Figure 13.

exists for *removing* the cobalt ion (at any valency level) from corrins. It would appear, therefore, that Nature can fashion the cobalamin structure without the use of cobalt as a template. This does not exclude other species (e.g., Mg, Zn) from consideration but rather indicates a further set of necessary experiments.

Epilogue

The story of corrin biosynthesis so far has yielded many surprises. One cannot cease to marvel at Nature's method of synthesizing this complex macrocyclic ligand by first forming uro'gen III, the precursor of heme and chlorophyll, and then undoing the ring system by ejecting a C_1 unit under the "pressure" of β-methylation, and finally recyclizing the secocorrin to reveal the cobalt-free ligand with its full panoply of stereochemistry, the overall process being that of *reductive* methylation. Indeed, on the evolutionary scale B_{12} may be a much more venerable compound than heme, for

a study of the most ancient microorganisms reveals[34,44] that several archaic anaerobes produced B_{12} but no heme, whereas the more developed aerobic bacteria oft-times synthesize heme but not vitamin B_{12}. It is also clear that much remains to be clarified before the mechanistic details of the uro'gen–corrin connection are finally settled.

(44) K. Decker, K. Jungermann, and R. K. Thauer, *Angew. Chem., Int. Ed. Engl.*, **9**, 138 (1970); J. DeLey and K. Kersters; *Compr. Biochem.*, **29B**, 29 (1975).

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Radiation-Induced Organic Hydrogen Isotope Exchange Reactions in Aqueous Solution

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A complete understanding of the chemical reactions which take place in a given system should incorporate

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a consideration of possible exchange reactions in which there is no net chemical change. Such identity reactions are usually not directly detectable unless a suitable isotope label is present. Kinetically, these reactions are almost invariably of first order with respect to the concentration of the isotope label.[1] Low concentrations of tritium can easily be estimated by liquid scintillation counting, and this technique permits even exceedingly

(1) H. A. C. McKay, *Nature (London)*, **142**, 997 (1938).

slow isotope exchange reactions (with half-lives of the order of a million years) between the solvent and C–H bonds of organic solutes to be followed. In such experiments tritium is initially present in the solvent as tritiated water. After a suitable reaction time the solute can be isolated, purified, and assayed for radioactivity. In a very slow exchange reaction only a fraction of 1% of the solute becomes tritiated. The initial rate of isotope exchange can then be deduced from the measured amount of tritium incorporation.

Hydrogen exchange reactions are well known for both aromatic and aliphatic solutes, for example in two of the compounds studied in our investigations, mesitylene and *tert*-butyl alcohol. In each case there is an acid-dependent hydrogen isotope exchange reaction[2,3] not involving any radiation-chemical processes. At relatively high concentrations of tritium in the solvent there is in addition a pH-independent isotope exchange which, unlike the acid-dependent reaction, has a rate proportional to the *square* of the tritium concentration.[4,5] This second-order dependence arises from the dual function of tritium as an isotope label and as a source of β radiation. Such self-irradiation has found some practical application as a labeling technique.[6,7] Isotope exchange can be induced also by much shorter exposure to more intense ^{60}Co γ-irradiation,[8] for which the rate of tritium uptake depends on the *first* power of tritium concentration.[9,10]

For a given concentration of tritium, the rate of the radiation-induced isotope exchange increases as the concentration of organic solute (aromatic[4,9] or aliphatic[5,11,12]) is increased, and it ultimately reaches a limiting value (Figure 1). This type of concentration dependence is typical of a radiation chemical system in which a solute competitively scavenges one or more of the highly reactive species generated in the solution. The limiting rate is reached when all radicals are scavenged by the added solute (about 10^{-3} M for aromatic solutes; about 1 M for aliphatic solutes).

The Radiation Chemistry of Water[13]

According to present-day ideas, the energy from ionizing radiation is deposited in water in localized regions, called "spurs". Within these spurs the so-called primary radiolysis products, principally OH·, H·, e_{aq}^{-}, and H$_3$O$^+$, are present in relatively high concentrations, whereas their overall (bulk) concentrations are much lower. These primary species can therefore react with

(2) J. R. Adsetts and V. Gold, *J. Chem. Soc. B*, 950 (1969).

(3) V. Gold and L. C. Gruen, *J. Chem. Soc. B*, 600 (1966).

(4) J. R. Adsetts and V. Gold, *Chem. Commun.*, 915 (1968); *J. Chem. Soc. B*, 1108, 1114 (1969).

(5) V. Gold and J. H. Rolston, *Chem. Commun.*, 208 (1970); *J. Chem. Soc. B*, 1795 (1970).

(6) D. H. T. Fong, J. L. Garnett, and M. A. Long, *J. Labelled Compd.*, 8, 695 (1972).

(7) D. H. T. Fong, C. L. Bodkin, M. A. Long, and J. L. Garnett, *Aust. J. Chem.*, 28, 1981 (1975).

(8) J. Kroh and A. M. Plonka, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, 14, 331 (1966); J. Kroh and E. Hankiewicz, *Int. J. Radiat. Phys. Chem.*, 1, 451 (1969); J. Baruel and O. Linde, *Radiochem. Radioanal. Lett.*, 2, 175 (1969).

(9) C. L. Brett and V. Gold, *Chem. Commun.*, 148 (1971); *J. Chem. Soc., Perkin Trans. 2*, 1437 (1973).

(10) J. H. Rolston and V. Gold, *J. Chem. Soc. B*, 1808 (1970).

(11) J. P. Garvey, V. Gold, M. E. McAdam, and A. Cooper, *Proc. R. Soc. London, Ser. A*, 346, 427 (1975).

