to induce complete exchange. When a less drastic separation procedure was used, such as allowing plumbic acetate to separate on cooling, no exchange was observed (154), a result which is more easily understood chemically. Fava has observed similar induced exchange during a study of Pb_3O_4 (157).

The situation regarding separation-induced exchange appears thus: the detection of complete exchange may arise from the separation procedure, especially if this involves chemical precipitation, in the process of which transient (labile) species may be produced. If more than one separation procedure is used (preferably involving a different type of method) with the same result, then this is some evidence for the correctness of the result. If the separation procedure has been used with similar inert molecules with no induced exchange, this also constitutes good evidence for the separation procedure not being the cause of complete exchange with the labile molecule.

2. Nonlinearity of exchange curve

A distinct curvature for the exchange plot might be expected under the following conditions (47, 352):

(*a*) *Nonequivalence of atoms in the molecule:* If, as in the case of phosphorus pentachloride mentioned above, there is a large difference in the rates of exchange of the nonequivalent atoms no difficulties arise. If, however, the rates of the two exchanges (considering *two* distinct types) had been comparable, then a log $(1 - F)$ versus time curve convex downwards would have been obtained. This might, under simplifying assumptions, be resolvable into the two linear first-order exchange components (343).

(*b*) *Chemical equilibria not established rapidly:* One of the assumptions used in the derivation of the first-order exchange law is that the exchange process is unaccompanied by a net chemical reaction. In a study of the rate of exchange of free carbonate ion and the complex ion $[Co(NH_3)_5CO_3]^+$, if exchange were initiated soon after the two reactants were mixed a curvature was obtained for the exchange plot. If, however, a solution of the two inactive exchange reactants was allowed to stand until aquation equilibrium had been attained (determined by separate experiments) and then exchange initiated, the semi-log plot was then linear. "Aging" of the solution for longer times did not affect the result (434). Luehr, Challenger, and Masters (311) have considered the case in which BX* undergoes thermal exchange with AX simultaneously with chemical conversion of BX to AX. If BX* is counted, then the rate expression is independent of the amount of BX converted to AX and is identical with equation 1. If AX is counted, it is necessary only to know how much BX has been converted to AX at the time when each sample is taken for counting. The kinetics of the conversion of BX to AX are immaterial. This has been illustrated for the Tl(I)–Tl*(III) exchange system under the conditions of a chemical conversion of Tl(III) to Tl(I). The rate constant so deduced (1.29 l. mole^{-1} min.$^{-1}$) agrees well with that observed for the ordinary exchange system (1.22 l. mole^{-1} min.$^{-1}$).

(*c*) *Catalytic effects:* Lewis, Coryell, and Irvine (300) found that the ingress of oxygen, even in amounts only enough to oxidize a small percentage of the cobaltous complex, markedly catalyzed the $Co(en)_3^{2+}$–$Co(en)_3^{3+}$ electron exchange. The effect disappeared within an hour or so and, provided the zero-time exchange was small because of this effect, the later linear portion of the resultant curve could be used to determine the true rate. The catalysis by oxygen was explained by the formation of a metastable cobaltous oxygen complex $[CoN_5O_2]^{2+}$ which exchanged more rapidly than did $Co(en)_3^{2+}(CoN_6)^{2+}$.

(*d*) Other possible causes of nonlinearity about which little further need be added include heterogeneity of exchange (343a), tracer isotope in secular or transient radioactive equilibrium with the parent (264), a case unlikely to be met in practice, and radiation-induced exchange (47). An example of the latter case arises during the radiation-induced O_2–H_2O exchange (221). Hydrogen peroxide is an inhibitor but until it attains a concentration of $10^{-5}M$ the exchange is fast; after this, it is much slower.

When changing rates of exchange are encountered it is possible sometimes to find the initial rate by extrapolating the exchange rates to early times. This procedure was adopted, for example, by Brown and Ingold (71) in their investigation of the exchange of chlorine between chloride ion and *cis*-$[Co(en)_2Cl_2]^+$ in methanol. The exchange of the second chlorine atom overlaps that of the first and the trans complex concurrently produced also has exchangeable chlorine. Extrapolation of the specific rate constants obtained at various stages of exchange to zero exchange gave the initial specific rate.

In the same way there was a continual loss of Cr(II) during the Cr(II)–$CrCl^{2+}$

electron-transfer exchange; Taube and King (448) extrapolated their observed rate to zero time to correct for this effect.

D. IMPORTANT CONSIDERATIONS IN THE INTERPRETATION OF EXCHANGE DATA

Before any detailed kinetic exchange studies can be undertaken there are several points which should be considered.

The nature and amount of the species likely to be present in the exchange mixture should be known. This is especially important when complex ions are involved in the study. Occasionally the conditions of the experiment can be adjusted so that only the two exchanging reactants are present; otherwise a knowledge of the stability constants governing the systems is essential in a detailed interpretation of the mechanism. The following examples, all involving electron-transfer processes, will illustrate this point. Hudis and Wahl (246) investigated the effect of fluoride ion upon the rate of the iron(II)–iron(III) exchange reaction in perchloric acid at 0.5 ionic strength. They measured the specific rate constant, k, defined by

$$R = k[\mathrm{Fe^{II}}][\mathrm{Fe^{III}}]$$

as a function of the fluoride-ion concentration. Since the formation constants of the iron(III)–fluoride complexes had been measured at this ionic strength (131), it was possible to correlate the variation of the specific rate constant with the free fluoride-ion concentration in terms of the various possible electron-transfer processes:

$$R(\text{overall rate}) = k_0[\mathrm{Fe^{3+}_{aq}}][\mathrm{Fe^{2+}_{aq}}] + k_1[\mathrm{FeF^{2+}}][\mathrm{Fe^{2+}_{aq}}] + k_2[\mathrm{FeF_2{}^{+}}][\mathrm{Fe^{2+}_{aq}}] + k_3[\mathrm{FeF_3}][\mathrm{Fe^{2+}_{aq}}] + k_4[\mathrm{FeF}_n^{x-}][\mathrm{Fe^{2+}_{aq}}] \quad (10)$$

In this way an intimate picture of the gross exchange process was obtained. Since iron(II)–fluoride complexes were considered not to form at the low fluoride concentrations used in most of the experiments (131) and in the acid concentrations used the amount of $\mathrm{Fe(OH)^{2+}}$ was negligible, these complex species were ignored for the purposes of the interpretation of the results.

Rossotti (404) has also stressed the importance of a knowledge of the equilibrium data in interpreting kinetic results by considering the exchange reaction between monovalent and trivalent thallium, which had been previously examined by two independent investigators (215, 385) with substantially the same experimental results. At the time of these investigations, however, the hydrolysis of trivalent thallium had not been quantitatively studied. With this information now available (48) Rossotti was able to show that the only important thallium(III) hydroxy complex present in the exchange solutions was $\mathrm{Tl(OH)^{2+}}$ and represented the overall exchange, R, in terms of two processes:

$$R = 0.154[\mathrm{Tl^{3+}}][\mathrm{Tl^{+}}] + 1.22[\mathrm{TlOH^{2+}}][\mathrm{Tl^{+}}] \quad (11)$$

Although the amount of $\mathrm{TlOH^{2+}}$ present in the various acidities of the exchange experiments never exceeded 10 per cent of the total Tl(III) present and was often much less, the higher specific rate constant for the electron transfer involving this ion and Tl^+ means that its contribution to the observed exchange is substantial. Monovalent thallium was completely unhydrolyzed, and the different interpretations of the two investigations (215, 385) arose mainly because of the absence of the hydrolysis data. The importance of such data is therefore self-evident, and although thallium(III) is hydrolyzed more readily than most metallic ions, similar considerations will obviously apply to other metal–ion electron-transfer processes.

Neumann and Brown (349) have simplified the apparent complexities of the Sb(III)–Sb(V) electron-transfer process in hydrochloric acid solution. The data can be interpreted if it is assumed that $SbCl_6^-$ is the Sb(V) species which exchanges with Sb(III). Previous difficulties apparently arose from the fact that the rate of formation of $SbCl_6^-$, rather than the electron-transfer process, is rate-determining under certain conditions.

When exchange studies in nonaqueous solvents are undertaken, it is equally important that the nature of the species present be considered. This point is well brought out in the exchange studies of organic bromine compounds with metal bromides (129, 153, 405); the results are equally pertinent, for example, to exchange between inorganic halogen compounds and halides in nonaqueous solvents. In the work of Evans and Sugden (153) the apparent bimolecular rate constant, k', for the exchange reaction:

$$n\text{-}C_4H_9Br + Br^{*-} \rightleftharpoons n\text{-}C_4H_9Br^* + Br^-$$

in acetone was observed to increase with decreasing concentration of lithium bromide. The latter is incompletely dissociated in acetone at the concentrations used, and

$$\begin{aligned} R &= k[C_4H_9Br][Br^-] = k[C_4H_9Br][LiBr]\alpha \\ &= \frac{-2.303}{t}\,\frac{[C_4H_9Br][LiBr]}{[C_4H_9Br] + [LiBr]}\log_{10}(1 - F) \end{aligned} \tag{12}$$

α, the degree of dissociation of lithium bromide, does not enter into the large expression because as far as distribution of Br^{*-} is concerned it does not distinguish lithium bromide and bromide ion because these are in rapid equilibrium. Then,

$$k\alpha = \frac{2.303}{t}\cdot\frac{1}{[C_4H_9Br] + [LiBr]}\log\left(\frac{1}{1 - F}\right) = k' \tag{13}$$

If the apparent bimolecular rate constant k' is therefore divided by α, to allow for this effect, an appreciably constant $k = k'/\alpha$ is obtained, as shown in table 1 (153). Undissociated lithium bromide exchanges very slowly with n-butyl bromide. No similar difficulties were encountered with the ethyl iodide exchange with sodium iodide in methyl alcohol, since it can be shown that over the concentration range used in the study, sodium iodide is almost completely dissociated in this solvent.

One of the assumptions made in the original derivation of the exchange law is that no net reaction accompanies the exchange. However, it is quite possible

TABLE 1

Data related to the exchange reaction between butyl bromide and lithium bromide in acetone solution (153)

$10^4[C_4H_9Br]$	$10^4[LiBr]$	α	$10^3k'$	$10^3k'/\alpha = 10^3k$
mole l.$^{-1}$	*mole l.*$^{-1}$		*l.mole*$^{-1}$ *min.*$^{-1}$	*l.mole*$^{-1}$ *min.*$^{-1}$
440–470	0.504	0.925	3.93	4.3
440–470	1.28	0.848	3.99	4.7
440–470	2.49	0.774	3.13	4.0
440–470	4.38	0.696	3.48	5.0
440–470	22.7	0.457	2.22	4.9
440–470	79.4	0.314	1.44	4.6
440–470	191.0	0.241	1.07	4.4

to obtain a first-order exchange law even when there is a net change (vide supra), so that it is important to verify that such a change in the type of species is not important. Otherwise the exchange behavior may apply to a species other than the one intended. For example, during the exchange study of $C^{14}N^-$ with the complex ion $Mn(CN)_6^{3-}$ (10) it was noticed that, although initially the color of the solution was orange-red, this faded to a pale yellow over 10 to 15 min. Obviously such behavior could have seriously vitiated the interpretation of the exchange results. It might be that it was the red form which was $Mn(CN)_6^{3-}$, which then changed to an entirely different yellow species. If the complex was dissolved in potassium cyanide solution and then potassium radiocyanide solution added immediately (red solution), the rate of exchange was similar to the normal results obtained on the yellow solution by allowing this color to develop before adding the potassium radiocyanide solution. This result, as well as subsidiary investigations of the color change, strongly suggested that the yellow solution does contain $Mn(CN)_6^{3-}$ and that the initial color is due to a slight impurity which does not affect the results. On the other hand, the slow fading in color of permanganate in strong acid (214) casts some doubts on the results of the exchange between Mn^{2+} and MnO_4^- in this solvent (4). It may be that an intermediate oxidation state and not MnO_4^- is involved in the exchange; however, a first-order exchange law is observed and the results obtained using two very different separation procedures are somewhat similar (4, 214), so that until the color change is understood, its importance cannot be fully assessed.

The drastic effect of small amounts of impurities on the reaction rates of complex ions has been noticed in several exchange studies. Ordinary distilled water induced some initial exchange of Cl^- and $AuCl_4^-$ and the usual log $(1 - F)$/time plot showed a distinct curvature. Redistilled water was used therefore to investigate the uncatalyzed exchange (391). The observation made in ordinary water led to a study of the induced exchange between these species by reducing agents, especially Fe^{2+} ion (392).

Rich and Taube (390) also found during the study of some exchange reactions of Cl^- and $PtCl_6^{2-}$ that the spontaneous exchange rate for the complex platinum(IV) ion derived from commercial $H_2PtCl_6 \cdot 6H_2O$ was much *less* than from prepared $Na_2PtCl_6 \cdot 6H_2O$ purified from rhodium, palladium, and iridium. Since the exchange is inhibited by (for example) $Fe(CN)_6^{3-}$ and $IrCl_6^{2-}$, it was concluded that the commercial specimen contained iridium or other possible inhibitors. Although in these two examples the anomalous results led to the uncovering of important effects, such behavior could result in incorrect results or interpretations if based on desultory experiments.

It is important that the chemical identity of the tracer used in an exchange study is completely characterized. It is certainly unsafe to assume that a labelled complex in tracer amounts will exist in the same chemical form as the added carrier even if both tracer and carrier have been subjected to the same chemical treatment. This is especially true of complex ions which undergo slow chemical substitution reactions. Sloth and Garner (420) encountered a good deal of difficulty because of this in their electron-transfer study of the $IrCl_6^{3-}$–$IrCl_6^{2-}$ exchange. Reduction of commercial H_2IrCl_6 containing Ir^{192} produced an Ir(III) tracer, which was assumed to be H_3IrCl_6 and which was therefore used to initiate exchange by addition to a mixture of inactive $IrCl_6^{3-}$ and $IrCl_6^{2-}$ ions. A slow and somewhat erratic exchange behavior was observed. If the Ir(III) tracer was then oxidized and reduced and the new Ir(III) tracer used in exchange studies, once again a slow rate (different from before) with an initial rapid drop was observed. Evidence was adduced that these tracers probably existed as Ir(III) aquo complexes, which might be expected to undergo slow charge-transfer reactions. Amongst others, a third tracer, unequivocally labelled as Na_2IrCl_6, was prepared by neutron irradiation of iridium metal, converting the irradiated material to solid Na_2IrCl_6 by heating a mixture of sodium chloride and the former with chlorine at 600°C. At no time was an inactive iridium compound added. The exchange reaction was rapid, using this material, as might be expected for the two anionic species (492). This behavior undoubtedly arises from the different reaction rates of carrier-free tracers and the different stability of intermediates in processes involving tracers. Related to this is the observation (274) that it is difficult to effect complete exchange between tracer amounts of fission iodine and macro amounts of iodine or iodide.

E. INCIDENTAL APPLICATIONS TO REACTION KINETICS

A feature of isotopic exchange reactions is that the overall concentrations of exchanging reactants do not change during the course of the exchange, which is simply a redistribution of isotopes. Factors such as pH and ionic strength which markedly influence the course of a reaction in solution also remain constant (at least in the ideal case). Exchange reactions should therefore serve as very useful systems for the testing of theories concerned with the influence of ionic strength and dielectric constant upon reaction rates. In view of this important advantage, it is rather surprising that so little work on these lines has been performed. Several inorganic systems have been studied with regard to the effects of ionic strength upon the exchange rate, but these effects have been used to confirm mechanisms rather than to test theories (10, 268, 308, 430). In organic systems the effect of the dielectric constant of the solvent on the rate of the hydrogen iodide–butyl iodide exchange (238) and the effects of pressure on the exchanges of *n*-propyl iodide and *n*-propyl bromide with alkali halides in ethanol have been investigated (346).

The rate of a photoinitiated exchange reaction can be used to determine quantum yields in a simple manner. For the general exchange reaction

$$AX + BX^* \rightleftharpoons AX^* + BX$$

in which exchange is initiated by light absorption by AX, the rate will be given by:

$$R = \phi I_{\text{abs}} = \phi I_0 E d a \tag{14}$$

(at low AX concentrations) where E is the extinction coefficient of AX and d the path length of the light. Combining equation 14 with equation 5, the exchange rate law may be written:

$$0.693/t_{\frac{1}{2}} = \phi I_0 E d(a/b + 1) \tag{15}$$

A study of the variation with intensity of the incident light of the exchange half-time at known reactant concentrations will thus evaluate the primary quantum yield, ϕ. This principle has been used in the $C^{14}O$–$COCl_2$ exchange system (435) to evaluate the primary quantum yield for the process:

$$COCl_2 + h\nu \rightarrow COCl + Cl$$

for which ϕ was found to be 1.00 at 2537 A. and 30°C. for both C^{12} and C^{14} molecules. The homomolecular exchange:

$$O_2^{16} + O_2^{18} \rightleftharpoons 2O^{16}O^{18}$$

is photosensitized by both chlorine and mercury vapor. The chlorine-initiated reaction has a quantum yield of much less than unity (360), whereas the mercury-sensitized reaction exhibits an overall quantum yield of 125 (267). Gazith and Noyes (185) have adopted the converse approach in assuming the primary quantum yield for iodine to deduce individual rate constants for the exchange between iodine and benzyl iodide.

The principle enunciated above is also applicable to radiation-induced exchanges for the deduction of G values, i.e., the number of molecules transformed per 100 e.v. of energy absorbed. The Ce(III)–Ce(IV) electron exchange is induced by unfiltered 50-kvp x-rays and in 0.8 N sulfuric acid the increased exchange rate is completely accounted for by the rate of Ce(IV) reduction. The G values for Ce(IV) reduction and for exchange are 3.28 and 3.2 ions/100 e.v., respectively (94). Exchange between water and dissolved oxygen is induced both photochemically and by Co^{60} γ-radiation and appropriate G values have been calculated (221). A kinetic study of the homomolecular H_2–T_2 exchange revealed that the exchange rate was proportional to the square root of the intensity of the absorbed β-radiation from the tritium (136).

III. Factors Influencing the Choice of a Tracer Isotope

A. AVAILABILITY OF ISOTOPES

The production of both radioactive and enriched stable isotopes has now advanced to the stage where the chemist may frequently choose from more than one isotope for use as a tracer element in an experiment. Generally speaking, the technical assay problems are considerably reduced if a radioactive isotope of an element is chosen. Moreover considerable dilution of a radioisotope can be tolerated in experiments (e.g., 10^6 is common), but dilution of a stable isotope is normally limited by the natural abundance of this isotope (e.g., deuterium or O^{18} cannot be diluted below their natural abundances of 0.016 per cent and 0.204 per cent, respectively). Nevertheless certain technical limitations, characteristic of radioisotopes alone, can modify the chemist's choice. The high neutron flux available in a nuclear reactor permits the production of suitable radioisotopes of many elements, most commonly by (n,γ) reactions, e.g., $Co^{59}(n,\gamma)Co^{60}$, although other reactions are important in several cases: e.g., $N^{14}(n,p)C^{14}$; $S^{32}(n,p)P^{32}$; $Cl^{35}(n,p)S^{35}$; $Li^6(n,\alpha)H^3$. The product nuclide of (n,γ) reactions is necessarily isotopic with the target element and this, combined with a low excitation cross-section or a long half-life of the product nuclide, may yield a radioisotope in only low specific activity; e.g., the activation cross-section for the $Be^9(n,\gamma)Be^{10}$ reaction is only 0.0085 barn, the Be^{10} product nuclide having a half-life of 2.7×10^6 yr. When such low specific activity is only attainable, the chemist may have to use large amounts of active material to obtain measurable disintegration rates, yet these concentrations may be too high for the desired experiment. This difficulty may sometimes be overcome, e.g., with Fe^{59}, by conducting the (n,γ) reaction on electromagnetically enriched material ($Fe_2^{58}O_3$) or utilizing a Szilard–Chalmers reaction (the recoil product from potassium ferrocyanide). A more serious objection is that neutron irradiation may only yield an isotope of inconveniently short half-life; e.g., Na^{24} (14.8 hr.), F^{20} (12 sec.). In selected cases, cyclotron bombardment may then be favored: e.g., $Li^7(d,n)Be^7$ (53 days); $O^{18}(p,n)F^{18}$ (112 min.); $Mg^{24}(d,\alpha)Na^{22}$ (2.6 yr.). For further details the review by Garrison and Hamilton should be consulted (184). Should both these production methods be unsuitable, several isotopes can be conveniently derived from separated fission products; e.g., ($Sr^{89} + Sr^{90}$) is abundantly available from this source, whereas Sr^{89} (reactor) and Sr^{85} (cyclotron) can only be produced in relatively low specific activities. Good accounts of the production of radioisotopes are contained in the texts of Kamen (275) and Whitehouse and Putman (473).

Despite the general availability of radioisotopes of most elements, there still remain some deficiencies, notably for nitrogen and oxygen. The cyclotron-produced isotopes N^{13} and O^{15} have half-lives of 10.1 and 2.1 min., respectively, which render them well-nigh useless for normal experiments. (For convenience, the half-life of the tracer should not be less than the duration of an experiment, although decay over some four half-lives in that time can usually be tolerated.) The choice of the enriched stable isotopes N^{15} and O^{18} is thus almost inevitable. Helium, boron, neon, magnesium, and aluminum are other elements which do not possess suitable radioisotopes or whose long-lived isotopes (e.g., Mg^{28}) are not yet generally available.

A further difficulty with radioisotopes arises when the energy of the emitted radiation is particularly low (e.g., tritium with a maximum β energy of 0.018

m.e.v. has a range of only 0.7 mg./cm.^{2} in matter) and specialized assay techniques, such as internal gas counting, become necessary. Deuterium is therefore the normally preferred tracer for hydrogen, but even in this case recent simplified techniques (87, 93) have rendered the task of counting tritium far less formidable than is commonly assumed.

Two distinct advantages of stable isotopes should be indicated. Firstly, duplicate assays of stable isotopic samples can be performed with present-day high-resolution mass spectrometers to a standard deviation error of ± 0.1 per cent. The assay of radioactive samples (especially solids) may be rapidly and conveniently performed to a standard deviation of ± 1 per cent, but further improved precision to even ± 0.5 per cent is difficult owing to irreproducibilities in sample preparation and to the inherent statistical uncertainty occasioned by the random nature of radioactive disintegrations. Secondly, the detection of the actual position of a stable tracer atom in a labelled molecule may be deduced frequently from the mass-spectral pattern obtained in the assay of the molecule. On the other hand, the position of a radioactive atom in a molecule can only be determined by a series of degradative steps, which in themselves must not cause isotopic exchange or rearrangements among the various positions in a molecule. When employing mass-spectrometric analysis, care should be taken to assign mass numbers correctly. For example, the alkaline oxidation of ammonium salts to nitrogen by hypobromite gave lines at mass number 44 due to traces of nitrous oxide formed during the reaction and at mass number 30 due to NO^+ formed by ionization cleavage of nitrous oxide (396). The latter might be incorrectly assigned to N_2^{15} and invalidate N^{15} experiments based on this reaction. A second limitation in using stable isotopes is the need for greatly increased dispersion in mass spectrometers when isotopes are used as tracers for elements of high atomic weight.

B. ASSAY PROCEDURES

1. *Radioactive isotopes*

In this section only general principles will be outlined; further details are readily available in standard texts (113, 174). In many radiotracer experiments the active sample is isolated from a reaction mixture as a precipitate. The accuracy of the subsequent assay largely depends upon the uniformity and reproducibility with which this solid can be mounted on a suitable support (such as a metal pan). The problem of sample mounting is especially serious for weak β-emitting nuclides such as C^{14} and S^{35} ($E_{\max} = 0.15$ m.e.v.) but is less important for higher-energy β-emitters (i.e., $E_{\max} > 0.6$ m.e.v., such as P^{32} 1.7 m.e.v.) and γ-emitters. In general the solid may be dissolved in a suitable reagent and evaporated in an assay pan (421), slurried in an inert solvent, and dried (91) or collected in either a filter cup or on filter paper (233). The precipitate chosen for the assay procedure must therefore be chemically and physically stable and amenable to a suitable method of sample mounting. Thus C^{14} is frequently assayed as barium carbonate, S^{35} as barium sulfate or benzidine sulfate, and P^{32}

as magnesium ammonium phosphate. The dried solid sample may then be positioned reproducibly under an end-window Geiger or scintillation counter (113) or inserted in an internal gas-flow proportional counter (397). To assay duplicate solid samples to a standard deviation of 1 per cent by this general method requires a fair degree of manipulative skill. If the sample can be assayed as a liquid in a skirted-wall Geiger counter, sample preparation and reproducibility are not major problems. Geiger counting of liquids is only possible for strong β-emitting nuclides ($E_{\max} > 0.5$ m.e.v.) and γ-emitting nuclides, but the liquid counting of weak β-emitting nuclides (notably C^{14} and S^{35}) in a gas-flow proportional counter (413), in the presence of a suitable liquid scintillator (222) or in a plastic-scintillator dish (437), is now feasible. When a high detection efficiency is required or when a weak β-emitter (e.g., tritium) is to be assayed, recourse must be normally made to gas-phase counting. In such cases the possible chemical form of the labelled gas is limited to those molecules which have suitable ionization characteristics. Methane, butane, and acetylene are frequently favored for the assay of both C^{14} and H^3, although less suitable gases such as H_2^3O can be introduced at a low pressure (87, 93) with a carrier gas used to operate the counter. Operation of a gas counter in the proportional, rather than the Geiger, region is preferred, owing to the higher stability and lower sensitivity to contaminant gases such as oxygen. A scintillation gas counter, which is very insensitive to gas impurities, has been recently described (437). Nevertheless from the manipulative viewpoint, all gas-counting methods are more complex than liquid- and solid-counting methods, which are to be preferred for most normal tracer experiments.

2. Stable isotopes

In principle it is possible to use the difference in any property of normal and isotopically enriched molecules as the basis of an assay method for an enriched stable isotope. This difference must be sufficiently large for convenient and accurate measurement. Kirshenbaum (281) has discussed the detailed procedures, difficulties, and relative merits of various assay methods for isotopic water, and Dole (134) has subsequently indicated more recent refinements to experimental techniques. The general principles enunciated are pertinent to all stable isotopes. Mass spectrometry, density measurements, and absorption spectrometry now appear to be the most favored analytical methods, although thermal conductivity (156) and refractometry (121) may also be employed. The mass spectrometer represents the most versatile instrument in that most chemical samples can be analyzed, although these samples must normally be converted into a suitable gas either by direct decomposition (281), e.g.,

$$\mathrm{Zn + CaO + HDO \xrightarrow{550°C.} CaZnO_2 + HD}$$

or by equilibration (110), e.g.,

$$\mathrm{CO_2^{16} + H_2O^{18} \rightleftharpoons CO^{16}O^{18} + H_2O^{16}}$$

the latter procedure requiring a knowledge of the relevant exchange equilibrium constant (Section VII). Density measurements are normally restricted to the analysis of isotopic water samples (D_2O and H_2O^{18}) and are frequently based on the use of either a micropycnometer (186) or a quartz temperature-float (297). This method gives results almost comparable to those for a routine mass spectrometer used in analyzing water samples and the instrumentation required is substantially less. Absorption-spectrometric methods (infrared, microwave, or ultraviolet) can be applied to any molecule exhibiting a distinct spectral shift on isotopic substitution. The method should be generally applicable to deuterium-labelled compounds, all of which exhibit gross spectral shifts (e.g., D-substitution in the boranes (278)) but can also be applied when the spectral shifts are much smaller (e.g., N^{15} substitution in nitrogen (256)). This method is eminently suitable for the assay of stable isotopes, since exchange or decomposition reactions can be followed without removal of samples from the reaction mixture. In all other assay methods for both stable and radioactive isotopes, samples must normally be removed from the reaction mixture (but see 500); this is especially inconvenient for gas-phase studies.

IV. Exchange Reactions in the Detection of Equilibria

The observation of isotopic exchange between two chemical species can be used to detect a chemical equilibrium involving these same species. The majority of examples where this principle has been used involve immeasurably fast exchange produced as evidence of the existence of rapid equilibria. Particularly is this the case with nonaqueous solvent systems where tracers have been mainly used in an attempt to detect the small amount of autoionization which is considered to exist in many protonic and nonprotonic solvents (30).

A. SOLVENT SYSTEMS

The addition of either tagged NH_4^+ or NH_2^- ions to liquid ammonia should rapidly lead to labelling in the solvent *via* the rapid dissociative equilibrium:

$$2NH_3 \rightleftharpoons NH_4^+ + NH_2^-$$

and in fact a rapid exchange between added $N^{15}H_4Cl$ and the solvent ammonia has been observed even at $-60°C$. (357). Unfortunately, another interpretation of this result is possible, since direct proton transfer will as easily explain the rapid exchange:

$$N^{15}H_4^+ + NH_3 \rightleftharpoons N^{15}H_3 + NH_4^+$$

Certainly, Ogg has shown from work with magnetic resonance spectra that the latter reaction is very fast, as well as the relevant one,

$$NH_2^- + NH_3 \rightarrow NH_3 + NH_2^-$$

with rate constants of the order of 10^{11} mole^{-1} cm.^{3} sec.$^{-1}$ (361a). Similarly, proton transfer rather than self-ionization of acetic acid might easily account for the rapid exchange of $CH_3C^{14}OO^-$ with CH_3COOH (154). With the oxygen-containing solvents (for example, sulfur dioxide) the situation is no better. The rapid exchange of the "base" tetramethylammonium pyrosulfite, $[(CH_3)_4]_2S_2O_5$ with $S^{35}O_2$ is probably better explained (265) by a mechanism involving a direct oxide-ion transfer:

$$S_2O_5^{2-} \rightleftharpoons SO_3^{2-} + SO_2 \qquad (1)$$

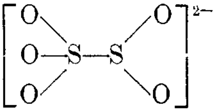
$$SO_3^{2-} + S^{35}O_2 \rightleftharpoons SO_2 + S^{35}O_3^{2-} \qquad (2)$$

rather than by the alternative one, which supports the idea of autoionization in sulfur dioxide (reaction 3):

$$S_2O_5^{2-} \rightleftharpoons SO_3^{2-} + SO_2 \qquad (1)$$

$$2S^{35}O_2 \rightleftharpoons S^{35}O^{2+} + S^{35}O_3^{2-} \qquad (3)$$

That the exchange takes place via equilibrium (1) alone is unlikely, since the pyrosulfite ion has the structure



with nonequivalent sulfur atoms and only half of the pyrosulfite sulfur would exchange with the sulfur of $S^{35}O_2$. The evidence for the mobility of oxide ions in liquid sulfur dioxide is strong. The fast exchange of oxygen (344) and the very slow exchange of sulfur (257) between sulfur dioxide and sulfur trioxide at room temperature led Huston (257) to suggest a mechanism involving an oxide-ion transfer:

$$SO_2 + SO_3 \rightleftharpoons SO^{2+} + SO_4^{2-} \text{ (or } SO_2 + 2SO_3 \rightleftharpoons SO^{2+} + S_2O_7^{2-}\text{)}$$

to account for these differences. A mechanism involving self-ionization of the sulfur dioxide (344) would necessarily lead to exchange in both cases:

$$2SO_2 \rightleftharpoons SO^{2+} + SO_3^{2-}$$

$$SO_3 + SO_3^{2-} \rightleftharpoons S_2O_6^{2-}$$

Mechanisms involving oxide-ion transfer processes have also been postulated for the observed catalysis by dissolved ionic halides of the thionyl bromide–sulfur dioxide (235) and the thionyl chloride–sulfur dioxide (320) exchanges. For the latter exchange, for example, a rate law

$$R = k[\text{catalyst}][\text{thionyl chloride}][\text{sulfur dioxide}]$$

was observed and the mechanism suggested was:

$$S^{35}O_2 + Cl^- \rightarrow S^{35}O_2Cl^- \text{ (fast)}$$

$$S^{35}O_2Cl^- + SOCl_2 \rightarrow S^{35}OCl_2 + SO_2Cl^- \text{ (slow)}$$

An oxide-ion transfer could account for the rapid exchange of N_2O_4 with $N^{15}O_3^-$ (108). An exchange result possibly free from objections of the kind outlined above involves nitrosyl chloride. The rapid exchange of Cl^{36-} with nitrosly chloride has been adduced as definite evidence for the self-ionization of this solvent (299). A nitrosonium-ion transfer mechanism seems much less likely, i.e.,

$$Cl^{*-} + NOCl \rightleftharpoons Cl^{*}NO + Cl^{-}$$

Both chloride ion and nitrosyl chloride, which would be the participating species in such a mechanism, are electron donors. Only kinetic studies of these very fast exchanges and the accumulation of rate laws will possibly resolve these ambiguities.

Does then the converse hold true that the *absence* of rapid exchange between dissolved solute and solvent invalidates the idea of rapid self-ionization of the solvent? Here again the results have to be treated with caution. The absence of exchange of thionyl compounds with liquid sulfur dioxide (197, 265, 337) might easily arise from incomplete ionization of the former, e.g., $SOCl_2 \rightleftharpoons SOCl^{+} + Cl^{-}$ to produce a species ($SOCl^{+}$) which did not exchange with the solvent. The negative result does mean, however, that *both* ionizations

$$2SO_2 \rightleftharpoons SO^{2+} + SO_3^{2-}$$

and

$$SOCl_2 \rightleftharpoons SO^{2+} + 2Cl^{-}$$

do *not* occur at the same time. Similar considerations apply to the slow exchange of acetic anhydride and acetic acid (154) and possibly of aluminum chloride and phosgene (258).

Exchange work in solvent systems is difficult experimentally. High-vacuum apparatus is invariably used and care has to be taken that, as far as possible, moisture is excluded. The purification of reactants and their preparation in an anhydrous condition are essential. Neat devices have been described for the addition of solute to solvent and for other manipulative techniques (e.g., 154). Although the separations used (invariably distillation methods) very probably preclude separation-induced exchange, separation times of less than several minutes are not easily attained. A table showing the application of exchange studies to solvent systems is given (table 2).

B. MISCELLANEOUS EQUILIBRIA

By the same kind of reasoning as in Section IV,A the absence of exchange may indicate that a certain reaction is "irreversible" and an upper limit may be assigned to the equilibrium constant. The hydration of hypophosphoric acid is known to lie well to the right, but a small amount of hypophosphoric acid, not easily detected by analytical methods, may remain when equilibrium is attained:

$$H_2O + H_4P_2O_6 \rightleftharpoons H_3PO_3 + H_3PO_4$$

The existence of a reversible equilibrium involving $H_4P_2O_6$, H_3PO_3, and H_3PO_4 will necessarily lead to phosphorus exchange between H_3PO_3 and H_3PO_4 provided

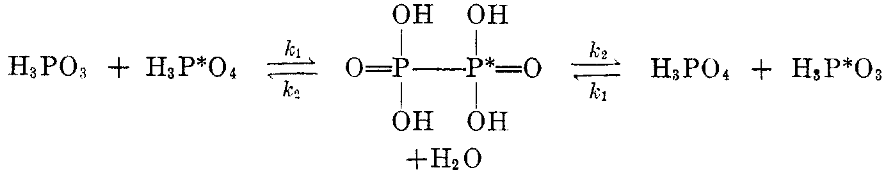
TABLE 2

Exchange in solvent systems

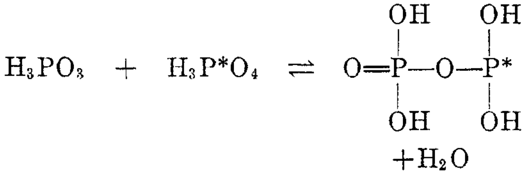
Solvent	Solute(s)	Temperature	Exchange Rate	Remarks	References
		°C.			
$COCl_2$	$AlCl_3^*$	0	$t_{\frac{1}{2}} \sim$ 12–60 hr.	Homogeneous; nonphotochemical; addition of halide does not catalyze exchange (see reference 235)	(258)
$COCl_2$	$CaCl_2^*$	25	<1% in 119 days	Heterogeneous	(258)
$COCl_2$	$NaCl^*$	25	1% in 113 days	Heterogeneous	(258)
CH_3COOH	CH_3C^*OONa		$t_{\frac{1}{2}} < 1$ min.		(154)
CH_3COOH	$(CH_3C^*OO)_2Pb$		$t_{\frac{1}{2}} < 1$ min.		(154)
CH_3COOH	$(CH_3C^*OO)_4Pb$		$t_{\frac{1}{2}} < 1$ min.		(154)
CH_3C^*OOH	$(CH_3CO)_2O$	25	$t_{\frac{1}{2}} \sim 10$ hr.		(154)
$(CH_3CO)_2O$	CH_3C^*OONa	Room temperature	Slow	Heterogeneous	(154)
$(CH_3CO)_2O$	$(CH_3C^*OO)_4Pb$	Room temperature	$t_{\frac{1}{2}} \sim 1$ min.		(154)
$(CH_3CO)_2O$	CH_3C^*OOH	0	$t_{\frac{1}{2}} \sim 5$ hr.		(154)
$(CH_3C^*O)_2O$	CH_3COCl	0	$t_{\frac{1}{2}} \sim 10$ hr.		(154)
NH_3	N^*H_4Cl	−33, −60	$t_{\frac{1}{2}} < 2$ min.		(357)
N_2O_4	$(CH_3)_4NN^*O_3$		Complete exchange		(108)
$NOCl$	$(C_2H_5)_4NCl^*$	−36	Complete within 3 min.	Nonphotochemical	(299)
S^*O_3	SO_2	132	1.5% (624 hr.)		(257)
S^*O_2	SO_3	132	None (72 hr.)		(257)
SO_3	SO_2^*	20	Moderately fast		(344)
S^*O_2	$[(CH_3)_4N]_2S_2O_5$	−21	$t_{\frac{1}{2}} < 20$ min.		(265)
		−75	Fast; 80% in 20 min.		
SO_2^*	$SOCl_2$	0	Negligible in 9 days		(197)
S^*O_2	S^*OCl_2	61	$t_{\frac{1}{2}} \sim$ 2–6 yr.		(265, 337)
S^*O_2	$SOBr_2$	25	$t_{\frac{1}{2}} \sim 1.9 \pm 0.4$ yr.		(265)
S^*O_2	S^*OBr_2, $(CH_3)_4NBr$	−22 to 25	$R = 2.50 \times 10^8 e^{-13,200/RT} \times [\text{catalyst}]$	Slight heterogeneous catalysis; KCl, KBr, RbBr, RbCl, and CsBr also catalyze	(235)
S^*O_2	S^*OCl_2, $(CH_3)_4NCl$	0–25	$R = 1.08 \times 10^7 e^{-14,700/RT} \times [(CH_3)_4NCl] [SOCl_2] [SO_2]$	HCl, aqueous HCl, and $AlCl_3$ very weak catalysis; mechanism suggested	(320)
SO_2	S^*OCl_2, RbCl	0–25	$R = 5.31 \times 10^6 e^{-14,700/RT} \times [RbCl] [SOCl_2] [SO_2]$	As for previous system	(320)
S^*OCl_2	SO_2, $(CH_3)_4NCl$	0–25	$R = 5.11 \times 10^6 e^{-13,600/RT} \times [(CH_3)_4NCl] [SOCl_2] [SO_2]$	As for previous system	(320)
SO_2	$(C_2H_5)_3NS^*O_2$	−70, −80	Complete exchange within 4 min.	Ready dissociation of complex	(234)
SO_2	$(C_2H_5)_3NS^*O_2H_2O$	−70, −80	Complete exchange within 4 min.	Ready dissociation of complex	(234)
$SOCl_2$	$(CH_3)_4NCl^*$	0	C 80 min.†	Also complete in SO_2 solvent (−20°)	(501)
$SOCl_2^*$	$SbCl_3$	0	C 40 min.		(501)
$POCl_3$	$(CH_3)_4NCl^*$	25	C 105 min.		(501)
$SeOCl_2$	KCl^*	21	C 50 min.		(501)
$SeOCl_2^*$	$FeCl_3$	40	C 150 min.		(501)

† The letter C preceding a listed time indicates that ⩾95 per cent exchange occurred at the lowest concentrations and temperature conditions.

that hypophosphoric acid has a symmetrical structure (331) but not if it possesses an unsymmetrical one:



$$H_3PO_3 + H_3P^*O_4 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \begin{matrix} OH & OH \\ | & | \\ O{=}P & {-}{-}P^*{=}O \\ | & | \\ OH & OH \end{matrix} + H_2O \underset{k_1}{\overset{k_2}{\rightleftharpoons}} H_3PO_4 + H_3P^*O_3$$



$$H_3PO_3 + H_3P^*O_4 \rightleftharpoons \begin{matrix} OH & & OH \\ | & & | \\ O{=}P & {-}O{-} & P^* \\ | & & | \\ OH & & OH \end{matrix} + H_2O$$

Wilson (483) observed negligible exchange between H_3PO_3 and $H_3P^{32}O_4$ in 26 days at 25°C. By placing an upper limit on the amount of exchange after this time, it was possible to assign a maximum value for k_1, and hence for the equilibrium constant for the reaction ($K = k_1/k_2$), since k_2 was known from independent hydrolysis experiments. Thus K was estimated to be less than 8×10^{-5} liter mole^{-1} at 25°C. in 5.6 N hydrochloric acid, assuming a symmetrical structure for hypophosphoric acid.