(12) V. Gold and M. E. McAdam, *J. Chem. Soc., Chem. Commun.*, 228 (1975); *Proc. R. Soc. London, Ser. A*, 346, 443 (1975).

(13) For a recent review see I. G. Draganić and Z. D. Draganić, "The Radiation Chemistry of Water", Academic Press, London, 1971.
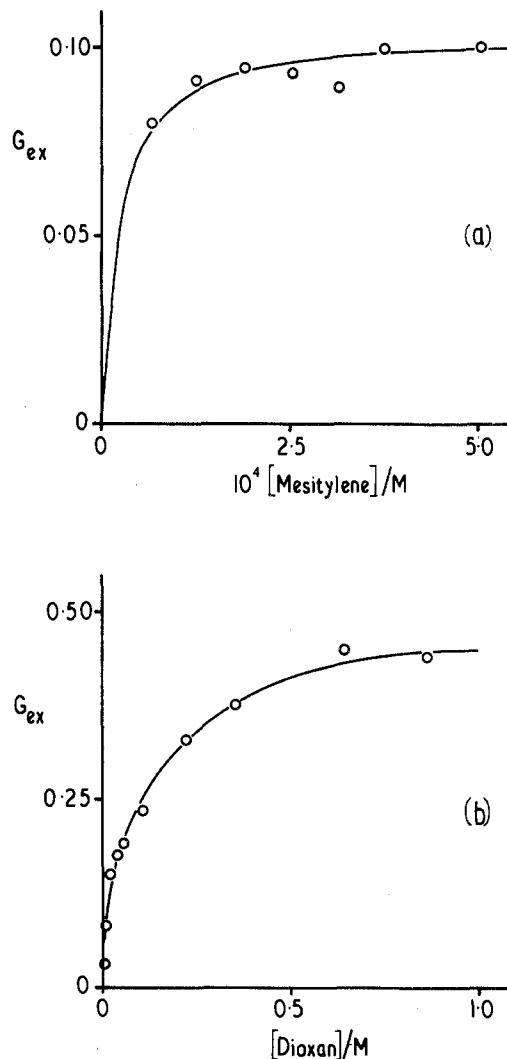
Figure 1. Rate of hydrogen isotope exchange as a function of substrate concentration. (a) Variation of G_{ex} with concentration of mesitylene. The data are taken from ref 9 and the values have been corrected for the small amount of radiation damage to the substrate. (b) Variation of G_{ex} with concentration of 1,4-dioxane (data from ref 12).

one another within this high-concentration region. Such intra-spur radical–radical reactions either lead to the "molecular products", H$_2$ and H$_2$O$_2$, or else they regenerate water. Alternatively, the primary species can diffuse into the bulk of solution and become homogeneously distributed prior to further reaction. Under conditions of low dose rate, such as those typically used in our studies of radiation-induced isotope exchange, the concentrations of primary radicals after escape into the bulk of solution are extremely low. Hence, except within spurs, radical–radical reactions of the primary species are very improbable. Those that have escaped into the bulk of solution (and become homogeneously distributed) are more likely to react with adventitious impurities, such as the residual oxygen that is present even in a degassed system.[9]

Reactions of homogeneously distributed radicals can be studied by the addition of low concentrations of reactive solutes; the concentrations commonly used are similar to those of aromatic solutes necessary in hydrogen isotope exchange studies. On the other hand, much higher concentrations of radical scavengers must be present so as to interfere with spur reactions that
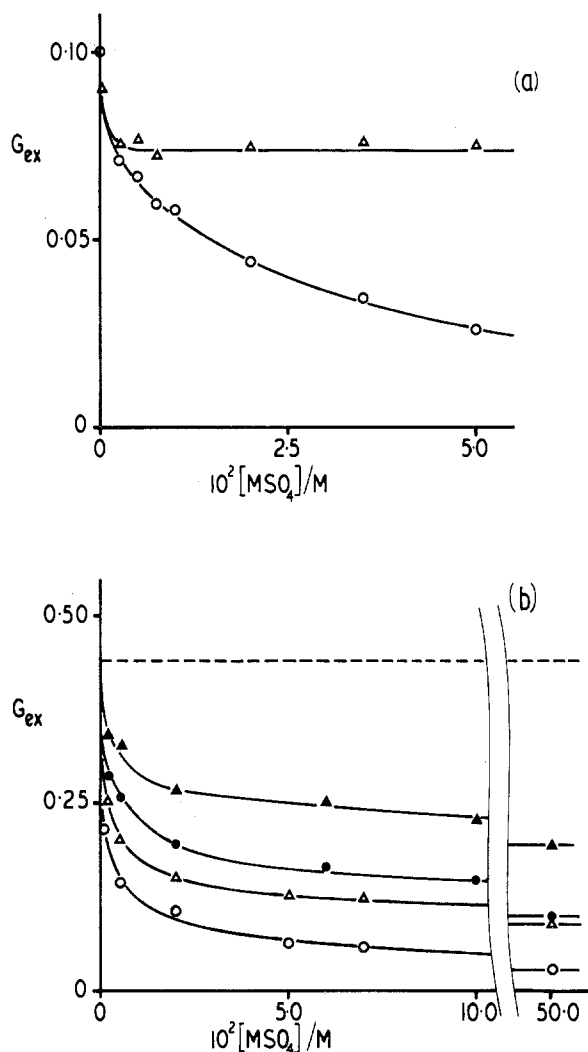
Figure 2. Effects of solvated electron, hydrogen atom, and hydroxyl radical scavengers on isotope exchange. (a) Variation of G_{ex} for benzene with concentration of added $CuSO_4$ (O) and $NiSO_4$ ($\triangle$) (data from ref 9). The hydrogen atom scavenger, $CuSO_4$, is clearly having the greater inhibitory effect. Maximum rate reduction with $NiSO_4$ is ca. 20%. (b) Variation of G_{ex} for 1,4-dioxane with concentration of the electron scavengers $CuSO_4$ (O), $NiSO_4$ ($\triangle$), $CoSO_4$ ($\bullet$), and $ZnSO_4$ ($\blacktriangle$) (data from ref 12). It can be seen that the added metal ions reduce G_{ex} to different limiting values. (- - -) Exchange in the absence of scavenger.

lead to the molecular products. These concentrations are similar to those of aliphatic solutes used in isotope exchange studies.