Owen and Johnson (367) have suggested that the slow exchange between arsenic trichloride and chlorine in carbon tetrachloride constitutes good evidence for the nonexistence of arsenic pentachloride, since rapid exchange would have been expected from a reversible equilibrium:

$$AsCl_3 + Cl_2 \rightleftharpoons AsCl_5$$

This argument presupposes that the formation of arsenic pentachloride in solution would be rapid, which seems reasonable in view of the rapid reaction between phosphorus trichloride and chlorine. The exchange is markedly catalyzed by traces of hydrogen chloride which seem always to be present and the observed exchange is believed to occur via hydrogen chloride:

$$HCl + AsCl_3 \rightleftharpoons HAsCl_4$$

with rapid HCl–Cl_2 exchange also occurring (266).

From the results of such experiments as these, evidence for the probable absence of a molecular species in solution may be deduced.

So far the discussion has centered mainly around rapid or very slow exchange. The value of these studies has been seen to be somewhat limited. If, however, the equilibrium is approached at a measurable rate, then it is possible to correlate exchange *rates* with *equilibrium* data obtained by other means (i.e., forward and reverse reaction rates and equilibrium constants). The "classical" example of this correlation is the study of exchange between labelled arsenic acid and inactive arsenious acids in the presence of I_3^- (484). This has been fully discussed by Crompton (122).

The results of exchange studies and the interpretation of the mechanism of the nitrogen pentoxide decomposition constitute a more recent example of both the detection of an equilibrium and its subsequent quantitative investigation.

Ogg (358) suggested that in the decomposition of nitrogen pentoxide the initial step involved a rapid equilibrium lying well to the left:

$$N_2O_5 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} NO_2 + NO_3 \quad \text{(rapid equilibrium)} \tag{1, 2}$$

and that the subsequent stages were:

$$NO_2 + NO_3 \xrightarrow{k_3} NO_2 + NO + O_2 \quad \text{(slow)} \tag{3}$$

$$NO + N_2O_5 \xrightarrow{k_4} 3NO_2 \quad \text{(rapid)} \tag{4}$$

This mechanism demanded that nitrogen pentoxide should exchange rapidly with nitrogen dioxide via the fast equilibrium (1, 2) (either nitrogen compound being tagged). Ogg (359) used the 10-min. N^{13} isotope to study the exchange of nitrogen pentoxide with $N^{13}O_2$ in carbon tetrachloride and found in agreement with his ideas that using approximately 0.1 M exchange reactants the exchange was fast ($t_{\frac{1}{2}} \sim 2$ min., 10°C.). The half-life of the decomposition of the nitrogen pentoxide under similar conditions would be as much as 60 hr. This constituted therefore the first experimental proof of the reversibility of the first step. The procedure involved quenching the exchange (which at the same time separated the exchanging species) by addition of alkali ($N_2O_5 \rightarrow NO_3^-$; $NO_2 \rightarrow NO_3^- + NO_2^-$) and following the decrease in activity of the NO_2^- (counted as silver nitrite) as a measure of the exchange. At the same time it was necessary to confirm that the NO_2^-–NO_3^- exchange did not occur in solution during these operations. The confirmation of step 1 in the gas phase (120, 362) was accomplished *without the necessity of a separation* by the elegant device of following the change in infrared absorption of a mixture of $N^{15}O_2$ and normal N_2O_5. The exchange reaction:

$$N_2^{14}O_5 + N^{15}O_2 \rightleftharpoons N_2^{15}O_5 + N^{14}O_2$$

leads to a diminishing amount of $N^{15}O_2$ which could be directly followed by a fast scanning spectrometer, using the very strong ν_3 fundamental band of nitrogen dioxide at 1621 cm.$^{-1}$ The exchange rate R was shown to be approximately represented by the relationship:

$$R \simeq 0.5\,[N_2O_5] \tag{16}$$

(at 27°C. and with 500 mm. of mercury partial pressure of carbon dioxide added to improve the resolution of the $N^{15}O_2$ P branch). This is essentially in agreement with the value obtained from a study of the reaction $N_2O_5 + NO \rightarrow 3NO_2$ (362), which is also presumed to be governed by the N_2O_5 bond-breaking stage (1).

$$N_2O_5 \underset{k_2}{\overset{k_1}{\rightleftharpoons}} NO_2 + NO_3 \tag{1, 2}$$

$$NO_3 + NO \xrightarrow{k_4} 2NO_2 \quad (k_4 \gg k_2)$$

Amell and Daniels (13) investigated the kinetics of the $N^{15}O_2$–N_2O_5 exchange in the gas phase. The exchange reaction was stopped at various times by adding sodium hydroxide solution in the same way as for the work with N^{13} (359). Sulfamic acid was added to destroy nitrite, and the nitrate remaining was converted into nitrogen gas with sodium hypobromite. The N^{15}/N^{14} ratio of the nitrogen gas was measured.

If the exchange proceeds via equilibrium 1, then because $k_1 \ll k_2$ the rate of exchange, R, will be given by

$$R = k_1[N_2O_5] = \frac{2.303}{t}\,\frac{2[N_2O_5][NO_2]}{2[N_2O_5] + [NO_2]}\log\left(1 - \frac{x_t}{x_\infty}\right) \qquad (17)$$

x_t and x_∞ representing the concentration of N^{15} in nitrogen pentoxide at times t and at equilibrium. A full account of the calculations involved in determining x_t/x_∞ from the experimental data is given by Amell and Daniels, whose paper should be consulted for these useful details. The data obtained conform with the value for $k_1 = 6 \times 10^{12}\, e^{-19,000/RT}$ sec.$^{-1}$ and this is, once again, in fair agreement with the rate constant and energy of activation obtained for the NO + N_2O_5 reaction under comparable experimental conditions. The kinetics of the decomposition of nitrogen pentoxide are fully discussed by Frost and Pearson (180).

The confirmation of the tautomeric equilibrium existing in an aqueous solution of hypophosphorous acid (489) illustrates the importance of the isotopic exchange approach.

The slow oxidation of hypophosphorous acid to phosphorous acid by various oxidants, including the halogens (489), iodate (223), and iodine monochloride (166), has been the subject of several investigations. The rate of oxidation is independent of the concentration of oxidizing agent provided this is sufficiently large. The results are best explained by the assumption of a slow, acid-catalyzed change from a normal form of the acid $[H_3PO_2]_I$ to an "active" form $[H_3PO_2]_{II}$. Virtually only the latter form (which is present in very small concentrations) is oxidized, and when the oxidant concentration is high, the tautomeric change (step 1) is the rate-determining step:

$$[H_3PO_2]_I \underset{k_2}{\overset{k_1}{\rightleftharpoons}} [H_3PO_2]_{II} \qquad (1, 2)$$

$$[H_3PO_2]_{II} + \text{oxidant} \xrightarrow{k_3} H_3PO_3 + \text{reductant} \qquad (3)$$

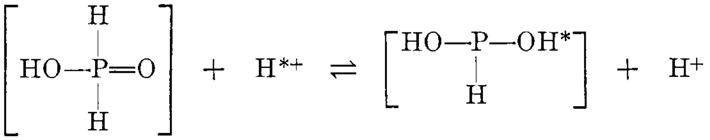
The irreversibility of step 3 is shown by the nonexchange of phosphorus between H_3PO_2 and H_3PO_3 even in the presence of iodine or iodide ion (67). Strong evidence for the reality of the proposed tautomeric forms has been provided by two independent studies of exchange between labelled water and hypophosphorous acid (69, 262). In one case HTO was used and the rate of increase in radioactivity of the dissolved acid determined (as precipitated thallous hypophosphite) (262). In the other work (69) the rate of loss of the deuterium content of D_2O was measured after contact with the acid. In both cases the rapid exchange of one hydrogen of the H_3PO_2 (in the hydroxyl group) was allowed for, and the exchange rate of the remaining two hydrogens was related quantitatively to the relevant oxidation rate constant. Considering the results of Jenkins and Yost (262): when hypophosphorous and oxonium acids only are present

$$R \text{ (exchange)} = k_1^{\mathrm{H}}[\mathrm{H^+}][\mathrm{H_3PO_2}] + k_1^{\mathrm{H_3PO_2}}[\mathrm{H_3PO_2}]^2 \tag{18}$$

and at 30°C. k_1^{H} and $k_1^{\mathrm{H_3PO_2}}$ are 3.3 ± 0.15 and 2.9 ± 0.14 liters mole^{-1} hr.$^{-1}$ Comparing these results with the study of the oxidation of hypophosphorous acid by iodine (196)

$$R \text{ (oxidation)} = k_1^{\mathrm{H}}[\mathrm{H^+}][\mathrm{H_3PO_2}] + k_1^{\mathrm{H_3PO_2}}[\mathrm{H_3PO_2}]^2 \tag{19}$$

where at 30°C. k_1^{H} and $k_1^{\mathrm{H_3PO_2}}$ are 21 and 7.6 liters mole^{-1} hr.$^{-1}$, the form of the rate equation and the values of the rate constants (bearing in mind isotope effects) are in good agreement with each other. The Russian workers (69) visualized the mechanism for the tautomerism (and the exchange path) as:



$$\left[\mathrm{HO{-}\overset{\displaystyle H}{\underset{\displaystyle H}{P}}{=}O}\right] + \mathrm{H^{*+}} \rightleftharpoons \left[\mathrm{HO{-}\underset{\displaystyle H}{P}{-}OH^*}\right] + \mathrm{H^+}$$

$[\mathrm{H_3PO_2}]_{\mathrm{I}}$ $[\mathrm{H_3PO_2}]_{\mathrm{II}}$

For a detailed discussion of this and other exchanges of inorganic molecules the reader is referred to an article by Brodskiĭ (64).

In the ion $\mathrm{H_2PO_2^-}$ exchange with $\mathrm{D_2O}$ is slower by a factor of 10^6–10^7 and an analogous tautomerism is probably unimportant (69). The nonexchange of $\mathrm{D_2O}$ with the one phosphorus–hydrogen bond of $\mathrm{H_3PO_3}$ (69) appears to rule out an analogous mechanism involving a pretautomerism of phosphorous acid which had been suggested (330) for the much slower subsequent oxidation of orthophosphorous to orthophosphoric acid. On the other hand, the rate of oxidation in water of dialkyl phosphites, $\mathrm{HPO(OR)_2}$, by excess iodine is independent of the iodine concentration and is the same rate as with bromine oxidation (356). The tautomerism, which has been proposed for this case also, should be checked by tagged water exchanges.

An exchange study of the $\mathrm{PH_3}$–$\mathrm{D_2O}$ system (471) has been used to assign an acid and base constant to phosphine. The $\mathrm{IO_3^-}$–$\mathrm{I_2^{131}}$ system (111, 342) constitutes a good example of the necessity of considering activity coefficients in assessing rate data and has been fully discussed in a previous review (15).

V. EXCHANGE REACTIONS AND MOLECULAR STRUCTURE

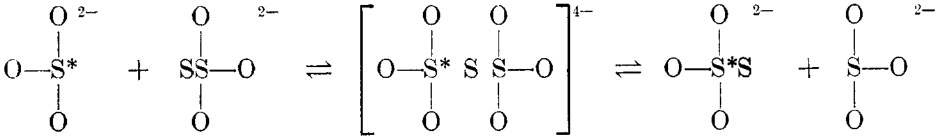
Exchange processes, which are usually carried out on nonreacting systems, can give information as to the structure of the exchanging species, the intermediates, and, in some cases, even the transition state. When diborane reacts with ammonia at −120°C. a salt-like solid of composition $\mathrm{B_2H_6 \cdot 2NH_3}$ is obtained. Burg (84) was able to show from deuterium-exchange studies that six hydrogen atoms were different from the other six. He studied the exchange of $\mathrm{B_2H_6 \cdot 2NH_3}$ with nearly pure $\mathrm{ND_3}$ at −78°C. and found that the $\mathrm{ND_3}$ was "diluted" with ordinary hydrogen to the extent of half of the hydrogens of the boron compound. In another experiment he showed that no loss of deuterium content of the ND_3 occurred in 60 hr. at 18°C. between $B_2H_6 \cdot 2ND_3$ and ND_3 and that even heating the mixture at 40°C. (during which extensive ammonolysis occurred) induced no exchange between B—H and N—D. These observations were in agreement with the favored structure $NH_4^+(H_3B \cdot NH_2 \cdot BH_3)^-$ and ruled out suggested alternatives such as $(NH_4)_2^{2+}(B_2H_4)^{2-}$. The deuterium content of the separated ND_3 was measured by vapor tension against that of known mixtures, using a differential tensiometer.

Another example of the different exchangeability of atoms within a molecule is afforded by phosphorus pentachloride. The phosphorus pentachloride–chlorine exchange in carbon tetrachloride (140) has been already referred to in Section II. The "zero-time" exchange of three of the five chlorine atoms followed by slow exchange of the remaining two constitutes unique evidence for the different reactivity of the equatorial and apical chlorines of the phosphorus pentachloride molecule, and also indicates a trigonal bipyramidal, rather than a tetragonal pyramidal, structure for phosphorus pentachloride.

An exchange study that yields information on the structure of the reactant (and possibly on the transition state) is the $S_2O_3^{2-}$–SO_3^{2-} exchange thoroughly examined by Ames and Willard (14). The exchange equilibrium corresponded to exchange of only one sulfur atom (the outer) of the thiosulfate group:

$$S^*O_3^{2-} + SSO_3^{2-} \rightleftharpoons SS^*O_3^{2-} + SO_3^{2-}$$

Since the rate R ($= k[SO_3^{2-}]\,[S_2O_3^{2-}]$ for most of the conditions studied) varied little with a pH change from 12 to 5, it appeared that both SO_3^{2-} and HSO_3^- were equally able to collide with $S_2O_3^{2-}$ and effect the transfer of sulfur. The species present in the solution under the conditions of the exchange were considered (including possible ion-pairs) and the suggested mechanism involved a symmetrical activated complex:



$$\mathrm{O{-}}\underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}^*}}{}^{2-} + \mathrm{S}\underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}}}\mathrm{{-}O}^{2-} \rightleftharpoons \left[\mathrm{O{-}}\underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}^*}}\ \mathrm{S}\ \underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}}}\mathrm{{-}O}\right]^{4-} \rightleftharpoons \mathrm{O{-}}\underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}^*}}\mathrm{S}^{2-} + \underset{\underset{\mathrm{O}}{|}}{\overset{\overset{\mathrm{O}}{|}}{\mathrm{S}}}\mathrm{{-}O}^{2-}$$

It is perhaps worth digressing a little here to point out that the existence (on paper) of a symmetrical transition state obviously does not mean that exchange will necessarily occur between two exchanging species. The SO_3^{2-}/SO_4^{2-} exchange, which is formally similar to the $SO_3^{2-}/S_2O_3^{2-}$ system, is extremely slow and possible reasons for this have been discussed (14). Whilst the exchange of thiocyanate ion and cyanide ion through the symmetrical transition state $(NCSCN)^{2-}$ might appear possible at first sight, in fact no exchange occurs (8).

A good example of the observation of exchange and the formulation of the activated complex comes from the Cr^{2+}-catalyzed $CrCl^{2+}$–Cl^- exchange (448). This exchange in perchloric acid is immeasurably slow in the absence of catalysts and does not arise from Cr^{2+}-catalyzed dissociation of $CrCl^{2+}$. From some preliminary experiments at 0°C. a rate law

$$R = 31[Cr^{2+}][Cl^-][CrCl^{2+}]$$

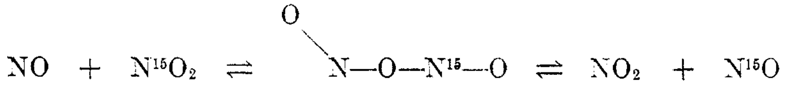
is indicated and the exchange path is considered to be via the equilibrium:

$$CrCl^{2+} + Cl^- + Cr^{2+} \rightleftharpoons CrCl_2^+ + Cr^{2+}$$

which lies well to the left. The reverse reaction is a known electron-transfer process (449). Since the activated complex is readily accessible from $CrCl^{2+}$, Cl^-, and Cr^{2+} ions, and the chromium–chlorine link is preserved during the process (from chloride tracer studies; see later), no juxtaposition of groups occurs during the process and the most reasonable formulation of the transition state appears to be (448):

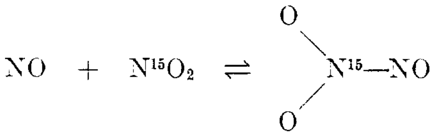
$$[Cr\text{---}Cl\text{---}Cr\text{---}Cl]^{3+}$$

Some care has to be taken however in assigning *molecular structure* on the basis of exchange experiments. The rapid exchange of NO and $N^{15}O_2$ at −35°C. was adduced (295) as proof that N_2O_3 had a symmetrical structure with an oxygen bridge:



$$NO + N^{15}O_2 \rightleftharpoons \overset{O\diagdown}{}N\text{—}O\text{—}N^{15}\text{—}O \rightleftharpoons NO_2 + N^{15}O$$

rather than a direct N—N link:



$$NO + N^{15}O_2 \rightleftharpoons \overset{O\diagdown}{\underset{O\diagup}{}}N^{15}\text{—}NO$$

It is, however, the structure of the activated complex that is suggested by these experiments. N_2O_3 in point of fact probably has the unsymmetrical structure (366).

Table 3 summarizes isotopic exchange investigations which have been conducted on compounds of elements of Groups I to VII. Broadly speaking, the findings of these investigations are similar to those described in Sections IV and V.

Key to table 3

Exchanging species: An asterisk denotes the labelled species used. When both species were labelled and used in separate experiments, both are marked with asterisks. The exchanging species are arranged according to the periodic classification. Within a periodic group, the exchanging species are arranged in order of increasing complexity. The species indicated are not necessarily those existing under the conditions of the exchange (e.g., pH will govern the predominant form).

Exchange conditions: Columns 3 and 4 indicate the concentrations (in nor-

TABLE 3

Isotopic exchange reactions of compounds of elements of Groups I to VII

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Group I			
H_2	H_2^*	42–52%	57–47%	643–737°		K; diffusion of air into reaction vessel prevented; lower rates than previously reported, $E = 59.8 \pm 0.4$; rate accelerated by oxygen traces (282a) and inhibited by NO and propylene (426)	(56a)
H_2	H_2^*	59–400 mm.	46–133 mm.	Induced by β-radiation	4–14 hr.	K; chain process; variation with intensity of β-radiation and total pressure investigated	(136)
H_2^*	OH^-	—	0.12–0.88		30–240 min. (100°)	K; suggested mechanism: $D_2 + OH^- \rightarrow D^- + DOH$; $HOH + D^- \rightarrow OH^- + HD$	(481)
H_2^*	NH_2^-	—	10^{-4}–10^{-3}	Liquid ammonia	30–110 min. (−53°)	Analogous kinetics and mechanism to those given in 481	(480)
$Na_2(Ph_4\text{-}PO)$†	Na^{*+}	—	—	Pyridine	C 6 min.		(35)
				Group II			
$Mg(HQ)_2$†	Mg^{*2+}				~30 min.	Heterogeneous	(407)
Chlorophylls *a* and *b*	Mg^*Cl_2	1.5 mg.	2.6 mg.	Absolute ethanol or 80% acetone	N 7 hr.		(39, 406)
				Group III			
BBr_3	Br_2^*			Liquid mixture	Complete exchange (59°)		(167)
BH_4^-	H_2^*O	1.5	Excess	pH 12	N 17 hr.		(187)
$B_2H_6 \cdot 2NH_3$	NH_3^*	Liquid solution			C 70 sec. (−80°)		(84)
$B_2H_6 \cdot 2NH_3^*$	NH_3^*				N 60 hr. (18°)	No exchange of protons in diborane during substantial ammonolysis	(84)
B_2H_6	H_2^*	0.025–0.096 (g.-atoms H per liter)	0.0086–0.042	Gas	42–109 (55°)	K; see 316	(322)
B_2H_6	$B_2H_6^*$	2.4–19 cm.	2.4–19 cm.	Gas	7–20 min. (24°)	K	(322)
B_2H_6	$B_2^*H_6$				Rapid (25°)	Postulated via BH_3 dissociation fragments	(416)

† Ph_4-PO = tetraphenylporphyrin. HQH = hydroxyquinoline.

B_5H_9	$B_5H_9^*$			Gas or liquid	N (room temperature); C (200°)	Absence of dissociation fragments	(416)
B_5H_9	$B_5^*H_9$			Gas or liquid	N 100° (liquid) N 250° (gas)		(416)
Al_{aq}^{3+}	H_2O^*	1.0	Excess	0.3–1.0 H^+	C 3 min.		(254)
$Al_2Cl_6^*$	HCl^*	7×10^{-4} mole (solid)	6×10^{-4} mole (gas)		~150 min.	Previous nonexchange (394) due to traces of moisture in Al_2Cl_6	(56)
Al_2Cl_6	HCl^*	21 cm.	16 cm.	Gaseous	C in <76 hr. (213)	N 12 hr. (21°)	(394)
$AlBr_3$	Br_2^*	$AlBr_3$ in liquid bromine			Complete exchange		(167)
$Al(oxalate)_3^{3-}$	$Oxalate^{*2-}$	0.03	0.01	pH 4.5–6.0	C 20 sec.		(307)
Ga_{aq}^{3+}	H_2^*O	1.0	Excess	0.3–1.2 H^+	C 2.5 min.		(254)
$TlCl_4^-$	Cl^{*-}	0.025	0.05	pH 2	C 1 min.		(391)
				Group IV			
CNO^-	C^*N^-	0.05	0.05	pH 10	N 43 hr.		(9)
CS_2	S_8^*	Excess	0.05		N 68 hr. (100°)	CS_2 may be used as solvent in S* studies	(116)
CS_2	H_2S^*	0.1	0.004	C_6H_6	N 95 hr. (120°)		(137)
CCl_4	HCl^*	48 mm.	10 mm.		N 15 hr.		(105)
SiF_6^{2-}	HF^*	0.17	0.017	pH 0.5–1.0	C 5 min.		(25)
$SiCl_4$	HCl^*	50 mm.	10 mm.		N 60 min.		(105)
$SiBr_4$	Br_2^*	$SiBr_4$ in liquid bromine			N 6 hr. (100°)		(167)
$SiBr_4$	$AlBr_3^*$				Complete exchange (100°)		(167)
SiI_4	I_2^*			Xylene	140 min. (130°)	C 60 min. (130°); melt; no solvent	(345)
$SnCl_4^*$	HCl^*	15–25 mm.	5.5 mm.	Gas	100 sec. (or less)	~50% induced exchange; catalyzed by pyrex or silica surface; inhibited by chlorine	(244)
$SnCl_4^*$	HCl^*	0.0004	0.015	Liquid	~40 sec. (−31°)	Slow diffusion of HCl from gas into solution involved	(244)
$SnCl_4^*$	HCl^*	0.0004	0.0003	Solid	Rapid (−78°)	Surface layer probably exchanges very rapidly; then slower diffusion into bulk	(244)
$SnBr_4$	Br_2^*	0.04	0.04	CCl_4	C 2 min.		(485, 127)
$SnBr_4$	Br_2^*	$SnBr_4$ in liquid bromine			Complete exchange		(167)
SnI_4	I_2^*	4×10^{-6}	10^{-6}	CCl_4	C 7 sec. (0°)		(273)
PbI_2	I^{*-}				C in time of precipitation of $(NH_4)_2PbI_4$		(97)
Th_{aq}^{4+}	H_2O^*	1.0	Excess	0.1 H^+	C 3 min.		(254)

TABLE 3—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Group V			
NH_4^+	H_2^*O	Used NH_4NO_3, $(NH_4)_2SO_4$, and NH_4Cl			1–10 min. (0°)	Exchange rate retarded by acid added to suppress $NH_4^+ + H_2O \rightarrow NH_3 + H_3O^+$ suggested exchange path	(68)
NH_4NO_3	H_2^*O			54% aqueous HNO_3	~3 min. (0°)	Also NH_4^+ salts and $C_4H_9OH^*$ in chloroform	(276)
NH_4^+	NO_2^-	0.23	0.23	0.01 H^+	N 92 min.	3.3 ± 2.6% exchange, 92 min.	(326)
NH_3^*	N_2H_4	10 mm.	10 mm.		C 5 sec.		(123)
NO_2^-	H_2O^*			pH 4–6		K; rate = $2.6 \times 10^8 \times [H^+]^2[NO_2^-]$	(16)
				0.08–0.2 *M* $HClO_4$		K; rate = $32[HNO_2]^2$ (0°)	(83)
NO_2^-	N_2^*	0.05			N 15 days	As expected; compare rapid exchange reported in reference 350	(271, 351)
$N^*O_3^-$	NO_2^-				N 30 min.		(13, 359)
NO_3^-	N_2^*	0.05			N15 days	As expected; compare rapid exchange reported in reference 350	(271, 353)
HNO_3	H_2O^*	46.8 mole per cent			4 hr.	K; marked rate increase for $HNO_3 > 40$ mole per cent	(79)
HNO_3	H_2O^*	8.2 mole per cent		0.003 mole per cent HNO_2	9 min.	Catalysis by HNO_2 marked below $[HNO_3]$ 40 mole per cent	(80)
$NH_2OH \cdot HCl$	N_2^*	0.1		pH = 7.3	N 1 day	As expected; compare rapid exchange reported in reference 350	(376, 271)
NH_2NO_2	H_2^*O				C 1 hr. (5°)		(291)
$Na_2N_2O_2$	H_2O^*			pH > 7	N 16 hr.	N_2O evolved; inactive	(58)
$Na_2N_2O_3$	H_2O^*			pH > 7	N	NO_2^- and N_2O evolved but inactive	(58)
N_2O	H_2O^*			Alkali or acid	N 40 hr.		(58)
NO	N_2^*O				N (750°)	No exchange during decomposition of N_2O	(178)
N^*O_2	NO	Total pressure ~2.5 cm.			C 15 sec. (−35°)	Suggests that structure of N_2O_3 is symmetrical (but see reference 366)	(295)
$N_2^*O_3$	NO				C 5 min. (−118°)	Heterogeneous; N_2O_3 solid	(295)
N_2O_5	N^*O_2	0.1	0.05	CCl_4	~2 min. (10°)		(359)
N_2O_5	N^*O_2	0.0002	0.0003	Gas (~5 cm. total pressure)	~100 sec.	K; $k = 6 \times 10^{12} \times e^{-19,000/RT}$ sec.$^{-1}$; enhanced rate in presence of NO; increase of pressure (50 cm. with CO_2) had little effect	(13, 362, 120)
PH_3	H_2^*O			pH 3.4–4.95 pH 10.0–11.75	10–270 hr. 5–210 hr.	K; *E* = 17.6; enhanced rate at higher acidities; acid and base catalyzed	(471)
PCl_3	Cl_2^*	0.04	0.06	CCl_4	C 5 min.		(286)
PCl_3	HCl^*	61 mm	8 mm.	Gaseous	C 45 min.		(105)

PCl$_3^*$	PCl$_5$			CCl$_4$	~1 hr.		(140, 139)
PCl$_3$	P$_4^*$	0.25	0.061	CS$_2$	~14 days		(338)
PCl$_5$	Cl$_2^*$	0.01–0.02	0.02–0.04	CCl$_4$	Three chlorine atoms exchanged rapidly; then 75–170 min.	K; exchange of apical chlorine atoms markedly accelerated by HCl and moisture (*cf.* 286); no simple rate law obtained; probably nonheterogeneous	(140, 139)
POCl$_3$	Cl^{*-}	Excess POCl$_3$			C 4 min. (18°)		(298)
POCl$_3$	Cl^{*-}	0.007	0.005	CHCl$_3$	40 min.	$E = 17.6$; bimolecular; $t_{\frac{1}{2}} = 4$ sec. (9°) in nitrobenzene	(298)
POCl$_3$	Cl^{*-}	0.007–0.024	0.007–0.04	Acetonitrile	9–36 sec. (−20°)	K; $E = 13.5$; bimolecular	(298)
POCl$_3$	Cl$_2^*$			CCl$_4$	>20 days		(140)
POCl$_3$	HCl*	12 mm.	9 mm.		N 30 min.		(105)
PBr$_3$	Br$_2^*$	0.03	0.04	CCl$_4$	C 3 min.		(286, 167)
AsCl$_3$	HCl*				C 60 min. (60°)		(105)
AsBr$_3$	Br$_2^*$	0.02	0.04	CCl$_4$	C 10 min.		(485, 167)
AsBr$_3$	Br$_2^*$	Solution of AsBr$_3$ in bromine			Complete exchange		(167)
Sb*Cl$_3$	SbCl$_5$	0.03–0.11	0.005–0.067	CCl$_4$	5–30 days dark (50°)	K; P; probably homogeneous	(34)
SbBr$_3$	Br$_2^*$			CS$_2$	C 1 hr. (50°)	Also complete exchange in CCl$_4$ and in absence of solvent (167)	(336)
SbF$_5$	HF*			Liquid	C 10 min.		(399)
As*Cl$_3$	As*Br$_3$	0.038 mole	0.039 mole		C 10 min. (132°)	Exchanged for 10 min. at 20°, then distilled	(339)
Sb*Cl$_3$	Sb*Br$_3$	0.05 mole	0.04 mole		C 10 min. (225°)	Exchanged for 10 min. at 100°, then distilled	(339)
AsCl$_3$	Cl^{*-}		Excess AsCl$_3$		C 4 min. (18°)		(298)
H$_3$P*O$_2$	H$_3$PO$_3$				N hours (70°)	No exchange in presence of I$_2$ or I$^-$ (*cf.* H$_3$AsO$_3$/H$_3$AsO$_4$ exchange)	(67)
H$_2$P*O$_2^-$	H$_2$PO$_3^-$				N hours (70°)		(67)
H$_2$PO$_2^-$	HP*O$_4^{2-}$	0.05	0.05	Neutral or acid	N 24 hr. (100°)		(374)
H$_2$PO$_2^-$	H$_2$P*O$_4^-$	0.1–1.0	0.1–1.0		N 4 days (280°)	H$_2$PO$_2^-$ all oxidized to H$_2$PO$_4^-$	(259)
H$_2$PO$_2^-$	H$_2^*$O				21 hr. (100°)	Rate accelerated by acetic acid and 0.1 *N* NaOH (decomposition)	(69, 262, 151)
H$_3$PO$_2$	H$_2^*$O				16 min.	K; one OH$^-$ exchanged rapidly	(69, 262, 151)
H$_3$PO$_2$	H$_2$O*			—	<10 min. (40°)	K	(70)
H$_2$PO$_2^-$	H$_2$O*			—	10 hr. (100°)	K	(70)
H$_3$PO$_3$	H$_2^*$O			—	N 45 hr.	Two OH$^-$ exchange rapidly	(69)
H$_3$PO$_3$	H$_2$O*			—	6.5 hr. (63°)	K	(70)
HPO$_3^{2-}$	H$_2$O*			—	N 10 hr. (100°)		(70)
H$_3$PO$_3$	H$_3$P*O$_4$	0.35	0.36	5.6 HCl	N 26 days	H$_4$P$_2$O$_6$ + H$_2$O → H$_3$PO$_3$ + H$_3$PO$_4$; $K > 8 \times 10^{-5}$	(483)
H$_3$PO$_3$	H$_3$P*O$_4$				N 4 days (280°)	H$_3$PO$_3$ all oxidized	(259)
HPO$_3^{2-}$	P*O$_4^{3-}$	0.4	0.4	2.8 NaOH	N 24 hr. (100°)		(483)

TABLE 3—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
Group V—*Concluded*							
H_3PO_4	H_2O^*			—	70 hr. (100°)		(70)
PO_4^{3-}, HPO_4^{2-}, or $H_2PO_4^-$	H_2O^*			—	No exchange		(70)
$H_2P^*O_4^-$	$(HPO_3)_n$	0.02	0.01	pH 2.0	N 2 min. (100°) N 3 min. (100°), pH 12	Indicates $H_4P_2O_7 \rightarrow HPO_3 + H_3PO_4$; irreversible	(219)
$H_2P^*O_4^-$	$H_2P_2O_7^{2-}$	0.017	0.008	pH 2.0	N 30 min. (100°) N 3 min. (100°), pH 12	Indicates $2HPO_3 + H_2O \rightarrow H_4P_2O_7$ and $H_4P_2O_7 + H_2O \rightarrow 2H_3PO_4$; both irreversible	(249)
$H_2P^*O_4^-$	$H_2P_2O_6^{2-}$	0.05	0.05	pH 1, 5, and 10	N (90°)		(333)
$H_2P^*O_4^-$	$(NaPO_3)_6$	0.015	0.03	Presence of 0.005 $(NaP^*O_3)_3$	N 25 hr.		(462)
$(NaP^*O_3)_3$	$(NaPO_3)_6$	0.005	0.03	pH 10	N 15 min. (100°)	Also N 25 hr. (25°) at pH = 2; N 0.17 hr. (100°) at pH = 5; indicates $(NaPO_3)_6 \rightarrow (NaPO_3)_3 \rightarrow Na_3PO_4$ (proposed mechanism of hydrolysis of $(NaPO_3)_6$ and occurring during exchange) is irreversible	(462)
$H_2P_2^*O_7^{2-}$	$(HPO_3)_n$	0.004	0.01	pH 2.3	N 1.5 min. (100°)		(249)
$P_2^*O_7^{4-}$	$H_2P_2O_6^{2-}$	0.005	0.005	pH 1, 5, and 10	N (90°)		(333)
$AsCl_3$	HCl^*	Liquid	10 mm.		C 60 min. (60°)		(105)
$AsCl_3^*$	HCl			CCl_4	C 6 min.		(367)
$AsCl_3^*$	Cl_2	0.02–0.20	0.03–0.11	CCl_4	2–15 hr.	K; catalyzed markedly by HCl (probably always present and precluding thorough study)	(367)
AsO_4^{3-}	$As^*O_3^{3-}$			1 NaOH	N 3 hr. (100°)		(484)
H_3AsO_4	$H_3As^*O_3$			HCl	N 3 hr. (100°)		(484)
H_3AsO_4	$H_3As^*O_3$	0.1–0.4	0.1–0.15	0.1–0.24 HCl, 0.01–0.1 KI, 0.1 NaCl	6 hr.	K; exchange takes place exactly through $H_3AsO_3 + I_3^- + H_2O \rightleftharpoons H_3AsO_4 + 3I^- + 2H^+$	(484)
$As^*O_4^{3-}$	AsS_4^{3-}				Fast		(318)
$As^*O_4^{3-}$	AsS_3^{3-}				N 20 min.		(318)
BiI_3	I^{*-}				C in time of precipitation of NH_4BiI_4		(97)
BiI_4^-	I^{*-}				C 5 min.		(126)
$As(S_2O_3)_3^{3-}$	As*(III)			2.0 HCl	$t_{\frac{1}{2}}$ few seconds (3°)		(414)
$Sb(S_2O_3)_3^{3-}$	Sb*(III)			2.0 HCl	$t_{\frac{1}{2}}$ few seconds (3°)	Faster than arsenic analog	(414)
$Bi(S_2O_3)_3^{3-}$	Bi*(III)			2.0 HCl	C few seconds (17°)		(414)

Group VI

O_2	O_2^*	20 cm.			N years		(363, 267)
O_2	O_2^*	2 cm.		In presence of O_3 (15 cm.)	3 min.	$O_3 \rightleftharpoons O + O_2$; $O + O^*O^* \rightarrow OO^* + O^*$	(363, 364)
O_2	O_2^*			$h\nu$ 2537 A. + mercury vapor	4 days	Quantum yield 125 for mercury-sensitized reaction	(267)
O_2	O_2^*	5 mm.	200 mm. Cl_2	Unfiltered mercury lamp	Several hours	Quantum yield $\ll 1$; involves ClO and ClO_2 intermediates	(360)
O_2	O_2^*	20 mm.	20 mm. N_2O_5			K; exchange faster than N_2O_5 pyrolysis; NO_4 postulated as intermediate	(361)
O_3	H_2O^*			0.04 $HClO_4$	N 5 days		
O_3	H_2O^*		—	In presence of 10^{-3} H_2O_2	10% exchange	(Accompanied by loss of O_3 and H_2O_2) Evidence for existence of OH exchange carrier: $H_2O^* + OH \rightarrow O^*H + H_2O$ $O^*H + O_3 \rightarrow HOO^* + O_2$ $HOO^* + O_3 \rightarrow OH + OO^* + O_2$ Inhibited by high $[NO_3^-]$ and low $[O_3]$ or $[H_2O_2]$	(170, 171, 182)
OH	H_2O^*	Hydroxyl radical generated by KO_3	Excess	pH 0.5–13.4	~10% exchange in evolved oxygen; rapid	Independent of pH (Grotthus type mechanism postulated)	(277)
S^{2-}	S^* (element)				C 1 hr. (90–100°)	S slowly dissolves	(461)
SF_6	HF^*			Vapor	N 45 min.		(399)
S_2Cl_2	S_8^*	Excess	0.03		30 min. (98°)	Postulated $S_8^* \rightleftharpoons S_6 + S_2^*$ (slow) $2S_2Cl_2 \rightleftharpoons S_2Cl_4 + S_2$ $R = k[S_8][S_2Cl_2]$; *cf.* 115	(115) (164)
S_2Cl_2	HCl^*	10 mm.	10 mm.	Gaseous	N 60 min. (60°)	N 180 min. (60°) with liquid S_2Cl_2	(105)
H_2S^*	S^*O_2			Variety of conditions	N in appreciable time before sulfur precipitates		(229)
H_2S^*	SO_2			$CHCl_3$	No exchange	Yellow solution formed containing S_nO_2; inactive SO_2 emitted on warming	(192)
SCN^-	C^*N^-	0.19	0.59	pH 0.5–14	N 160 hr.	Precludes formation of $NCSCN^{2-}$ as transition state	(8)
KSCN	S^* (element)	0.1	~0.01	Alcohol	N 5 days	N 5 hr. (115°) in isoamyl alcohol–xylene mixture (287)	(26)
NH_4SCN	S^* (element)	0.05	~0.005	Acetone	N 21 days	Preparation of SCN^- irreversible: $CN^- + S \rightarrow SCN^-$	(26)
SCN^-	S^{*2-}	0.1	0.1	Slightly alkaline	N 2 days (100°)	N 23 days (pH 13), (8)	(230)
$(SCN)_2$	KS^*CN			CCl_4–acetone CCl_4–acetic acid	C, minutes		(75)

TABLE 3—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Group VI—*Concluded*			
$(SCN)_2$	KS*CN			CCl_4-acetic acid, acetic anhydride	Slow	Large induced exchange	(75)
SCN^-	$S^*_2O_3^{2-}$				N 26 hr.		(66)
SO_2	S^*O_3				N 17 hr. (200°), slight 24 hr. (335°)	Slight, 15 hr. (280°) with water	(460, 461)
$H_2S^*O_4$	SO_2	Excess 97.2% H_2SO_4			~7.5 hr. (211°)	Probably homogeneous in liquid phase; $E_{act} \sim 22.0$; rate $\gg SO_2$, SO_3 gas exchange	(351)
$S_2O_3^{2-}$	HS^{*-}			1 NaOH	N room temperature; C 24 hr. (100°)	Suggested $S_2O_3^{2-} \rightleftharpoons S + SO_3^{2-}$; $E \sim 15$ (14)	(460, 461)
$S^*_2O_3^{2-}$	$S^*O_3^{2-}$	0.06	0.2	pH 5.0	10 min. (89°)	K; $k = 2.3 \times 10^6 e^{-14,500/RT}[S_2O_3^{2-}][SO_3^{2-}]$ Slight change in rate or E from pH 5–14	(14, 460, 461)
$S^*_2O_3^{2-}$	$S_2O_4^{2-}$	0.015	0.015	pH 6	N 75 min.	(N 44 hr.; pH 13)	(147, 146)
$S^*_2O_3^{2-}$	$S_3O_6^{2-}$	0.1	0.1	pH 7–10	100 min. (50°)	K; pH independent rate 7–10; homogeneous; enhanced by bi- and trivalent cations at constant μ	(163, 158)
$S^*_2O_3^{2-}$	$S_nO_6^{2-}$	0.15	0.15	$n = 3, 4, 5, 6$	Rapid	Supports the reaction: $O_3SS \vdots SSO_3^{2-} + S^*SO_3^{2-} \rightleftharpoons O_3SSS^*SO_3^{2-} + SSO_3^{2-}$	(158)
$S^*SO_3^{2-}$	$HOCH_2SO_2Na$	0.002	0.002		N 5 days		(226)
$S^*O_3^{2-}$	$S_2O_4^{2-}$	0.006	0.005	1 *N* NaOH	N 90 sec.	C 10–20 sec. (pH 1, 7)	(224)
$HS^*O_3^-$	$S_3O_6^{2-}$	0.007	0.002	pH ~ 7	N 96 hr.		(224)
$S^*O_3^{2-}$	$S_2O_6^{2-}$				No exchange		(161)
$S^*O_3^{2-}$	$S_3O_6^{2-}$					Second order; $E \sim 10$ kcal.	(162, 161)
SO_3^{2-}	$S^*O_4^{2-}$		0.1*N* HCl or alkali		N 35 hr. (100°)		(460, 461)
$S^*O_3^{2-}$	$OOCCH_2SSO_3^{2-}$	0.005–0.02	0.002–0.02	pH 7	30–150 min.	K; data for other organic thiosulfates included	(368)
SO_4^{2-}	$S_3O_6^{2-}$				N 26 hr. (25°)		(65)
$S^*O_4^{2-}$	S^{2-}			Alkaline solution	N 36 hr. (100°)		(460, 461)
$S^*O_4^{2-}$	$S_2O_8^{2-}$	0.001	0.001	pH 1, 7, and 10	N 7 days (room temperature)		(395, 148)
$S^*O_4^{2-}$	$S_2O_8^{2-}$	1.5×10^{-3}	7.7×10^{-4}	Water or concentrated acetic acid	N 12 hr. (34°)	$S_2O_8^{2-} \rightleftharpoons SO_4^{2-} + SO_4$ not important in persulfate oxidation	(144)
$S^*O_4^{2-}$	$S^*_4O_6^{2-}$			Neutral or weakly acid	N 44 hr.		(147, 146)

H_2SO_4	H_2O^*	3-15 f	16-49 f		3 min. to 3 yr.	K; activation energy depends on $[H_2SO_4]$	(498)
SO_2Cl_2	$H_2S^*O_8$					Partial exchange during hydrolysis of SO_2Cl_2; not consistent with any of several suggested mechanisms	(227)
$H_2Se^*O_3$	H_2SeO_4	0.1	1.4		N 2 days (100°)	N 14 days (68°) in presence of H_2O_2, indicating that oxidation of H_2SeO_3 by H_2O_2 does not involve H_2SeO_3-H_2SeO_4 couple	(248)
$SeOCl_2$	Cl^{*-}				C 55 min. (18°)		(298)
$SeBr_4^*$	Br_2^*			CS_2	C 1 hr. (45°)		(386)
$Cr_2O_7^{2-}$	$Cr^*(III)$	Equal concentrations		Neutral or pH ~ 3	N 2 hr.	Not affected by I^- (*cf.* arsenite-arsenate)	(341)
TeI_6^{2-}	I^{*-}				C 5 min.		(126)
Group VII							
F_2	HF^*	0.003-0.02	0.001-0.03	Gas	50 min. (194°)	K; heterogeneous by metal fluoride metal coating; N room temperature (130)	(3, 130, 399)
ClF_3^*	F_2	0.0004-0.016	0.008-0.036	Gas	19 min. to 4 hr. (194°)	K; part heterogeneous (metal fluoride surface); homogeneous due to dissociation $ClF_3 \rightleftharpoons ClF + F_2$	(2, 44)
BrF_5^*	F_2	0.0005-0.005	0.006-0.035	Gas	30 min. to 2.5 hr. (193°)	K; mainly heterogeneous via BrF_5-F_2 complex	(2, 44)
IF_7^*	F_2	0.001-0.02	0.003-0.03	Gas	30-60 min. (194°)	K; part heterogeneous (metal fluoride surface); homogeneous $IF_7 \rightleftharpoons IF_5 + F_2$	(2, 44)
ClF_3	HF^*			Liquid or gas	C 10 min.	All HF-fluorohalide exchanges consistent with a mechanism of the type:	
BrF_3	HF^*			Liquid or gas	C 10 min.		
BrF_5	HF^*			Liquid or gas	C 10 min.	$HF + BrF_3 \rightleftharpoons BrF_2^+ + HF_2^-$	(399)
IF_5	HF^*			Liquid	C 10 min.	Probably not heterogeneous in gas-phase exchanges	
IF_7	HF^*			Gas	C 10 min.		
ClF_3^*	BrF_3			Liquid or gas	C 10 min.		
Cl_2^*	HCl	0.0015	0.0085	Gas	16 hr. (fluorocarbon surface)	Faster with pyrex surface and adsorbed water (503); $P(t_{\frac{1}{2}} = 40$ min.) Probably through $Cl_2^* \rightleftharpoons Cl^* + Cl$ $Cl^* + HCl \rightleftharpoons HCl^* + Cl$	(266, 130)
Cl_2	Cl^{*-}	<0.01	0.15	0.5 H_2SO_4 + 0.06 acetanilide	C < 10^{-3} sec.	Competition of Cl_2-Cl^- exchange with fast chlorination of acetanilide (known rate); probably via $Cl_2 + Cl^- \rightleftharpoons Cl_3^-$	(310, 211, 452)
Cl_2	Cl^*O_2	0.03	0.04	0.06 HCl	N 66 min.		(132)
Cl^-	Cl^*O_2	0.1	0.04	0.05 $HClO_4$	N 60 min.	Also N 55 min. (pH 7)	(132)
Cl^{*-}	Cl^*O_2	0.03	0.02	0.03 HOCl; pH 6.2	Slight, 67 min.	Accompanying $ClO_2 \rightarrow ClO_3^-$ reaction	(132)
Cl_2^*	ClO_3^-	0.015-0.025	0.75-1.0	2.0-4.5 H_2SO_4	N 90 min.	N 60 min. (93°, sealed tube, decomposition); *cf.* reference 302, which gives $t_{\frac{1}{2}} = 90$ min.	(447)

TABLE 3—*Concluded*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
Group VII—*Concluded*							
Cl^{*-}	ClO_3^-			Solids	N 60 min. (510°)		(73, 60)
Cl^{*-}	ClO_4^-				N 60 min. (510°)		(73, 60)
Cl^*O_2	$Cl^*O_2^-$	10^{-4}	5×10^{-3}	pH ~ 5	~6 sec.	Also ~6 sec. (0.5 $HClO_4$)	(132)
ClO_2^-	$Cl^*O_3^-$	0.04	0.14	0.73 H_2SO_4	No activity in evolved ClO_2 after 20% chlorite decomposition (15 min.)	$2H^+ + ClO_2^- + Cl^*O_3^- \rightarrow H_2O + Cl^*O_2$; much less than acid disproportionation of $HClO_2 \rightarrow$ inactive ClO_2; i.e., $ClO_2^- + ClO_3^-$ slow indicated by exchange (132)	(447)
Cl^*O_2	ClO_3^-	0.04	0.05	pH ~7 or ~1	N 43 min.	Therefore $2ClO_2 + H_2O \rightleftharpoons 2H^+ + ClO_2^- + ClO_3^-$; not path for ClO_2–ClO_2^- exchange	(132)
ClO_2^-	OCl^{*-}	0.05	0.017	0.1 OH^- (0.017 Cl^- present)	<5% 45 min.	Probably via Cl_2^*, ClO_2^- or $HOCl^*$, ClO_2^-	(447)
Cl^*O_2	ClO_4^-	0.04	0.05	0.05 $HClO_4$ (0.05 ClO_3^- present)	N 43 min.		(132)
$Cl^*O_3^-$	ClO_4^-	0.056	0.056		N 2 yr.	N 1 hr. (99°); N 19.5 hr. at pH 1 or 13	(294)
ClO_4^-	H_2O^*	1.45	Excess	4.5 $HClO_4^-$	C 1 day		(254)
Br_2^*	HBr	Equal pressures; total pressure 0.5-2.0 mm.		Gas	0.14 0.75 sec. C 2 min. (CCl_4, 454)	SiO_2 wool increases rate ($t_{\frac{1}{2}} \sim 0.06$ sec.); heterogeneous, *cf.* 130; non-P; not radiation induced; irreproducibility precludes kinetics	(260, 213, 62, 303, 301)
Br_2	Br^-	1.5	0.8		C 1 min.		(204, 133, 167, 400)
Br_{aq}^{*-}	$Br_{org.}^{*-}$	0.15–2.0	0.15–2.0	Ethanol, acetone, or glycerol	C 1 min. (−30°)	Disagrees with reference 62 (who found slow exchange)	(465)
Br_2^*	BrO_3^-	0.0024	0.082	1.65 $HClO_4$	35 hr.	K	(47, 302, 380)
Br^-	BrO_3^-				N 8 days (100°)		(380)
BrO_3^{*-}	H_2O	0.02–0.80	Excess			K; $E = 14.2$	(497)
I_2	HI^*			Gas	Fast	Also fast in dry pentane	(301)
I_2	I^{*-}				C 1 min.		(250, 272, 133, 231)
I_{aq}^{*-}	$I_{org.}^{*-}$	0.15–2.0	0.15–2.0	Ethanol, acetone, or glycerol	C 1 min. (−30°)	Disagrees with reference 62	(465)
I_2	I atoms					$k \simeq 8 \times 10^{10}$ ml. mole^{-1} sec.$^{-1}$; E = 2–3 kcal. indirectly from iodine/*trans*-diiodoethylene exchange	(355)
I_2^*	I (pyridine)$^+$	10^{-1}–10^{-7}	2×10^{-2}	Pyridine	C in time of mixing	Exchange independent of complex organic anion	(284)

KI_3 8	I^{*-}				C 15 sec.	Polyiodide solution formed by shaking KI solid with I^--I_2(aq)	(375)
I^{*-}	IO_3^-	0.005	0.1	Neutral	N 67 days (50°)		(342, 380)
I^{*-}	IO_3^-	~0.1	0.14	Scaled tubes (100-300°)	100 min. (250°)	K; $E = 32$	(490)
I_2	IO_3^-	0.22-1.0	0.001-0.002	0.001-0.002 HIO_3	12 days	K; 0.2 $HClO_4$; $t_{\frac{1}{2}} \sim 50$ days	(342, 111, 250)
I_2^*	IO_4^-			0.5 HNO_3	Slow	Rate decreases with decreasing acid; comparable to IO_3^--I_2 couple	(119)
$I^*O_3^-$	IO_4^-	0.030	0.030	N HNO_3	100-200 days (98°)		(119, 118)
I^-	IO^-				C min.		(231)
ICN	I^{*-}			Water, water-dioxane	C min. (0°)		(499)
ICN	C^*N^-			Acetone, alcohol	C min. (−80°)		
ICN	I_2^*			Water, water-dioxane	C min. (30°)		(499)
				Heptane	C min. (0°)		(499)
ICl	I_2^*			0.4 *N* HCl	C 5 min. (18°)		(502)
MnO_4^-	Mn^{*2+}	0.002-0.016	0.007-0.001	1.5-3.0 *M* $HClO_4$	20 hr.	K; $R = k[H^+]^{1.0-1.6}[Mn^{2+}]^{1.0-1.6}[MnO_4^-]^{0.0-0.6}$; inhibited by MnO_2 which precipitates under these conditions much later than as given in reference 382	(4)
MnO_4^-	Mn^{*2+}				N 15 min.	Precludes $3Mn^{2+} + 2MnO_4^- \rightarrow 5Mn(IV)$; rapid; MnO_2 precipitated completely during this time,	(382)
MnO_4^-	Mn^{*2+}	0.0009-0.0013	0.0003-0.0006	1.0-2.0 HNO_3	8-16 hr.	K; different separation from that given in reference 4; some agreement with rate given in reference 4; color change during exchange	(214)

malities or molarities for reactants in solution or millimeters of mercury pressure for gaseous reactants) of the exchanging species listed in columns 1 and 2, respectively. Column 5 refers to any other important condition(s) employed in the experiment. Unless indicated in column 5, all experiments were performed in water.

Exchange rate: The times listed in column 6 denote the exchange half-times. The letter N preceding a listed time signifies that $\leqslant 5$ per cent exchange occurred at the highest concentrations and temperature conditions. The letter C preceding a listed time indicates that $\geqslant 95$ per cent exchange occurred (usually within the separation time) at the lowest concentrations and temperature conditions. When no quantitative information is available, the rate is denoted simply by "fast" or "slow". All temperatures refer to 20–30°C., or room temperature, unless otherwise specified.

Remarks: Included in this column is an indication that a kinetic study was performed (K), that an activation energy for a simple mechanism was obtained ($E = x$ kcal./mole), or that the exchange was photosensitive (P).

References: When more than one reference is given, then the stated conditions of the exchange refer to the first reference cited, and unless otherwise stated the results of the other studies confirm the general conclusions of the first.

VI. Rates and Mechanisms of Exchange of Complexes of the Transitional Elements

The coördination complexes of the transitional elements represent compounds in which the following factors, all of which influence the lability of molecules, can be varied at will: the oxidation state of the central atom in otherwise identical molecules, the nuclear charge of the central metal atom in a series of analogous molecules, the stereochemical configuration and bond hybridization in complexes of the same element, and the number and electronegativity of groups coördinated to a metal atom.

If a series of compounds react by identical mechanisms with a common reagent, then a measure of the bond labilities will be reflected in the relative values for the respective rate constants. Such an assumption is not without objections, however, since the final equilibrium states for the various reaction systems will probably differ and the more significant quantity for comparison purposes is the extent to which the equilibrium states are approached in a given time or the "degree of attainment" of the reactions, as originally discussed by De Donder (135). Thus a "labile" molecule may undergo reaction with a low rate constant because of an unfavorable equilibrium position for that reaction. Taube (445) has discussed this point in an earlier review.

The measurement of the rate of isotopic exchange of a ligand bound in a coördination complex (and somewhat less favorably the corresponding rate for the central metal atom) with its corresponding "free" entity in solution is not subject to this complicating factor. Since the heat of reaction for an isotopic exchange is essentially zero, the free-energy change for the process, which will always be negative, is derived directly from the entropy of isotopic mixing.

The equilibrium state for an isotopic exchange is known to be always that corresponding to random distribution of the labelling isotope between the exchanging reactants (with perhaps slight allowance for isotope effects) and failure to observe exchange is, for ligands at least, a direct indication of inert chemical bonds.

The processes of dissociation and solvolysis detectable by nontracer techniques provide one type of reaction path by which isotopic exchange can occur. The other important reaction path is that involving direct bimolecular collision and replacement of (say) a ligand in a coördination complex by a labelled free ligand in solution. Such a process is detectable only by the use of isotopic tracers ("direct exchange path"); its rate and its contribution to the overall exchange rate are of the greatest significance in estimating labilities.

It has been possible to classify coördination compounds as either "ionic" or "covalent" depending on the state of electron pairing in the molecules as shown by their measured magnetic moments (369). While it is often the case that "ionic" compounds undergo rapid exchange reactions, examples will be presented later of "ionic" complexes which exhibit relatively slow rates of exchange. Conversely, several "covalent" complexes undergo fairly rapid exchange reactions. Other considerations then besides the nature of the bonding are involved. Increasing acceptance is now being given to the classification (85, 445) of bonds as either "outer orbital" (e.g., $4S4P^34D^2$) in which, owing to the use of d orbitals of higher principal quantum number, the number of unpaired electrons in the compound is that in the free ion of the central metal atom, or "inner orbital" (e.g., $3D^24S4P^3$), in which maximum electron pairing normally occurs with the use of lower quantum number d orbitals. A classification of inner-orbital hexacovalent complexes into "labile" and "inert" classes by virtue of available d orbitals (445) is extremely effective and for such complexes a prediction of exchange rates is simple. However, it must be remembered that while the magnetic moment indicates the ground state of the coördination complex it cannot indicate the importance of any higher-energy states in a molecule. In complexes formed by the coördination of rather electronegative ligands, an outer-orbital paramagnetic state may be only slightly above the diamagnetic state in energy (445). Accordingly, whilst a complex may exhibit a magnetic moment characteristic of "inner-orbital" bonding, it may undergo isotopic exchange according to the properties of the more polar, higher-energy state (see page 796). Such polarization effects are well known in organic chemistry and are now appearing in inorganic chemistry as more quantitative exchange and other studies on coördination complexes are performed.

A. RELATIVE ADVANTAGES OF METAL AND LIGAND EXCHANGE

In general, the rate of exchange of the metal atom will be complicated by the interaction of the metal M with the complex MX_n to form all possible intermediate species, in concentrations determined by their relevant stability constants. Such interactions frequently lead to practical difficulties in the separation of the exchanging species and may be one of the basic causes of the phenomenon of induced exchange. Furthermore, precipitation commonly occurs on addition of a metal ion to a metal-complex anion, as Long (308) has observed for example in the exchange of Ni^{*2+} with $Ni(CN)_4^{2-}$. All that one can say about such studies is that exchange is fast (or slow) compared with the rate of precipitation of that salt, which often occurs in a fraction of a second. Metal–complex interaction can also cause difficulties in the interpretation of exchange data. Wolfgang and Dodson (487) studied the exchange of Hg_{aq}^{2+} with $HgCN^+$ and $Hg(CN)_2$ by allowing the equilibrium amounts of the three inactive species to form and then injecting a highly active Hg^{*2+} solution of extremely low concentration. By separating the Hg^{2+} ion as the iodate, it was shown that the slow exchange observed was that between Hg^{2+} and $HgCN^+$ at low concentrations of mercuric cyanide. At high concentration of mercuric cyanide, the disproportionation reaction:

$$Hg^{2+} + Hg(CN)_2 \rightleftarrows HgCN^+ + HgCN^+$$

provided an additional path for isotopic exchange and suitable allowance was necessary. These difficulties do not arise when, owing to their relatively low stability, the formation of intermediate complexes is unimportant and the parent complex can exist with significant concentrations of the free metal ion: e.g., $Fe(phen)_3^{2+}$ (407) and $Ni(tetrameen)_2^{2+}$ (476).[2] A further exception arises when the central atom is coördinated with a single polydentate chelate: e.g., $Fe(EDTA)^-$ (268) or chlorophyll (407). However, it will be appreciated that if the aim of a research is to measure the lability of the M—X bond in a complex MX_n, then the probability that isotopic exchange will be observed for the central atom M is considerably less than the corresponding probability of ligand exchange, requiring as it does the rupture of only one or two M—X bonds for mono- and bidentate ligands. It has been pointed out (72) that for some complexes of Fe(II), Fe(III), and Ni(II) the rates of metal and ligand exchange are approximately equal. In such cases the first M—X bond rupture is probably a slow bimolecular aquation which is followed by rapid heterolysis. However, this concept is admitted (72) to be of limited applicability. Moreover Taube (445) has described a kinetic scheme for which it is possible for ligand exchange to be measurable whilst the metal exchange would be immeasurably slow. The study of metal exchange in such an instance would give a false estimate of the lability of the complex. On the other hand, rapid exchange of a metal ion with its corresponding entity bound in a complex is a definite indication of high lability within the complex.

From the foregoing discussion it would appear that the study of ligand exchange in coördination complexes has definite advantages over the corresponding study of metal exchange. Nevertheless some difficulties are encountered when ligand-exchange studies are performed on intermediate species of a thermodynamic series. Whilst Hg^{*2+} exchanges very slowly with mercuric cyanide, C^*N^- ion is observed to exchange very rapidly (9). This is due to the formation

[2] phen = 1,10-phenanthroline; tetrameen = 2,3-dimethyl-2,3-diaminobutane; EDTA = ethylenediaminetetraacetic acid.

of $Hg(CN)_3^-$ and $Hg(CN)_4^{2-}$, containing equivalent cyanides, from which cyanide is "torn" by the separation procedure (addition of silver ion). Thus the "exchange rate" observed is in reality the rate of formation of $Hg(CN)_3^-$. Therefore ligand exchanges should be conducted on the last thermodynamic member of a series, e.g., MA_6^{n+}, to avoid this complication. Metal–ion exchanges can be carried out on the first member, e.g., MA^{n+}, which can usually exist with an excess of M^{n+} with the formation of negligible amounts of higher complexes. If a suitable separation method is available, these experiments provide a convenient means of measuring the lability of MA^{n+}. Another practical difficulty arises in the actual preparation of suitably labelled ligands, but with increasing availability of labelled starting materials, these difficulties are steadily disappearing.

B. COMPLEXES OF COÖRDINATION NUMBER FOUR

1. Exchange of the central atom

Duffield and Calvin (142) performed one of the earliest (kinetic) isotope-exchange studies on the exchange of a series of copper chelate compounds (mostly salicylaldehyde derivatives) with copper acetate in pyridine solution. The general reaction may be represented as:

$$\mathrm{Cu(II)Ke_2 + Cu^*(II) \rightleftharpoons Cu^*(II)Ke_2 + Cu(II)}$$

where Ke_2 represents either two bidentate chelates or one quadridentate chelate. Whilst copper salicylaldehyde itself exhibited complete exchange in 15 sec. (the time of separation), other substituted salicylaldehyde–chelate complexes exhibited longer half-times which, in the case of bis-(salicylaldehyde-ethylenediimine)copper was several hours at room temperatures. Since the exchange half-time of the latter complex was proportional to the reciprocal of the reactant concentration (both reactants being of equal concentration), the exchange rate could be described by a second-order rate law (Section II,B). Mechanisms based on a dimer of the complex (for which $t_{\frac{1}{2}} \propto c^{-\frac{1}{2}}$) or proceeding via S_N1 ionization and recombination (for which $t_{\frac{1}{2}}$ is independent of c) could therefore be rejected. The mechanism suggested was one involving direct bimolecular collision, with the complexed copper atom being directly replaced by the "free" copper atom. This process would require considerable energy of activation to effect simultaneous rupture of four metal–ligand bonds. It would seem highly likely that the copper chelate complex becomes substantially modified on solution in pyridine such that a complex with one or two coördinated pyridine ligands is formed. The resultant complex might be considerably more labile to substitution. If such a process were operative, the observed lability would be that of the intermediate solvated complex rather than that of the parent complex. A further conclusion drawn from this work was that the higher the polarographic reduction potential of the chelated complex (and hence the higher the stability of the complex), the slower the rate of isotopic exchange. It now appears that any general relation between exchange rate and thermodynamic stability is not to be expected, since the factor which principally determines exchange rates is the activation energy required to rupture the appropriate metal–ligand bonds, which in turn is largely determined by the electronic structure of the chelated metal atom. In the present series of copper complexes derived from very similar chelating agents, the orders of increasing activation energies for substitution and increasing thermodynamic stabilities are parallel. Such a circumstance cannot be generally expected.

West (468) has considered the relation between bond type (as indicated by magnetic moment measurements) and the exchange rate of cobalt(II) complexes of substituted salicylaldehyde bidentates with cobalt acetate in water and pyridine solutions. Most of these complexes exhibit magnetic moments of about 4.5 Bohr magnetons, indicating three unpaired electrons in the Co(II) orbitals; the corresponding "outer-orbital" bonds would be expected to be labile to isotopic exchange. This was indeed observed, exchange being complete within the separation time of 1 min. at 20°C. On the other hand, cobaltous phthalocyanine does not exchange with cobaltous acetate in pyridine over many hours at 30°C. This result is also consistent with the electronic state of the central cobalt atom in the phthalocyanine complex, which possesses a bond moment corresponding to dsp^2, inner-orbital bonding. That this result is not due to the solvent is shown by the equally negligible exchange with cobaltous sulfate of the water-soluble ammonium cobaltous phthalocyaninetetrasulfonate. The Co(II) complex derived from the quadridentate chelate N,N'-disalicylidene-ethylenediamine exchanges "instantaneously" with cobaltous acetate in pyridine at 30°C. and with reactant concentrations of $10^{-2}M$ in the absence of oxygen (470). Reducing the reactant concentrations to $10^{-4}M$ and the temperature to 15°C. enabled exchange half-times of the order of 20 min. to be measured. The salicylidene-ethylenediamine cobalt(II) complex readily absorbs oxygen to form oxygenated species (215a) and the exchange half-time thereby increases from 20 min. to some 3 hr.

This example illustrates the point that many of the earlier exchange studies, conducted at a single reactant concentration and temperature and reported to exhibit "instantaneous" exchange, could be profitably repeated under more suitable conditions of lower concentrations and temperature and earlier separation times. Should kinetic studies be thereby possible, much more quantitative information will be forthcoming as compared to the large amount of purely qualitative observations which has accumulated at present. Indeed, subsequent discussions will cite several kinetic studies of exchange systems exhibiting half-times of a minute or less. The supreme example is the elegant study by Sheppard and Wahl (417) of the MnO_4^-/MnO_4^{2-} electron exchange, whereby half-times of 3–12 sec. were reproducibly measured.

Like the copper(II) bidentate complexes, N,N'-disalicylidene-o-phenylenediamine cobalt(II) exhibits a second-order rate law for exchange with cobaltous acetate. West (470) suggests an analogous bimolecular collision mechanism between the complex and free cobalt, but the observed activation energy of 17 kcal./mole (23 kcal. for the copper complex) seems rather low for such a mechanism involving a complex of considerable stability. Consideration should again be given to possible modification of the complex by coördination of solvent pyridine molecules.

Studies of the exchange of nickel with tetracoördinated nickel complexes (212, 263) reveal that significant modification of the bonding in such complexes can occur in certain solvents (e.g., methyl cellosolve, pyridine). Whilst certain solid diamagnetic nickel complexes exchange extremely slowly with nickel chloride in methyl cellosolve at room temperature, other diamagnetic solid complexes which dissolve in methyl cellosolve or pyridine with obvious modification of the dsp^2 bonding to sp^3d^2 by solvent coördination, exchange readily. Basolo and Matoush (38) have isolated crystalline compounds of hexacoördinated Ni(II) containing two molecules of solvent pyridine. Thus while bis-(*N*-methylsalicylaldimine)nickel forms such a paramagnetic compound and readily exchanges with nickel chloride in pyridine, bis-(salicylaldehyde-ethylenediimine)-nickel remains tetracoördinated in pyridine and does not exchange. The inertness of this latter complex to isotopic exchange might appear puzzling when it is recalled that copper acetate in heated pyridine will displace nickel from bis-(salicylaldehyde-ethylenediimine)nickel (377). Apart from the fact that the conditions are somewhat more drastic than in the case of the exchange studies, this net replacement reaction must involve a large free-energy decrease in passing from a less stable to a very stable state; the much smaller free-energy change for the exchange reaction arises only from the entropy of isotopic mixing.

It has been pointed out (28, 470) that whereas the order of increasing thermodynamic stability of chelated complexes for the first transition series is Co $<$ Ni $<$ Cu $>$ Zn, with zinc complexes somewhat less stable than cobalt complexes, this order is not maintained for studies of the rate of isotopic exchange (see table 4). The apparently anomalous position of nickel was then attributed to considerable solvation of nickel chloride in pyridine. However, the relative stabilities (and labilities) of the planar, tetrahedral, and octahedral configurations of the complex, when solvation is possible, are probably additional factors determining such an order. It should be reiterated that there is no *a priori* reason for a correlation between thermodynamic stability and exchange lability.

Long (308) has performed an interesting study of the exchange of nickel between pairs of nickel complexes. The exchanges $Ni^*(NH_3)_x^{2+}$–$Ni(CN)_4^{2-}$ and $Ni^*(en)_3^{2+}$–$Ni(CN)_4^{2-}$ exhibit half-times of less than 1 min. at 23°C., whereas the systems $Ni^*(C_2O_4)_2^{2-}$–$Ni(CN)_4^{2-}$ and $Ni^*(tartrate)^-$–$Ni(CN)_4^{2-}$ exhibit half-times of 3 hr. and 46 hr., respectively. Increase of ionic strength reduces the exchange rate of the former two systems but increases the rate of the latter systems. This presumably indicates rate-determining steps involving oppositely

TABLE 4

Exchange rates of metal complexes of bis-salicylaldehyde-ethylenediimine

Metal	Cu	Ni	Co	Zn
Concentration (*M*)	0.015	0.01	0.017	0.01
Exchange temperature	25°C.	Room	30°C.	25°C.
Exchange rate	$t_{1/2}$ = 2.1 hr.	None after 48 hr.	Complete in 6 min.	Complete in 0.5 min.
Reference	(142)	(212)	(470)	(28)

charged ions and like-charged ions in the two types of systems. Long points out that the exchange rate between oppositely charged complex ions is fast but is slow for like-charged ions. This generalization is of course only applicable to a series of complexes involving a metal atom in the same electronic state in each complex.

That the electronic structure of the central metal atom is not always the predominating factor determining exchange rates is shown by the immeasurably slow exchange of the central atom with chlorophyll (39, 406), cupric pheophytin (407), and zinc phthalocyanine (28). From a consideration of their available bonding orbitals and the behavior of other complexes of the same metals, all these compounds would be expected to be extremely labile, as found for instance with the rapid exchange of magnesium ion and zinc ion with the 8-hydroxyquinolate complexes (28, 407). Undoubtedly the rupture of the four metal–nitrogen bonds necessary for exchange to proceed is made difficult by the fused-ring structure of these complexes. Indeed the only exception to the general rule of inertness of these "fused-ring" compounds appears to be the disodium tetraphenylporphyrin complex, which rapidly exchanges with sodium iodide in pyridine (35). Owing to their large size, the sodium atoms lie well outside the plane of the porphyrin ring, thereby rendering them more susceptible to substitution and exchange reactions.

An examination of the work performed so far on the exchangeability of the central atom in tetracoördinated complexes reveals that a large fraction of these studies has not provided the chemist with entirely new data. It has however confirmed already known ideas regarding the structure and lability of these complexes and the importance of solvolytic equilibria in determining their apparent lability.

2. Exchange of ligands

Several kinetic studies of ligand exchange have been reported, especially for the square complexes of Pt(II) and Au(III), and some indications have now emerged of the relative importance of the various mechanisms by which these exchanges can proceed. Therefore the results obtained from these studies appear to have much more relevance to the quantitative estimation of bond labilities than those studies concerned with the exchange of the central atom.

Grinberg and Nikolskaya (202) have studied the exchange rates of a series of Pt(II) complexes:

$$(\mathrm{PtX_4})^{2-} + \mathrm{X}^{*-} \rightleftharpoons (\mathrm{PtX_4^*})^{2-} + \mathrm{X}^-$$

where X is CN, I, Br, or Cl. The order of increasing exchange rate (i.e., decreasing half-time) appeared to be opposite to the order of increasing thermodynamic stability of the complex anions (202) (see table 5). However, it is not known if these four exchange systems even proceed by the same mechanism and what relative contribution aquation makes to the observed exchange rate in each case. Therefore these figures, as such, cannot be taken as a direct quantitative measure of the labilities of the respective metal–ligand bonds.

A more detailed kinetic study (203) of the $(\mathrm{PtBr_4})^{2-}$–Br^{*-} system revealed that the rate is approximately first order in complex concentration but independent of the bromide-ion concentration. This observation is consistent with either of two mechanisms in aqueous solution:

(*a*) Rate-determining S_N1 dissociation:

$$(PtBr_4)^{2-} \underset{\text{fast}}{\overset{\text{slow}}{\rightleftarrows}} (PtBr_3)^- + Br^-$$

$$(PtBr_3)^- + Br^{*-} \underset{\text{slow}}{\overset{\text{fast}}{\rightleftarrows}} (PtBr_3Br^*)^{2-}$$

(*b*) Rate-determining S_N2 aquation followed by rapid "anation" of the intermediate aquo complex:

$$(PtBr_4)^{2-} + H_2O \underset{\text{fast}}{\overset{\text{slow}}{\rightleftarrows}} (PtBr_3H_2O)^- + Br^-$$

$$(PtBr_3H_2O)^- + Br^{*-} \underset{\text{slow}}{\overset{\text{fast}}{\rightleftarrows}} (PtBr_3Br^*)^{2-} + H_2O$$

However, when the K_2PtBr_4 was allowed to "age" in aqueous solution before being mixed with the labelled potassium bromide solution, the exchange rate increased with the "age" of the solution. This "aging" represents the gradual establishment of the equilibrium concentration of the intermediate aquo complex; mechanism (*b*) is therefore favored. The observed exchange rate of $PtBr_4^-$ with bromide ion thus represents the rate of aquation of the former ion and not, as might have been inferred in the absence of a kinetic study, the rate of direct Br^-–ligand exchange. Indeed, as will transpire in subsequent discussions, there are very few unambiguous and authentic examples of direct ligand exchange of transition metal complexes in aqueous solution. This is due to the relatively high nucleophilic character, i.e., complexing power, of the solvent water molecules. Kinetic exchange studies of aqueous systems normally reveal either partial, or sometimes complete, aquation superimposed on the rate of any direct ligand exchange. The rate constant for aquation (and the observed overall exchange rate) will however give some indication of the magnitude of the bond lability.

An example of these considerations is provided by the very thorough study of the $PtCl_4^{2-}$–Cl^{*-} exchange system performed by Grantham, Elleman, and Martin (195). All the experiments to be described were performed in the dark

TABLE 5

Exchange rates of PtX_4^{2-} *ions*

X^-	Concentration of Complex	$t_{\frac{1}{2}}$
	M	*minutes*
CN^-	0.037	1
I^-	0.103	5
Br^-	0.05	8
Cl^-	0.072	280

because of the photosensitivity of this exchange system; such effects are discussed in Section VI,F. The $PtCl_4^{2-}$ ion undergoes reversible aquation:

$$PtCl_4^{2-} + H_2O \underset{k_2}{\overset{k_1}{\rightleftharpoons}} PtCl_3H_2O^- + Cl^-$$

the rate term for the forward reaction being $k_1[PtCl_4^{2-}]$ and that for the reverse being $k_2[PtCl_3H_2O^-][Cl^-]$. The $PtCl_3H_2O^-$ ion, as a weak acid, can be readily titrated with sodium hydroxide, and from a potentiometric titration curve the equilibrium constant for aquation was determined to be 0.018 mole/l. at 25°C. The reversible aquation of the $PtCl_4^{2-}$ ion, the rate of which could be readily measured, provides one possible path for the exchange of free chloride ion. The authors found that the rate of chloride exchange in freshly prepared K_2PtCl_4 solutions of high chloride content (i.e., with $PtCl_3H_2O^-$ initially absent) could be accounted for (to within 10 per cent) by the assumption that aquation was the sole mechanism for exchange; e.g., for reactant concentrations of 0.017 (complex) and 0.27 (chloride) at 25°C. the observed exchange half-time was 15.3 hr., whilst that calculated from the previously measured rate of aquation was 16.8 hr. Hence the direct exchange of chlorine–ligands proceeds, at the most, at 10 per cent of the rate of exchange via aquation. However, using aged K_2PtCl_4 solutions (i.e., solutions which had been left for at least 20 hr. to attain the equilibrium concentration of up to 60 per cent of $PtCl_3H_2O^-$ before exchange was initiated) the observed chloride exchange rate is significantly greater than that calculated on the assumption that the aquation path is solely responsible for exchange. Under the reaction conditions employed, the rate of formation of the diaquo species $PtCl_2(H_2O)_2$ is too slow to account for this increased exchange rate and thus the direct exchange:

$$PtCl_3H_2O^- + Cl^{*-} \rightleftharpoons PtCl_3^*H_2O^- + Cl^-$$

must be significant. This exchange process is described by the rate law:

$$R = k'[PtCl_3H_2O^-]$$

In this case it would seem that the mechanism does involve S_N1 dissociation of the complex, since the rate of the alternative S_N2 aquation is known to be slow. The detailed mechanism may then be written:

$$PtCl_3H_2O^- \overset{\text{slow}}{\rightleftharpoons} [PtCl_2H_2O] + Cl^-$$

$$[PtCl_2H_2O] + Cl^{*-} \underset{\text{slow}}{\rightleftharpoons} PtCl_2Cl^*H_2O^-$$

The measured entropy of activation (table 6) is also in accord with this S_N1 dissociation process. It is interesting to note that the chloride ion can compete favorably with the solvent water molecule for reaction with the uncharged intermediate $PtCl_2H_2O$. However, with the charged parent $PtCl_4^{2-}$ ion, the coulombic energy barrier is such that the chloride ion does not react at a significant rate as compared to that of the water molecule.

The kinetic data in table 6 have been obtained for this exchange system.

TABLE 6

$PtCl_4^{2-}$-Cl^- *exchange*

	k_1	k_2	k'
25°C	0.14 $hr.^{-1}$	7.7 l. $mole^{-1}$ $hr.^{-1}$	0.16 $hr.^{-1}$
$\Delta H^\ddagger$, kcal./mole	21	15	25
$\Delta S^\ddagger$, e.u.	−8	−18	+2

This exchange study has therefore provided a direct quantitative estimate of the lability of the platinum–chlorine bond in the $PtCl_3H_2O^-$ ion (rate constant of direct exchange, k') but it cannot provide a similar estimate for the $PtCl_4^{2-}$ ion since the rate constant k_1 refers to the process of aquation. The rate of the direct ligand exchange in $PtCl_4^{2-}$ could probably be derived from a study in nonaqueous solvents, but this lability is still not necessarily relevant to water, for which most data are required. The rate constants for the primary aquation of $PtCl_4^{2-}$ and $PtBr_4^{2-}$ are, respectively, 0.14 and 3.6 $hr.^{-1}$ at 25°C., but the ratio of these rate constants is not necessarily an estimate of their relative bond labilities. If the hydration equilibrium is more displaced in favor of the aquo ion in the case of $PtBr_4^{2-}$ than for $PtCl_4^{2-}$ (for which $K = 0.018$), then the ratio of the rates at which the equilibrium states are approached, i.e., the relative bond labilities, will be less than the ratio 3.6/0.14. If, however, the hydration equilibrium constants for the two complex ions are approximately the same, then it would be correct to state that the platinum–bromine bond in $PtBr_4^{2-}$ is 25 times more labile with respect to aquation than the platinum–chlorine bond in $PtCl_4^{2-}$.