In order to compare the importance of exchange reactions with other radiation chemical processes, the reaction rate is best expressed as the G value for exchange, G_{ex}. In general, the G value for a given radiation chemical event is defined as the number of such events occurring per 100 eV (16 aJ) of energy absorbed. For instance, for ^{60}Co γ radiation the yield of solvated electrons escaping into the bulk of solution, $G(e_{aq}^-)$, is about 2.7, and the molecular yield of hydrogen peroxide, $G(H_2O_2)$, is about 0.7. G values are dependent on the radiation type, and for tritium β radiation the yield of the molecular products is higher and the bulk yield of primary radicals is lower than the corresponding yields found for ^{60}Co γ radiation. The G_{ex} values given in Figure 1 and 2 are not corrected for any isotope effects, either in the formation of primary radiolysis products from water or in their subsequent reactions (see also ref

9 and 12). In effect the calculation of G_{ex} values assumes that the observed number of *tritium* exchange events is equal to the *total* number of hydrogen exchange events multiplied by the fractional abundance of tritium in water.

Ionizing radiation produces in water highly reactive oxidizing and reducing radical species ($OH\cdot$, $H\cdot$, e_{aq}^-), and all three of these primary radicals have been found by us to play a role in hydrogen isotope exchange reactions of different kinds, with mechanisms quite unlike those of acid-catalyzed exchanges. The relative importance of the different primary radicals in a given exchange reaction can be assessed by the effect upon the exchange rate of added solutes with known reactivity toward these radicals.

It must be appreciated that $H\cdot$ and e_{aq}^- are interconvertible by the acid–base reactions 1 and 2.

$$e_{aq}^- + H_2O \xrightleftharpoons{slow} H\cdot + OH^- \tag{1}$$

$$e_{aq}^- + H_3O^+ \xrightarrow{rapid} H\cdot + H_2O \tag{2}$$
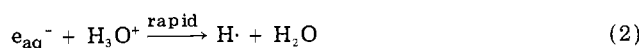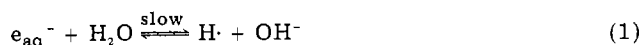
Isotope Exchange Involving Hydrogen Atoms

For benzene and for other aromatic compounds in aqueous solution a limiting exchange rate is reached at relatively low concentrations of solute (ca. 10^{-3} M; see Figure 1a).[4,9] Taken in conjunction with the known reactivity of the substrate toward the three primary radicals,[14,15] this result implies the involvement of a homogeneously distributed primary radiolysis product. Hydroxyl radicals react with simple aromatic compounds by addition rather than by hydrogen atom abstraction,[16] a process which leads to hydroxylation or oxidation and not to isotope exchange. Hydrogen atoms and solvated electrons also react by addition,[14,15] but in these cases addition reactions provide possible routes to hydrogen exchange.[4,9] The relative importance, in exchange reactions, of hydrogen atom and electron addition to aromatic substrates, in aqueous solution at neutral pH, is shown by the effects of added copper(II) and nickel(II) ions.[4,9] These ions are equally reactive toward solvated electrons, but copper(II) ions are much more reactive than nickel(II) ions toward hydrogen atoms.[17] It is observed that the isotope exchange is more strongly inhibited by copper(II) ions (Figure 2a). This result points to the hydrogen atom as being the principal species responsible for initiating tritiation. The first step of the reaction is visualized as an addition reaction (eq 3).
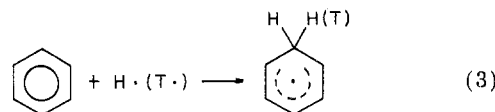
The cyclohexadienyl radical formed in step 3 reverts to starting material, some of which will be tritium-labeled. A number of mechanisms are conceivably

(14) M. C. Sauer and B. Ward, *J. Phys. Chem.*, **71**, 3971 (1967).
(15) B. D. Michael and E. J. Hart, *J. Phys. Chem.*, **74**, 2878 (1970).
(16) L. M. Dorfman, R. E. Buhler, and I. A. Taub, *J. Chem. Phys.*, **36**, 549, 3051 (1962).
(17) Compilations of the reaction rate constants of the primary species include: (a) M. Anbar and P. Neta, *Int. J. Appl. Radiat. Isot.*, 18, 493 (1967). (b) M. Anbar, M. Bambenek, and A. B. Ross, *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.*, No. 43 (1973). (c) L. M. Dorfman and G. E. Adams, *ibid.*, No. 46 (1973). (d) M. Anbar, Farhataziz, and A. B. Ross, *ibid.*, No. 51 (1975).