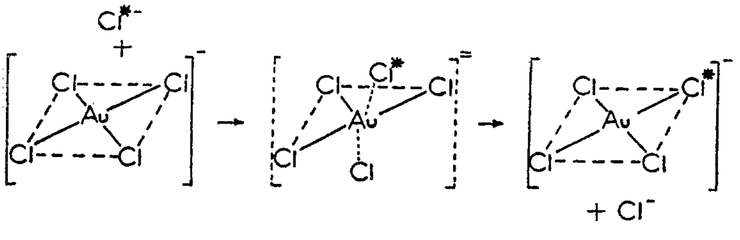
Rich and Taube (391) have studied the analogous Au(III) system:

$$AuCl_4^- + Cl^{*-} \rightleftharpoons AuCl_4^{*-} + Cl^-$$

which undergoes quite rapid exchange ($t_{\frac{1}{2}}$ less than 5 min. at 0°C.) as compared to the Pt(II) system ($t_{\frac{1}{2}}$ about 15 hr. at 25°C.). Moreover under the experimental conditions employed, negligible aquation of $AuCl_4^-$ occurs in contrast to $PtCl_4^{2-}$. The rate law for exchange is:

$$R = k_1[AuCl_4^-] + k_2[AuCl_4^-][Cl^-]$$

where $k_1 = 0.20$ $min.^{-1}$ and $k_2 = 11.0$ l. $mole^{-1}$ $min.^{-1}$ at 0°C. The k_2 term is good evidence for the direct participation of Cl^- and $AuCl_4^-$ in the activated complex and S_N2 chlorine–ligand exchange must be occurring. The detailed mechanism of this process was postulated to involve utilization of the vacant p orbital in the $AuCl_4^-$ ion by the incoming chloride ion, the activated $AuCl_5^{2-}$ complex thereby approximating to a trigonal-bypyramid in configuration:



(Such a mechanism is probably applicable to most square coplanar complexes and has also been suggested (9, 313) for the extremely rapid exchange of the —CN ligands in the tetracyanides of Pd(II), Zn(II), Ni(II), and Hg(II).) The mechanism of the process described by the k_1 term is far less certain. The large entropy decrease on activation (−50 e.u.) might suggest a rate-determining S_N2 hydrolysis of the square complex via an octahedral activated complex involving two solvent water molecules. In support of this view, Rich and Taube point out that the observed exchange rate by this path is about four times the rate of hydrolysis, a factor to be expected if the hydrolyzed species $AuCl_3OH^-$ completely exchanges the three remaining chlorine ligands before reverting to the parent $AuCl_4^-$ ion.

It is noteworthy that although $AuCl_4^-$ and $PtCl_4^{2-}$ are isoelectronic, their behavior to isotopic exchange is very different (195). The exchange of the gold compound is about 200 times faster than that of the platinum compound under comparable conditions and occurs by fundamentally different processes. Whilst a direct S_N2 ligand exchange represents a substantial fraction of the total exchange for $AuCl_4^-$, this path accounts for only 10 per cent (at the very most) of the total rate of $PtCl_4^{2-}$. Undoubtedly this may be attributed to the higher charge barrier for Cl^- exchange with $PtCl_4^{2-}$. The $PtCl_3H_2O^-$ ion, of the same formal charge as $AuCl_4^-$, also does not undergo direct bimolecular chloride-ion exchange but rather S_N1 dissociation, due possibly to the labilizing influence of the $—OH_2$ ligand. Nevertheless the gold–chlorine bonds in $AuCl_4^-$ must be much more labile than the platinum–chlorine bonds in $PtCl_3H_2O^-$.

Provided sufficient kinetic investigations are performed, a quantitative evaluation of trans effects (387) may be forthcoming from exchange studies on tetracoördinated complexes. The magnitude of the trans effect appears to be intimately connected with the electronegativity of ligands in the various complexes; for a given central atom, this factor also largely determines the lability of the metal–ligand bonds. The exchange of —Cl ligands is reported (201) to be faster in *cis*-$K_2Pt(NO_2)_2Cl_2$ than in K_2PtCl_4, but until the relative contributions of aquation and direct exchange are known for the former complex, further quantitative deduction would seem premature.

C. COMPLEXES OF COÖRDINATION NUMBER SIX

1. *Exchange of the central atom*

As in the case of tetracoördinated complexes, most studies of the exchange of hexacoördinated central atoms have been concerned with those complexes which have been already classified as "ionic" or "covalent" from magnetic moment measurements. Thus free ferric ion does not exchange with ferricyanide or ferrocyanide ("covalent") but undergoes complete exchange in a few seconds with the ferri-tris-oxalate ion ("ionic") (207, 208). Whilst a series of "ionic" Co(II) tris-phenanthroline and some 5-substituted phenanthroline complexes exhibit rapid exchange with free Co^{2+}_{aq}, bis-tripyridyl-cobalt(II) exhibits a measurable exchange half-time (2.8 hr.) at 15°C. and at 0.005 *M* reactant concentrations (469). West suggested on the basis of these results that the latter compound would have $3d^24s4p^3$ bond hybridization (inner orbital) with the one unpaired electron promoted to the 5*s* state. This is to be contrasted with the outer-orbital $4s4p^34d^2$ bonding of the former complexes. Williams (479) has pointed out that whereas the dipyridyl and phenanthroline Co(II) complexes exhibit weak absorption between 450 and 600 mμ ($\epsilon_{\max} = 10$) and are labile, the tripyridyl complex exhibits strong absorption over the range 400–500 mμ ($\epsilon_{\max} > 1000$). This latter complex is relatively inert, like the covalent Fe(II) dipyridyl and phenanthroline complexes (e.g., the slow exchange of $\mathrm{Fe(phen)_3}^{2+}$ with $\mathrm{Fe}^{2+}_{\mathrm{aq}}$) (407, 474), which also display a very strong absorption in this region.

Although ferric-ethylenediaminetetraacetate (FeY^-, Y = EDTA) is "ionic," the exchange rate with $\mathrm{Fe}^{3+}_{\mathrm{aq}}$ is relatively slow and Jones and Long (268) were able to study the kinetics of this system. The rate of exchange was markedly pH dependent, and by conducting experiments over narrow pH ranges in which one mechanism predominated, the rate law at 25°C. could be represented as:

$$R = 0.47\,[\mathrm{FeY^-}][\mathrm{H^+}]^3 + 0.015\,[\mathrm{FeY^-}][\mathrm{Fe^{3+}}] + 0.14\,[\mathrm{FeY^-}][\mathrm{FeOH^{2+}}] \quad (20)$$

although the second rate term may include the first power of the hydrogen-ion concentration. The exchange rate exhibited a small positive salt effect at high acidities (when the first kinetic term predominates) and a small negative salt effect at lower acidities (when the second and third kinetic terms predominate). The three postulated exchange mechanisms are:

(1) $\mathrm{FeY^-} + 2\mathrm{H^+} \rightleftarrows \mathrm{H_2FeY^+}$ (rapid)

$\mathrm{H_2FeY^+} + \mathrm{H^+} \xrightarrow{\text{slow}} \mathrm{Fe^{3+}} + \mathrm{H_3Y^-}$

(2) $\mathrm{FeY^-} + \mathrm{Fe^{*3+}} \rightleftarrows \mathrm{Fe^*Y^-} + \mathrm{Fe^{3+}}$

(3) $\mathrm{FeY^-} + \mathrm{Fe^*OH^{2+}} \rightleftarrows \mathrm{Fe^*Y^-} + \mathrm{FeOH^{2+}}$

A knowledge of the entropies of activation would probably enable some decision to be made as to the detailed mechanism of processes 2 and 3, but in view of the complexity of the system such a temperature-dependence study would need to be of the highest precision to obtain significant data. The analogous $\mathrm{Fe^{*2+}}$–$\mathrm{FeY^{2-}}$ exchange reaction proceeds at a very high rate, which has been correlated with the comparatively high dissociation constant (10^{-14}). A similar kinetic study was therefore precluded, but measurable half-times were reported (309) in exploratory experiments on the $\mathrm{Co^{*2+}}$–$\mathrm{CoY^{2-}}$ and $\mathrm{Ni^{*2+}}$–$\mathrm{NiY^{2-}}$ systems, with a similar pH dependence in the latter system as for the $\mathrm{Fe^{*3+}}$–$\mathrm{FeY^-}$ system.

It seems that *a priori* the exchange reactions of metal ethylenediaminetetraacetate complexes will be complicated, with several paths being available for exchange. This is apparent from the kinetic studies of substitution of $\mathrm{CdY^{2-}}$ with $\mathrm{Cu^{2+}}$ (1) and of the substitution of $\mathrm{PbY^{2-}}$ with $\mathrm{Zn^{2+}}$ (63). In the former example four different reaction paths are available to the $\mathrm{Cu^{2+}}$ ion by collision with the anions $\mathrm{CdY^{2-}}$, $\mathrm{CdHY^-}$, $\mathrm{HY^{3-}}$, and $\mathrm{H_2Y^{2-}}$. The bimolecular rate constant is divisible into three terms:

$$k = k_1 + k_2[\mathrm{H^+}] + k_3[\mathrm{H^+}]^2 \quad (21)$$

over the pH range 4 to 5. The $\mathrm{Fe^{*3+}}$–$\mathrm{FeY^-}$ exchange study was conducted from pH 1 to 2.5, and it is interesting to note that a third-order dependence on hydrogen-ion concentration arises in these acidities. For the Cu^{2+}–CdY^{2-} reaction a similar dependence could arise at these low pH values, implying reaction with H_3Y^-. The ferric exchange system is unfortunately complicated by the occurrence of hydrolyzed species at low acidities. This complication would not be as serious for the analogous Ni^{*2+}–NiY^{2-} exchange system and a detailed kinetic study would seem well worthwhile.

2. *Exchange of monodentate ligands*

Kinetic studies of the rate of ligand exchange in hexacoördinated complexes in aqueous solution reveal that water again plays a significant role. In the interpretation of such studies it would be of considerable significance if the rate of water–ligand exchange in these complexes could be evaluated. Not only would such measurements assist in the general understanding of the lability of complex ions but they would serve to compare the kinetic behavior of neutral-ligand exchange systems to that observed with charged ligands in exchange and substitution reactions. Moreover the first step in ligand exchanges is frequently one of aquation and it is desired to ascertain the detailed mechanism of the subsequent "anation" reaction leading to the appearance of a labelled ligand in the complex. This anation reaction is often described by a rate law consistent with either an S_N1 or an S_N2 mechanism. Hunt and Taube (254) have illustrated this problem with reference to the reaction:

$$Co(NH_3)_5H_2O^{3+} + Cl^- \rightleftarrows Co(NH_3)_5Cl^{2+} + H_2O$$

which proceeds in the forward sense according to the rate term

$$k[Co(NH_3)_5H_2O^{3+}]\ [Cl^-]$$

This rate law is compatible with either of two mechanisms:

(*a*) S_N1:

$$Co(NH_3)_5H_2O^{3+} \rightleftarrows Co(NH_3)_5{}^{3+} + H_2O \quad \text{(rapid equilibrium)}$$

$$Co(NH_3)_5{}^{3+} + Cl^- \underset{k_2}{\overset{k_1}{\rightleftarrows}} Co(NH_3)_5Cl^{2+}$$

(*b*) S_N2:

$$Co(NH_3)_5H_2O^{3+} + Cl^- \underset{k_2'}{\overset{k_2}{\rightleftarrows}} Co(NH_3)_5Cl^{2+} + H_2O$$

For the S_N1 mechanism the rate of formation of $Co(NH_3)_5Cl^{2+}$ must be less than the rate of the exchange of water with $Co(NH_3)_5H_2O^{3+}$, but for the S_N2 mechanism no such restriction applies. A discrimination between these two possible mechanisms is thus possible, at least in principle, from a measurement of the rate of water–ligand exchange.

The rate of the exchange reaction:

$$Co(NH_3)_5H_2O^{3+} + H_2O^{18} \rightleftarrows Co(NH_3)_5H_2O^{18\ 3+} + H_2O$$

exhibits (410) first-order dependence on the concentration of the pentammineaquo ion. In an endeavor to ascertain whether the anation of $Co(NH_3)_5H_2O^{3+}$ by SO_4^{2-} proceeds via an S_N1 or an S_N2 mechanism, Rutenberg and Taube (410) observed that the water exchange half-time increased from 24 to 27.8 hr. on the addition of 0.33 *M* sodium sulfate and 0.50 *M* sodium bisulfate. This would seem compatible with S_N1 dissociation followed by competition of SO_4^{2-} and H_2O for the intermediate $Co(NH_3)_5^{3+}$ ion, thereby leading to a decreased rate of water exchange (i.e., increased half-time). An S_N2 process would tend to exhibit a slight increase in the rate of water exchange on addition of SO_4^{2-} due to the reaction:

$$Co(NH_3)_5H_2O^{3+} + SO_4^{2-} \rightarrow Co(NH_3)_5SO_4^{+} + H_2O$$

It should be pointed out that these observations merely indicate that the S_N1 mechanism predominates over the S_N2 mechanism; the latter is not completely excluded.

The general technique employed (176, 253, 254) in studying the exchange of hexaaquo cations with solvent water was to mix an aqueous cation solution with water labelled with H_2O^{18}. At suitable times the water was distilled off *in vacuo*, equilibrated with normal carbon dioxide, the latter analyzed, and the extent of exchange calculated. However, since the water coördinated to a cation represented only a small fraction of the total water in the system, experiments were of necessity conducted at high salt concentrations (>0.5 *M*) with high analytical precision in order to follow the exchange accurately. Under these conditions Al_{aq}^{3+}, Fe_{aq}^{3+}, Co_{aq}^{3+}, Ga_{aq}^{3+}, and Th_{aq}^{4+} exchanged completely in the separation time of 3 min. at 25°C. (254), but Cr_{aq}^{3+} exhibited a half-time of about 40 hr. which was independent of acidity (253). A more detailed study by Plane and Taube (378) revealed that with both ClO_4^- and NO_3^- in the presence of perchloric acid, the exchange rate could be expressed as:

$$R = k[Cr_{aq}^{3+}][\text{anion}] \qquad (22)$$

Under the high concentration conditions employed, it is difficult to discriminate between salt effects (due to the effect of ionic atmospheres) and actual chemical effects (involving direct participation of the anion in the activated complex). Plane and Taube favor the latter interpretation and suggest that the anion operates such that a water molecule in the anion hydration sphere is replaced by a water of the cation hydration sphere, the interaction thereby reducing the energy required to remove a water ligand from the cation. However, Mackenzie and Milner (314) found no specific effects for the Cr_{aq}^{3+}–H_2O^{18} exchange in the absence of acid, although the exchange rate does depend upon the ionic strength. Accordingly the anion-exchange mechanism was proposed:

$$Cr(H_2O)_6^{3+} + X^- \rightleftarrows Cr(H_2O)_5X^{2+} + H_2O$$

$$Cr(H_2O)_5X^{2+} + X^- \rightleftarrows Cr(H_2O)_4X_2^{+} + H_2O$$

which is equivalent to an isomerization reaction (or hydrolysis when $X^- = OH^-$). In solutions containing no acid the direct exchange, with $X^- = OH^-$, was assumed to predominate, but in the presence of acid other specific anions bring about the exchange reaction. The specific effects noted by Plane and Taube were thus attributed to steric factors, since the exchange rate is claimed to decrease with increasing anion size ($Cl^- > Br^- > NO_3^- > ClO_4^-$). However the observed variation is well within experimental error. It is noteworthy that the addition of hydrochloric acid to the Cr_{aq}^{3+}–H_2O^{18} system causes immediate exchange of two water ligands, followed by a very much slower exchange of the remaining four water ligands. This is presumably due to the rapid formation of the stable $Cr(H_2O)_4Cl_2^+$ ion with expulsion of two water ligands.

By precipitating Cr_{aq}^{3+} as $CrPO_4 \cdot 6H_2O$ and studying the appearance of O^{18} in this fraction, Hunt and Plane (251) have been able to study the Cr_{aq}^{3+}–H_2O^{18} exchange system at low salt concentrations (0.05 M) in perchloric acid. No specific anion effects were observed, the exchange rate being expressible by the term $k_1[Cr(H_2O)_6^{3+}]$ [compared to the equation (equation 22) quoted by Plane and Taube]. In the presence of nitrate ion and perchlorate ion slight differences in exchange rate occurred at $\mu = 0.7$ but these could be attributed to activity effects; the extrapolated value of k_1 at $\mu = 0$ and 27°C. is 2.07×10^{-4} min.$^{-1}$ for both these anions. The activation energy for exchange is 27.6 ± 1 kcal./mole in the presence of acid at all salt concentrations and 31 ± 4 kcal./mole in the absence of acid; the difference in activation energies, if significant, may be some support for the anion-exchange mechanism of Mackenzie and Milner.

From the observed decrease of O^{18} content in water on complete exchange with Cr_{aq}^{3+}, Hunt and Taube (254) were able to confirm experimentally that the hydration number of Cr^{3+} was 6.0 ± 0.2, a suitable allowance being applied for isotopic fractionation effects (see Section VII,C). With other aquo cations which undergo rapid —OH_2 ligand exchange, the hydration numbers must be deduced from the isotopic exchange equilibrium constant. However, the adaptation of flow methods to a study of these rapid rates may still permit the direct measurement of the hydration numbers of labile cations (444, 446). It is interesting to enquire as to the probable reason for the slow exchange of Cr_{aq}^{3+} on the one hand and the rapid exchange of Al_{aq}^{3+}, Ga_{aq}^{3+}, Co_{aq}^{3+}, and Fe_{aq}^{3+} on the other. The Cr^{3+} ion is by no means exceptional (254) in this series of ions with respect to factors such as ionic radius, hydration energy, hydrolysis constant, or halide stability constants. The difference must be due to the differing electronic states of the metals coördinated as the aquo cations. On formation of inner-orbital d^2sp^3 bonds, all the $3d$ orbitals of Cr(III) are occupied. Therefore with an S_N2 mechanism operative necessitating the formation of a heptacoördinated activated complex, either one $3d$ electron would have to be promoted to a $4d$ state or the incoming group would have to utilize a single $4d$ orbital with consequent formation of a relatively unstable activated complex. A relatively slow rate of —OH_2 ligand exchange for Cr(III) thus appears reasonable; this explanation is also probably applicable to all ligand exchanges of Cr(III). In the case of Al_{aq}^{3+}, Fe_{aq}^{3+}, and Ga_{aq}^{3+} the —OH_2 ligands utilize outer-orbital sp^3d^2 bonds and rapid exchange, possibly by S_N1 dissociation, is to be anticipated. At first sight the rapid water exchange of Co_{aq}^{3+} (176) may seem surprising, although Taube (445) has interpreted this as evidence for the greater stabilization by —OH_2 ligands of a paramagnetic Co(III) state (and hence rapid exchange). However, the experiments on Co^{3+}_{aq} were complicated by the presence of Co^{2+}_{aq}, which was independently shown to undergo rapid water exchange. A rapid electron exchange between Co^{2+}_{aq} and Co^{3+}_{aq} could cause an apparent rapid exchange of water in Co^{3+}_{aq}.

This same principle has been used (378) to obtain an estimate of the rate of electron exchange between Cr^{3+}_{aq} and Cr^{2+}_{aq}. As distinct from Cr^{3+}_{aq}, Cr^{2+}_{aq} undergoes rapid exchange of ligand water, the change being complete in less than 2 min. On the addition of 0.16 M Cr^{2+} to 1 M Cr^{3+} ($t_{\frac{1}{2}}$ normally 27 hr.) the exchange half-time for Cr^{3+}_{aq}–H_2O^{18} was 2.1 hr. The extent of the catalytic effect by Cr^{2+}_{aq} is governed by the rate of the electron exchange between Cr^{2+}_{aq} and Cr^{3+}_{aq} and it was thereby possible to set an upper limit of 0.028 l. mole^{-1} min.$^{-1}$ to the rate constant of this reaction. The principle should be generally applicable to other ligand exchanges in complexes of two valency states of a given metal. The sole requirement is that one complex should be labile, and the other relatively inert, to ligand exchange.

Adamson and Wilkins (11) attempted to measure the rate of direct bimolecular exchange of SC*N with $Cr(NH_3)_5SCN^{2+}$, $Co(NH_3)_5SCN^{2+}$, and *trans*-$Co(en)_2(SCN)_2^+$ but found that aquation of all these complexes was quite substantial in the times required to investigate the rates of direct —SCN exchange. To increase the sensitivity of the rate measurements, the systems were followed using labelled complex ion and measuring the rate of appearance of activity in the free thiocyanate ion for small degrees of aquation. The competing processes of aquation and exchange may then be written (neglecting isotope effects):

Aquation: $MA_5SCN^{2+} + H_2O \xrightarrow{k_1} MA_5H_2O^{3+} + SCN^-$

$MA_5SC^*N^{2+} + H_2O \xrightarrow{k_1} MA_5H_2O^{3+} + SC^*N^-$

Direct exchange: $MA_5SC^*N^{2+} + SCN^- \overset{k_2}{\rightleftharpoons} MA_5SCN^{2+} + SC^*N^-$

and it was shown that the first-order rate constant for the appearance of activity in SCN^- (k_{app}) could be expressed as:

$$k_{app} = k_1 + k_2[SCN^-]_0 \qquad (23)$$

Any direct exchange should then appear as a dependence of k_{app} upon $[SCN^-]_0$. With $Cr(NH_3)_5SCN^{2+}$ the direct exchange term was only a few per cent of k_1 at 70°C.; k_2 must thus be less than 0.015 l. mole^{-1} hr.$^{-1}$ at this temperature. At 90°C. with $Co(NH_3)_5SCN^{2+}$, k_{app} did increase with concentration of free thiocyanate ion, but this increase was shown to be due to a specific catalysis of the aquation rate by thiocyanate ion. This catalysis does not occur in the aquation of $Cr(NH_3)_5SCN^{2+}$. (A similar catalytic effect by sulfate ion has also been observed by Taube and Posey (451) in the aquation of $Co(NH_3)_5SO_4^+$.) The difference in catalytic effects for the chromium and cobalt pentammine complexes was attributed to the operation of an S_N2 mechanism for Cr(III) complexes and an S_N1 mechanism for Co(III) complexes. Whilst removal of an uncharged $—OH_2$ ligand by S_N1 dissociation of $Co(NH_3)_5H_2O^{3+}$ would not be expected to be influenced by ion-pair formation (as shown in the case of SO_4^{2-}; vide supra), the removal of a charged ion by S_N1 dissociation of $Co(NH_3)_5SCN^{2+}$ could be reasonably assumed to be accelerated by anion pairing.

This question of ion-pair formation may also be relevant to a study (71) of the exchange and substitution reactions of *cis*-$Co(en)_2Cl_2^+$ in absolute methanol. The Cl^- exchange and SCN^-, Br^-, and NO_3^- substitutions proceed by first-order kinetics and presumably indicate rate-determining S_N1 dissociation of the dichloro complex. The S_N2 formation of an intermediate methylato complex could, however, exhibit similar kinetics. The strongly nucleophilic ions OCH_3^-, N_3^-, and NO_2^- showed partial second-order kinetics which were interpreted by Brown and Ingold as evidence for direct bimolecular replacement. An alternative explanation is that in terms of ion-pair formation, with these strongly nucleophilic ions inducing S_N1 dissociation of a —Cl ligand. In direct physical terms, however, the distinction between ion-pair-induced S_N1 dissociation and direct S_N2 substitution is a somewhat academic point, i.e.,

$$Co(en)_2Cl_2^+ \cdot OCH_3^- \xrightarrow{\text{slow}} Co(en)_2Cl^{2+} \cdot OCH_3^- + Cl^-$$

or

$$Co(en)_2Cl_2^+ + OCH_3^- \rightarrow Co(en)_2Cl \cdot OCH_3^+ + Cl^-$$

For purposes of discussion it is probably sufficient to interpret these results as evidence for bimolecular ligand replacement. Whilst this study in nonaqueous media is of considerable importance in itself, the basic problem of devising methods for studying bimolecular ligand exchange in aqueous solution, in the presence of aquation, still remains. Ettle and Johnson (152) in some very early work investigated the exchange of chlorine ligands in *cis*- and *trans*-$Co(en)_2Cl_2^+$ and *cis*-$Co(en)_2(H_2O)Cl^{2+}$ with free chloride ion in aqueous solution. With the two isomers of $Co(en)_2Cl_2^+$ no evidence for direct exchange of chlorine was found in a contact time dictated by the relatively rapid aquation of the complexes, although at 80°C. and a contact time of 35 sec. a slight amount of exchange occurred with the monoaquo complex. In the isomerization:

$$trans\text{-}Co(en)_2Cl_2^+ \rightleftarrows cis\text{-}Co(en)_2Cl_2^+$$

in the presence of NaCl*, complete randomization of activity occurred. Since direct chloride exchange is relatively slow, this transfer of Cl^{*-} is attributed to the aquation reactions:

$$cis\text{- and } trans\text{-}Co(en)_2Cl_2^+ \rightleftarrows Cl^- + Co(en)_2(H_2O)Cl^{2+}$$
$$\rightleftarrows 2Cl^- + Co(en)_2(H_2O)_2^{3+}$$

Moreover the catalysis of the inversion of *d*-*cis*-$Co(en)_2Cl_2$ by added potassium chloride cannot be attributed to "inversion by substitution" (a mechanism extremely common for organic compounds), since direct ligand exchange does not occur.

A rather extensive survey has been conducted of the exchange of cyano ligands

TABLE 7

Exchange rates and stability constants of cyanide complexes

Complex	Stability Constant	Approximate Concentration of Dissociating Product in 0.1 *M* Solution	Exchange Rate
$Hg(CN)_4^{2-}$	10^{-42}	10^{-6}	"Instantaneous"
$Fe(CN)_6^{3-}$	10^{-44}	10^{-6}	Very slow
$Fe(CN)_6^{4-}$	10^{-37}	10^{-5}	Very slow
$Ni(CN)_4^{2-}$	10^{-22}	10^{-4}	"Instantaneous"
$Mn(CN)_6^{3-}$	10^{-27}	10^{-4}	Measurable

in two-, four-, six- and eight-coördinated complexes (9, 313). The dicyano complexes of Hg(II), Ag(I), and Cu(I), the tetracyanides of Zn(II), Hg(II), Ni(II), and Pd(II), and the hexacyanides of Cr(II) and V(III) all exchange in the time of reactant separation, whilst the hexacyanides of Fe(II), Fe(III), Co(III), the pentacyanoaquo complexes of Fe(II), the pentacyanonitroso complex of Fe(III), and the octacyanide of Mo(IV) undergo very slow ligand exchange. These results are a good illustration of the independence of ligand exchangeability and thermodynamic stability, as shown in table 7. It is important to appreciate that the amount of free cyanide ion produced by dissociation of a complex cyanide is unimportant compared with the rate at which this cyanide ion is produced. It is the latter which determines the rate of —CN ligand exchange. The dissociation of cyanide complexes is frequently very slow and the stability constants are calculated from electrode potential measurements (293) which only depend on rapid electron transfers.

Adamson, Welker, and Wright (10) found that the exchange rate of $Mn(CN)_6^{3-}$ with cyanide ion was first order in complex-ion concentration, but independent of free cyanide concentration, pH (from about 9 to 11), and ionic strength. The authors conclude that only one charged reactant is involved, that this reactant is not a hydrolyzed species, and that the rate-determining step in the exchange is one of the following:

(*a*) S_N1 dissociation:

$$Mn(CN)_6^{3-} \underset{\text{fast}}{\overset{\text{slow}}{\rightleftarrows}} Mn(CN)_5^{2-} + CN^-$$

(*b*) S_N2 aquation:

$$Mn(CN)_6^{3-} + H_2O \overset{\text{slow}}{\rightleftarrows} [Mn(CN)_6H_2O^{3-}] \overset{\text{fast}}{\rightleftarrows} Mn(CN)_5H_2O^{2-} + CN^-$$

The entropy of activation is −44.2 e.u., which is considered too large for a normal unimolecular reaction and hence the S_N2 aquation is favored. The latter path proceeds via a heptacoördinated complex formed, it is postulated, by using an available inner *d* orbital (the ground state of Mn(III) being $3d^2d^1d^1D^2D^2S^2P^2P^2P^2$). This process requires little energy for Mn(III) (which would attain an inert gas structure in the activated complex), rather more energy for Cr(III), and considerable energy for Co(III), Fe(II), and Fe(III), since in these cases promotion of electrons to higher orbitals must occur. The observed decrease in lability towards cyanide exchange was explained in this way. Somewhat similar, although more general, ideas have been described by Taube in his effective classification of hexacoördinated compounds (445).

MacDiarmid and Hall (313) subsequently observed completely analogous kinetic behavior for $Co(CN)_6^{3-}$, $Fe(CN)_6^{4-}$, and $Cr(CN)_6^{3-}$ and postulate the same aquation mechanism as invoked for $Mn(CN)_6^{3-}$. The observation of increasing exchange rate with decreasing pH constitutes further support for the aquation mechanism. It is to be noted that in all these cases of complex cyanides, the observed rate of ligand exchange is determined by the rate of aquation of the complex. The cyanide ion presumably does not enter into the seventh coördination position because of the relatively high concentration of water and the uncharged nature of the latter.

Adamson (5) has studied the exchange in the absence of oxygen of free cyanide with the cyanide complex of Co(II), which was shown to have the empirical formula $K_3Co(CN)_5$ rather than $K_4Co(CN)_6$. In solution the ion could exist as either $Co(CN)_5H_2O^{3-}$ or $Co(CN)_5^{3-}$. The latter possibility is favored, since the cyanide exchange is complete in a separation time of 2 min., which probably indicates that a S_N2 exchange mechanism operates, utilizing a vacant orbital in the complex (as already mentioned for planar complexes). The exchange behavior of $Co(CN)_5H_2O^{3-}$ would be expected to be similar to that of $Co(CN)_6^{3-}$, which is very slow (9).

The exchange of single atoms within a ligand was first studied qualitatively some twenty years ago (22, 149, 365), especially with the exchange of hydrogen atoms in ammonia ligands with deuterium oxide. Quantitative studies of the hydrogen exchange in $Co(NH_3)_6^{3+}$ and $Co(en)_3^{3+}$ revealed (20) that the rate is inversely proportional to the hydrogen-ion concentration, a result which constitutes evidence for metal amide formation, as in the following kinetic scheme:

$$Co(ND_3)_6^{3+} \rightleftharpoons Co(ND_3)_5ND_2^{2+} + D^+$$

$$Co(ND_3)_5ND_2^{2+} + H_2O \xrightarrow{\text{slow}} Co(ND_3)_5ND_2H^{3+} + OH^-$$

$$H^+ + OH^- \rightleftharpoons H_2O$$

The greater the orbital overlap in the cobalt–nitrogen σ-bond formed in such ammine complexes, the lower will be the electron distribution on the nitrogen atom and hence the greater the probability of acid dissociation. Thus a complex more inert to substitution should exhibit a higher probability of acid dissociation. The product (K) of the exchange rate constant and the number of exchangeable hydrogen atoms can be taken as a measure of the probability of acid dissociation of the ammine complexes; these values are 4.54×10^{-6} for $Co(NH_3)_6^{3+}$ and 5.27×10^{-6} for $Co(en)_3^{3+}$ at 25°C. and seem to be in accord with these ideas. The rate of exchange for Co(III) complexes is greater than that for the tetrammines of platinum and palladium, indicating a higher acid strength, the higher the central atom valency (19). The K values for $Pd(NH_3)_4^{2+}$, $Pt(NH_3)_4^{2+}$, and $Co(NH_3)_6^{3+}$ at 0°C. are 1.17×10^{-8}, 2.48×10^{-8}, and 13.8 ×

10^{-8}, respectively. Moreover $Pd(NH_3)_4^{2+}$ exchanges not only by the acid dissociation mechanism (at pH about 7) but at low pH exchanges also by reversible dissociation of ammonia. More qualitative studies have been reported for the ions $Co(NH_3)_4(NO_2)_2^+$, $Co(NH_3)_4CO_3^+$ (22), and $Cu(NH_3)_4^{2+}$ (150). In view of the importance of such measurements, further studies of such ammine–water exchanges are desirable.

3. Exchange of bidentate ligands

An early study by Long (307) of the tris-oxalato complexes of metals revealed that whereas the Co(III) and Cr(III) complexes did not exchange with free aqueous C^{11}-labelled oxalate in half an hour at 50°C. and 35°C., respectively, the corresponding complexes of Fe(III) and Al(III) exchanged in the time of reactant separation. This is evidence for the inner-orbital type of bonding in the former pair of complexes and outer-orbital bonding in the latter pair. The short half-life of C^{11} (20.5 min.) prevented Long from studying the Co(III) and Cr(III) complexes over a longer period of time to investigate the possibility of a slow exchange. The exchanges of tris-oxalato and tris-malonato complexes of Fe(III) with their free C^{14}-labelled ligand ions have also been recently studied (99). The measured magnetic moments of both complexes indicate these complexes to be constituted of outer-orbital bonds. Rapid exchange for both complexes is claimed, but inspection of the experimental results for the malonate complex reveals an exchange half-time of about 30 min. If this is significant, the slower half-time for the malonato complex may reflect the increased stabilization to exchange of the six-membered ring as compared to the five-membered ring in the oxalato complex. It then follows that the ferrimalonate complex might be resolvable.

An interesting ligand-exchange study (100) of the salicylaldehyde type quadridentate complexes of nickel has been recently reported. Bis-(salicylaldoxime)-nickel and bis-(*N*-methylsalicylaldimine)nickel were shown to be paramagnetic in pyridine solution, owing presumably to formation of an octahedral adduct incorporating two pyridine solvent molecules which could be precipitated from pyridine solution by water. These two complexes exchange rapidly in pyridine with C^{14}-labelled salicylaldoxime and methylsalicylaldimine, whilst bis-(salicylaldehyde-ethylenediimine)nickel, which is diamagnetic both as a solid and in solution, does not undergo ligand exchange. However, although a dynamic equilibrium appears to exist in pyridine solution between diamagnetic and paramagnetic forms of bis-(salicylaldehyde-*o*-phenylenediimine)nickel, no ligand exchange was observed. This result, at first rather surprising, was attributed to the quadridentate ligand occupying four planar positions in the complex, and the two pyridine molecules in the paramagnetic (labile) form thereby must assume trans rather than cis positions. For exchange to occur with the free quadridentate ligand ion, either four nickel–ligand bonds must be ruptured simultaneously (S_N1) or an activated complex of coördination number eight must be formed (S_N2). Since either alternative would require a high activation energy, ligand exchange is slow. This study indicates that stereochemical requirements can, under certain circumstances, outweigh the influence of the electronic structure of the central metal atom. It would be interesting to study quadridentate ligand exchange with a nickel complex which was labile with regard to nickel exchange (e.g., bis-(salicylaldehyde-trisethylenediimine)nickel (212)) to further test these ideas.

Whilst $Zn(en)_3^{2+}$, $Cu(en)_2^{2+}$, and $Hg(en)_2^{2+}$ exchange completely with labelled ethylenediamine in a minimum separation time of 3 sec. at 0°C., $Ni(en)_3^{2+}$ exhibits exchange half-times of the order of a few seconds. Popplewell and Wilkins (383) have shown that since the exchange rate is first order in concentration of $Ni(en)_3^{2+}$ but independent of free ethylenediamine concentration, then an S_N2 associative mechanism involving ethylenediamine is excluded. Whether the rate-determining step involving $Ni(en)_3^{2+}$ is one of S_N1 dissociation or S_N2 reaction with water is undecided. The ligand exchange of $Ni(en)_3^{2+}$ is immeasurable at 20°C., as is reported (263) for the exchange of nickel with the complex ion at the same temperature. A study of the latter exchange system also at 0°C. would therefore be of considerable interest.

Some quantitative information has now been gained on the influence of neutral ligands upon the carbonato–ligand lability in the complex ions $Co(NH_3)_4CO_3^+$ (217, 220), $Co(NH_3)_5CO_3^+$ (434), and $Co(en)_2CO_3^+$ (241). The general rate law for the exchange of free carbonate ion with the carbonato ligand in the three complexes may be written:

$$R = k_1[\text{complex}][\text{total carbonate}] + k_2K[\text{complex}][H^+] \qquad (24)$$

where the first term represents the rate of direct ligand exchange and the second term that of aquation. The equilibrium constant, K, refers to the hydration equilibria known to occur (290, 371) with such carbonato complexes:

$$Co(NH_3)_5CO_3^+ + H_3O^+ \rightleftharpoons Co(NH_3)_5HCO_3^{2+} + H_2O$$

For the pentammine carbonato complex $K = 2.5 \times 10^6$ (289) and in the region of pH 9, only about 1 per cent of the carbonato complex will exist in the bicarbonato form. Contrary to the original interpretation (220), isotope effect (Section VII,C) and conductometric studies now suggest that both the bidentate complexes exist substantially in the monodentate forms $Co(NH_3)_4H_2O \cdot CO_3^+$ and $Co(en)_2H_2O \cdot CO_3^+$ in aqueous solution. Whilst the hydration equilibrium constants are unknown for these two complexes, the measured value for the pentammine complex will be assumed in the succeeding discussion.

The rate constant k_1 represents the rates of the direct carbonato–ligand exchange processes and in view of the additional facts now available on the hydration equilibria, these processes are best represented in terms of the predominant species existing under the experimental conditions:

$$Co(NH_3)_4H_2O \cdot CO_3^+ + HC^*O_3^- \xrightleftharpoons{{}_{\mathrm{T}}k_1} Co(NH_3)_4H_2O \cdot C^*O_3^+ + HCO_3^-$$

$$Co(NH_3)_5CO_3^+ + HC^*O_3^- \xrightleftharpoons{{}_{\mathrm{P}}k_1} Co(NH_3)_5C^*O_3^+ + HCO_3^-$$

$$Co(en)_2H_2O \cdot CO_3^+ + HC^*O_3^- \xrightleftharpoons{{}_{\mathrm{E}}k_1} Co(en)_2H_2O \cdot C^*O_3^+ + HCO_3^-$$

rather than as previously represented:

$$Co(NH_3)_4H_2O\cdot HCO_3^{2+} + HC^*O_3^- \overset{k_1}{\rightleftarrows} Co(NH_3)_4H_2O\cdot HC^*O_3^{2+} + HCO_3^-, \text{ etc.}$$

Moreover, the postulation of this latter exchange process does not completely explain the pH dependence of the exchange rate and yields values of k_1 which seem too high for a normal ion-ion substitution reaction (from 8 to 40 l. mole^{-1} min.$^{-1}$ at 25°C. for all three complexes).

The rate constant k_2 was originally identified with the aquation processes:

$$Co(NH_3)_4H_2O\cdot HCO_3^{2+} + H_2O \xrightarrow{{}_{\mathrm{T}}k_2} Co(NH_3)_4(H_2O)_2^{3+} + HCO_3^-$$

$$Co(NH_3)_5HCO_3^{2+} + H_2O \xrightarrow{{}_{\mathrm{P}}k_2} Co(NH_3)_5H_2O^{3+} + HCO_3^-$$

$$Co(en)_2H_2O\cdot HCO_3^{2+} + H_2O \xrightarrow{{}_{\mathrm{E}}k_2} Co(en)_2(H_2O)_2^{3+} + HCO_3^-$$

This detailed mechanism of aquation may have to be modified in the light of H_2O^{18} tracer studies (252, 384) which indicate that the aquation of carbonato complexes, in acid at least, involves rupture of the oxygen–carbon bond in the carbonato ligand rather than the cobalt–oxygen bond and that aquation is therefore a process of decarboxylation (82) rather than hydrolysis. The implied processes:

$$Co(NH_3)_4H_2O\cdot HCO_3^{2+} \xrightarrow{k_2} Co(NH_3)_4H_2O\cdot OH^{2+} + CO_2, \text{ etc.,}$$

are equally consistent with the observed exchange kinetics. Detailed kinetic studies of the three exchange systems have yielded the rate constants shown in table 8, which have been expressed at 25°C. and at an ionic strength of approximately 0.04. (Stranks (430) has shown that ionic strength has little effect on the direct exchange rate for the tetrammine complex above 0.01 but does influence the rate of the aquation rate slightly. However, the chief interest is in the results for the direct exchange rate.) Taube (445) has suggested that in hexacoördinated Co(III) complexes increasing electronegativity of ligands causes greater stabilization of an excited paramagnetic state relative to the diamagnetic ground state of the Co(III) complex. Hence more electronegative ligands should result in a complex more labile to substitution. Applying this concept

TABLE 8

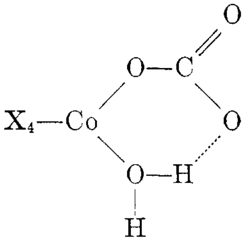
Rate constants for exchange of Co(III) *carbonato complexes*

Parent Complex	k_1	k_2*	k_2†
	l.mole^{-1} sec.$^{-1}$ × 10^3	*sec.$^{-1}$ × 10^2*	*l.mole^{-1} sec.$^{-1}$ × 10^3*
$Co(NH_3)_4CO_3^+$	0.35	1.0	0.18
$Co(NH_3)_5CO_3^+$	2.6	6.4	1.1
$Co(en)_2CO_3^+$	0.25	0.55	0.10

* Calculated on the basis that aquation is S_N1 decarboxylation.

† Calculated on the basis that aquation is a direct S_N2 process.

to the carbonato complexes, all of which react in the monodentate form, the anticipated order of rate constants for direct ligand exchange would be ${}_{\mathrm{T}}k_1 > {}_{\mathrm{E}}k_1 > {}_{\mathrm{P}}k_1$, since an $—OH_2$ ligand occurring in the first two complexes only is much more electronegative than either an $—NH_3$ or an —en ligand. The apparently exceptional position of the pentammine complex might be due to more significant hydrogen bonding in the other two complexes, with the formation of six-membered rings which are relatively inert to direct ligand exchange.



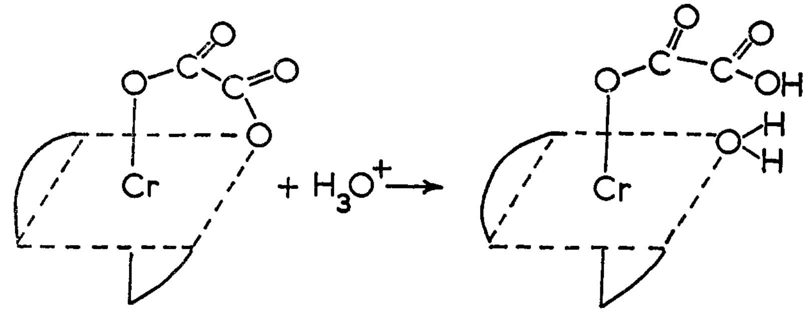
A similar order of rate constants appears to hold for the rate of aquation but these values are of less quantitative significance since the hydration equilibrium constants, K, are unknown for the ethylenediamine and tetrammine-carbonato complexes. The exchange of free carbonate ion with $Co(tn)_2CO_3^+$ (where tn = trimethylenediamine) is inconveniently slow below 40°C. (E_{act} = 25 kcal.), whereas exchange of the previous carbonato complexes is measurable between 0°C. and 25°C. (E_{act} = 15–20 kcal.). In the former case exchange is considered to proceed (219) via the hydrated intermediate $Co(tn)_2HCO_3\cdot OH^+$ and steric effects are undoubtedly important in determining the much slower exchange rates. Additional studies on the influence of other neutral ligands upon the carbonato–ligand lability would assist in a greater understanding of these effects.

D. EXCHANGE AND RACEMIZATION PROCESSES

Comparison of the rates of exchange and of racemization of an optically active complex ion can help in an understanding of the mechanism of the latter process. Once again ligand exchange is the more useful (see Section VI,A) and there are three obvious relationships between the two rates, all of which have been observed.

(*a*) *The rates of exchange can be slower than the rate of racemization.* In the now classical exchanges of Long (306, 307), it was shown that for both $Co(oxalate)_3^{3-}$ and $Cr(oxalate)_3^{3-}$ no exchange occurred (separately) between these ions and C^{11}-tagged oxalate within 25 min. at 50°C. and 35°C., respectively. At these temperatures the half-life of inversion of both ions is approximately 15 min. (86). With C^{14}-labelled oxalate no exchange with $Co(oxalate)_3^{3-}$ occurs until direct decomposition of the complex becomes significant (412). This decomposition involves the entry of a water molecule into the complex (117), which permits the exchange of an oxalate ligand. The rupture of an oxalate group as a whole from the complex as the means of racemization is therefore excluded by these results. Further insight into the racemization mechanism is afforded by some recent work of Carter, Odell, and Llewellyn (305). The exchange of H_2O^{18}

with Cr(oxalate)$_3^{3-}$ was observed at a much faster rate than the exchange of C^{13}-oxalate with the latter. In addition *all* the twelve oxygen atoms of the complex took part in the exchange. The reaction



was proposed as the initial step in the racemization, H$_2$O^{18} exchange and concomitant aquation to Cr(oxalate)$_2$(H$_2$O)$_2^-$, involving "one-ended" dissociation of the oxalate group.

(*b*) *The rates of exchange and racemization are the same.* The loss of optical activity from the *cis*-Co(en)$_2$Cl$_2^+$ ion in absolute methanol is identical with the rate of exchange of lithium radiochloride with the *first* chlorine atom of the complex ion (71) (see table 9).

$$cis\text{-Co(en)}_2\text{Cl}_2^+ \rightarrow \underset{\substack{\text{(Optically}\\ \text{inactive)}}}{\text{Co(en)}_2\text{Cl}^{2+}} + \text{Cl}^-$$

It has been shown that the exchange of labelled phenanthroline with Ni(phen)$_3^{2+}$ in neutral and in alkaline pH occurs by a dissociative mechanism and that the rate constant is identical with the racemization rate constant under comparable conditions (478). This work extends that showing similarity of rates of acid dissociation and accompanying racemization of the Ni(phen)$_3^{2+}$ ion (37). In these cases then a dissociative mechanism with rapid racemization of the complex fragment can completely account for the racemization observed. In view of the measurable exchange rates reported for Ni(en)$_3^{2+}$ with labelled ethylenediamine in methanol at 0°C. (383) it might be possible to resolve this ion if the attempt were made at fairly low temperatures and if the racemization of Ni(en)$_3^{2+}$ were a dissociative mechanism, as seems probable from the behavior of Ni(phen)$_3^{2+}$ and Ni(dipy)$_3^{2+}$ (dipy = dipyridyl).

TABLE 9

Exchange and racemization rate of complex ions

Complex Ion	Exchange Rate Constant	Racemization Rate Constant (as defined in reference 37)	Conditions	Reference
Co(en)$_2$Cl$_2^+$.....	1.4 × 10^{-4} sec.$^{-1}$	1.35 × 10^{-4} sec.$^{-1}$	35.8°C.; μ = 0.04; CH$_3$OH	(71)
Ni(phen)$_3^{2+}$.....	90 × 10^{-4} min.$^{-1}$	92 × 10^{-4} min.$^{-1}$	45.0°C.; pH = 6.8	(478)
Ni(phen)$_3^{2+}$.....	113 × 10^{-4} min.$^{-1}$	111 × 10^{-4} min.$^{-1}$	45.0°C.; pH = 13	(478)

(*c*) *The rate of exchange may be faster than the rate of racemization.* Holden and Harris (241) have studied the rate of racemization of carbonato-bis-(ethylenediamine)cobalt(III) chloride and of its exchange with $HC^{14}O_3^-$. They have suggested that the racemization is an intramolecular process and that each complex ion species postulated to be present in the exchanging solution racemizes independently of the others.

$$\text{Rate} = k_1[\mathrm{Co(en)_2CO_3H_2O^+}] + k_2[\mathrm{Co(en)_2CO_3(OH)^+}] + k_3[\mathrm{Co(en)_2HCO_3H_2O^{2+}}] + k_4[\mathrm{Co(en)_2(H_2O)_2^{3+}}] \quad (25)$$

In this case, however (unlike (*a*)), the process is slower than the exchange rate, which proceeds via dissociative and associative mechanisms (vide supra) apparently not involving racemization. Rapid exchange of labelled ligand with $Zn(en)_3^{2+}$ (383), $Al(oxalate)_3^{3-}$, and $Fe(oxalate)_3^{3-}$ (307) compared with the reported resolution and relatively slow racemization of these complex ions may be other examples of instances where dissociative processes responsible for exchange do not directly lead to racemization (445).

E. EVIDENCE FOR UNUSUAL OXIDATION STATES

Rich and Taube (391) observed that the use of ordinary laboratory distilled water in the Cl^{*-}–$AuCl_4^-$ exchange system caused a rapid induced exchange of some 30 per cent in the first 20 sec., but that thereafter the exchange proceeded with half-times of the order of 1 to 4 min. A subsequent detailed study of this induced process (392) revealed that the exchange system was exceedingly sensitive to traces of certain reducing agents, notably Fe^{2+}. Even storage of solutions in green bottles, for instance, generated sufficient Fe^{2+} to cause a significant amount of induced exchange. A $6 \times 10^{-7} M$ ferrous sulfate solution causes 50 per cent exchange of 0.015 M Cl^{*-} with 0.006 M $AuCl_4^-$ in 5 sec. (uncatalyzed half-time 3 min. at 0°C.) and for every Fe^{2+} ion oxidized by $AuCl_4^-$, about 10^4 chloride-ion substitutions are effected. Whilst the one-electron reducing agent VO^{2+} is also capable of inducing the exchange, the two-electron reducing agents Sn(II) and Sb(III) are relatively ineffective although easily oxidized by $AuCl_4^-$. Since Au(I) was shown to exert no catalytic effect, Rich and Taube conclude that the active species is gold in the oxidation state +2, which is efficiently formed by one-electron reduction of Au(III) by Fe^{2+} and VO^{2+}, but only in very low concentration by Sn^{2+} or Sb^{3+}.

A kinetic study of the Fe^{2+}-induced exchange led to the following postulated mechanism:

$$(1)\quad \mathrm{Fe^{2+}} + \mathrm{AuCl_4^-} \xrightarrow{k_1} \mathrm{Fe(III)} + \mathrm{Au^{II}_{Cl}}$$

$$(2)\quad \mathrm{Au^{II}_{Cl}} + \mathrm{Cl^{*-}} \rightleftharpoons \mathrm{Au^{II}_{Cl*}} + \mathrm{Cl^-} \quad \text{(very rapid)}$$

$$(3)\quad \mathrm{Au^{II}_{Cl*}} + \mathrm{AuCl_4^-} \xrightarrow{k_3} \mathrm{Au^{II}_{Cl}} + \mathrm{AuCl_4^{*-}}$$

$$(4)\quad \mathrm{2Au(II)} \xrightarrow{k_4} \mathrm{Au(I)} + \mathrm{Au(III)} \quad \text{(chain terminating)}$$

In accordance with this mechanism, a function of the amount of induced exchange varied linearly with the square root of the initial ferrous concentration, thereby enabling k_1 to be evaluated as 1.8×10^4 l. mole^{-1} min.$^{-1}$ and lower limits to be set to k_3 and k_4 of 10^8 l. mole^{-1} min.$^{-1}$ and 10^{10} l. mole^{-1} min.$^{-1}$, respectively, all at 0°C. The actual form of the Au(II) complex is unknown but it is possibly either $\mathrm{AuCl_4^{2-}}$ or $\mathrm{AuCl_3^-}$, so that reaction 3 will involve either electron transfer or chlorine-atom transfer. The great substitution lability of $\mathrm{Au^{II}_{Cl}}$ as compared to $\mathrm{AuCl_4^-}$ was attributed to the possibility of states of different coördination number for Au(II) having nearly the same energy such that the energy required for removal of $\mathrm{Cl^-}$, e.g.,

$$\mathrm{AuCl_4^{2-} \rightarrow AuCl_3^- + Cl^-}$$

is very small.

The exceptional substitution lability of an intermediate oxidation state of an element also serves to explain induced exchanges observed in the chloride exchange with $\mathrm{PtCl_6^{2-}}$. Rich and Taube (390) found that the spontaneous exchange rate for $\mathrm{PtCl_6^{2-}}$ derived from commercial samples of $\mathrm{H_2PtCl_6}$ is much less ($t_{\frac{1}{2}}$ = approx. 50 min. at 25°C.) than that for $\mathrm{PtCl_6^{2-}}$ samples freed from traces of iridium ($t_{\frac{1}{2}}$ = a few seconds). Both oxidizing agents ($\mathrm{IrCl_6^{2-}}$, $\mathrm{Cl_2}$, $\mathrm{Fe(CN)_6^{3-}}$) and some reducing agents (barium diphenylaminesulfonate and hydroquinone) reduce the exchange rate to very low values by destroying the postulated catalytic species of Pt(III). For discussion purposes the form of Pt(III) was assumed to be $\mathrm{PtCl_5^{2-}}$ in the exchange mechanism:

$$\mathrm{PtCl_5^{2-} + Cl^{*-} \rightleftarrows PtCl_5^{*2-} + Cl^-}$$

$$\mathrm{PtCl_5^{*2-} + PtCl_6^{2-} \rightleftarrows PtCl_5^*Cl^{2-} + PtCl_5^{2-}}$$

The introduction of $\mathrm{PtCl_4^{2-}}$ serves to catalyze the $\mathrm{PtCl_6}$–$\mathrm{Cl^{*-}}$ exchange due to the equilibrium:

$$\mathrm{PtCl_4^{2-} + PtCl_6^{2-} \rightleftarrows 2PtCl_5^{2-}}$$

The authors further make the interesting suggestion that, in the absence of inhibitors, the spontaneous exchange rate of $\mathrm{PtCl_6^{2-}}$ with chloride ion may be due to the generation of $\mathrm{PtCl_5^{2-}}$ by β-radiation from the $\mathrm{Cl^{36}}$ tracer. The intermediate +3 oxidation state is also important in the $\mathrm{PtCl_4^{2-}}$–$\mathrm{Cl^{*-}}$ exchange system, which is also strongly catalyzed by Ce(IV),

$$\mathrm{Ce(IV) + PtCl_4^{2-} + Cl^- \rightarrow Ce^{3+} + PtCl_5^{2-}}$$

but not by chlorine (which presumably bypasses the Pt(III) state); e.g., at 0°C. 1 per cent exchange occurs in 30 min. with 0.01 M $\mathrm{PtCl_4^{2-}}$ and 0.03 M $\mathrm{Cl^{*-}}$ but in the presence of 5×10^{-4} M Ce(IV) the initial induced exchange rate has a half-time of about 30 sec. Moreover, the relatively slow exchange of $\mathrm{PtCl_6^{2-}}$ with $\mathrm{Pt^*Cl_4^{2-}}$ is inhibited by oxidizing agents (notably $\mathrm{IrCl_6^{2-}}$) and the exchange mechanism is probably:

$$\mathrm{PtCl_5^{2-} + Pt^*Cl_4^{2-} \rightleftarrows PtCl_4^{2-} + Pt^*Cl_5^{2-}}$$

$$\mathrm{Pt^*Cl_5^{2-} + PtCl_6^{2-} \rightleftarrows PtCl_4^{2-} + Pt^*Cl_6^{2-}}$$

$$\overline{\mathrm{Pt^*Cl_4^{2-} + PtCl_6^{2-} \rightleftarrows PtCl_4^{2-} + Pt^*Cl_6^{2-}}}$$

In a similar way evidence has been adduced (95) for Tl(II), since the thermal exchange of Tl(I)–Tl(III) is accelerated by $Fe(CN)_6^{4-}$ and the x-ray-induced exchange also involves this intermediate valency species.

These isotopic exchange studies have provided significant kinetic evidence for the relative lability of intermediate oxidation states of gold, thallium, and platinum. There is no other evidence for the existence of these valency states in aqueous solution, although the isolation of a few solid compounds has been claimed (283, 293). Such work might be extended to other transitional elements with considerable profit and yield results which would otherwise be difficult to obtain (415).

F. PHOTOCHEMICAL EFFECTS

The $PtCl_6^{2-}$–Cl^{*-} exchange system was also found to be strongly photosensitive, owing probably to the production of the active Pt(III) catalytic species in the reaction:

$$PtCl_6^{2-} \xrightarrow{h\nu} PtCl_5^{2-} + Cl$$

e.g., in the dark $t_{\frac{1}{2}}$ is 50 min. but in bright sunlight exchange is complete in 10 min. Since high quantum yields were found, the exchange mechanism cannot involve hydrolysis, which exhibits a quantum yield of less than unity. Similarly the $PtCl_6^{2-}$–$Pt^*Cl_4^{2-}$ exchange system is photosensitive and the photosensitive reaction is inhibited by oxidants such as $IrCl_6^{2-}$ which, when present in 10^{-5} M concentration, reduce the rate to measurable values ($t_{\frac{1}{2}} \sim 5$ min.). It is interesting to note that whereas the $PtCl_4^{2-}$–Cl^{*-} exchange is photosensitive, the $AuCl_4^-$–Cl^{*-} system is insensitive (at least to ordinary sunlight) and the active Au(II) catalytic species cannot be photogenerated in appreciable concentrations.

The exchanges of cyanide ion with $Mo(CN)_8^{4-}$, $Fe(CN)_6^{3-}$ (9), $Fe(CN)_6^{4-}$, $Co(CN)_6^{3-}$, $Cr(CN)_6^{3-}$, $Fe(CN)_5NO^{2-}$, and $Fe(CN)_5H_2O^{3-}$ (313) are all markedly accelerated by sunlight. Previous photochemical experiments by MacDiarmid and Hall (312) have shown that for the first four complex ions, at least, photocatalyzed aquation occurs via the process:

$$M(CN)_x^{-y} + H_2O \rightarrow M(CN)_{x-1}(H_2O)^{1-y} + CN^-$$

or

$$(M(CN)_x^{-y} + H_3O^+ \rightarrow M(CN)_{x-1}(H_2O)^{1-y} + HCN)$$

which is the same primary step postulated for the thermal exchange of cyanide ion with such complex cyanides (vide supra). However, both $Mn(CN)_6^{3-}$ and $Mn(CN)_6^{4-}$ show no photosensitivity in exchange or in aquation. On the basis of these observations MacDiarmid and Hall conclude that only those cyano complexes which are relatively inert to acids will be photosensitive to both exchange and aquation. At 25°C. the cyanide exchanges with both $W(CN)_8^{3-}$ and $W(CN)_8^{4-}$ (194) exhibit half-times of the order of two years, but radiation from a 100-watt incandescent light reduced the exchange half-times to about 10 days. Since under the conditions of complete light absorption the exchange rate is independent of both complex-ion and cyanide-ion concentrations, the rate-determining step must be the photoactivation step:

$$4W(CN)_8^{3-} + 2H_2O \xrightarrow{h\nu} 4W(CN)_8^{4-} + 4H^+ + O_2$$

At the lower pH resulting from this photolytic reaction, the $W(CN)_8^{4-}$ ion undergoes aquation with generation of free cyanide ion,

$$W(CN)_8^{4-} + H_2O \rightarrow W(CN)_7(H_2O)^{3-} + CN^-$$

thereby buffering the excess hydrogen ion and creating a photostationary state.

These studies show that photocatalysis must always be considered in studying exchange reactions of transitional metal complexes, especially when the metal atom is capable of photoreduction. Detailed actinometric studies on systems of the type described above should permit the evaluation of primary quantum yields (see Section II,E).

Summarizing then, the most important factor determining exchange rates is usually the electronic state of the central atom. Should the complex contain inner-orbital bonding, then exchange of both ligand and metal atom will normally be relatively slow. If an additional bond orbital exists for use in the activated complex, then even for inner-orbital complexes rates of ligand exchange will be rapid, as will those of outer-orbital complexes. However, even for these "labile" complexes important kinetic data should be obtainable by adjustment of reaction conditions: e.g., lower temperatures and nonaqueous solvents; lower reactant concentrations; earlier observation times and fast-reaction techniques.

Another important factor is the electronegativity of the attached ligand. Highly electronegative ligands will tend to increase the importance of the labile outer-orbital state of a complex of a given metal, thereby leading to greater exchange rates. Nevertheless more studies need to be performed on series of complexes in which small gradations of ligand electronegativity occur before the effects of electronegativity on lability can be satisfactorily evaluated.

The stereochemistry of the ligand is an important consideration. Multidentate chelates (especially with "fused" rings) often undergo reduced rates of metal exchange.

The coördinating power of the solvent must also be considered, since often a complex may be considerably modified in solution by actual coördination of solvent molecules in the complex. In this respect water and pyridine are the most notable examples. Moreover the process of solvolysis of the complex frequently competes with—sometimes to the exclusion of—the process of direct ligand or metal exchange. The effects of ionic strength, pH, photosensitivity, and susceptibility to inhibitors and catalysts (especially when intermediate oxidation states are attainable) are additional factors to be considered in evaluating isotopic exchange data.

G. COMPREHENSIVE TABLE OF LITERATURE DATA (TABLE 10)

Key to table 10

Exchanging species: An asterisk denotes the labelled species used. When both species were labelled and used in separate experiments, both are marked with

TABLE 10

Exchange reactions of complexes of the transitional elements†

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Vanadium group			
$V(CN)_6^{3-}$	C^*N^-	0.026	0.026	pH 9	C 1 min.		(313)
				Chromium group			
$Cr(H_2O)^{2+}$	H_2O^*	0.4	Excess	0.4 $HClO_4$	C 2 min.		(378)
$Cr(H_2O)_6^{3+}$	H_2O^*	0.4–1.4	Excess	1.8–5.2 ClO_4^- 0.01–1.1 H^+	25–80 hr.	K; $E = 24$	(378, 253, 254)
$Cr(H_2O)_6^{3+}$	H_2O^*	3.0	Excess	No added acid	12 hr. (30°)	K; $E = 31$	(314)
$Cr(H_2O)_6^{3+}$	H_2O^*	0.05–1.1	Excess	0.1–0.5 $HClO_4$	17–58 hr.	K; $E = 28$	(251)
$Cr(H_2O)_6^{3+}$	H_2^*O				Rapid		(314)
$Cr(CN)_6^{4-}$	C^*N^-	0.026	0.026	pH 11.3	C 40 sec.		(313)
$Cr(CN)_6^{3-}$	$Cr^*(H_2O)_6^{3+}$	0.01	0.01	pH 3–4	36 hr.	Decomposition at this pH (9)	(329)
$Cr(CN)_6^{3-}$	$CrCl_2(H_2O)_4^+$	0.005	0.005	0.05 HCl	N 72 hr.		(329)
$Cr(CN)_6^{3-}$	$Cr(ac)_3$	0.008	0.008	pH 3–4 (acetic acid)	≈16 days		(329)
$Cr(CN)_6^{3-}$	C^*N^-	0.05	0.05	pH 10	~24 days	Increased at low pH (decomposition)	(9)
$Cr(CN)_6^{3-}$	C^*N^-	0.026	0.026		~40 days	P	(313)
$Cr(SCN)_6^{3-}$	$Cr^*(H_2O)_6^{3+}$	0.01	0.01	0.05–2.0 H^+	N 72 hr.		(329)
$Cr(SCN)_6^{3-}$	$Cr^*Cl_2(H_2O)_4^+$	0.007	0.007	0.07 HCl	N 24 hr		(329)
$Cr(SCN)_6^{3-}$	S^*CN^-				Slow		(198)
$Cr(H_2O)_5Cl^{2+}$	Cl^{*-}				Slow	Increased by Cr^{2+}	(448)
$Cr(H_2O)_4Cl_2^+$	Cl^{*-}	1.6	2.2		Slow		(429)
$Cr(H_2O)_3F_3$	$Cr^*(H_2O)_6^{3+}$	0.16	0.1	0.01 HNO_3	~4 days	Decreased at 1.0 HNO_3	(280)
$Cr(H_2O)_4SO_4^+$	$S^*O_4^{2-}$				270 min. (30°)		(168)
$Cr(urea)_6^{3+}$	$Cr^*(H_2O)_6^{3+}$	0.04	0.1	1.0 HNO_3	N 16 hr.		(280)
$Cr(NH_3)_5NC^*S^{2+}$	SCN^-	0.01–0.20	0.06–0.40	pH 2.5	Hours (80°)	K	(11)
$Cr(oxalate)_3^{3-}$	$Cr^*(H_2O)_6^{3+}$	0.01	0.01	0.02 $HClO_4$	N 72 hr.		(329)
$Cr(oxalate)_3^{3-}$	$Cr^*(H_2O)_4Cl_2^+$	0.005	0.005	0.05 HCl	N 1 hr.		(329)
$Cr(oxalate)_3^{3-}$	$Oxalate^{*2-}$	0.06	0.01		N 25 min.	(35°) $t_{\frac{1}{2}}$ ~ 25 min. (racemization)	(306)
$Cr(en)_3^{3+}$	$Cr^*(H_2O)_6^{3+}$	0.1	0.1	1 HNO_3	N 50 hr. (40°)	Some decomposition	(280)
$Cr(en)_3^{3+}$	en*	0.1	0.16	1 HNO_3	N 70 hr. (40°)	Accompanied by irreversible aquation	(477)
$Mo(CN)_8^{4-}$	C^*N^-	0.05	0.05	pH 10	N 11 days	P	(9)

$W(CN)_8^{4-}$	C^*N^-	0.01	0.17	pH 11.1	~500 days (dark)	Increased at pH 9.5 (decomposition); P	(194, 31)
$W(CN)_8^{4-}$	C^*N^-	0.01–0.02	0.16–0.32	pH 10.9–11.2	10–12 days (light)	K	(194)
$W(CN)_8^{3-}$	C^*N^-	0.01–0.02	0.15–0.32	pH 9.0–10.4	~500 days	P; increased at pH 9.5 (decomposition)	(194, 31)
				Manganese group			
$Mn(CN)_6^{4-}$	C^*N^-	0.026	0.026	pH 11.8	C 6 min.		(313)
$Mn(CN)_6^{3-}$	C^*N^-	0.01–0.02	0.05–0.10	pH 9–11	35–80 min. (0°)	K; *E* = 8.5	(10, 9, 313)
$Mn^*(oxalate)_3^{3-}$	Mn_{aq}^{*2+}	0.01	0.005	0.1 oxalic acid	C 5 sec.		(382)
$Mn(AA)_3$	Mn^{*2+}			Methanol	Fast	Also manganous benzoylacetonate; fast (both Szilard-Chalmers)	(141)
				Iron group			
Fe_{aq}^{3+}	H_2O^*	1.0	Excess	0.4–1.2 H^+	C 3.5 min.	Slower at lower acidities (polynuclear forms)	(254)
$Fe(CN)_6^{4-}$	Fe_{aq}^{*2+}	0.2	>0.2		None within precipitation time	Precipitate forms on mixing	(453)
$Fe(CN)_6^{4-}$	C^*N^-	0.025	0.025	pH 10.3	N 77 hr.	$t_{1/2}$ = 33 hr. (light)	(313, 9, 202)
		0.025	0.045	pH 3.5	53 hr.	K; P	(313)
$Fe^*(CN)_6^{3-}$	Fe_{aq}^{*3+}	0.07	0.14		N 6 days	P	(453, 207, 208)
$Fe(CN)_6^{3-}$	C^*N^-	0.1	0.3	pH 9.5	N 64 hr.	Increased at low pH (decomposition)	(99)
$Fe(CN)_6^{3-}$	C^*N^-	0.05	0.05	pH 10	N 5 days	P	(9, 313)
$Fe(CN)_5H_2O^{3-}$	C^*N^-	0.025	0.025	pH 10	38 hr. (dark)	P; increased at low pH (decomposition)	(313)
$Fe(CN)_5NO^{2-}$	C^*N^-	0.025	0.025	pH 10.3	5.5 days (dark)	P; decreased at low pH	(313)
$Fe(CN)_6^{3-}$	$Fe^*(oxalate)_3^{3-}$	—	—	pH 1.2	N 10 min.		(208)
$Fe(oxalate)_3^{3-}$	Fe_{aq}^{*3+}	0.005	0.005	pH 1.5	C 5 min.		(208, 207)
$Fe(oxalate)_3^{3-}$	$Oxalate^{*2-}$	0.06	0.01	pH 4.5–6	C 20 sec. (35°)		(307, 99)
$Fe(malonate)_3^{3-}$	$Malonate^{*2-}$	0.14	0.11		~30 min.	Decomposition during long separation time	(99)
$Fe^*(dipy)_3^{2+}$	Fe_{aq}^{*2+}	0.01	0.01	pH 1.5	~5 hr.	K; *E* = 14.9	(407, 474)
$Fe^*(phen)_3^{2+}$	Fe_{aq}^{*2+}	0.01	0.02	pH 1.5	~97 min.	K; *E* = 19.4	(407, 474)
$Fe(EDTA)^{2-}$	Fe_{aq}^{*2+}	0.01	0.01	pH 2–5	$t_{1/2}$ < 1 min.	Nitrogen atmosphere	(268)
$Fe(EDTA)^-$	Fe_{aq}^{*3+}	0.006–0.025	0.006–0.025	pH 1–2.5	25 min. to 40 hr.	K	(268)
Ferrimethemoglobin	Fe_{aq}^{*3+}	0.0006	0.0007	pH 3.6	N 48 hr.		(208)
$Ferri(Ph_4\text{-}PO)$	Fe_{aq}^{*3+}			Acid-ethanol-benzene	N 5 days		(407)

TABLE 10—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
Iron group—*Concluded*							
Ferri(proto-PO)	Fe_{aq}^{3+}	0.0003	0.0001	Alcoholic HCl	N 60 days		(407)
Ferrihemoglobin	Fe_{aq}^{*3+}	10^{-5}	10^{-5}		N 30 hr.		(407)
Ferri(PP)	Fe_{aq}^{*3+}			80% acetone	N 48 hr.		(407)
$OsCl_6^{2-}$	Cl^{*-}	0.06	0.06	0.1–2.0 H^+	N 63 days (50°)		(292)
Cobalt group							
Co_{aq}^{2+}	H_2O^*	1.55	Excess	3.0 $HClO_4$	C 2 min. (1°)		(176)
Co_{aq}^{3+}	H_2O^*	0.4–0.5	Excess	4.0 $HClO_4$	C 2 min. (0°)	Presence of about 0.5 *M* Co_{aq}^{2+}	(176)
$Co(CN)_5^{3-}$	C^*N^-	0.02	0.03		C 2 min.		(5)
$Co(CN)_6^{3-}$	Co_{aq}^{*2+}	0.005	0.005		N 2.5 days		(169)
$Co(CN)_6^{3-}$	C^*N^-	0.05	0.05	pH 11	N 8 days	Slightly increased at pH 4	(9)
$Co(CN)_6^{3-}$	C^*N^-	0.025	0.022	pH 2	Slight exchange, 75 hr.	P	(313)
$Co^*(NH_3)_6^{3+}$	Co_{aq}^{2+}	0.01	0.01		N 6 days (50°)	N 3.5 hr. in 1 *M* HCl (323)	(243, 441, 169)
$Co^*(NH_3)_6^{3+}$	Co_{aq}^{3+}	0.01	0.01	0.5 H_2SO_4	N 90 min.	Some Co_{aq}^{2+} formed during exchange	(243)
$Co(NH_3^*)_6^{3+}$	H_2O	0.008–0.08	Excess	pH 4.7	14.5–57 min.	K	(20, 22, 149, 365)
		0.04	Excess	pH 5.6	8.5 min.		
$Co(NH_3)_5H_2O^{3+}$	H_2^*O				All H exchange		(365)
$Co(NH_3)_5H_2O^{3+}$	H_2O^*	0.02–0.12	Excess	0.01–0.07 $HClO_4$	24 hr.	K	(410)
$Co(NH_3)_5NCS^{2+}$	SC^*N^-	0.02–0.17	0.34–0.54	pH 2.5	Hours (90°)	K	(11)
$Co(NH_3^*)_5Cl^{2+}$	H_2O	0.02	Excess	pH 3	5 hr. (38°)	C 1 min. at pH 12	(6)
$Co(NH_3)_5Cl^{2+}$	Co_{aq}^{*2+}	0.005	0.005		N 14 hr.		(169)
$Co(NH_3)_5Br^{2+}$	Br^{*-}				N 2 hr.	Also from Szilard–Chalmers data	(7)
$Co(NH_3)_5NO_2^{2+}$	H_2^*O				All H exchange	Also *trans*-$Co(NH_3)_4(NO_2)_2^+$ (slow) (19)	(365)
$Co(NH_3)_5CO_3^+$	$C^*O_3^{2-}$	0.006–0.04	0.003–0.05	pH 8.8–10	70 min.–20 hr. (0°)	K	(434)
$Co(NH_3)_4CO_3^+$	H_2^*O				Several hours	Reference 33 reports rapid	(21, 365)
$Co(NH_3)_4CO_3^+$	$C^*O_3^{2-}$	0.005–0.09	0.007–0.036	pH 9.4–10.1	3–16 hr.	K; effect of μ studied (430)	(220, 217)
$Co(NH_3)_4(H_2O)_2^{3+}$	H_2O^*				Slow		(384)
$Co(NH_3)_4(H_2O)_2^{3+}$	H_2^*O				Fast		(33)
$Co(NH_3)_3(NO_2)_3$	Co_{aq}^{*2+}	0.005	0.005		N 1 hr. (99°)		(169)
$Co(NH_3)_3(NO_2)_2Cl$	Co_{aq}^{*2+}	0.005	0.005		N 5 hr.		(169)

$Co(en^*)_3^{3+}$	$H_2\overset{*}{O}$	0.02–0.09	Excess	pH 4.7	27–67 min.	K	(20)
$Co(en)_3^{3+}$	Co_{aq}^{*2+}	0.008	0.008		N 24 hr.		(468, 441)
$Co(en)_3^{3+}$	en*	0.04	0.20	pH 7.0	N 65 hr. (100°)		(477)
$Co(en)_2(NC^*S)_2^+$	SCN^-	0.05	0.05	pH 6.5	Hours (80°)		(11)
cis-$Co(en)_2Cl_2^+$	Cl^{*-}				N 15 sec. (80°)	Considerable aquation in this time	(152)
trans-$Co(en)_2Cl_2^+$	Cl^{*-}				N 25 sec. (80°)	Considerable aquation in this time	(152)
$Co(en)_2(H_2O)Cl^+$	Cl^{*-}				Slight; 35 sec. (80°)	Probably occurs via reversible aquation	(152)
cis-$Co(en)_2Cl_2^+$	Cl^{*-}	0.002	0.04	Methanol	100 min. (36°)	K	(71)
$Co(pn)_2Cl_2^+$	Co_{aq}^{*2+}	0.005	0.005		N 5 hr.		(169)
$Co(en)_2CO_3^+$	$C^*O_3^{2-}$	0.01–0.06	0.005–0.03	pH 9.2	3-8 hr.	K	(241)
$Co(phen)_3^{2+}$	Co_{aq}^{*2+}	0.005	0.005		$t_{\frac{1}{2}} < 28$ sec. (15°)		(469)
$Co(5CH_3\text{-}phen)_3^{2+}$	Co_{aq}^{*2+}	0.005	0.005		$t_{\frac{1}{2}} < 36$ sec. (15°)		(469)
$Co(5NO_2\text{-}phen)_3^{2+}$	Co_{aq}^{*2+}	0.005	0.005		$t_{\frac{1}{2}} < 25$ sec. (15°)		(469)
$Co(CO_3)_3^{3-}$	$C^*O_3^{2-}$	1.0	1.0		N 15 hr.		(319)
$Co(oxalate)_3^{3-}$	$Oxalate^{*2-}$	0.06	0.01		N 25 min. (50°)		(307)
$Co(AA)_3$	Co^{*2+}	0.008	0.008	Pyridine	~80 days (30°)		(468)
$Co(AA)_2(H_2O)_2$	Co^*Ac_2	0.008	0.008	Pyridine	C 50 sec.		(468)
$Co(NN)_3$	Co^{*2+}	0.003	0.003	Pyridine	≈20–30 days		(468)
$Co(S)_2$	Co^*Ac_2	0.008	0.008	50% pyridine	C 40 sec.		(468)
$Co(Ph\text{-}SM)_2$	Co^*SO_4	0.008	0.008	Pyridine	C 50 sec.		(468)
$Co(3Tol\text{-}SM)_2$	Co^*Ac_2	0.008	0.008	Pyridine	C 45 sec.		(468)
$Co(2Anisyl\text{-}SM)_2$	Co^*Ac_2	0.008	0.008	Pyridine	C 40 sec.		(468)
$Co(OH\text{-}SM)_2$	Co^*SO_4	0.008	0.008	Pyridine	C 18 min.	Slower in oxygen	(468)
$Co(dien)_2^{3+}$	Co_{aq}^{*2+}	0.10	0.10		N 15 min.	Also from Szilard-Chalmers data	(441)
$Co(trpy)_2^{2+}$	Co_{aq}^{*2+}	0.005	0.005		2.8 hr. (15°)		(469)
$Co(EDTA)^{2-}$	Co_{aq}^{*2+}	0.005	0.005	pH 2.4–5	Fast		(309)
$Co(EDTA)^-$	Co_{aq}^{*2+}	0.005	0.005	pH 2.8	Slow		(309)
$Co(SE)$	Co^*Ac_2	0.0001	0.0001	Pyridine	20 min. (15°)	Much slower in oxygen	(470)
$Co(SP)$	Co^*Ac_2	0.0017–0.017	0.0017–0.017	Pyridine	48 min. to 7.5 hr. (15°)	K; $E = 17$	(470)
$Co(X)$	Co^*Ac_2	0.008	0.008	Pyridine	2 days		(468)
$Co(P)$	Co^*Ac_2	0.004	0.008	Pyridine	N 5 days		(468)
$Co(P\text{-}tetrasulfonate)$	Co_{aq}^{*2+}	0.001	0.017	pH 1	N 13 days		(468)
$Co(meso\ PO)$	Co^*Ac_2			Pyridine	Slow	Nitrogen atmosphere	(24)
Vitamin B*12	Co_{aq}^{*++}			pH 2–12	N 14 days (55°)	No exchange on conversion to cobalamins	(59, 32, 155)

TABLE 10—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Cobalt group—*Concluded*			
$Rh(en)_3^{3+}$	Rh_{aq}^{3+}				Slow	No exchange with $P^*O_4^{3-}$ (155); Szilard-Chalmers	(428)
$IrBr_6^{2-}$	Br^{*-}	0.010	0.01		Slow		(198)
$Ir^*Cl_6^{2-}$	$Ir(py)_2Cl_4$	0.005	0.009		*N* 1.5 hr. (hot)		(200)
$Ir(en)_3^{3+}$	Ir_{aq}^{3+}				Slow	Szilard-Chalmers	(428)
				Nickel group			
$Ni(CN)_4^{2-}$	Ni_{aq}^{*2+}	0.007	0.006	pH 4-8	N 1 min.	Precipitate forms on mixing; increased rate at low pH	(308)
$Ni(CN)_4^{2-}$	C^*N^-	0.005	0.02	pH 6.5-10.5	C 30 sec.	Extraction separation	(308)
$Ni(CN)_4^{2-}$	C^*N^-	0.05	0.05	pH 10	C 3 min.	Precipitation separation	(9)
$Ni(CN)_4^{2-}$	$Ni^*(NH_3)_x^{2+}$	0.005	0.005	0.3 *M* NH_3	C 25 sec.	Measurable at high μ	(308)
$Ni^*(CN)_4^{2-}$	$Ni^*(en)_3^{2+}$	0.005	0.005	pH 11	C 30 sec.	Measurable at pH 7 (decomposition) and high μ	(308)
$Ni(CN)_4^{2-}$	$Ni^*(oxalate)_2^{2-}$	0.007	0.007	pH 6-8, 0.007 potassium oxalate	N 9 min.	Measurable at pH 4 (decomposition) and high μ	(308)
$Ni(CN)_4^{2-}$	$Ni^*(tartrate)^-$	0.005	0.005	pH 10, 0.01 potassium tartrate	46 hr.	$t_{\frac{1}{2}} = 5$ hr. ($\mu = 2.4$)	(308)
$Ni(S)_2 \cdot 2H_2O$	$Ni^*(ClO_4)_2$			Methyl cellosolve	C 5 min.		(263)
$Ni(SM)_2$	$Ni^*(ClO_4)_2$			Methyl cellosolve	C 5 min.		(263)
$Ni(SM)_2$	(S^*M)			Pyridine	C 5 min.		(100)
$Ni(OH\text{-}SM)_2$	$Ni^*(ClO_4)_2$			Methyl cellosolve	C 5 min.		(263)
$Ni(OH\text{-}SM)_2$	$(OH\text{-}S^*M)$			Pyridine	C 5 min.		(100)
$Ni(Me\text{-}SM)_2$	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	C 5 min.		(212)
$Ni(Me\text{-}SM)_2$	$(Me\text{-}S^*M)$			Pyridine	C 5 min.	C 1 min. (dioxane); C 5 min. (ethanol)	(100)
$Ni(SPT)_2$	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	C 10 min.		(212)
$Ni(Me_2G)_2$	Ni^*Cl_2	0.005	0.005	Pyridine	~ 14 hr.		(212)
$Ni(Me, Bu\text{-}G)_2$	$Ni^*(ClO_4)_2$			Methyl cellosolve	~ 20 hr.	C 48 hr. (pyridine)	(212, 263)
$Ni(Me, Bz\text{-}G)_2$	$Ni^*(ClO_4)_2$			Acetone	N 1 hr.		(263)
$Ni(HQ)_2$	Ni^*Cl_2	0.005	0.005	Pyridine/methyl cellosolve	C 5 min.		(212)
$Ni(Et_2\text{-}DC)_2$	Sulfur*			Xylene	N 3 days (140°)		(201)
$Ni(Pr_2\text{-}DC)_2$	$Ni^*(ClO_4)_2$			Acetone	N 1 hr.	NH_3 induces complete exchange	(263)
$Ni(iso\text{-}am_2\text{-}DC)_2$	$Ni^*(ClO_4)_2$			Acetone	N 1 hr.	NH_3 induces complete exchange	(263)
$Ni(en)_3^{2+}$	Ni_{aq}^{*2+}				C 5 min.		(263)
$Ni(en)_3^{2+}$	en*	0.005-0.05	0.001-0.01		5-10 sec. (0°)	K	(383)