possible for this reaction (eq 4). Some of the more

$$(4)$$
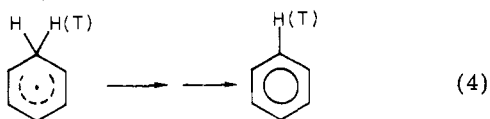
obvious possibilities, such as unimolecular loss of a hydrogen atom or bimolecular disproportionation of two radicals into benzene and cyclohexadiene, have been discounted for the experimental conditions employed (e.g., tritiated cyclohexadienes were not formed along with tritiated benzene).[9] Oxidation by molecular oxygen present in low concentrations during the early stages of the reaction even in degassed solutions is a much more favorable alternative. There remains also a possibility that the chain propagation reaction (eq 5)

$$(5)$$
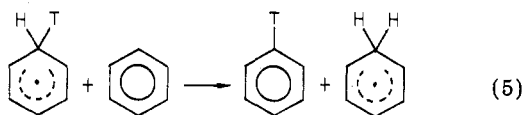
provides a route to labeled benzene. However, in the presence of copper(II) or similar oxidizing transition metal ions, it would seem that formation of the cyclohexadienyl cation (reaction 6) and subsequent proton

$$(6)$$
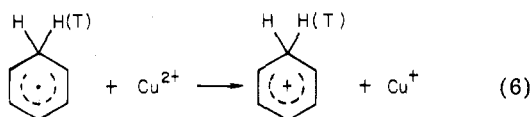
loss (reaction 7) represent the overwhelmingly pre-


$$(7)$$

$$(8)$$
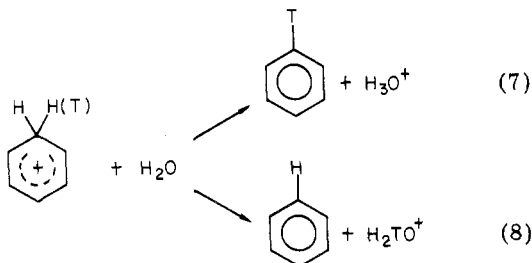
dominant route.

Because of a kinetic isotope effect, nearly all cyclohexadienyl radicals with tritium in the methylene position are expected to lose protium (reaction 7) rather than tritium (reaction 8) and hence to lead almost exclusively to the tritiated starting material (a conclusion which is independent of the mechanism of step 4). The rate of formation of tritiated starting material is therefore very nearly the same as the rate of reaction 3 (*with tritium*).[9]

It follows that relative rates of reaction 3 for different aromatic substrates can be deduced from competition experiments in which the formation of tritiated species is observed. Such studies can involve either direct competition between different aromatic substrates or, more conveniently, competition between a common hydrogen (tritium) atom scavenger and various aromatic species in turn.[9] Copper(II) ions proved a suitable scavenger for this purpose. Their oxidizing behavior toward cyclohexadienyl radicals also served to minimize any possible side reactions of these radicals (see above), and the very high reactivity of copper(II) toward electrons helped to suppress electron-induced exchange (see below). Some relative rate constants for reaction 3 (with tritium) derived in this manner are given in

Table I. The relative reactivities exhibited in the isotope exchange reaction are in accord with the view that the hydrogen atom behaves as if it were a mildly electrophilic reagent.

Isomer distribution studies show that radiation-induced hydrogen isotope exchange occurs mainly at the ortho positions in anisole and toluene, but is approximately statistical in chloro- and fluorobenzenes.[18] For the halogenobenzenes, both tritiated starting material and tritiated benzene are isolated from the reaction medium.[19] This indicates that tritium attack can occur at unsubstituted and substituted ring positions (ipso attack) (see eq 9 and 10).

$$(9)$$

$$(10)$$

X = Cl, Br, or I
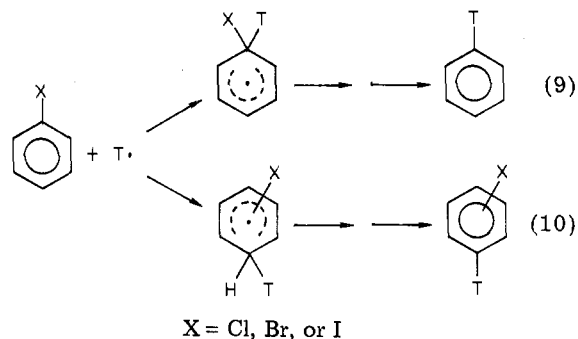
Hydrogen isotope exchange can be induced also by nonradiolytically generated hydrogen atoms. Photolysis of an acidified solution of potassium iodide and benzene in tritiated water leads to tritium incorporation into the aromatic compound[20] according to eq 11–12, followed by 3–4.

$$I^- + h\nu \to I\cdot + e_{aq}^- \tag{11}$$

$$e_{aq}^- + H_2TO^+ \to H\cdot(T\cdot) + HTO\ (H_2O) \tag{12}$$
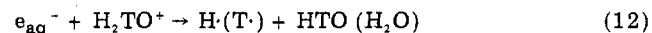
Isotope Exchange Involving Solvated Electrons

A more detailed analysis of the effects of added copper sulfate and nickel sulfate on the β-radiation-induced exchange in degassed neutral aqueous solutions of benzene revealed that about 20% of the tritiation under these conditions is induced by solvated electrons (see Figure 2a).[9] Electron-induced hydrogen exchange had earlier been reported for experiments carried out under very different conditions.[21] The γ irradiation of hydrogen-saturated (0.08 M) alkaline solutions (pD 13.8) of benzene in heavy water was found to lead to extensively deuterated benzene (in addition to other products). These conditions are much more favorable to the occurrence of electron reactions than those used in our β radiolyses.

Aromatic tritiation induced by solvated electrons is clearly shown when the photolysis of tritiated aqueous solutions of potassium iodide containing benzene is carried out at relatively high pH.[22] At low pH the electrons are converted into hydrogen atoms which then react with benzene, inducing isotope exchange, according to reactions 3 and 4. As the pH is increased, electrons are less extensively converted into hydrogen

(18) C. L. Brett, V. Gold, and G. Perez, *J. Chem. Soc., Perkin Trans. 2*, 1450 (1973).

(19) C. L. Brett and V. Gold, *Chem. Commun.*, 1426 (1971); *J. Chem. Soc., Perkin Trans. 2*, 1453 (1973).

(20) V. Gold, M. A. Major, and M. J. Gregory, *J. Chem. Soc., Faraday Trans. 1*, **70**, 965 (1974).

(21) M. H. Studier and E. J. Hart, *J. Am. Chem. Soc.*, **91**, 4068 (1969).

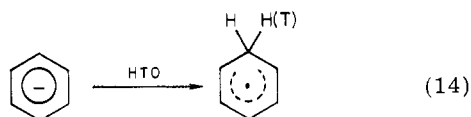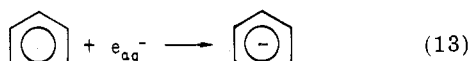(22) V. Gold and M. A. Major, *J. Chem. Soc., Faraday Trans. 1*, **70**, 977 (1974).

Table I
Relative Reactivities of a Series of Aromatic Compounds
toward Tritium Atoms[a]

	$\dfrac{k^T{}_{ArX}}{k^T{}_{Cu(II)}}$[b]	$\dfrac{k^T{}_{ArX}}{k^T{}_{benzene}}$[c]
Mesitylene	42.5	8.5
tert-Butylbenzene	19.0	3.8
Anisole	13.5	2.7
Toluene	11.0	2.2
Bromobenzene	5.5	1.1
Chlorobenzene	5.5	1.1
Fluorobenzene	5.0	1.0
Benzene	5.0	(1.0)
Benzonitrile	4.5	0.9
Trifluoromethyl-benzene	2.0	0.4

[a] Data from ref 9. [b] Calculated directly from the inhibitory effect of added copper(II) ions on the isotope exchange reaction. A value for $k^T{}_{ArX}$ can be estimated by assuming a value for $k^T{}_{Cu(II)}$ which may be approximated to the rate constant for the reaction of copper(II) ions with *hydrogen* atoms, $k^H{}_{Cu(II)}$. However, the values reported for the latter reaction[17d] vary by well over an order of magnitude, and any estimates of $k^T{}_{ArX}$ from the above data will therefore also be subject to such an error. In addition, any comparison of derived values of $k^T{}_{ArX}$ with literature values of $k^H{}_{ArX}$ will need to take into consideration possible kinetic isotope effects. [c] Calculated from the relative values in the preceding column.

atoms, and the exchange rate falls (Figure 3). It does not, however, reach zero, except in the presence of the efficient electron scavengers N_2O or NO_3^-. All the exchange observed at pH >7 in the absence of electron scavengers is initiated by solvated electrons (reactions 13 and 14). The cyclohexadienyl radical formed via

$$\text{(benzene)} + e_{aq}^- \longrightarrow \text{(benzene radical anion)} \tag{13}$$

$$\text{(benzene radical anion)} \xrightarrow{HTO} \text{(cyclohexadienyl radical, H H(T))} \tag{14}$$

reactions 13 and 14 is oxidized to benzene (cf. reactions 6–8). Under the conditions referred to in Figure 3 exchange is evidently less efficiently induced by solvated electrons than by hydrogen atoms. This is true also for β radiolysis. The difference in efficiency probably occurs because e_{aq}^- is more reactive than H· toward impurities (e.g., O_2), but less reactive than H· toward benzene.

Isotope Exchange Involving Hydroxyl Radicals and Solvated Electrons

For saturated aliphatic solutes in aqueous solution the limiting value toward which the exchange rate increases is reached only at high concentrations of substrate (ca. 1 M; see Figure 1b).[5,11,12] A consideration of the known reactivity of the various substrates toward the primary radicals[17] and of the radiation chemistry of aqueous solutions (see above) suggests that the limiting rates are attained only at high concentrations because of the involvement of a spur process. If isotope exchange is indeed initiated only within spur regions, then this in turn suggests the possible participation of a radical–radical reaction.

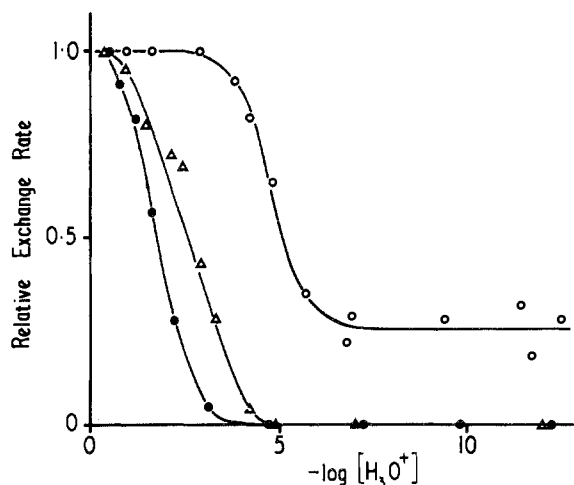Exchange has been observed in degassed aqueous