$Ni(tetrameen)_2^{2+}$	Ni_{aq}^{2+}	0.005	0.015		67 min.	K	(476)
$Ni(dipy)_3^{2+}$	Ni^{*2+}				5 min.		(263)
Ni(AE)	Ni^*Cl_2	0.005	0.005	Pyridine	N 2 days	N (methyl cellosolve)	(212)
Ni(SE)	$Ni^*(ClO_4)_2$			Methyl cellosolve	N 2 days	N (pyridine and ethyl cellosolve)	(212, 263)
Ni(SE)	S*E			Pyridine	N 24 hr.		(100)
Ni(3OMe-SE)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	N 2 hr.		(212)
Ni(4OH-SE)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	N 2 hr.		(212)
Ni(ST)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	C 5 min.		(212)
Ni(3OMe-ST)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	C 5 min.		(212)
Ni(SD)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	C 5 min.		(212)
Ni(SP)	Ni^*Cl_2	0.005	0.005	Methyl cellosolve	N 44 hr.	N pyridine	(212)
Ni(SP)	S*P			Pyridine	N 90 hr.		(100)
$Ni^*(EDTA)^{2-}$	Ni_{aq}^{*2+}	0.002	0.002	0.2–9.6	C 1 min.; N 24 hr.	K; complex pH dependence of rate	(309)
$Pd(CN)_4^{2-}$	C^*N^-	0.05	0.05	pH 10	C 3 min.		(9)
$PdCl_4^{2-}$	Cl^{*-}				Fast		(198)
$PdBr_4^{2-}$	Br^{*-}				Fast		(198)
$Pd(N\overset{*}{H}_3)_4$	$H_2\overset{*}{O}$	0.07	Excess	pH 6.6	120 min. (0°)	K	(19)
				pH 7.7	13 min. (0°)	K	
$Pt(CN^*)_4^{2-}$	CN^{*-}	0.04	0.16		~1 min.		(202)
$Pt(SCN)_4^{2-}$	S^*CN^-				Fast		(198)
$Pt(SCN)_6^{2-}$	S^*CN^-				Fast		(198)
$PtCl_4^{2-}$	Cl^{*-}	0.004–0.017	0.06–0.27		13.2–15.3 hr.	K; $PtCl_3(H_2O)$ initially absent	(195, 390, 202)
		0.004–0.017	0.01–1.0		4–19 hr.	K; $PtCl_3(H_2O)$ present in equilibrium concentration (2–60%)	(195)
$PtBr_4^{2-}$	Br^{*-}	0.05	0.20		~ 6 min.	Rate depends on "aging time"; see 195	(198, 202, 203)
PtI_4^{2-}	I^{*-}	0.1	0.4		~4 min.		(202)
$PtCl_6^{2-}$	Cl^{*-}	0.02	0.005	pH 1.5	Few seconds	K; P; increased by $PtCl_4^{2-}$; decreased by $Fe(CN)_6^{3-}$	(390)
$PtCl_6^{2-}$	Cl^{*-}	0.008			60 min. (50°)		(201)
$Pt^*Cl_6^{2-}$	*cis*-$Pt(NH_3)_2Cl_4$	0.008	0.014		N in hot during recrystallization		(200)
$Pt^*Cl_6^{2-}$	$PtCl_4^{2-}$	0.005	0.005	pH 2	~ 1 hr.	P; $t_{\frac{1}{2}} < 30$ sec.	(390, 200)
$PtBr_6^{2-}$	Br^{*-}	0.15	0.35		C 30 min. (100°)		(199)
$PtBr_6^{2-}$	Br^{*-}				N 2 hr.	P	(7, 198)
PtI_6^{2-}	I^{*-}	0.005			30 min. (18°)		(201)
$Pt(N\overset{*}{H}_3)_4^{2+}$	H_2O	0.14	Excess	pH 5.5	35 min.	K	(19)

TABLE 10—*Continued*

Exchanging Species		Exchange Conditions			Exchange Rate	Remarks	References
				Copper group			
$Cu(CN)_2^-$	C^*N^-	0.026	0.026	pH 9.8	C 2 min.		(313)
$CuBr_2^-$	Br^{*-}				Fast		(126)
$CuBr_3^-$	Br^{*-}				Fast		(126)
$Cu(NH_3)_4^{++}$	H_2^*O	0.7	Excess		Fast		(150, 33)
$Cu(glycine)_2$	Cu_{aq}^{*++}				Measurable (?)		(200)
$Cu(AA)_2$	Cu^*Ac_2			Chloroform	C 2 min.		(408)
$Cu(S)_2$	Cu^*Ac_2	0.008	0.008	Pyridine	C 15 sec.		(142)
$Cu(SM)_2$	Cu^*Ac_2	0.008	0.008	Pyridine	C 15 sec.		(142)
$Cu(Me\text{-}SM)_2$	Cu^*Ac_2	0.008	0.008	Pyridine	$t_{\frac{1}{2}} < 15$ sec.		(142)
$Cu(en)_2^{2+}$	en^*	0.001	0.002		C 3 sec. (0°)		(383)
Cu(SN)	Cu^*Ac_2	0.008	0.008	Pyridine	1 min.		(142)
Cu(SE)	Cu^*Ac_2	0.0015–0.015	0.0015–0.015	Pyridine	2.1–26 hr.	K; $E = 23$	(142)
Cu(SP)	Cu^*Ac_2	0.008	0.008	Pyridine	9 hr. (50°)	Also from Szilard-Chalmers data (242)	(142)
Cu(AE)	Cu^*Ac_2	0.004	0.004	Pyridine	37 hr.		(142)
Cu(PP)	Cu^{*2+}			80% acetone	N 48 hr.		(407)
$Cu(S_2O_3)_2$	Cu_{aq}^{*2+}			0.5 HCl	Fast		(414)
$Ag(CN)_2^-$	C^*N^-	0.026	0.026	pH 10.3	C 2 min.		(313)
$AuCl_4^-$	Cl^{*-}	0.003–0.012	0.003–0.076	pH 0–3	0.77–4.2 min. (0°)		(391, 392)
$HAuCl_4$	HCl	0.002	0.016	β,β′-Dichlorodiethyl ether	C 30 sec.		(455)
				Zinc group			
Zn_{aq}^{2+}	H_2O^*	0.2	Excess	$0.4\ HClO_4$	C 2 min.		(378)
$Zn(CN)_4^{2-}$	C^*N^-	0.026	0.026	pH 10.3	C 2 min.		(313)
$Zn(SCN)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(296)
$Zn(AA)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec. (0°)	Also benzoylacetonate and nicotinylacetonate	(296)
$Zn(DT)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.	Also aqueous alcohol (315)	(28)
$Zn(HQ)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(28)
$Zn(A)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(28)
$Zn(Me\text{-}SM)_2$	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(28)
$Zn(en)_3^{2+}$	en^*	0.02	0.16		C 6 sec. (0°)		(383)
Zn(SE)	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(28)

Zn(SP)	Zn^*Ac_2	0.001	0.001	Pyridine	C 30 sec. (0°)		(28)
Zn(AE)	Zn^*Ac_2	0.01	0.01	Pyridine	C 30 sec.		(296)
$Zn(EDTA)^{2-}$	Zn^{*2+}			pH 3–11	C 1 min.		(458)
Zn(P)	Zn^*Ac_2	0.002	0.002	Pyridine	N 35 days		(28)
Hg_{aq}^{2+}	H_2O^*				Not rapid		(45)
$Hg(CN)^+$	Hg^{*++}	0.007–0.03	0.001–0.02	pH 2.6	15–88 min.	K; in presence of equilibrium amount of $Hg(CN)_2$	(487)
$Hg(CN)_2$	C^*N^-	0.05	0.05	pH 10	C 15 sec.		(9)
$Hg(CN)_4^{2-}$	C^*N^-	0.02	0.02	pH 10	C 5 min.		(9)
$HgCl_2$	Cl^{*-}	0.001	0.002		C 1 min.		(391)
$HgCl_4^{2-}$	Cl^{*-}	0.3	1.0		C 1 min.		(391)
$HgBr_2$	Br_2^*	0.002	0.001	CS_2	C 2 min. (<0°)		(137)
HgI_2	I^{*-}				C 2.5 min.		(380)
HgI_4^{2-}	I^{*-}	0.0005	0.3		C 30 sec.		(125, 380)
$Hg(en)_2^{2+}$	en*	0.006	0.01		C 6 sec. (0°)		(383)

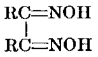
†

en = ethylenediamine
pn = propylenediamine
dien = diethylenetriamine
tetrameen = 2,3-dimethyl-2,3-diaminobutane
phen = 1,10-phenanthroline
dipy = 2,2′-dipyridyl
tripy = 2,2′,2″-terpyridine
AAH = acetylacetone
$EDTA\cdot H_4$ = ethylenediaminetetraacetic acid

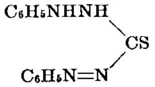
SH = salicylaldehyde
NNH = α-nitroso-β-naphthol
HQH = hydroxyquinoline
PO = porphyrin
PP = pheophytin
Ac = acetate
P = phthalocyanin
X = 4,4′-dicarbethoxy-3,3′,5,5′-tetramethyldipyrromethene

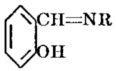
TABLE 10—*Concluded*

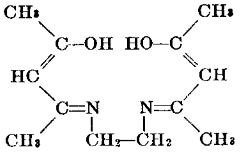
For the following chelating agents, all indicated substitutions refer to the R position: e.g., dimethylglyoxime is indicated by Me_2GH.

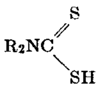
GH =


$$\begin{array}{l} RC{=}NOH \\ \;| \\ RC{=}NOH \end{array}$$

DTH =


SMH =


AEH₂ =


DCH =


For chelates based on the general structure

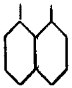
SEH_2 : R = $(CH_2)_2$

STH_2 : R = $(CH_2)_3$

SDH_2 : R = $(CH_2)_4$

$SPTH_2$: R = $(CH_2)_3NH(CH_2)_3$

SPH_2 : R =


SNH_2 : R =


asterisks. Within a periodic group the exchanging species are arranged in order of increasing complexity. The species indicated are not necessarily those existing under the conditions of the exchange (e.g., pH will govern the predominant form).

Exchange conditions: Columns 3 and 4 indicate the concentration (in normalities or molarities) of the exchanging species listed in columns 1 and 2, respectively. Column 5 refers to any other important condition(s) used in the experiment. Unless otherwise indicated, all experiments were performed in water.

Exchange rate: Times listed in column 6 denote the exchange half-times. The letter N preceding a listed time signifies that $\leqslant 5$ per cent exchange occurred at the *highest concentration and temperature conditions.* The letter C preceding a listed time indicates $\geqslant 95$ per cent exchange occurred (usually within the separation time) at the *lowest concentration and temperature conditions.* All temperatures refer to 20–30°C., or room temperature, unless otherwise specified.

Szilard–Chalmers evidence of bond lability (fast or slow) is given only when no direct exchange results are available. When no quantitative information is available the rate is denoted simply by "fast" or "slow."

Remarks: Included in this column is an indication that a kinetic study was accomplished (K), that an activation energy for a simple mechanism was obtained ($E = x$ kcal./mole), or that the exchange was photosensitive (P).

References: When more than one reference is given, then the conditions of the exchange refer to the first reference and, unless otherwise stated, the results of the other studies confirm the general conclusions of the first.

VII. Isotope Effects in Exchange Reactions

In many isotopic exchange studies it is assumed that the reaction rate of the labelled molecule is identical with that of the "parent" molecule. However, the fact that isotopes such as D, N^{15}, and O^{18} can be concentrated by various chemical techniques is but one practical example of significant differences in isotopic reaction rates. The purpose of this section will be to examine the expected magnitude of such "isotope effects" and the limitations thereby imposed on quantitative exchange studies. It will also be indicated how a knowledge of isotope effects can be applied to the elucidation of the structure of exchanging molecules. Unless special new principles are involved, no mention will be made of the isotope effects exhibited by deuterium- or tritium-labelled molecules, since thorough reviews on both types of reactions have been recently published (193, 475).

A. THEORETICAL TREATMENT

The calculation of isotope effects in exchange reactions can be placed on a relatively firm theoretical basis. Consider the general exchange reaction:

$$aA + bB^* \rightleftharpoons aA^* + bB$$

where the superscript * denotes the heavier (normally the labelling) isotope. We may write the equilibrium constant of this reaction as:

$$K = \left(\frac{A^*}{A}\right)^a \Big/ \left(\frac{B^*}{B}\right)^b \tag{26}$$

the quantities (A*/A) and (B*/B) being the specific activities (or per cent atom abundance) of A and B. In most reactions the equilibrium constant should be unity if no differences in isotopic reaction rates occur; i.e., at exchange equilibrium the specific activities of the A and B molecular species should be equal. Conversely, a deviation of K from unity will indicate the existence of an isotope effect. For comparison purposes, an isotope effect will be defined by the relation:

$$\text{Percentage isotope effect} = 100(K - 1) \tag{27}$$

the chemical exchange equations being always written such that $K > 1$; e.g., if $K = 1.0775$ then a "7.75 per cent isotope effect" will be said to be operative in the exchange system.

From statistical mechanics, equation 26 may be written in the form:

$$K = \left(\frac{Q_{\mathrm{A}^*}}{Q_{\mathrm{A}}}\right)^a \Big/ \left(\frac{Q_{\mathrm{B}^*}}{Q_{\mathrm{B}}}\right)^b \tag{28}$$

where the Q's indicate the total partition functions of the indicated molecules. The equilibrium constant for an isotopic exchange reaction may thus be derived directly from the calculated partition-function ratios for the two pairs of isotopic molecules. The partition-function ratio for two isotopic molecules is expressed rigidly by the equation:

$$\frac{Q^*}{Q} = \frac{\sigma}{\sigma^*}\left(\frac{M^*}{M}\right)^{3/2} \sum_i e^{-E_i^*/kT} \Big/ \sum_i e^{-E_i/kT} \tag{29}$$

where σ, σ^* are the symmetry numbers of the isotopic molecules, M, M^* are the molecular weights, and E_i, E_i^* refer to the energy of the i^{th} state of the respective molecules. All these energies are calculated relative to the same minimum of the potential energy curve, the shape of which is assumed to be the same for the two isotopic molecules. Expressing the total partition function as a product of the separate translational, vibrational, and rotational partition functions (since a ratio is only involved, the electronic partition function can be neglected for all but hydrogen isotopes) and employing the Teller–Redlich product theorem, Urey (459) has shown that equation 29 reduces to the form for a polyatomic molecule:

$$f = \left(\frac{Q^*}{Q}\right)\left(\frac{m}{m^*}\right)^{3/2n} = \frac{\sigma}{\sigma^*}\prod_i \frac{u_i^*}{u_i} \cdot \frac{e^{-u_i^*/2}}{e^{-u_i/2}} \cdot \frac{1 - e^{-u_i}}{1 - e^{-u_i^*}} \tag{30}$$

where $u_i = hc\omega_i/kT$ and ω_i is the frequency (strictly the zero-order frequency) of the i^{th} vibrational mode of the appropriate molecule,
m, m^* = the atomic weights of the isotopic atoms,
n = the number of equivalent exchangeable atoms or groups,

and f is conventionally called the "isotopic partition-function ratio." For a diatomic molecule f is given by the analogous equation:

$$f = \left(\frac{Q^*}{Q}\right)\left(\frac{m}{m^*}\right)^{3/2n} = \frac{\sigma}{\sigma^*}\frac{u^*}{u}\frac{e^{-u^*/2}}{e^{-u/2}}\frac{1 - e^{-u}}{1 - e^{-u^*}} \tag{30a}$$

The equilibrium constant of the general exchange reaction may then be written as simply:

$$K = f_A/f_B \tag{31}$$

Whereas the calculation of the total partition function of a single molecule is quite complex, the estimation of an isotopic partition-function ratio is comparatively straightforward. The expressions for f do not require a knowledge of moments of inertia but simply the various vibrational frequencies of the two isotopic molecules. For the purposes of numerical calculation, equations 30 and 30a may be simplified into more convenient forms. Urey (459) has defined the quantities:

$$\chi_i = (u_i + u_i^*)/4 \tag{32}$$

$$\delta_i = (u_i - u_i^*)/2 \tag{33}$$

and equation 30 becomes for all isotopes except those of hydrogen

$$\ln f = \ln (\sigma/\sigma^*) + \sum_i \ln (u_i^*/u_i) + \sum_i \coth \chi_i\delta_i \tag{34}$$

with an analogous equation for diatomic molecules. Bigeleisen and Mayer (55) quote an alternative expanded form of equation 30 such that:

$$f = \frac{\sigma}{\sigma^*}(1 + \sum G(u_i)\Delta u_i) \tag{35}$$

where

$$\Delta u_i = u_i - u_i^* \tag{36}$$

and

$$G(u_i) = \frac{1}{2} - \frac{1}{u_i} + \frac{1}{e^{u_i} - 1} \tag{37}$$

Numerical values of the function $G(u_i)$ are listed for values of u_i varying from 0.00 to 25.00 at intervals of 0.10.

The deduction of equation 30 is based on several assumptions. The assumptions that the vibrational molecular motions are harmonic and that there is no interaction between vibration and rotation are open to some criticism, as is the use of observed fundamentals (ν) rather than zero-order frequencies (ω). When sufficient data are available to make allowance for such effects, the error incurred by the assumptions is not as great as might be imagined; e.g., at 273°K. the corrected f values for C^{14}-substituted carbon monoxide and hydrogen cyanide are 1.2162 and 1.2805 compared to the uncorrected values of 1.2155 and 1.2815 (440). In other molecules the errors may be greater, but the lack of suitable data precludes correction for such effects especially for polyatomic molecules. In the case of exchanges between gases and liquids, neglect of the relative vapor pressures of the isotopic compounds may lead to errors of up to 1 per cent in the calculated exchange equilibrium constants (459). Nevertheless it will be appreciated that because a ratio of f values is employed in the calculation of exchange equilibrium constants, errors, which may be quite large for single molecules, tend to cancel out. Under normal temperature conditions (0–100°C.) the uncertainties enumerated may only amount to an error of a fraction of a per cent in the final exchange equilibrium constants. This is well within experimental errors encountered in most tracer experiments.

Except for deuterated molecules, the vibrational frequencies for isotopically substituted molecules are frequently unknown and must be calculated from the frequencies of the normal molecules. For any diatomic molecule, the harmonic oscillator approximation relates the vibrational frequencies to the reduced masses (μ) of the isotopic molecules thus:

$$\omega_e^*/\omega_e = \sqrt{\mu/\mu^*} = \rho \tag{38}$$

and for the anharmonic coefficients:

$$\omega_e^* \chi_e^* = \rho^2 \omega_e \chi_e \tag{39}$$

always assuming the force constants for the isotopic molecules to be identical. For polyatomic molecules, the Teller–Redlich product rule (236) gives the product of the ω^*/ω values for all vibrations of a given symmetry type as a function of the masses of the atoms and the geometrical structure of the molecule. When more than one genuine vibration belongs to a particular symmetry type, then insufficient independent equations are available for calculating separate frequencies. Recourse must then be made to normal vibration equations, of which the valence-force approximation is most suitable. For instance, the stretching frequencies (ν_1, ν_3) of a linear XYZ molecule (e.g., HCN) are given by:

$$4\pi^2(\nu_1^2 + \nu_3^2) = k_1\left(\frac{1}{m_x} + \frac{1}{m_y}\right) + k_2\left(\frac{1}{m_y} + \frac{1}{m_z}\right) \tag{40}$$

$$16\pi^4 \nu_1^2 \nu_3^2 = \frac{m_x + m_y + m_z}{m_x m_y m_z} k_1 k_2 \tag{41}$$

If the molecule is isotopically substituted on atom Y, then the isotopic frequencies will be given by:

$$\frac{\nu_{1i}^2 + \nu_{3i}^2}{\nu_1^2 + \nu_3^2} = \frac{k_1\left(\frac{1}{m_x} + \frac{1}{m_y^i}\right) + k_2\left(\frac{1}{m_y^i} + \frac{1}{m_z}\right)}{k_1\left(\frac{1}{m_x} + \frac{1}{m_y}\right) + k_2\left(\frac{1}{m_y} + \frac{1}{m_z}\right)} \tag{42}$$

$$\frac{\nu_{1i}^2 \nu_{3i}^2}{\nu_1^2 \nu_3^2} = \frac{m_y}{m_y^i} \cdot \frac{m_x + m_y^i + m_z}{m_x + m_y + m_z} \tag{43}$$

where k_1 and k_2, the stretching force constants for the X—Y and Y—Z bonds, are assumed to be equal for the isotopic molecules and i denotes the isotopic species. For more complex molecules the isotopic frequencies will be a function of atomic masses, force constants, and bond angles. In actual practice the computation of the isotopic frequencies is often the most time-consuming part of the calculation of f values. Whilst normal vibration equations never completely describe the vibrations of a polyatomic molecule, they are quite accurate in estimating isotopic spectral shifts.

The magnitude of an exchange equilibrium constant depends on the relative magnitudes of the isotopic partition-function ratios (f) for the two molecular species. Inspection of equation 30 shows that the value of f for a pair of isotopic molecules depends on (*a*) the ratio of symmetry numbers σ/σ^* and (*b*) the spectral shifts on isotopic substitution. The ratio σ/σ^* is always unity if the molecule contains either one exchanging atom or several structurally equivalent atoms all undergoing exchange. Since this situation is encountered in all normal isotopic exchange reactions, the symmetry number ratio may be ignored in subsequent discussions. The ratio σ/σ^* differs from unity only when homomolecular ("randomizing" or "scrambling") exchange reactions are studied. In practice this only arises with enriched stable isotopes and tritium. For example, in the exchange system:

$$CO_2^{18} + CO_2^{16} \rightleftharpoons 2CO^{18}O^{16}$$

the equilibrium constant will be given by

$$K = \frac{\sigma_{18}\,\sigma_{16}}{\sigma_{18,16}^{2}} \times \frac{Q_{18,16}^{2}}{Q_{18}\,Q_{16}} \tag{44}$$

The symmetry number of a molecule may be defined as "the number of indistinguishable positions into which the molecule can be turned by simple rigid rotation" (482). Two such positions exist for the $O^{16}—C—O^{16}$ and $O^{18}—C—O^{18}$ molecules but only one for $O^{16}—C—O^{18}$. The symmetry number ratio will then be $2 \times 2/1^2 = 4$. Furthermore, to a very good approximation the partition function of a molecule such as $CO^{18}O^{16}$ is the geometric mean of those for CO_2^{18} and CO_2^{16} (the "rule of the geometric mean" (53)). The expected exchange equilibrium constant would be 4; the accurate calculated value is 3.9990 at 0°C. (459). Similarly for N^{15} homomolecular reactions, e.g.,

$$N_2^{14} + N_2^{15} \rightleftharpoons 2N^{14}N^{15}$$

the expected value of 4 is very close to that calculated of 3.9918 at 0°C. (459). Regardless of its value, the ratio of symmetry numbers cannot lead to isotopic enrichment since it merely represents the relative probabilities of forming symmetrical and unsymmetrical molecules. Therefore isotope effects in exchange reactions must arise from effect (*b*).

The magnitude of isotopic spectral shifts (and hence f) is determined by the form and size of the molecular vibrational frequencies, the temperature, the mass difference between labelling isotope and parent nuclide, and the atomic weight of the element undergoing isotopic substitution. For compounds of a given element the value of f at a given temperature will be greater the higher the vibrational frequencies in the molecule. Table 11 lists typical data for the C^{14} exchange of the cyanogen halides with free cyanide ion (440). It is seen that the isotope effect steadily decreases with decreasing vibrational frequencies. Therefore sub-

TABLE 11

Exchange of C^{14}-cyanogen halides with cyanide ion

Halide	ν_1	ν_2*	ν_3	f_{273}	$100(K - 1)$
	cm.$^{-1}$	cm.$^{-1}$	λ		
$ClC^{12}N$..........	729	397	2201	1.2992	9.02
$ClC^{14}N$..........	718	378	2102		
$BrC^{12}N$.........	580	368	2187	1.2824	7.61
$BrC^{14}N$.........	567	352	2091		
$IC^{12}N$...........	470	321	2158	1.2650	6.15
$IC^{14}N$...........	457	304	2066		

* ν_2 is doubly degenerate.

stantial isotopic discrimination may be anticipated in any exchange reaction between one molecule having high vibrational frequencies (strong bonds) and the other molecule having low vibrational frequencies (weak bonds). This important generalization is the basis for many applications of exchange isotope effects to chemical problems. The greatest isotope effects will occur when one of the exchanging species is an atom or a free monatomic ion of the element, for which the value of f is unity.

The value of f tends to a maximum value of $(1 + \Delta u_i/2)$ at low temperatures (equation 35), this value being simply determined by the difference in zero-point energies for the two isotopic molecules. At very high temperatures the value of Δu_i becomes vanishingly small and no isotope effect occurs. A typical variation in an exchange equilibrium constant with temperature is for the system:

$$C^{13}O + C^{12}O_2 \rightleftharpoons C^{13}O_2 + C^{12}O$$

$100(K - 1)$....	9.8	8.6	5.5	3.8	2.9
°A............	273	298	400	500	600

Bigeleisen (51) has pointed out that for several isotopes of a single element the relative isotope effects are directly proportional to the mass difference between the respective isotopes and the parent nuclide. Thus tritium isotope effects will be twice those for deuterium, and carbon-14 effects twice those for carbon-13. This can be seen from an inspection of table 12. Tudge and Thode (456) have calculated equilibrium constants for S^{34}/S^{32} exchange systems and the isotope effects for S^{35}/S^{32} exchanges; i.e., $100(K - 1)$ will be simply 1.5 times those quoted values. Similar considerations apply to Cl^{37}/Cl^{35} and Cl^{38}/Cl^{35} exchanges. For all the exchange systems listed in table 12, the tracer isotope will preferentially concentrate in the first-named species of the pair.

The exchange equilibrium constants approach unity with increasing atomic weight. Fluctuations do occur in this trend, owing to the influence of additional vibrations in some compounds and to the varying vibrational frequencies among analogous compounds. It will be seen that for tracers above atomic weight 40,

TABLE 12

Some typical exchange equilibrium constants

Exchanging Reactants	100(K − 1)	Exchanging Reactants	100(K − 1)	Reference
$C^{13}O_2-C^{12}O$	9.4	$C^{13}O_3^{2-}-C^{12}O_2$	1.2	(459)
$C^{14}O_2-C^{12}O$	18.8	$C^{14}O_3^{2-}-C^{12}O_2$	2.4	(440)
$N^{15}O_2-N^{14}O$	4.0	$N^{15}O_3^{-}-N^{14}O_2$	5.3	(422)
$(CO_2^{18})^{\frac{1}{2}}-CO^{16}$	1.3	$(CO_2^{18})^{\frac{1}{2}}-(CO_3^{16\ 2})^{1/3}$	2.2	(459)
$S^{34}O_2-(S_8^{32})^{1/8}$	3.4	$S^{34}O_3-S^{32}O_2$	4.1	(456)
$S^{35}O_2-(S_8^{32})^{1/8}$	5.1	$S^{35}O_3-S^{32}O_2$	6.0	
$Cl^{37}O_2-(Cl_2^{35})^{\frac{1}{2}}$	2.7	$Cl^{37}O_3-Cl^{35}O_2$	1.8	(459)
$Cl^{38}O_2-(Cl_2^{35})^{\frac{1}{2}}$	4.0	$Cl^{38}O_3-Cl^{35}O_2$	2.7	
		$Br^{81}O_3^{-}-(Br^{79})^{\frac{1}{2}}$	0.8	(459)
		$I^{129}O_3^{-}-(I_2^{1\ 7})^{\frac{1}{2}}$	0.28	(459)
		$I^{131}O_3^{-}-(I_2^{127})^{\frac{1}{2}}$	0.56	

very little isotopic discrimination is likely. Measurable isotope effects are very likely for the important elements carbon, nitrogen, oxygen, phosphorus, sulfur, and chlorine in addition to hydrogen. For carbon, nitrogen, and oxygen exchange systems, effects up to a maximum of 20 per cent are possible provided of course that the exchange in a given system proceeds at a convenient rate. Isotopic partition-function ratios have been calculated for isotopes of hydrogen, lithium, boron (459), carbon (440, 459), nitrogen (422), oxygen (459), sulfur (456), and chlorine, bromine, and iodine (459).

B. LIMITATIONS IMPOSED BY ISOTOPE EFFECTS IN EXCHANGE REACTIONS

The general first-order exchange law (Section II) was first derived by McKay (325), neglecting the possibility of isotope effects. If isotope effects do occur (218), then the exchange still proceeds according to an accurate first-order rate law provided the tracer concentration is negligible. For simple bimolecular exchange mechanisms, the first-order rate law holds to within 1 per cent for even 100 per cent abundance of "tracer" isotope if the isotope effect is less than 2 per cent (77). For an isotope effect of 10 per cent the first-order law is only followed up to 20 per cent tracer abundance. In the case of a dissociative type of mechanism the first-order law is again followed accurately for isotope effects up to 10 per cent and tracer concentrations up to 10 per cent abundance. For tracer concentrations above these limits significant departures from the simple exchange law are possible. Apart from deuterium, such effects are only probable in highly enriched samples of C^{13}, N^{15}, or O^{18}.

Although most exchange reactions will therefore be adequately described by a first-order law, neglect of isotope effects can introduce serious errors in the deduction of rate constants from kinetic studies. The observed exchange rate is that for the tracer, but the purpose of an exchange study is to determine the exchange rate for the unlabelled "parent" compound. Harris (218) has shown that for an isotopic exchange proceeding via a bimolecular mechanism and exhibiting significant isotope effect, the rate law is:

$$R = \frac{-2.303}{t} \frac{\epsilon ab}{\epsilon a + b} \log_{10}(1 - F) \tag{45}$$

(compared with equation 1). The isotope effect factor ϵ is identified with the exchange equilibrium constant, K. The rate of the exchange should therefore be calculated from the measured exchange half-time thus:

$$R = \frac{0.693}{t_{\frac{1}{2}}} \cdot \frac{\epsilon ab}{\epsilon a + b} \tag{46}$$

Furthermore it is common practice to calculate x_∞ from the simple equation 4. If an isotope effect is operative, the tracer will preferentially concentrate in one of the exchange species. Under these conditions the appropriate expression is:

$$x_\infty = \epsilon b x_0 / \epsilon a + b \tag{47}$$

for BX* initially labelled.

If isotope effects were neglected, the exchange rate (R') calculated from equation 5 would obviously be in error, this error varying with the concentration ratio $f = a/b$. The relation between the apparent rate R' and the true rate (R), i.e., the exchange rate of the unlabelled molecules, is:

$$R'/R = 1 - \left(\frac{\epsilon - 1}{\epsilon}\right)\left(\frac{1}{f + 1}\right) \tag{48}$$

For the isotopes of the important elements carbon, nitrogen, and oxygen, an isotope effect of 10 per cent is quite possible; i.e., $\epsilon = 1.10$. For $f = 0.1$, the error in R' is 8.3 per cent; for $f = 1$, 4.5 per cent; and for $f = 10$, 0.8 per cent. Hence if the existence of an isotope effect is suspected in an exchange yet cannot be measured, the true rate can be determined by exchanging a high concentration of an unlabelled reactant with a low concentration of labelled reactant. However, the more satisfactory procedure is always to calculate or measure the exchange equilibrium constant.

A knowledge of isotope exchange equilibrium constants is essential in precision mass-spectrometric analyses depending on equilibration of one compound with another. A notable example is the analysis of H_2O^{18} by equilibration with carbon dioxide (110), for which the equilibrium constant is 1.047 at 25°C.

The occurrence of isotope effects in exchange reactions is an important cause of variations in the isotopic abundances of chemicals derived from natural sources. A knowledge of the equilibrium constants is of substantial importance in drawing conclusions as to the previous history of samples but such geochemical topics will not be pursued further in the present review.

C. EXPERIMENTAL EXCHANGE EQUILIBRIUM CONSTANTS

An exchange equilibrium constant is most readily determined by the measurement of the equilibrium isotopic composition of the two exchanging molecular species (equation 26). Since isotopic equilibrium is reached in eight or ten exchange half-times, this method presumes a knowledge of the exchange rate. It should be appreciated that these equilibrium measurements demand high precision in isotopic assays. Frequently the isotope effect is not greater than 10 per cent, a value which is becoming comparable to the experimental errors especially for radiotracers. Moreover it is important that the separation procedure does not disturb the isotopic compositions of the two molecular species. A system in which such effects are serious is the C^{14} exchange between cyanogen iodide and cyanide ion in dioxane solutions (261), for which the calculated equilibrium constant is 1.052 at 30°C. (440). The observed equilibrium constant is the ratio of the specific activities of the cyanogen iodide fraction to that of the cyanide-ion fraction; the following results were obtained at 30.6°C.:

K	1.08 ± 0.02	1.15 ± 0.02	1.18 ± 0.03	1.28 ± 0.02	1.29 ± 0.03
Per cent dioxane	0	20	28	40	60

In dioxane solution the rate of the exchange is very fast compared to the rate of precipitation of cyanide ion as silver cyanide. It was postulated that there was an isotope effect in the precipitation reaction and that the system continuously equilibrated with the remaining cyanide. Under these conditions the observed equilibrium constant will vary with the relative concentrations of cyanogen iodide and cyanide ion.

Frequently secondary decomposition reactions become serious when an exchange reaction must be equilibrated for some ten half-times. Melander (328) has considered the exchange

$$AX + BX^* \underset{\beta}{\overset{\alpha}{\rightleftharpoons}} AX^* + BX$$

in which α is the isotope effect for the forward reaction and β is that for the reverse reaction; $\alpha/\beta = K$. If y be the isotopic composition of BX (y_0 at $t = 0$) and z that for AX ($z = 0$ at $t = 0$), then it may be shown that:

$$\frac{d}{dt}\left(\frac{y}{y_0}\right)_{t=0} = -\frac{\alpha R}{a} \quad \text{and} \quad \frac{d}{dt}\left(\frac{z}{y_0}\right)_{t=0} = +\frac{\alpha R}{b} \tag{49}$$

Thus the instantaneous time rate of change of the activities in both fractions at zero time should provide a measure of αR, where R is the rate of exchange of the unlabelled molecules. If AX is initially labelled, then βR could be similarly measured. Whilst this proposal is theoretically sound it would be extremely difficult to realize in practice except where large isotope effects occur. No experimental attempts have yet been reported.

Another method of estimating the isotope effect is to measure exchange rates separately with two isotopes of the same element: e.g., T and D; C^{14} and C^{13}. In both these examples the ratio of exchange rates for the two isotopes will be in the same ratio as the rate ratio for the lighter isotope compared to the parent isotope. Yankwich and McNamara (488) found the ratio of C^{13} to C^{14} rates to be 1.038 ± 0.028 for exchange of carbonate ion with carbonato-bis-(ethylenediamine)cobalt(III), thereby indicating the probable absence of any isotope effect.

With stable isotopes especially, exchange reactions may be conducted in a cascade or multistage system, thereby amplifying small isotope effects up to considerable overall separation factors. For instance, an overall N^{15} enrichment of 2.5 was achieved with the system:

$$N^{15}O(g) + HN^{14}O_3(aq) \rightleftharpoons N^{14}O(g) + HN^{15}O_3(aq)$$

although the equilibrium constant for a single stage was only 1.045 (424). The preparation of 99.8 per cent N^{15} has been recently achieved using this exchange system (425). Similarly a separation factor of 3.0 was achieved by multistage exchange of $N^{15}O$ with nitrogen dioxide (423). Repetitive exchange between gaseous chlorine and aqueous chloride ion yielded an overall Cl^{37}/Cl^{35} separation of 1.048 or an equilibrium constant of approximately 1.004 with the Cl^{37} concentrating in the gas phase (409).

Urey (459) has summarized many exchange systems in which a direct comparison of calculated and observed isotope effects is possible; within the rather large experimental error, reasonable agreement is found. More recently the equilibrium constant for the β-induced exchange

$$H_2 + T_2 \rightleftharpoons 2HT$$

has been measured (321) as 2.87 ± 0.06 at 28°C., compared with the theoretical value of 2.57 (50, 269, 459). The significant difference was attributed either to the higher effective temperature in the electron beam of the mass spectrometer or to the fact that an equilibrium in a radiation field (in this case the tritium particles) may differ from the thermodynamic equilibrium constant. The latter point is one of considerable interest and merits closer attention. A similar effect has been observed (494) in the recently studied γ-ray-induced exchange between D_2O and dissolved hydrogen. The measured equilibrium constant for the system:

$$NH_3 + HD \rightleftharpoons NH_2D + H_2$$

was reported (373) as 5.26 ± 0.1 and 4.92 ± 0.1 for duplicates at 295°K.; the calculated value is 5.82 (281). The exchange equilibrium constant for the system

$$C^{14}O + COCl_2 \rightleftharpoons CO + C^{14}OCl_2$$

is adequately predicted over a 500°C. temperature range and a variety of experimental conditions (431, 433). The relatively large isotope effect, e.g., 9.9 per cent at 20°C., was shown from kinetic studies (435) to arise from a multiplication of isotope effects for the equilibrium:

$$COCl \rightleftharpoons CO + Cl$$

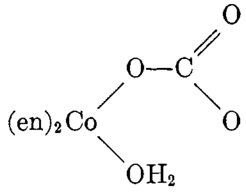
and for the decomposition reaction:

$$COCl + Cl_2 \rightarrow COCl_2 + Cl$$

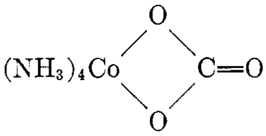
Substantial data have now accumulated on isotope effects in systems of the type:

$$Co(NH_3)_4CO_3^+ + HC^{14}O_3^- \rightleftharpoons Co(NH_3)_4C^{14}O_3^+ + HCO_3^-$$

for which Stranks and Harris (438, 439) first reported an equilibrium constant of 0.875 at 0°C., increasing steadily to 0.900 at 30°C. The C^{14} tracer thus concentrated in the free carbonate ion, which is presumably the more strongly bonded state of carbon. For the corresponding ethylenediamine complex $Co(en)_2CO_3^+$, Yankwich and McNamara (488) reported an equilibrium constant of 0.991 ± 0.014 for C^{13} exchange and 0.990 ± 0.019 for C^{14} exchange at 25°C. Stranks claimed (432) that a distinct isotope effect occurred in this system with K varying from 0.981 ± 0.005 at 0°C. to 0.993 ± 0.005 at 56°C. for C^{14} exchange. The difference between the magnitude of isotope effects for two apparently similar complexes has been attributed (216) to the existence of the second complex in the monodentate form



as distinct from the bidentate form for the other complex



in which considerable modification of the carbonate group could occur. In support of this view the monodentate complex $Co(NH_3)_5CO_3^+$ exhibited (432) an equilibrium constant of 1.0000 ± 0.0055 at 0°C. Saito and Lazard (411) have recently repeated the measurements on the tetrammine complex and, using unenriched C^{13} for both complex and carbonate, observed an equilibrium constant of 1.00 (compared to that expected from the C^{14} results of 0.95). However when labelled carbonate ion was used, K varied from 0.85 to 0.97 for C^{14} exchange and from 0.94 to 1.00 for C^{13} exchange. The equilibrium constant more nearly approached unity, the more the complex was "purified" by recrystallization. These observations seem compatible with the existence of a nonexchanging impurity in the carbonato complex, but Saito and Lazard could find no additional evidence for this impurity. However there appears to be some correlation between the water content of the solid carbonato complex and the expected percentage impurity (e.g., a sample for which Saito and Lazard observed $K = 0.94$, corresponding to an impurity of 6 per cent, has a water content of 0.90 mole of water per mole of complex; another sample having an expected impurity of 15 per cent has a water content of 0.79 mole of water per mole of complex). A provisional explanation may be that the bidentate form of the complex is not in rapid equilibrium with the monodentate form $Co(NH_3)_4CO_3 \cdot H_2O^+$ and the former is the nonexchanging entity. A variation in the equilibrium constant with temperature would thus be the gradual irreversible conversion of the bidentate form to the monodentate form. With more study, investigations of this type of system may throw light on the actual form of existence of coördination complexes in aqueous solution.