Figure 3. pH dependence of the exchange rate in benzene initiated by photolysis of deaerated aqueous potassium iodide solution. The relative exchange rates in the absence of added scavenger (O) and in the presence of 10^{-3} M $NaNO_3$ (△) or 0.024 M N_2O (●) are plotted as a function of $-\log [H_3O]^+$ (data from ref 22). A relative exchange rate of unity is assumed for exchange in the absence of added scavenger at low pH. (Benzene concentration 3.8 mM.)
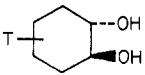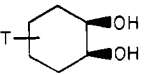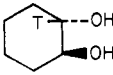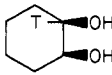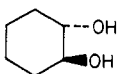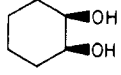
solutions of *tert*-butyl alcohol,[23] 1,4-dioxane,[12] *cis*- and *trans*-cyclohexane-1,2-diol,[11] and tartaric acid,[24] as well as in aerated solutions of *tert*-butyl alcohol, cyclohexanol, and isopropyl alcohol.[5] For dioxane and *tert*-butyl alcohol the limiting rate reached at ca. 1 M substrate concentration is not an absolute limit. At higher concentrations (≥3 M) the rate increases again as the mole fraction of the organic component increases.[23] These effects in mixtures cannot be discussed simply in terms of the basic radiation chemistry of water, and fall outside the scope of this review.

Saturated aliphatic compounds, such as ethers and alcohols, are unreactive toward solvated electrons, but they undergo hydrogen abstraction reactions with hydroxyl radicals and hydrogen atoms.[17] The hydroxyl-radical scavengers, Br^-, N_3^-, and SCN^-, have a very similar effect on the exchange rate of dioxane. At concentrations comparable to that of the substrate (≲1 M), all three almost completely inhibit the isotope exchange.[12] Thus, both the hydroxyl radical and the organic free radical, formed from the aliphatic solute by hydrogen atom abstraction, are implicated in the mechanism. However, tritiation of dioxane can additionally also be inhibited by perchloric acid,[12] and exchange in *trans*-cyclohexane-1,2-diol can be inhibited by nitrous oxide.[11] In acidic solutions solvated electrons are converted into hydrogen atoms, while in the presence of nitrous oxide they are converted into hydroxyl radicals.[13] Thus the conversion of e_{aq}^- into H· or OH·, both of which are hydrogen-abstracting species, does not increase the amount of exchange but, on the contrary, causes a large decrease. The presence of an organic free radical in a tritiated aqueous medium is therefore *by itself* not sufficient to result in isotope exchange, but the presence of solvated electrons is additionally required. Other scavengers of solvated electrons, such as bivalent transition metal cations

(23) V. Gold, M. E. McAdam, and A. Pross, *J. Chem. Soc., Faraday Trans. 1*, **72**, 755 (1976).
(24) M. Colosimo, J. P. Garvey, V. Gold, and E. Leonidou, *J. Chem. Soc., Perkin Trans. 2*, 1595 (1975).

Table II
**Steric Course of Radiation-Induced Tritium Exchange between Water and Cyclohexane-1,2-diols[a]**

|	Tritiated products, %			
	Non-α-substitution		α-Substitution	
Starting isomer				
 (±)-*trans*-diol	64.5	Zero	27 (retention)	8.5 (inversion)
 cis-diol	Zero	64	28.5 (inversion)	7.5 (retention)

[a] Data from ref 11.

(Figure 2b) or the nitrate anion, also inhibit aliphatic isotope exchange.[11,12,25] It therefore appears that, in the absence of any other added solute, aliphatic hydrogen isotope exchange involves a radical–radical reaction between the organic free radical R· and e_{aq} within the spur regions of solution.[12]

At first sight it seems surprising that metal ions at quite low concentrations (see Figure 2b) can efficiently inhibit spur reactions, in contrast to the high concentrations required to cause a substantial reduction in the yield of molecular products in the radiolysis of water. Perhaps replacement of the OH radical by a less reactive organic radical causes a change in the structure of the spur region (to a "looser" spur) which renders the electron more easily scavengeable. A similar modification of spurs may occur when the solvated electron is replaced by a lower valence-state transition-metal ion.[26]

According to the proposed mechanism, eq 15 and 16

(15)

(16)
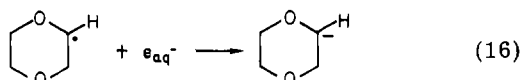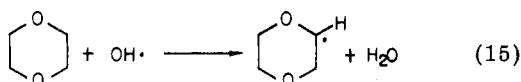
then represent the sequence of reactions of the primary radicals with dioxane as solute. Subsequent or concomitant protonation (tritonation) of the carbanion by the solvent (reaction 17) leads to the (labeled) parent

(17)
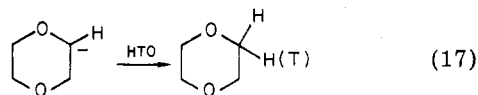
compound.

There is a parallel to reactions 16 and 17 in the reduction of radicals by radical anions (which can *for this purpose* be regarded as complexed electrons in solution).[27,28]

From the foregoing discussion it is clear that the hydroxyl radical alone cannot initiate exchange. Equally it is apparent that the original suggestion[5] that

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(26) G. V. Buxton, F. Dainton, and D. R. McCracken, *J. Chem. Soc., Faraday Trans. 1*, 69, 243 (1973).

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a reaction of substrate with the solvated electron is by itself sufficient to induce exchange is invalid. This is shown not only by the inhibitory effect of hydroxyl radical scavengers but also by our results on the steric course of aliphatic hydrogen isotope exchange (see below).[11]

Hydrogen atoms are formed in radiolysis in smaller yields than are hydroxyl radicals, and their reaction with substrates does not appear to play a major role in our experiments. Neither does the hydrogen atom seem to react with the organic free radical to yield starting material, since in acidic solutions, when all of the solvated electrons are converted into hydrogen atoms, the exchange rate is small.[12] (However, under the conditions used, the substrate itself will be the principal scavenger of hydrogen atoms.)