In studying the exchange of H_2O^{18} with the first hydration sphere of cations, Feder and Taube (165) have observed distinct fractionation effects. The general equilibrium may be represented as:

$$H_2O_h^{16} + H_2O_l^{18} \rightleftharpoons H_2O_h^{18} + H_2O_l^{16}$$

for which

$$K = \frac{[H_2O_h^{18}]}{[H_2O_h^{16}]} \bigg/ \frac{[H_2O_l^{18}]}{[H_2O_l^{16}]} = \frac{W_h^{18}}{W_h^{16}} \bigg/ \frac{W_l^{18}}{W_l^{16}} \tag{50}$$

where the W's represent the number of water molecules. Setting $W_l^{18}/W_l^{16} = R$ (R_0 is the ratio with no salt present) then it follows that the fractionation factor, α, is given to a good approximation by:

$$\alpha \equiv (R_0/R - 1) = nm(k - 1)/55.5 \tag{51}$$

where m is the molality of the solute and n the number of water molecules in the first hydration sphere. It is found that the quantity α/m is a function solely of the cation; e.g., α/m is equal for magnesium chloride and magnesium perchlorate or for sodium chloride, sodium iodide, and sodium perchlorate, but is different for magnesium chloride and sodium chloride. Moreover α is a linear function of m up to 12 molal solutions. A substitution inert ion such as $Co(en)_3^{3+}$ has a very small value of α/m. The exchange equilibrium between the cationic hydration sphere and other water molecules is in competition with the equilibrium

$$H_2O^{16}(l) + H_2O^{18}(g) \rightleftharpoons H_2O^{18}(l) + H_2O^{16}(g)$$

which has a value of 1.0088 at 25°C. (466). When the bonding in the hydration sphere is strong, a relatively large fractionation effect will offset this opposing equilibrium and α is observed to be positive with O^{18} concentrating in the hydration sphere: e.g., Al^{+++}, Mg^{++}, Li^+, Ag^+. Conversely, with relatively weak bonding in the hydration sphere α becomes negative: e.g., Cs^+, NH_4^+, K^+. In the case of sodium ion the two opposing fractionation effects balance and α is zero. From such measurements the product of the hydration number, n, and the exchange equilibrium constant for the hydration sphere, K, is obtained. The problem remaining is to separate this product and determine n. The most promising approach seems to be (446) the comparison of observed effects for unknown cations with that for a known cation such as Cr_{aq}^{3+} or comparing the method with a method based on the electronic absorption spectrum of colored cations of known hydration number in inert solvents (175). Direct calculation of K according to the methods outlined above is rendered very difficult because of the lack of suitable spectroscopic data.

Taube (446) has suggested that this exchange equilibrium approach may be quite useful in solvation studies in liquid ammonia in which solvent–solvent interaction is less and the lower temperatures attainable will enhance the discrimination effect. Another application would be to a study of outer-sphere association, i.e., whether a ligand actually replaces coördinated water or whether it interacts by outer-sphere association. Only when the ligand replaces the water will any marked change in the fractionation effect occur.

No difference was observed in the rates of exchange of $C^{12}O$ and $C^{14}O$ with carbon monoxide adsorbed on iron at −78°C. (145). However, O^{16} is preferentially adsorbed on copper surfaces (43), presumably owing to an exchange equilibrium between gaseous oxygen molecules and chemisorbed oxygen atoms. This isotope effect appears to be greater for the chemisorbed layer than for oxide films of 150–2500 A. thickness. Dole and Lane (134a) have found that O^{16} is preferentially chemisorbed on clean metal surfaces at room temperature. Steel surfaces exhibit a 2.5 per cent O^{16}/O^{18} equilibrium effect, whilst the effect varies from 7.4 to 5.2 per cent for copper, depending on the extent of oxidation of the surface. The authors hope to gain information on the mechanism of the formation of oxide films from such studies.

VIII. The Tracing of Tagged Atoms Through Chemical Reactions

A. DETECTION OF BOND CLEAVAGE

The occurrence of bond fission during a chemical reaction can be easily shown by carrying out the reaction in the presence of the suspected fission fragment suitably labelled. Provided direct exchange processes are unimportant, then appearance of labelling in the product(s) supports bond cleavage during the reaction. Two simple examples will make this clear.

Inactive potassium chlorate decomposed in the presence of labelled potassium chloride at 510°C. to inactive potassium perchlorate (60, 73). This indicated that complete bond cleavage of the chlorate to chloride did not occur during the decomposition and excluded a proposed mechanism (188):

$$KClO_3 \rightarrow KCl + 3O$$

$$KCl + 4O \rightarrow KClO_4$$

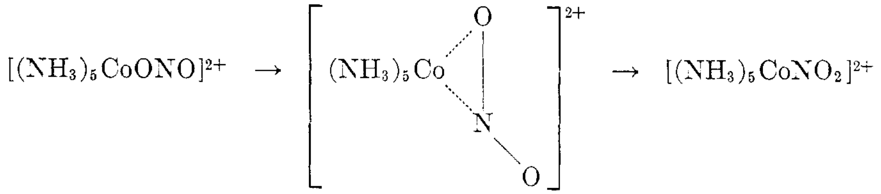
The complex ion $Co(NH_3)_5Cl^{2+}$ reacts rapidly with a slight excess of Cr^{2+}_{aq} in perchloric acid to form $CrCl^{2+}$. If this reaction was carried out in the presence of excess Cl^{*-}, the amount of active chlorine found attached to the final $CrCl^{2+}$ was less than 0.5 per cent. This immediately confirms the suspicion that during the electron-transfer reaction the cobalt–chlorine link is not severed until after the chromium–chlorine link has almost formed, and that the activated complex must have an arrangement

$$[(NH_3)_5Co\text{---}Cl\text{---}Cr]^{4+}$$

permitting the chlorine transfer from cobalt to chromium without exchange with chloride ion in solution (449, 450). Neither $Co(NH_3)_5Cl^{2+}$ nor $CrCl^{+}$ exchanges chlorine rapidly with chloride ion in aqueous solution.

By a logical extension of this method it is possible to differentiate between an intramolecular and a dissociative mechanism for a chemical reaction. Murmann and Taube (335) have investigated the $Co(NH_3)_5ONO^{2+}$–$Co(NH_3)_5NO_2^{2+}$

isomeric change using oxygen-18. This isomerization is believed to be intramolecular from the facts that the rate in solution is independent of nitrite concentration (370) and that the change occurs easily even in the solid state (12). It was observed (335) that when O^{18}-enriched $Co(NH_3)_5ONO^{2+}$ (either oxygen atom labelled separately) isomerized in the presence of normal nitrite ion in normal water at pH 5 or 6, no equilibration of oxygen occurred. The intramolecular mechanism was therefore confirmed and was pictured as:



The nitrito (or nitro) compound was converted into nitrite ion, which with sodium azide under carefully controlled conditions gave nitrous oxide (see below), which is easily purified and can be analyzed directly in a mass spectrometer. No difficulties arise from exchange between $Co(NH_3)_5ONO^{2+}$ and H_2O or between $Co(NH_3)_5NO_2^{2+}$ and nitrite ion under the conditions of the transformation.

A useful and novel way of detecting bond cleavage during chemical processes is by utilizing the phenomenon of "randomizing" (Section VII,A). The method is normally limited to stable isotopes (apart from tritium) which can be obtained in high enrichments. Using a remarkably similar approach Higginson and Sutton (239) and, independently, Cahn and Powell (89) investigated the mechanism of the oxidation of hydrazine by various oxidizing agents. N^{15}-enriched hydrazine containing amounts of the various possible species governed by the equilibrium:

$$N^{15}H_2N^{15}H_2 + N^{14}H_2N^{14}H_2 \rightleftharpoons 2N^{15}H_2N^{14}H_2$$

$$K = \frac{[N^{15}H_2N^{14}H_2]^2}{[N^{15}H_2N^{15}H_2][N^{14}H_2N^{14}H_2]} = 4 \quad \text{(Section VII,A)} \qquad (52)$$

was mixed with an excess of "ordinary" hydrazine. In the mixture the statistical equilibrium requirements will, naturally, no longer be satisfied. If in the oxidation of this mixed hydrazine no N—N bond fission occurs, then the nitrogen gas produced will have precisely the same abundance ratios 29/30 and 29/28 as those calculated for the hydrazine mixture with $29/30 \times 29/28 \neq 4$. This is the situation when the 4e oxidants IO_3^-, Tl(III), or $Fe(CN)_6^{3-}$ are used:

$$N_2H_4 \xrightarrow{-4e} N_2$$

and this means that, for example, postulated bimolecular schemes of the following type are untenable:

$$N_2H_4 \rightarrow H_2N—N \rightarrow H_2N—N{=}N—NH_2 \rightarrow N_2H_4 + N_2$$

With other oxidants, however, less than four equivalents of oxidant per hydrazine molecule are used, and ammonium ion is formed as well as nitrogen. This shows that some nitrogen–nitrogen bond cleavage must occur during the oxidation, the amount of which can be estimated from the extent of approach to the statistical equilibrium ("randomization"). Although the limiting $1e^-$ oxidants of hydrazine are not attained in practice, Ce(IV) closely approaches this behavior; the evolved nitrogen is now almost 50 per cent randomized and a short extrapolation to the ideal $1e^-$ oxidant indicates that in this case half the total nitrogen came from a *single* hydrazine molecule and half from two separate cleaved hydrazine molecules. Clearly, schemes which have been suggested like

$$\mathrm{N_2H_4 \rightarrow NH_2NH \rightarrow NH_2NHNHNH_2 \rightarrow 2NH_3 + N_2}$$

are not valid here either, because this would lead to 100 per cent randomizing. The mechanism suggested from this study involved the initial steps:

$$\mathrm{2H_2NNH_2 \quad \rightarrow \quad 2H_2NNH\cdot \quad \rightarrow \quad H_2\overset{a}{N}{-}\overset{a}{N}H{-}\overset{b}{N}H{-}\overset{b}{N}H_2}$$

Since the middle nitrogens *a* and *b* originate from different hydrazine molecules, loss of terminal NH_2 successively to form ammonia would mean that *complete* randomizing would be expected to occur:

$$\mathrm{H_2\overset{a}{N}{-}\overset{a}{N}H{-}\overset{b}{N}H{-}\overset{b}{N}H_2 \quad \rightarrow \quad H_3\overset{a}{N} \;+\; H\overset{a}{N}{=}\overset{b}{N}{-}\overset{b}{N}H_2}$$

$$\mathrm{H\overset{a}{N}{=}\overset{b}{N}{-}\overset{b}{N}H_2 \quad \rightarrow \quad \overset{a}{N}{\equiv}\overset{b}{N} \;+\; \overset{b}{N}H_3}$$

If, however, the intermediate N_3H_3 underwent tautomerism, rapid compared with the rate of loss of the final ammonia, the nitrogen evolved would in this case

$$\mathrm{H\overset{a}{N}{=}\overset{b}{N}{-}\overset{b}{N}H_2 \;\rightleftharpoons\; H_2\overset{a}{N}{-}\overset{b}{N}{=}\underset{b\;b}{\overset{b}{N}H} \;\rightleftharpoons\; H_3\overset{a}{N} \;+\; \overset{b}{N}{\equiv}\overset{b}{N}}$$

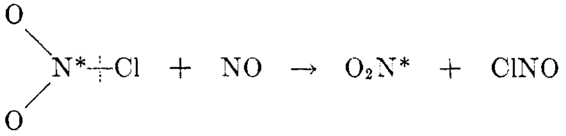
originate from one hydrazine molecule (H_2NNH_2) and the combined behavior would account for the observed 50 per cent randomization only.

Many oxidants such as Fe(III), V(V), and $Cr_2O_7^{2-}$, behave in an intermediate fashion and with simultaneous occurrence of the two types of reaction. In considering its isotopic composition the evolved nitrogen in these cases can be regarded as made up of nitrogen (*a*) unrandomized and (*b*) randomized. A straight-line plot of percentage randomization of nitrogen gas against per cent nitrogen gas by one-electron oxidations (from the oxidant stoichiometry) can be constructed, and the experimental results for various oxidants (using excess, to avoid isotope fractionation effects) are found to lie on this plot with the oxidants iodate ion and Ce(IV) at extreme ends of the line, thereby giving support to the dual mechanism.

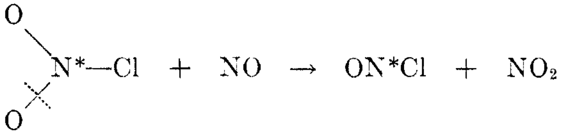
Obviously such an approach is not possible by radioactive tracer methods, since a determination of "fine structure" is necessary by some physical method, such as mass spectrometry.

The randomizing of highly enriched O^{18} oxygen gas by "normal" ozone has been studied by Ogg and Sutphen (363, 364). A very thorough discussion of the experimental methods and of the interpretation of mass-spectrometric examination of products, etc. is included in the paper describing this work (364).

So far the discussion has been concerned only with the detection of bond cleavage. Frequently when more than one mode of breakage is possible, tracer studies can detect the position of bond cleavage. Once again the principle involved here is simple. A reactant molecule is labelled at a particular position and made to react; the pure products, after separation, are analyzed for the tagged atom. To illustrate this point one might consider the reaction between nitryl chloride and nitric oxide, for which two mechanisms may be formulated. Mechanism 1 involves transfer of a chlorine atom, while mechanism 2 involves transfer of an oxygen atom:



(1)



(2)

If the nitryl chloride were tagged with nitrogen, then the tagged nitrogen would appear in one or other of the products depending on whether mechanism 1 or mechanism 2 applied (173). The success of such an experiment must depend on the nonexchange between nitrogen dioxide and nitrosyl chloride and between nitric oxide and nitryl chloride. Three examples taken from widely different researches will be used to illustrate the potentialities of the method.

Bunton and Llewellyn (82) have determined the actual position of bond cleavage in tracer experiments reminiscent of the classical ester-hydrolysis experiments of Polanyi and Szabo (379). The aquation and hydrolysis of acetatopentammino-cobalt(III) ion by O^{18}-enriched reagents produced acetate ion which contained very little O^{18}, proving that only cobalt–oxygen bond fission occurred:

$$H_2O^{18} + [(NH_3)_5Co{\vdots}O\text{—}COCH_3]^{2+} \rightarrow [(NH_3)_5Co(O^{18}H_2)]^{3+} + CH_3COO^- \qquad (S_N1 \text{ or } S_N2)$$

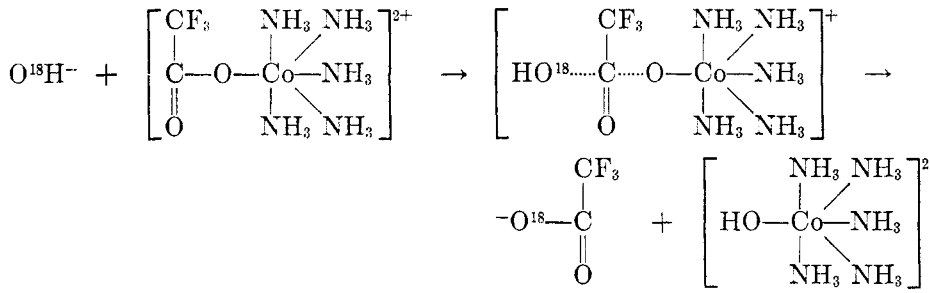
$$O^{18}H^- + [(NH_3)_5Co{\vdots}O\text{—}COCH_3]^{2+} \rightarrow [(NH_3)_5Co(O^{18}H)]^{2+} + CH_3COO^- \qquad (S_N2)$$

With trifluoroacetatopentammino-cobalt(III) ion, by contrast, there was substantially complete fission of the carbon–oxygen bond in the hydrolysis experiment (but not in the aquation experiments), leading to O^{18}-enriched trifluoroacetate (of content *about* 50 atom per cent from the water):

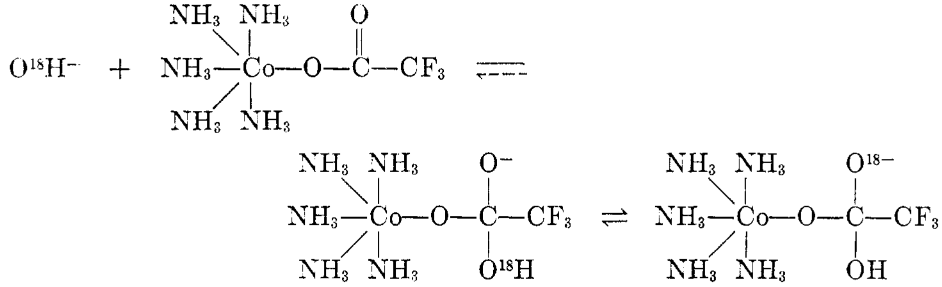
$$O^{18}H^- + [(NH_3)_5Co\text{—}O{\vdots}COCF_3]^{2+} \rightarrow [(NH_3)_5Co(OH)]^{2+} + CF_3COO^{18-} \qquad (B_{AC}2)$$

The accuracy of the experiments did not allow a differentiation between two possible bimolecular mechanisms: (I) when one of the two atoms of the isolated carboxylate will be derived from water (50 per cent), and (II) involving formation of a short-lived intermediate which will incorporate a small amount of O^{18} and lead to a carboxylate containing slightly more than 50 per cent isotopic abundance of water.

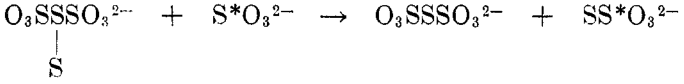
Mechanism I:



Mechanism II:



An experiment which throws light not only on the mode of bond fission but also on the structure of one of the reactants involves the reaction between tetrathionate and sulfite ions to form trithionate and thiosulfate ions, first studied and discussed by Christiansen and Drost-Hansen (98). If the tetrathionate structure contained a branched sulfur chain, then treatment of inactive tetrathionate with active sulfite would be expected to lead to active thiosulfate:



$$\underset{\displaystyle S}{O_3S\underset{|}{S}SO_3^{2-}} + S^*O_3^{2-} \rightarrow O_3SSSO_3^{2-} + SS^*O_3^{2-}$$

and not, as is observed, to inactive thiosulfate (98).

$$O_3SSSSO_3^{2-} + S^*O_3^{2-} \rightarrow O_3SSS^*O_3^{2-} + SSO_3^{2-}$$

This result is best explained by a nucleophilic displacement of a thiosulfate group in the linear nonbranched polythionate ion by a sulfite ion, as suggested by Foss (172). The possibility that the middle sulfur atoms are labile (as they are in certain alkyl polysulfides including diethyl tetrasulfide (205, 206)) and form thiosulfate with active sulfite is also ruled out by this experiment. Later Fava and Divo (159) confirmed these results in a more extensive study in which specifically labelled tetrathionate was decomposed by inactive sulfite and the actual position of activity in the trithionate determined by mild alkaline decomposition:

$$2SS^*O_3{}^{2-} \xrightarrow{I_2} O_3S^*SSS^*O_3{}^{2-}$$

$$O_3S^*SSS^*O_3^{2-} + SO_3^{2-} \rightarrow O_3S^*SSO_3^{2-} + SS^*O_3^{2-}$$

$$SS^*O_3^{2-} + 2Ag^+ + H_2O \rightarrow Ag_2S + H_2S^*O_4$$

$$2O_3S^*SSO_3^{2-} + 2OH^- \rightarrow O_3S^*S^{2-} + O_3SS^{2-} + S^*O_4^{2-} + SO_4^{2-} + 2H^+$$

A final, more complicated example is the reaction between hydrazoic and nitrous acids to give nitrous oxide and nitrogen (104).

$$H\overset{a}{N}\overset{b}{N}\overset{a}{N} + H\overset{c}{N}O_2 \rightarrow \overset{a}{N}\overset{c}{N}O + \overset{a}{N}\overset{b}{N} + H_2O$$

Although it is apparent in this case how the bond cleavage might occur to give the desired products, tracer methods provide a unique solution to this problem. The nitrogens of hydrazoic acid and of nitrous oxide are nonequivalent and do not undergo intramolecular exchange reactions (103, 106). There are three parts to the study:

(*a*) The reaction between $NaN^{15}O_2$ (containing 3.28 per cent N^{15}) and inactive NaN_3 (normal N^{15} content = 0.37 per cent) was initiated by adding 5 per cent acetic acid solution, and the evolved nitrous oxide was converted to nitrogen gas by burning with excess hydrogen catalytically on platinum. The nitrous oxide had enriched N^{15}, while the nitrogen gas had normal nitrogen.

$$HNNN + HN^{15}O_2 \rightarrow N_2^{15}O + N_2$$

1.82 0.37 exptl.% N^{15} content

$$\frac{0.37 + 3.28}{2} = 1.83 \text{ (calculated)}$$

(*b*) Inactive $NaNO_2$ and $KN^{15}NN^{15}$ (containing 1.52 per cent N^{15}) were mixed and reacted as before. Both the nitrous oxide and the nitrogen gas contain N^{15}:

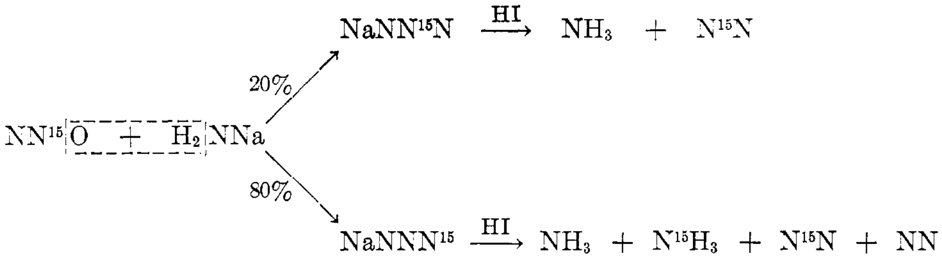
$$HN^{15}NN^{15} + HNO_2 \rightarrow N_2^{15}O + N_2^{15}$$

0.95 0.97 exptl. % N^{15} content

$$\frac{1.52 + 0.37}{2} = 0.95 \text{ (calculated)}$$

These experiments indicate that the middle nitrogen atom (*b*N) of the hydrazoic acid is always found in the nitrogen gas.

(*c*) A third and final experiment is necessary to find which of the two nonequivalent nitrogen atoms of nitrous oxide is enriched or whether there is even uniform labelling. In experiments (*a*) and (*b*) only a gross "tracing" of the nitrous oxide has been attempted. The actual location is accomplished by reacting purified nitrous oxide (obtained from $NaN^{15}O_2$ and NaN_3) with sodium amide, when the known isotopic reaction (already examined by Clusius (103, 106)) occurs:



The isotopic composition of the azide formed is determined by reduction to ammonia and nitrogen with hydrogen iodide and subsequent analysis (106). It might have been expected that only $NaNN^{15}N$ would have been formed from the reaction of $NN^{15}O$ with sodium amide, but surprisingly this is not the case, a fact only established by tracer studies of this kind. Therefore only $NN^{15}O$ is formed from reaction (*c*) and the nitrogen–oxygen bond remains intact throughout. The results are therefore in agreement with the equation first given and the postulated mechanism is reasonable.

$$\overset{a}{N}\overset{b}{N}\overset{a}{N}^- + \overset{c}{N}O^+ \rightleftharpoons \overset{a}{N}\overset{b}{N}\overset{a}{N}\overset{c}{N}O \rightarrow \overset{a}{N}\overset{b}{N} + \overset{a}{N}\overset{c}{N}O$$

Clusius has reviewed his work using N^{15}, which consists mainly of examples from organic chemistry but includes discussion of the techniques involved (101).

B. DETERMINATION OF MOLECULAR STRUCTURE

The observation of tracer movement through a chemical reaction or sequence of chemical reactions can give information on the structure of an intermediate which may or may not be stable. When the intermediate is a stable chemical substance, this method forms the basis of the frequently used determination of the equivalence or nonequivalence of atoms in a molecule by synthesis and decomposition. The structures of disulfur trioxide and nickel cyanide, for example, have been investigated by this means.

If dry sulfur, containing S^{35}, is added to excess liquid sulfur trioxide and the blue-green solid obtained ($S_2^{35}O_3$) is decomposed by adding dioxane, radioactive sulfur is re-formed with similar specific activity as the original in addition to the inactive compound of sulfur trioxide with dioxane.

TABLE 13

Analysis of reaction products from $N_2^{15}O$

		Calculated for $NN^{15}O$	Calculated for $N^{15}NO$	Calculated for 1:1 Mixture
Per cent N^{15} in N_2 (found)	1.21	1.24	1.68	1.46
Per cent N^{15} in NH_3 (found)	1.55	1.53	0.66	1.10
Total per cent N^{15}	3.96	4.02	4.02	4.02

$$S^{35} + SO_3 \rightarrow S^{35}SO_3 \xrightarrow{\text{dioxane}} S^{35} + SO_3\cdot\text{dioxane}$$

This provides strong evidence for an unsymmetrical formula for S_2O_3 (23). The structure SSO_3^{2-} was assigned to the thiosulfate ion in a related manner (18).

Although an attempt to study the exchange of Ni^{*2+} with $Ni(CN)_4^{2-}$ was thwarted by rapid precipitation of nickel cyanide, Long (308) has cleverly used this interaction to show that the latter most probably has the structure $NiNi(CN)_4$. Nickel^{63} chloride solution was mixed with potassium tetracyanonickelate at pH 4–8 and the resultant suspension of nickel cyanide treated with excess alkaline dimethylglyoxime. The nickel dimethylglyoxime obtained had the same specific activity as the original nickel and this was explained on the following basis:

$$Ni^{*2+} + Ni(CN)_4^{2-} \rightarrow Ni^*Ni(CN)_4$$

$$Ni^*Ni(CN)_4 + 2Me_2GH \rightarrow Ni^*(Me_2G)_2 + Ni(CN)_4^{2-} + 2H^+$$

A more complicated example of tracer synthetic and degradative studies affording insight into the structure of an inorganic molecule is the work of Goehring and Ebert (189). The four sulfur atoms of sulfur nitride, S_4N_4, were shown to be equivalent, in agreement with either the "cradle-like" structure involving many resonance forms (332) or the "cage-like" structure based on infrared and Raman spectra (304). Briefly the method involved the formation of sulfur nitride from S(II)- and S*(IV)-containing compounds and its subsequent degradation to an S(II) and an S(IV) compound. The equilibration of sulfur activity in the final products confirmed the equivalence of the sulfur atoms in S_4N_4.

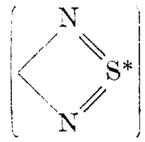
Sulfur nitride was prepared from the quantitative reaction in pyridine between thiazyl chloride $(ClS^*N)_3$ and inactive tetrasulfur tetraimide $(SNH)_4$:

$$4(ClS^*N)_3 + 3(SNH)_4 \rightarrow 6S_4^*N_4 + 12HCl$$

The specific activity of the sulfur nitride was one-half of that of the original thiazyl chloride (both assayed as barium sulfate). The decomposition of sulfur nitride into two sulfur compounds was effected in two different ways:

(1) $$N_4S_4^* + PbI_2 \xrightarrow{\text{liquid NH}_3} Pb(N{=}S^*)_2$$

$$N_4S_4^* + HgI_2 \xrightarrow{\text{liquid NH}_3} Hg$$



(2) $$N_4S_4^* + 4C_5H_{10}NH \rightarrow 2(C_5H_{10}N)_2S^* + 2S^*({=}N{-}H)_2$$

In both cases the two products had the same specific activity, once again in terms of barium sulfate after oxidation. Table 14 lists molecular structures that have been investigated by the methods outlined in this section.

The value of tracers in throwing light on even the structure of an unstable intermediate in a chemical reaction is well illustrated by the work of Taube and

TABLE 14

Synthesis and decomposition tracer experiments

Reactants	Intermediate	Mode of Decomposition and Products	Remarks	References
$CuBr(s) + \frac{1}{2}Br_2^*(g)$	$CuBr_2^*(s)$	Heat; $CuBr^*(s) + \frac{1}{2}Br_2^*(g)$		(381)
$AuBr(s) + Br_2^*(l)$	$AuBr_3^*(s)$	Heat; $AuBr^*(s) + Br_2^*(g)$		(381)
$HgI_2 + 2I^{*-}$	HgI_4^{*2-}	Ag^+; heat; $HgI_2^* + 2AgI^*$		(380)
Plumbite* + plumbate	$Pb_3^*O_4$	Boiling KOH solution; plumbite* + plumbate	Lead atoms are unequivalent	(157)
		Dilute HNO_3; plumbite* + plumbate*	Dilute HNO_3 induces exchange (*cf.* 491)	(157)
$Tl^{*3+} + 3Tl^+ + 6Cl^-$ (or Br^-)	$2Tl_2^*Cl_6$ (or $Tl_2^*Br_6$)	$Tl^{*3+} + 3Tl^+$	Thallium atoms are unequivalent	(324)
$PBr_3(l) + Br_2^*(l)$	$PBr_5^*(s)$	Heat; $PBr_3^*(l) + Br_2^*(g)$		(96, 381)
$Sb^{5+} + Sb^{*3+}$	$M_2Sb^*Cl_6$	$Sb^{*5+} + Sb^{*3+}$	Fast Sb^{III}-Sb^{V} electron transfer interferes	(457)
$S^* + SO_3$	$S_2^*O_3$	Treat with dioxane; $S^* + SO_3$ dioxane	Support for $S = SO_3$	(23)
$S^* + (C_2H_5)_2S_2$	$(C_2H_5)_2S_3^*$	NaOH; $S^* + (C_2H_5)_2S_2$	S—S links in $(C_2H_5)_2S_3$	(206)
$S^* + SO_3^{2-}$	$S_2^*O_3^{2-}$	Silver salt heated in water (18) or heated 5.5 hr. (125°) in acid (14); $Ag_2S^* + SO_4^{2-}$ or $S^* + SO_2$	Sulfur unequivalent in thiosulfate	(14, 18)
$(ClS^*N)_3 + S_4N_4H_4$ or $(ClS^*N)_3 + S_7NH$	$S_4^*N_4$	Treated with PbI_2 and liquid NH_3 gives $Pb(N{=}S^*)_2$ Treated with HgI_2 and liquid NH_3 gives $Hg(N_2S^*)$ Treated with $C_5H_{11}N$ gives $(C_5H_{10}N)_2S^* + S^*(NH)_2$	N_4S_4 contains equivalent sulfur atoms	(189)
$S_4N_4 + S^*O_3$	$S_3^*N_2O_6$	Hydrolysis; inactive SO_2	Activity of $S_3N_2O_6$ is two-thirds that of the original; shows that $2SO_3$ enter $S_3N_2O_5$; hydrolysis result supports cyclic structure for $S_3N_2O_6$	(191)
$Cr_2^*(SO_4)_3 + CrO_4^{2-}$	Solid with $Cr^{3+}:CrO_4^{2-}$ ratio = 2:1	$HClO_4$; $Cr_2^*(SO_4)_3 + CrO_4^{2-}$	At no stage are the chromium atoms equivalent	(27)
$Ni^{*2+} + Ni(CN)_4^{2-}$	$Ni^*(CN)_2$	Dimethylglyoxime (Me_2GH); $Ni^*(Me_2G)_2 + Ni(CN)_4^{2-}$	Supports $NiNi(CN)_4$ structure for $Ni(CN)_2$	(308)

Dodgen (447) and of Bothner-By and Friedman (61), both being good examples of the method and reasoning involved.

The reaction between chlorite and chlorine at neutral pH is very fast and goes virtually to completion (at this pH chlorine exists mostly as hypochlorite and chloride)

$$\mathrm{HOCl} + 2\mathrm{ClO_2^-} \rightarrow 2\mathrm{ClO_2} + \mathrm{Cl^-} + \mathrm{OH^-}$$

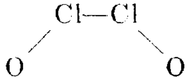
and

$$\mathrm{HOCl} + \mathrm{ClO_2^-} + \mathrm{OH^-} \rightarrow \mathrm{ClO_3^-} + \mathrm{Cl^-} + \mathrm{H_2O}$$

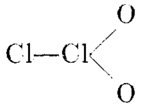
Chlorate ion is appreciably reduced by chloride ion in strong acid in the fairly rapid reaction

$$2\mathrm{Cl^-} + 2\mathrm{ClO_3^-} + 4\mathrm{H^+} \rightarrow \mathrm{Cl_2} + 2\mathrm{ClO_2} + 2\mathrm{H_2O}$$

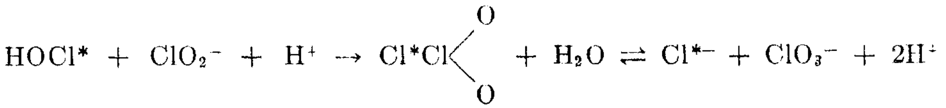
In both cases when labelled chlorine or labelled chloride, respectively, is used, the chlorine dioxide evolved only contains ~6 per cent of the activity expected if random distribution of the activity amongst all the chlorine atoms had occurred (447). The fact that the chlorine atoms of the two reactants for the most part remain distinct indicates that the major path is *not* via a symmetrical intermediate



or OCl but via an unsymmetrical one, e.g.,

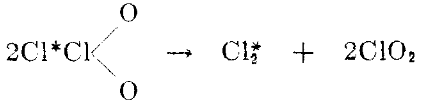


The very similar departure from ideality (which would be 0 per cent activity in chlorine dioxide) in both cases strongly suggests that a common intermediate is involved. An explanation which satisfies these observations and is in agreement with the observed kinetics of the chloride–chlorate reaction is:



$$\mathrm{HOCl^*} + \mathrm{ClO_2^-} + \mathrm{H^+} \rightarrow \mathrm{Cl^*ClO_2} + \mathrm{H_2O} \rightleftharpoons \mathrm{Cl^{*-}} + \mathrm{ClO_3^-} + 2\mathrm{H^+}$$

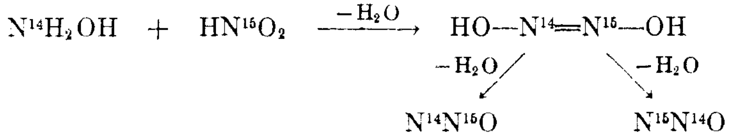
followed by



$$2\mathrm{Cl^*ClO_2} \rightarrow \mathrm{Cl_2^*} + 2\mathrm{ClO_2}$$

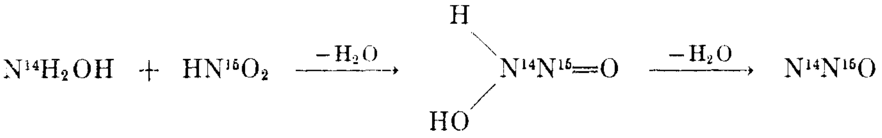
A prerequisite for the success of such an experiment is the demonstration that $\mathrm{ClO^-}$ and $\mathrm{ClO_2^-}$ (447), $\mathrm{Cl_2}$ and $\mathrm{ClO_3^-}$ (447), $\mathrm{Cl_2}$ and $\mathrm{ClO_2}$ (132), $\mathrm{ClO_3^-}$ and $\mathrm{ClO_2}$ (132), $\mathrm{ClO_2}$ and $\mathrm{Cl^-}$ (132) do not exchange to complicate the interpretation.

The mechanism of the reaction between nitrous acid and hydroxylamine to form nitrous oxide has been investigated using both N^{15} and O^{18} stable isotopes (61). This study affords a good illustration of the method of assignment of spectrometer mass numbers to particular isotopic species and the care with which this must be carried out. The results showed that when $NH_2OH \cdot HCl$ was mixed with sodium nitrite containing N^{15}, the small amount of $N^{15}N^{15}O$ produced indicated that no "randomizing" had occurred. Reaction via (say) nitroxyl, NOH (which has been a postulated intermediate), could therefore be excluded, since such an intermediate would mean that the two nitrogens of nitrous oxide would have originated randomly from the two starting nitrogen compounds. The excess N^{15} was approximately equally distributed between $N^{15}N^{14}O$ and $N^{14}N^{15}O$, so that the nitrogen atoms originated one from NH_2OH and one from NO_2^- and a symmetrical intermediate, probably hyponitrous acid, is involved:



$$N^{14}H_2OH + HN^{15}O_2 \xrightarrow{-H_2O} HO{-}N^{14}{=}N^{15}{-}OH$$
$$\xrightarrow{-H_2O} N^{14}N^{15}O \qquad \xrightarrow{-H_2O} N^{15}N^{14}O$$

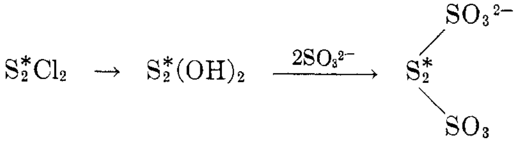
The reaction at pH = 1 produced about twice the amount of $N^{14}N^{15}O$ compared to $N^{15}N^{14}O$ and a reaction path involving an unsymmetrical intermediate, possibly *N*-nitrosohydroxylamine, is now important:



$$N^{14}H_2OH + HN^{15}O_2 \xrightarrow{-H_2O} \begin{smallmatrix}H\\HO\end{smallmatrix}\!\!>N^{14}N^{15}{=}O \xrightarrow{-H_2O} N^{14}N^{15}O$$

By concurrently studying this acid reaction in H_2O^{18}, it was shown that approximately all of the excess oxygen was found as $N^{14}N^{15}O^{18}$ and $N^{14}N^{14}O^{18}$ and little, if any, as $N^{15}N^{14}O^{18}$. Because of this result, rapid O^{18} exchange could not have occurred between NH_2OH and H_2O or $H_2N_2O_2$ and H_2O, and O^{18} most probably entered the $N^{14}N^{15}O^{18}$ molecule via exchange between $HN^{15}O_2$ or $H_2ONN^{15}O$ and H_2O. Thus from this work information regarding mechanism, the structure of intermediates, and exchange processes was obtained, combining several important principles.

Finally some recent Russian work on the formation of tetrathionate using radiosulfur (66) demonstrates the advantage of labelled atoms in the elucidation of mechanism. The example is deliberately chosen in order to show the methods available for establishing the exact location of tagged atoms in a molecule, a particularly important consideration with polyatomic molecules. Potassium tetrathionate was prepared from S^{35}-tagged S_2Cl_2 and inactive sulfur dioxide. The tetrathionate had a specific activity of sulfur one-half the value of that of the original compound when the original S_2Cl_2 and the tetrathionate were assayed as benzidine sulfate. It is apparent from this result that the two sulfur atoms of S_2Cl_2 have been diluted by two inactive sulfur atoms from two sulfite molecules in agreement with the proposed mechanism:



$$S_2^*Cl_2 \rightarrow S_2^*(OH)_2 \xrightarrow{2SO_3^{2-}} S_2^*\begin{cases}SO_3^{2-}\\ SO_3\end{cases}$$

(1604 counts/ min./mg. S) (818 counts/ min./mg. S)

The distribution of active sulfur within the tetrathionate was determined by using the rapid quantitative reaction with cyanide ion.

$$O_3SS_2^*SO_3^{2-} + 3CN^- + H_2O \rightarrow SO_4^{2-} + S_2^*O_3^{2-} + S^*CN^- + HCN$$

(818 counts/ min./mg. S) (inactive) (812 counts/ min./mg. S) (1560 counts min./mg. S)

and the distribution of active sulfur in the thiosulfate determined by the reaction with silver ion in hot solution:

$$S^*SO_3^{2-} + 2Ag^+ + H_2O \rightarrow Ag_2S^* + H_2SO_4$$

(812 counts/ min./mg. S) (1586 counts/ min./mg. S) (inactive)

The sulfur compounds, after separation, were all converted into sulfate by Carius oxidation and assayed as benzidine sulfate, as before. The reaction with cyanide ion is not complicated by SCN^--$S_2O_3^{2-}$ exchange (66), and although $S_4O_6^{2-}$–$S_2O_3^{2-}$ exchange is rapid (158) it occurs only by intact $S_2O_3^{2-}$ exchange and so cannot affect the activity distribution in the tetrathionate:

$$O_3SS^* \vdots S^*SO_3^{2-} + S^*SO_3^{2-} \rightarrow O_3SS^*S^*SO_3^{2-} + S^*SO_3^{2-}$$

In addition, the two sulfur atoms of thiosulfate are nonequivalent and do not undergo mutual exchange. This stability has been particularly useful in the synthesis of specifically labelled polythionates.

C. SIGNIFICANCE OF ISOTOPE EFFECTS IN UNIDIRECTIONAL REACTIONS

That the reaction rate of a heavier isotopic molecule should differ from that of the parent molecule may be seen from an inspection of the Arrhenius equation:

$$k = Ae^{-E/RT} \tag{53}$$

The preëxponential factor, related in the simple collision theory to the collision number of a molecule, will be reduced on isotopic substitution. Isotopic substitution will also cause a reduction in the fundamental vibrational frequencies with a consequent lowering of the zero-point energy of the isotopic molecule. For most reactions this results in a higher activation energy for the heavier isotopic molecule (see the recent review by Wiberg (475)). Since for all common elements the tracer isotope is heavier than the parent isotope, the tracer molecule usually reacts more slowly than the unlabelled molecule. As for exchange reactions, this is most serious for elements of atomic weight less than about 40. A knowledge of the magnitude of isotope effects is important in interpreting quantitative tracer results and can lead to valuable conclusions regarding mechanism.

In accordance with current convention, a ratio of isotopic reaction rates will be defined as:

$$\epsilon = \frac{\text{reaction rate of the tracer molecule}}{\text{reaction rate of the parent molecule}} = \frac{k^*}{k} \tag{54}$$

If a difference in reaction rates does exist, ϵ normally will be less than unity. The isotope effect in a unidirectional reaction will be defined as $100(1 - \epsilon)$; i.e., if $\epsilon = 0.85$, a "15 per cent isotope effect" will be operative.

In unidirectional reactions, care must be taken to distinguish between "intermolecular" and "intramolecular" isotope effects. The decomposition of C^{13}-labelled nickel carbonyl (41, 42) involves the following alternative rate-determining steps:

$$\mathrm{Ni(CO)_4} \xrightarrow{k_1} \mathrm{Ni(CO)_3\cdot} + \mathrm{CO}$$

$$\mathrm{Ni(CO)_3C^*O} \xrightarrow{k_2} \mathrm{Ni(CO)_3\cdot} + \mathrm{C^*O}$$

$$\mathrm{Ni(CO)_3C^*O} \xrightarrow{k_3} \mathrm{Ni(CO)_2C^*O\cdot} + \mathrm{CO}$$

The intermolecular isotope effect ($\epsilon = 4k_2/k_1$) evaluates the relative rates of decomposition of a labelled and an unlabelled nickel carbonyl molecule. (The factor of 4 must be included, since with tracer concentrations of C^{13}, each labelled nickel carbonyl molecule will only contain one isotopic atom.) Furthermore, within an individual labelled molecule there is the possibility that either labelled or unlabelled carbon monoxide will split off and the intramolecular isotope effect will be $\epsilon = 3k_2/k_3$. The intramolecular isotope effect therefore evaluates the relative probability of rupture of a C^{12}—C^{13} bond compared to a C^{12}—C^{12} bond.

1. Theory of isotope effects in unidirectional reactions

Wiberg (475) has already described the theoretical treatment by Bigeleisen of isotopic reaction rates and a summary only will be given here. For the reaction:

$$\mathrm{AB} \longrightarrow \text{products}$$

$$\mathrm{AB^*} \longrightarrow \text{products}^*$$

where the asterisk denotes the molecule substituted with the heavy (tracer) isotope, the ratio of rate constants is given by:

$$\frac{k}{k^*} = \frac{\kappa}{\kappa_*}\,\frac{\sigma}{\sigma_*}\,\frac{\sigma_*^\ddagger}{\sigma^\ddagger}\,\frac{Q^\ddagger}{Q_*^\ddagger}\,\frac{Q_*}{Q}\left(\frac{\mu_*}{\mu}\right)^{1/2} \tag{55}$$

where κ = the relevant transmission coefficient,
σ = the symmetry number,
μ = the effective mass of the activated complex along the coördinate of decomposition,

Q = the complete partition function for unit volume, and
‡ refers to the activated state.

Setting the ratios of both transmission coefficients and symmetry numbers to unity and neglecting the "tunnel effect" (valid for isotopes other than hydrogen isotopes above 0°C.), the simplified equation is obtained:

$$\frac{k}{k^*} = \left(\frac{\mu_*}{\mu}\right)^{1/2} \{1 + \sum_i G(u_i)\Delta u_i - \sum_i G(u_i^\ddagger)\Delta u_i^\ddagger\} \qquad (56)$$

where the function $G(u)$ has already been defined (equation 37). Equation 56 is separable into two factors: (*1*) the "reduced mass effect," evaluating the ratio of the rupture frequencies of the critical bonds within the two isotopic activated complexes; (*2*) the "zero-point energy effect," evaluating the isotopic shift of the equilibrium between reactants and activated complex (i.e., the isotopic equilibrium constant for "exchange" between reactants and activated complex). The reduced masses are usually calculated from the masses of the two atoms joined by the bond undergoing rupture (419). The calculations of the $G(u)$ functions are in principle the same as already described for exchange reactions (q.v.). The vibrational frequencies of the activated complex are of course unknown. The crude approximation is frequently made of setting the force constant of the rupturing bond to zero and leaving all other force constants unchanged; the "vibrational frequencies" of the activated complex can then be calculated by, say, normal valence force equations. The estimation of the isotopic partition-function ratio for the activated complex is the most unsatisfactory feature of the theoretical calculations and must always be remembered in the "comparison of theory and experiment."

For normal reactions involving bond rupture, the force constants of the reactants are greater than those of the activated complex; i.e., $\sum G(u)\Delta u > \sum G(u^\ddagger)\Delta u^\ddagger$. Or, expressed in terms of exchange between reactants and activated complex, the heavier isotope will preferentially concentrate in the reactants which have the higher isotopic partition-function ratio. Hence the reaction rate of the lighter (parent) molecule will be greater than that for the heavier (tracer) molecule. However for reactions in which the rate-determining step is one of ring closure, the force constants of the activated complex may be greater than those for the reactants. Provided

$$\sum G(u^\ddagger)\Delta u^\ddagger > \sum G(u)\Delta u + \tfrac{1}{2} \ln (\mu_*/\mu)$$

the heavier molecule could react faster than the ligher molecule. A "reverse" isotope effect observed in an organic reaction (427a) could not be substantiated (402).

For intramolecular reactions involving the same molecule $\Delta u = 0$ and there is evidence that $\Delta u^\ddagger = 0$ (52). An intramolecular isotope effect is thus solely determined by the reduced mass effect and will be substantially less than intermolecular effects, since the zero-point energy term principally determines the magnitude of k/k^*.

Bigeleisen (49) has calculated "maximum isotope effects" for common isotopes, but these values are based on the admittedly drastic assumption that the activated complex is an assemblage of free atoms. The magnitude of an intermolecular isotope effect can often be roughly estimated from the isotopic partition-function ratios for reactants and products: e.g., in the acidic decomposition of $HC^{14}O_3^-$ to $C^{14}O_2$. The f values for these two molecules are, respectively, 1.451 and 1.397 at 20°C. (440). Since the activated complex would be intermediate in characteristics and allowance should be made for the $(\mu_*/\mu)^{\frac{1}{2}}$ factor, an isotope effect of not greater than 4 per cent might be reasonably predicted. In general, isotope effects in unidirectional reactions will be only slightly greater than those observed or predicted in comparable exchange systems.

2. Practical limitations imposed by isotope effects

If an isotope effect is operative, serious difficulties can arise when a labelled reactant or product is sampled at various stages of a reaction. For the general reaction scheme:

$$A + B \rightarrow X + Y + Z$$

$$A^* + B \rightarrow X^* + Y + Z$$

in which an intermolecular isotope effect is occurring, the specific activity ${}_AS_f$ of reactant A at a fraction of reaction f is related (41, 138, 495) to that at zero fraction of reaction, ${}_AS_0$, by the relation:

$$ {}_AS_f/{}_AS_0 = (1 - f)^{\epsilon - 1} \tag{57}$$

where ϵ is defined by equation 54. Alternatively the specific activity of the labelled product is described (439) by:

$$ {}_XS_\gamma/{}_AS_0 = \epsilon(1 - \gamma)^{\epsilon - 1} \tag{58}$$

where ${}_XS_\gamma$ is the specific activity of a small product increment collected over an interval of reaction γ between fraction of reaction f and $(f + \Delta f)$, whilst ${}_AS_0$ and ϵ retain their previous significance. When the increment γ is small, ${}_XS_\gamma$ will approximate to the specific activity of the product of fraction of reaction f. Figure 1 illustrates the variation in the specific activity of both reactant and product with the fraction of reaction for a 10 per cent isotope effect (a probable value for isotopes of carbon, nitrogen, and oxygen). The fractional product is collected at each 10 per cent of reaction.

A common experimental procedure for isotopic assays involves the conversion of a separated labelled molecule into a more suitable chemical form for assay purposes; e.g., a carbon compound converted to carbon dioxide or barium carbonate. Figure 1 shows that serious errors could arise if (say) the product were sampled in small fractions as reaction was proceeding. A sample collected between 85 per cent and 95 per cent reaction would have a specific activity 20 per cent higher than that of the product collected up to 10 per cent reaction. For the reaction of deuterated water with zinc at 400°C., the error involved in such a procedure has been recently measured experimentally (232). At 50 per cent conversion a correction of 42 per cent must be applied to the observed isotopic

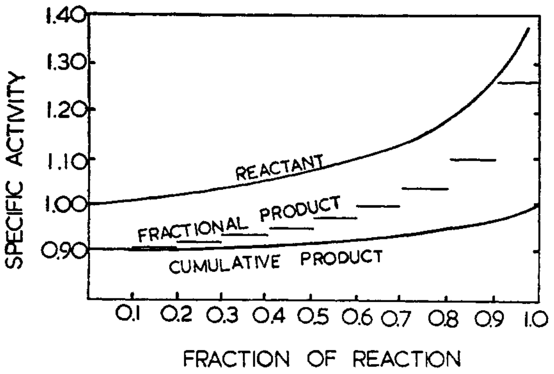


FIG. 1. Variation in the specific activity of both reactant and product with the fraction of reaction for a 10 per cent isotope effect.

abundance of hydrogen. To insure an error of less than 5 per cent in the D/H ratio, at least 99 per cent conversion is necessary. Melander (327) has derived an expression for the specific activity of a reactant as a function of fraction of reaction for the condition that the labelled atom occupies only one of several equivalent positions within the molecule, e.g., in tritium-labelled benzene. The functional form of his relation is completely analogous to equation 57 and indicates that errors due to isotope effects are less the greater the number of equivalent positions within the molecule.

Hence it is an unwise procedure to sample labelled materials at different fractions of reaction unless the magnitude of the isotope effect is known or semiquantitative results only are required. The procedure for overcoming these difficulties is to allow the reaction to proceed to completion, insure that all the labelled product is thoroughly mixed, and then, if desired, divide the product into fractions and proceed with the isotopic assay. The collected total product will of course have the same specific activity as the original reactant. With intramolecular isotope effects, the specific activity of the two labelled products will still differ when these products are completely collected. The interpretation of isotopic assays of samples derived from an intramolecular reaction must be subject to these limitations. The magnitude of the error will, however, be less than that for intermolecular effects.

3. Determination and interpretation of isotope effects

As a minimum, the observation of an isotope effect in a reaction indicates that rupture of a bond to the isotopic atom is involved in the rate-determining step. This step is of course the slowest one involving the isotopic molecule. Especially if a labelled solvent is used, the slowest step for the solvent may not necessarily be the rate-determining step for the overall reaction mechanism. Should it be possible to compare a calculated isotope effect with an accurately measured value, then further valuable conclusions can be drawn as to the more detailed structure of the activated complex and the possible importance of pre-equilibria.

With deuterium compounds it is possible to measure the rate of reaction of a completely deuterated compound and compare this with the reaction rate of the normal compound. Thus a recent study of the Fe^{++}–Fe^{+++} exchange system in deuterium oxide showed that the exchange rate was half of that in ordinary water (245). The direct participation of water in the activated complex and the rate-determining rupture of an oxygen–hydrogen bond is therefore indicated. Similarly, the rates of hydrolysis of either $Co(ND_3)_5Cl^{2+}$ in water or of $Co(NH_3)_5Cl^{2+}$ in deuterium oxide are approximately half the corresponding rate for $Co(NH_3)_5Cl^{2+}$ in water (6). This is confirmatory evidence for the preëquilibrium:

$$Co(NH_3)_5Cl^{2+} + OH^- \rightleftharpoons Co(NH_3)_4(NH_2)Cl^+ + H_2O$$

already indicated from nontracer studies (183) and the observation of isotopic exchange of hydrogen (6). With all radiotracers and many stable tracers it is impracticable to measure the reaction rate of a pure isotopic molecule, and to measure isotope effects recourse must be made to a differential method based on equations 57 and 58 or suitable analogs. Equation 58 shows that a rapid method of estimating ϵ is to determine the specific activity of the product for the first few per cent of reaction and compare this with the initial specific activity of the reactant; the ratio of these two specific activities is then equal to ϵ. This approach is very useful in preliminary work designed to ascertain the magnitude of a possible isotope effect (403), but it can be difficult experimentally if the reaction under study is at all rapid. A more accurate procedure is to sample the reactant or product at definite fractions of reaction and determine ϵ from an appropriate log-log plot. If the specific activity of accumulated product at a definite fraction of reaction (${}_{X}S_f$) is compared with the initial specific activity of reactant (${}_{A}S_0$), ϵ is given by the expression:

$$\epsilon = \ln (1 - rf)/\ln (1 - f) \qquad (59)$$

where $r = {}_{X}S_f/{}_{A}S_0$ (427). For an intramolecular reaction the ratio of specific activities of the two alternative products at complete reaction is equal to ϵ.

Differences in reaction rates of Li^7 and Li^6 isotopes have been detected. Repetitive precipitation of lithium carbonate from concentrated lithium chloride solutions altered the Li^7/Li^6 ratio from 12.48 to 14.03 (463). A single partial precipitation of the carbonate alters the ratio from 12.87 to 13.07 and slightly less for the orthophosphate (92). Cameron (92) points out that such isotope effects could affect the determination of the atomic weight of lithium by Richards and Willard (393), who purified their lithium salts by several partial precipitations of lithium fluoride. The importance of these effects is shown by the variation in the Li^7/Li^6 ratio from 12.44 to 12.93 for commercial chemicals and 12.47 to 12.72 for minerals (92).

The heterogeneous combustion of carbon monoxide between 560°C. and 700°C. exhibits the rate ratios $k^{13}/k^{12} = 0.984 \pm 0.002$ and $k^{14}/k^{12} = 0.959 \pm 0.004$ (29). On the assumption that adsorption is the rate-controlling step, it was shown that the relative rates of adsorption for isotopic molecules would be given by:

$$\frac{v_2}{v_1} = \left(\frac{m_1}{m_2}\right)^{\frac{1}{2}} e^{-(E_2-E_1)/kT} \simeq \left(\frac{m_1}{m_2}\right)^{\frac{1}{2}} \tag{60}$$

for a small difference in zero-point energies ($E_2 - E_1$) and a high temperature. The predicted rate ratios are then 0.983 for $C^{13}O$ and 0.966 for $C^{14}O$, values which agree well with those observed. (This ratio of adsorption rates also follows from the classical collision frequencies of the molecules with the vessel walls, neglecting any difference in the activation energies for adsorption.) On the other hand the homogeneous combustion of carbon monoxide at 580°C. exhibits no isotope effect. For the mechanism

$$CO + O_3 \rightarrow CO_2 + O + O$$

$$O + O_2 \rightarrow O_3$$

the activated complex was treated as O—C···O—M, where $M \equiv O_2$ is a point mass. The Bigeleisen equation thereby predicts no measurable isotope effect.

The intermolecular isotope effect in the decomposition of C^{13}-labelled nickel carbonyl (vide supra) is expressed by the relation

$$k_1/4k_2 = 1.0481 - 6.7 \times 10^{-5}t\ (°C). \tag{61}$$

between 30°C. and 105°C. (42). In the theoretical calculation of the effect Bernstein (42) considered the vibrational frequencies of the activated complex to be identical with those of the reactant molecule except those involving stretching of the ruptured bond; these frequencies were assumed to be zero. The calculated value is substantially greater than the experimental but if slight weakening of the carbon–oxygen bond in the activated complex is considered, better agreement is obtained. Bernstein points out that whilst a measured isotope effect may help to establish certain allowable properties of the activated complex, it cannot reveal the individual importance of single vibrations in a multi-atom activated complex.

As more confidence is gained in the theoretical prediction of isotope effects, then the measurement of isotope effects may become a useful tool in discriminating between possible mechanisms or elaborating already postulated mechanisms. Fry and Calvin (181) found isotope effects of 2.7 per cent and 5.5 per cent for the decomposition of C^{13}- and C^{14}-labelled oxalic acid at 103°C. The authors show that it is necessary to postulate an acid-base equilibrium before the rate-determining step to obtain calculated isotope effects of 3.1 per cent and 6.0 per cent. Had this preëquilibrium been neglected, the predicted effects would have been 3.8 per cent and 7.2 per cent. No C^{14}-isotope effects have been observed in the acidic decomposition of carbonatotetramminocobaltic nitrate (439), the pyrolysis of carboxyl-labelled lithium acetate at 490°C. (398), or the decarboxylation of barium adipate at 350°C. (54). The thermodecomposition of mercury formate at 80°C. (403) exhibits a measurable isotope effect.

Isotope effects should be useful in identifying a particular process or distinguishing between processes in catalytic reactions. The isotope effect will be characteristic of a particular process at a given temperature, whereas kinetic data such as rate constants and activation energies are composite quantities involving many variables. The reduction of hydrogen peroxide by Ti(III) exhibits an O^{18} isotope effect of only 0.5 per cent at 5°C., whereas reduction by Sn(II), Fe(II), Cr(II), and Cu(I) causes effects of 6 per cent (88). Reduction by Ti(III) was postulated to involve a $1e^-$ change, but the other reducing agents were assumed to proceed predominantly via a $2e^-$ change. For the latter the oxygen–oxygen bond is supposed to be completely severed in the activated complex, thereby leading to a calculated maximum isotope effect of 6.1 per cent. For $1e^-$ reduction the oxygen–oxygen bond is merely loosened; a zero-point energy effect will persist in the activated complex and a small isotope effect should result. That the isotope effect for the Fe^{3+}-catalyzed decomposition of hydrogen peroxide is the same as for the Fe(II) reduction is adduced in favor of a mechanism involving Fe(II) as a reduction intermediate rather than HO_2 in the former reaction. The O^{18}-isotope effect in the oxidation of hydrogen peroxide decreases with the mass of the halogen oxidant: I_2, 2.4 per cent; Br_2, 1.3 per cent; Cl_2, 1.0 per cent.

In the photolysis of hydrogen peroxide two mechanisms may be proposed:

Mechanism I:

$$H_2O_2 + h\nu \rightarrow 2OH \tag{1}$$

$$OH + H_2O_2 \rightleftharpoons HO_2 + H_2O \tag{3}$$

$$2HO_2 \rightleftharpoons H_2O + O \tag{4}$$

Mechanism II:

$$H_2O_2 + h\nu \rightarrow H_2O + O \tag{1'}$$

$$O + H_2O_2 \rightleftharpoons OH + HO_2 \tag{2}$$

The O^{18}-isotope effect for the production of water varies with acidity from 1.1 per cent to 1.9 per cent. Hunt and Taube (255) favor mechanism II, since although no variation in isotope effect should occur with acidity in the primary absorption process, reaction 2 could be rewritten as

$$O^* + OOH^- \rightleftharpoons O^*O + OH^-$$

thereby introducing an exchange equilibrium which could account for the observed variation in the isotope effect.

Bernstein and Pars (45) have studied the O^{18}-isotope effect in the reaction of hydroxide ion with Hg^{2+}_{aq} and Ag^{+}_{aq}. The fractionation factor $\alpha = (O^{16}/O^{18})_{oxide}/$

TABLE 15

Tritium isotope effects in the isomerization of cyclopropane

Gas pressure (mm.)	0.4	45	77	80	700
100(1 − ε) (equation 54)	0.4	8.9	7.9	8.8	12.9
Experimental error	1.0	—	1.1	1.7	2.7

TABLE 16

Chemical reactions studied by tracer methods

Reaction studied	Distribution of tracer products	Remarks	References
Nitrogen			
$N_2^*H_4$ oxidation with IO_3^-, Tl(III), and $Fe(CN)_6^{3-}$	N_2 nonrandomized	No N—N bond fission during oxidation	(89, 239)
$N_2^*H_4$ oxidation with Ce(IV), Fe(III), Fe(III)-Cu(II) mixtures, Ce(IV)-Cu(II) mixtures, V(V), MnO_4^-, and $Cr_2O_7^{2-}$	N_2 partly randomized (+ NH_3)	Partial N—N bond fission, the amount depending on the oxidizing agents	(89, 239)
N_2H_4 heated ($5N_2H_4 \rightarrow 6NH_3 + 2N_2 + H_2$)	N_2 partly randomized	Partial N—N bond fission in agreement with postulated free-radical mechanism	(389)
$N^*H_2CON^*H_2$ treated with hypobromite	N_2 nonrandomized	Unimolecular mechanism; both nitrogen atoms of N_2 from one urea molecule	(467)
N^*H_3 oxidized with OBr^- in presence of N_2H_4 or NH_2OH ($2NH_3 + 3OBr^- \rightarrow N_2 + 3H_2O + 3Br^-$)	No $N_2^*H_4$ or N^*H_2OH	N_2H_4 or NH_2OH probably not intermediate in reaction or in side production of N_2O (*cf.* 107) or NO_3^- (102)	(396)
$H\overset{a}{N}\overset{b}{N}\overset{a}{N} + H\overset{c}{N}O_2$	$\overset{a}{N}\overset{c}{N}O + \overset{a}{N}\overset{b}{N}$	Detection of position of bond cleavage	(104)
$Na\overset{a}{N}H_2 + O\overset{b}{N}\overset{c}{N}$	$Na\overset{a}{N}\overset{b}{N}\overset{c}{N}$ (20%) and $Na\overset{a}{N}\overset{c}{N}\overset{b}{N}$ (80%) + $\overset{a}{N}H_3$		(103)
$NH_2NH_2 + C_2H_5ON^*O$	$[NNN^*]^-$	Product used in subsequent experiments	(106)
$HNNN^*$ acid reduction	$\frac{1}{2}N_2 + \frac{1}{2}N^*H_3$ and $\frac{1}{2}N_2^* + \frac{1}{2}NH_3$	Central and outer nitrogens different; ring structure for azide grouping ruled out	
$HNNN^*$ alkaline aluminum reduction	$\frac{1}{2}N_2H_4 + \frac{1}{2}N^*H_3$ and $\frac{1}{2}N_2^*H_4 + \frac{1}{2}NH_3$		(106)
$HNNN^*$ acid permanganate oxidation	$\frac{1}{2}HN^*O_3 + \frac{1}{2}N_2 + \frac{3}{2}H_2O$ $\frac{1}{2}HNO_3 + \frac{1}{2}NN^* + \frac{3}{2}H_2O$ (+ by-product N_2O)		
$NH_2SO_3H + HN^*O_3$	ON^*N		(103)
$NH_2OH \cdot HCl + NaN^*O_2$	No randomizing of N_2O obtained	NOH intermediate ruled out	(61)
(Natural pH)	N^*NO and NN^*O in similar amounts	Symmetrical intermediate	(61, 103)
(pH 1)	$[NN^*O] > [N^*NO]$	Unsymmetrical intermediate also involved in two reaction paths	(61)
$NaN^*O_2 + (NH_4)_2SO_4$ (99% N^{15})	NN^* (97.3%); no randomizing	Both nitrogen atoms of N_2 from one ammonium nitrite molecule	(101)
Decomposition of N^*NO at 750°	No randomization in N_2	Rules out N atom-NO chain mechanism; in agreement with unimolecular decomposition mechanism	(178)
Decomposition of $N^{15}H_4N^{14}O_3$	$N^{15}N^{14}O$	Dehydration mechanism	(177)
Oxygen			
$KClO_3^* + MnO_2$	Evolved O_2^* lower isotopic abundance than $KClO_3$	$[KClO_3 + MnO_2]$ intermediate	(182)

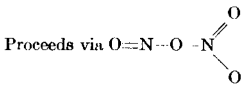
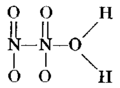
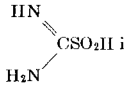
$KClO_3 + MnO_2^*$	Evolved O_2^* 20% isotopic abundance of MnO_2^*	Cyclic oxidation-reduction involving 20% of MnO_2	(65)
$4MnO_4^- + 4O^*H^-$	$4MnO_4^{2-} + 2H_2O + O_2^*$	O_2 completely derived from solvent; MnO_4^{2-} exchanges with solvent	(442)
Oxidation of H_2O_2 by Ce(IV), MnO_4^-, Cl_2, HClO, $Cr_2O_7^{2-}$, H_5IO_6 in presence of H_2O^*	O_2 contains no O^*	O—O bond preserved	(81, 88)
Decomposition of H_2O_2 by Pt, Ag, MnO_2, Fe(III), I^--I_2, Br^--Br_2 in presence of H_2O^*	O_2 contains no O^*	O—O bond preserved	(81, 88)
Reduction of H_2O_2 by Ti(III), Fe(II), Sn(II), Cr(II), Cu(I) in presence of H_2O^*	0.5% isotope effect with Ti(III) 6% isotope effect with other reductants	$1e^-$ oxidation of Ti(III) $2e^-$ oxidation of other reductants	(88)
$H_2O_2 + H_2O^* + h\nu(2537$ A.)	Evolved O_2 contains no O^*	O_2 derived from H_2O_2	(255)
$NO_2^{*-} + H_2O_2 \rightarrow H_2O + NO_3^-$	NO_2^{n*-} at high $[NO_2^-]$; $n = 1$ varying to $n = 2$ at low $[NO_2^-]$	At high $[NO_2^-]$ $ONO^*O^*H + NO_2^- \rightarrow ONO^* + O_2NO^* + H^+$ At low $[NO_2^-]$ $ONO^*O^*H \rightarrow O_2^*NO^- + H^+$	(16)
$2NO_2 + H_2O^* \rightarrow NO_2^- + NO_3^- + 2H^+$	At low $[NO_2]$ 1.4 O^* atoms per NO_3^- 0.7 O^* atoms per NO_2^-	Proceeds via 	(17)
	At high $[NO_2]$ 1.0 O^* atoms per NO_3^-; O^* in NO_2^- variable from 0 to > 1	Proceeds via activated complex 	
	Sulfur		
$S^*S^\dagger O_3^{2-} + I_2$	$O_3S^\dagger S^*S^*S^\dagger O_3^{2-}$	Expected mechanism	(66, 228)
$2SS^*O_3^{2-} + 3HgCl_2 + 2H_2O$	$HgCl_2 \cdot 2HgS + 2S^*O_4^{2-} + 4Cl^- + 4H^+$		(228)
$O_3SS^*SO_3^{2-} + CO_3^{2-}$	$O_3SS^{*2-} + SO_4^{2-} + CO_2$		(65)
$O_3S^*SSS^*O_3^{2}\ + 3HgCl_2 + 4H_2O$	$HgCl_2 \cdot 2HgS + 4S^*O_4^{2-} + 4Cl^- + 8H^+ + 2S$		(228)
$S_4O_6^{2-} + S^*O_3^{2-}$	$O_3SSS^*O_3^{2-} + S_2O_3^{2-}$	Nonbranched chain for $S_4O_6^{2-}$ $S_5O_6^{2-}$ similar but complicated	(98)
$S_2O_8^{2-} + S^{1*}O_3^{2-}$	$S_2^{1.5*}O_6^{2-} + S^{0.5*}O_4^{2-}$		(493)
$S_2O_7^{2-} + S^{1*}O_3^{2-}$	$S_2^{1*}O_6^{2-} + SO_4^{2-}$		(493)
$S_4^*O_6^{2-} + SO_3^{2-}$	$S_3^*O_6^{2-} + S_2^*O_3^{2-}$	Extended study of 98	(159)
$O_3S^*S^\dagger S^\dagger S^*O_3^{2-} + S^{\ddagger 2-}$	$2S^\dagger S^*O_3^{2-} + S^\ddagger$	Bond cleavage $O_3SS \vdots SSO_3^{2-}$ with slight side reaction (225)	(228)
$O_3S^*SSS^*O_3^{2-} + S^{2-}$	$O_3S^{*2-} + SS^*O_3^{2-} + 2S$	~3% of main reaction	(225)

TABLE 16—*Concluded*

Reaction studied	Distribution of tracer products	Remarks	References
	Sulfur—*Continued*		
$O_3SS_2^*SO_3^{2-} + 3CN^- + H_2O$	$SO_4^{2-} + S^*SO_3^{2-} + S^*CN^- + 2HCN$		(66)
$O_3SS_3^*SO_3^{2-} + 4CN^- + H_2O$	$S^*SO_3^{2-} + SO_4^{2-} + 2S^*CN^- + 2HCN$		(66)
$S^*Cl_2 + 2HSO_3^-$	$O_3SS^*SO_3^{2-}$		(65)
$S_2^*Cl_2 + 2HSO_3^-$	$O_3SS_2^*SO_3^{2-}$		(66)
$4SO_2 + 2H_2S^* + 6OH^-$	$3S^*SO_3^{2-} + 5H_2O$	Consistent with mechanism: $2HS^{*-} + HSO_3^- \rightarrow 2S^* + S + 3OH^-$ $OH^- + HSO_3^- \rightarrow SO_3^{2-} + H_2O$ $3SO_3^{2-} + 2S^* + S \rightarrow 2S^*SO_3^{2-} + SSO_3^{2-}$	(347)
$S^{1*}SO_3^{2-} + SO_3^{2-}$ in presence of sodium arsenite	$O_3SS^{3/4*}SO_3^{2-}$ and $O_3SS^{3/4*}S^{3/4*}SO_3^{2-}$	Indicates quantitative distribution of activity	(65, 66)
$5S^{1*}SO_3^{2-} + 4H^+$ at −10° (in presence of arsenite)	$S_3^{1*}(SO_3)_2^{2-} + 2SO_4^{2-} + H_2S^{2/3*} + 2S^{2/3*} + H_2O$	Arsenic acts to transfer thiosulfate sulfide (S′) sulfur to two other thiosulfates to form pentathionate	(66)
$2S^{1*}SO_3^{2-} + 4H_2O_2$	$O_3S^{1/4*}S^{1*}S^{1/4*}O_3^{2-} + S^{1/2*}O_4^{2-}$		(65)
$S^*SO_3^{2-}$ + $HOCH_2SO_2Na$ in presence of Co^{2+}	CoS (60–70% specific activity of original)	S not formed therefore by simple mechanism such as: $H_2O + H_2SO_2 + H_2S^*SO_3 \rightarrow H_2S^* + 2H_2SO_3$	(226)
$S^*SO_3^{2-}$ +  $HN{=}C(SO_2H)NH_2$ in presence of Cd^{2+}	CdS (48–85%)		
$S^*SO_3^{2-} + CoSO_2$ in presence of Co^{2+}	CoS (35–55%)		
$SS^*O_3^{2-} + Na_2S_2O_4$ in presence of Cd^{2+}	CdS (∼8%)		
$CoSO_2 + Na_2S^*$	CoS^* (100% original activity)	All sulfur originates from Na_2S	(226)
$HOCH_2SO_2Na + S^*SO_3^{2-} + I_2$ (acid)	S^*		(226)
$SO_3 + S^*Cl_2$ (50°)	$SO_2 + S^*OCl_2$	80–90% of sulfur in $SOCl_2$; direct oxygen atom transfer from SO_3 to SCl_2	(340)
$S_3N_2O_2 + 3S^*O_3$	$S_3N_2O_5 + 3S^*O_2$	SO_3 only an oxidant and sulfur of SO_3 does not enter $S_3N_2O_5$ molecule	(191)
$S_4N_4 + SOCl_2 + S^*O_2$	$S_3N_2O_2$ inactive	One S from $SOCl_2$, two S from S_4N_4, and no S from SO_2 in formation of $S_3N_2O_2$ mechanism proposed	(190)
$S_4N_4 + S^*OCl_2 + SO_2$	$S_3N_2O_2$ one-third original activity		
$2S^*S_2N_2O_2$ decomposition	$S_4N_4 + 2S^*O_2$		(190)

	Halogens		
$KClO_3 \rightarrow KClO_4$ in presence of KCl^* at 510° for 60 min.	$KClO_4$ inactive	Rules out: $KClO_3 \rightarrow KCl + 3O$ $KCl + 4O \rightleftharpoons KClO_4$	(60, 73)
$H_2O + IO_4^- + 2I^{*-}$	$I_2^* + 2OH^- + IO_3^-$		(334)
$HCl^*O + 2ClO_2^-$ (pH ~ 7)	$2ClO_2 + Cl^{*-} + OH^-$	Observed ClO_2 activity: 5–8% of that expected for complete mixing of chlorine activities	(447)
$HCl^*O + ClO_2^-$ (pH ~ 7)	$ClO_3^- + Cl^{*-} + H^+$	ClO_3^-: 9%	(447)
$Cl_2^* + 2HClO_2$ (pH = 0.5)	$2ClO_2 + 2Cl^{*-} + 2H^+$	ClO_2: 5–7%	(447)
$2Cl^{*-} + 2ClO_3^- + 4H^+$ (4.5 *M* H_2SO_4)	$Cl_2^* + 2ClO_2 + 2H_2O$	ClO_2: 3–6%	(447)
	Miscellaneous		
$Co(NH_3)_5Cl^{2+} + Cr^{2+}$ in presence of Cl^{*-}	$CrCl^{2+}$ inactive	No free Cl^- produced	(443, 450)
$CrCl_3$ (solid) $+ Cr^{2+}$ in presence of Cl^{*-}	$CrCl^{2+}$ almost inactive		(450)
$CrCl_2^+ + Cr_{aq}^{2+}$	$CrCl^{2+}$ almost inactive		(450)
$Co(NH_3)_5ONO^{2+}$ isomerization in presence of H_2O^* or NO_2^{*-}	$Co(NH_3)_5NO_2^{2+}$ unenriched	Intramolecular process	(335)
$Co(NH_3)_5OCOCH_3^{2+} + H_2O^*$ (or O^*H^-)	CH_3COO^- unenriched	Co—O bond fission	(82)
$Co(NH_3)_5OCOCF_3^{2+} + H_2O^*$	CF_3COO^- unenriched	Co—O bond fission	(82)
$Co(NH_3)_5OCOCF_3^{2+} + O^*H^-$	CH_3COO^- enriched	C—O bond fission (CH_2ClCOO^- and CCl_3COO^- intermediate behavior)	(82)
$Co(NH_3)_5CO_3^+ + 2H^+ + H_2O^*$	$Co(NH_3)_5H_2O^{3+}$ CO_2 normal abundance	No Co—O bond cleavage; aquation proceeds by decarboxylation	(252) (82)
$Co(NH_3)_4CO_3^+ + 2H^+ + H_2O^*$	$Co(NH_3)_4(H_2O)(H_2O^*)^{3+} + CO_2$	Confirms mechanism: $Co(NH_3)_4CO_3^+ + H^+ + H_2O \rightarrow Co(NH_3)_4(H_2O^*)(CO_3H)^{2+} \rightarrow Co(NH_3)_4(H_2O^*)(OH)^{2+} + CO_2$	(384)

$(O^{16}/O^{18})_{water}$, was 1.018 for Hg^{2+}_{aq} when 1 ml. of 1 *M* sodium hydroxide was added to 100 ml. of 1 *M* mercuric nitrate, using reagents of normal isotopic abundance. Since tracer experiments showed that the oxygen of the precipitated mercuric oxide was derived exclusively from the cation hydration sphere and not from the solvent water, the fractionation may be interpreted as a kinetic isotope effect in the proton transfer from hydrate water to hydroxide ion. Inspection of figure 1 will show that in the early stage of such an intermolecular reaction, the lighter isotope would preferentially appear in the product oxide. For silver ion, $\alpha = 1.016$ when silver ion was added to excess hydroxide ion, but for the reverse addition α was less than 1.013. This somewhat surprising result might be interpreted in terms of a very rapid exchange equilibrium (either between hydroxide ion and water or between the hydrate water and free water) combined with another isotope effect in the slower precipitation reaction. This is similar to that previously discussed for the fractionation effects in the $CNI-CN^-$ exchange system (Section VII,C).

A further significant application of isotope effects may be illustrated in the unimolecular isomerization of tritium-labelled cyclopropane to propylene. According to the Lindemann theory of unimolecular reactions, at high gas pressures the concentration of activated molecules is maintained by collision and the rate-determining step is the decomposition of the activated molecules. Therefore if rupture of a bond attached to a labelled atom is involved in the latter step, an isotope effect should occur. At low pressures, the concentration of activated molecules is no longer maintained and the slow step is the transfer of energy by collision, for which practically no isotope effect should occur. Such behavior was observed by Weston (472) when the isomerization of tritiated cyclopropane was performed in the region of 500°C. (see table 15). Reactions involving inorganic molecules which exhibit unimolecular characteristics might be similarly investigated.

Table 16 summarizes chemical reactions which have been studied by tracer methods. Reactions are classified according to the periodic group of the element labelled in the reaction study. Where atoms are designated by superscript letters, a study has been performed which has established the fate of all the indicated atoms in the reactant molecule; normally this involves multiple labelling. An asterisk(s) for the reaction product(s) denotes the fate of the labelling atom(s). Where a quantitative study of the tracer distribution among products has been performed, this is indicated by the tracer concentrations relative to a unit concentration of tracer in the original reactant.

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