It is implicit in these ideas that the aliphatic exchange reaction should be observed only if the compound is itself unreactive toward solvated electrons.

Further confirmation of the involvement of an organic free radical intermediate comes from the study of the stereochemistry of isotope exchange using the isomeric *cis*- and (±)-*trans*-cyclohexane-1,2-diols (Table II).[11] Whichever diastereoisomer is present initially, the preferential product of radiation-induced tritiation at the α positions is the *trans*-diol. Moreover, in both cases, the ratio of *trans*-diol to *cis*-diol for the α-tritiated product is the same. This shows clearly the formation of a common intermediate. The product ratio probably reflects the greater stability of the cyclic organic free radical (or carbanion) in a configuration with the adjacent hydroxy groups arranged axial–equatorial.[11] For tartaric acid, where there is no such steric restriction in the free radical formed by hydrogen abstraction, isotope exchange at the chiral centers proceeds to approximately equal extents with retention and with inversion of configuration.[24] Studies with inositols have also shown the occurrence of β-radiation-induced tritium exchange with retention and with inversion,[7] but a full explanation of these results will require detailed consideration of conformational preferences in very concentrated solutions.

In the case of the cyclohexanediols (Table II), substitution also occurs quite readily at non-α-positions, and that is why, even for the *cis*-diol, the starting isomer is the predominant tritiated product. This suggests, as does a consideration of the proposed mechanism, that even simple hydrocarbons should be able to undergo

Table III
A Summary of the Principal Steps Involved in Radiation-Induced Hydrogen Isotope Exchange in Aqueous Solution

| System	Oxidizing agent	Reducing agent	
RH/THO	OH·(H·)	e_{aq}^-	Oxidation precedes reduction
RH/THO/M²⁺	OH·(H·)	$M^+(e_{aq}^-)$	
ArH/THO {low pH / high pH	O_2? / O_2^- (H_2TO^+, THO)	H· / e_{aq}^-	Reduction precedes oxidation
ArH/THO/M²⁺ (low pH)	M²⁺	H·	

radiation-induced hydrogen isotope exchange. There is also indirect evidence that methyl radicals in aqueous solution react with solvated electrons to yield methane.[29] Direct evidence for isotope exchange in aliphatic hydrocarbons in aqueous solution is difficult to obtain because of their low solubility in water, although radiation-induced tritiation of cyclohexane has been observed in an aqueous dioxane medium containing tritiated water.[23]

Involvement of Metal Ions in Isotope Exchange

Apart from inhibiting the exchange which occurs in their absence, the metal ions themselves (or their reaction products) can mediate in tritiation of organic substrates. For the aromatic systems it seems likely that the copper(II) ion plays such an additional role by acting as oxidizing agent toward cyclohexadienyl radicals[9] (reaction 6). Oxidizing reactions of this type are well documented, particularly for aliphatic free radicals.[30]

The inhibitory role of bivalent metal ions in aliphatic hydrogen isotope exchange is ascribed principally to their reaction with solvated electrons. In particular for the cases of Ni^{2+}, Co^{2+}, and Zn^{2+}, reaction of the bivalent cation with the organic free radical derived from dioxane cannot contribute appreciably to the inhibition of aliphatic hydrogen isotope exchange.[12] However, different metal ions show different inhibitory effects. In particular, the maximum decrease obtainable in the rate of aliphatic exchange depends on the metal ion used as inhibitor (Figure 2b).[11,12,25] The most effective inhibitors (>90% inhibition) in the case of dioxane are Cu^{2+} and Ag^+, both of which are very reactive toward e_{aq}^-. For the other metal ions studied, their effectiveness (as measured by the limiting dioxane exchange rate at high metal ion concentrations; see Figure 2b) is in the order $Ni^{2+} > Co^{2+} > Zn^{2+}$.

In any radiation chemical system it is important to consider the reactivity of the metastable (or stable) products formed during the scavenging action of solutes. The residual aliphatic exchange (i.e., the reaction not suppressed by metal ions) is thought to involve reduction (reaction 18) of the organic free radical by such

$$(18)$$
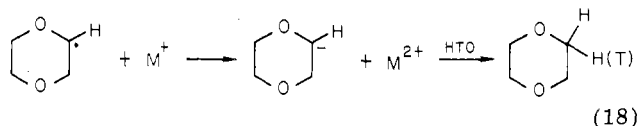
a species, namely the monovalent ion M^+ formed by the scavenging of electrons by M^{2+} ions. On this basis the results for exchange in dioxane place the relative reducing powers of the monovalent species toward the organic free radical in the sequence $Zn^+ > Co^+ > Ni^+$.

Other studies have illustrated the reducing power of such metal cations,[26,31-35] and similar relative reactivities have been inferred.[36,37]

The reaction between organic radicals and monovalent metal ions may involve a transient carbanion (eq 18). Alternatively it may proceed through the intermediacy of an organometallic cation such as that suggested by Kelm et al.[38]

Reactions other than (18) between an organic radical, R·, and M^+ are also possible. Polarographic studies suggest that the reduction of *tert*-butyl alcohol radicals leads to isobutene,[38,39] and that of the radical from 1,4-dioxane to an open-chain product.[40] Clearly, these types of reaction must also be considered to contribute to the aqueous radiation chemistry of aliphatic compounds.

Conclusions

The general theme which seems to run through the radiation-induced identity reactions is that they each involve one oxidation and one reduction step. The order in which these processes occur is determined essentially by the nature of the substrates and their chemistry, and by the experimental conditions. Hydrogen atoms and electrons initiate exchange by addition to an unsaturated system. Subsequent oxidation, either by oxygen or by added metal ions (e.g., Cu^{2+}), and proton (triton) loss lead back to starting material. On the other hand, when exchange is initiated by hydroxyl radicals the first reaction involves hydrogen atom abstraction from a saturated system. Subsequent reduction, either by solvated electrons or by metastable valence-state metal ions (e.g. Ni^+), and protonation (tritonation) by the solvent regenerate starting material. The various steps are summarized in Table III; they illustrate the facility of moving up and down the redox ladder via radical processes. The reactions involved are relatively clear because only a few species are present in irradiated aqueous solutions. This ability to oscillate between redox states via radical reactions is a more general possibility whenever free radicals are generated.

All of the identity reactions discussed above are undetectable when there is no isotope label in the

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solvent. Solutes, such as ethanol and methanol, which are apparently inert toward solvated electrons are often used in relatively high concentrations to assist in elucidating radiation chemical processes occurring immediately after the deposition of energy in aqueous solutions. It is now clear from our findings that reactions between the radiation products of these solutes (i.e., the aliphatic free radicals) and the solvated electrons should always be considered for such systems, particularly since it is in the spur regions where early processes occur. In addition, it is also to be expected that isotope exchange reactions may take place in more complex molecules, for example, carbohydrates. If such

exchange occurs at a chiral center, then, by analogy with our observations with cyclohexane-1,2-diols, the reaction may lead not only to the parent compound but also to an inversion product. Radiation-induced hydrogen isotope exchange reactions may therefore deserve consideration not only in an analysis of the radiation chemistry of aqueous solutions and of the chemistry of simple free radicals but also in a discussion of radiobiological processes.

Complexes of Cations in Unstable Oxidation States in Aqueous Solutions as Studied by Pulse Radiolysis

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The radiolysis of water has been the subject of many recent studies. The detailed mechanisms of the primary steps leading to the decomposition of water by ionizing radiation have not been fully elucidated. However the results clearly indicate that the primary processes occurring during the radiolysis of water and dilute aqueous solutions may be summarized by eq 1.[1] These

$$H_2O \xrightarrow{\gamma, e^-} e_{aq}^-, \cdot H, \cdot OH, H_2, H_2O_2, H_3O^+ \tag{1}$$
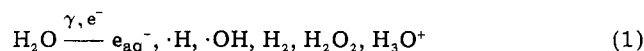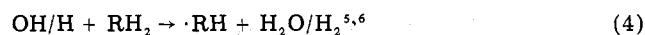
products are formed in a homogeneous solution within less than 100 ns after the radiation is absorbed. The yields of these primary products in dilute aqueous solutions are $G_{e_{aq}} = 2.65$, $G_{OH} = 2.65$, $G_H = 0.60$, $G_{H_2} = 0.45$, and $G_{H_2O_2} = 0.75$[1] (where G is the number of product molecules formed per 100 eV absorbed by the solution).

The radicals e_{aq}^-, OH, and H are strong single-electron redox reagents. The use of these reagents is complicated by the fact that nearly equal amounts of very strong reducing (e_{aq}^-, H·) and oxidizing (·OH, H·) reagents are formed simultaneously. However, work under strong oxidizing or reducing conditions is made possible by applying one of the following reactions:
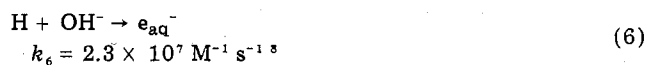
$$e_{aq}^- + N_2O \rightarrow N_2 + O^- \tag{2}$$
$$k_2 = 5.6 \times 10^9 \text{ M}^{-1} \text{ s}^{-1}{}^2$$

followed by

$$O^- + H_2O \rightleftarrows OH + OH^- \tag{2a}$$
$$pK_2 = 11.9 \pm 0.2^3$$

$$e_{aq}^- + H_3O^+ \rightarrow H \tag{3}$$
$$k_3 = 2.3 \times 10^{10} \text{ M}^{-1} \text{ s}^{-1}{}^4$$

$$OH/H + RH_2 \rightarrow \cdot RH + H_2O/H_2{}^{5,6} \tag{4}$$

(where RH_2 is a saturated aliphatic compound and the radical $\cdot RH$ is a reducing agent, an oxidizing agent, or unreactive, depending on the nature of RH_2 and the system studied; see below).

$$OH + H_2 \rightarrow H + H_2O \tag{5}$$
$$k_5 = 6 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}{}^7$$

$$H + OH^- \rightarrow e_{aq}^- \tag{6}$$
$$k_6 = 2.3 \times 10^7 \text{ M}^{-1} \text{ s}^{-1}{}^8$$

Furthermore, a series of other strong single-electron redox reagents can be produced by adding appropriate solutes, e.g., I_2^-,[9,10] Br_2^-,[9,11] $(NCS)_2^-$[12] in solutions containing N_2O and I^-, Br^-, or NCS^-, respectively; Cl_2^- in acidic solutions containing Cl^-;[9,13] O_2^- or HO_2 de-

Dan Meyerstein was born in Jerusalem, Israel, and earned his M.Sc. and Ph.D. (1965) degrees at the Hebrew University of Jerusalem. After holding a year's postdoctoral fellowship at the Chemistry Division, Argonne National Laboratory, he received a joint appointment in the Chemistry Department, Nuclear Research Centre-Negev, and the Chemistry Department of Ben Gurion University of the Negev, where he is Associate Professor of Chemistry. Dr. Meyerstein's field of interest is the study of inorganic redox reactions as studied by pulse-radiolytic, electrochemical, and stopped-flow techniques.

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