Radiolytic Displacement of Substituent Groups in Benzene by Hydrogen (Tritium)

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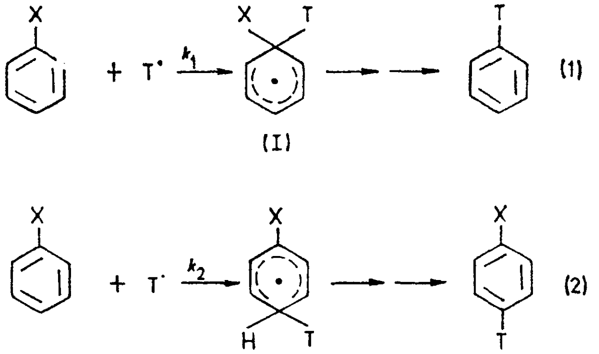
The experimental work examines the extent to which β-radiation-induced hydrogen exchange of aromatic substrates in aqueous solution with the solvent is accompanied by displacement of a substituent group in the aromatic compound. Radiation-induced substituent displacement is observed to any significant extent only for the halogenobenzenes (PhI > PhBr > PhCl). A dual function is ascribed to copper(II) ions, which act as inhibitor of both exchange and substituent displacement: they act as oxidising agent towards hydrogen atoms and substituted cyclohexadienyl radicals with attendant formation of the corresponding cations. This model explains why, in the case of bromobenzene, copper(II) ions inhibit the substituent displacement reaction more than the tritium exchange.

BENZENE and its derivatives undergo hydrogen exchange with solvent water when the solutions are exposed to β-[1,2] or γ-radiation.[2] By use of selective scavengers it has been shown that this reaction proceeds by way of the primary formation of hydrogen atoms in the solvent, at least when electron scavengers are present.[1,2] In the absence of electron scavengers the evidence points to some additional initiation of the reaction by solvated electrons.[3] The hydrogen atom-initiated substitution has been studied in some detail by use of tritium tracer in the solvent.[1,2] The occurrence of the exchange reaction is recognisable by tritium labelling of the aromatic substrate, and the process can be detected even at quite low rates of reaction. These experiments, in most of which tritium also fulfilled the role of an internal radiation source, have led to a reactivity pattern for the attack of hydrogen (tritium) atoms on monosubstituted derivatives of benzene.[4]

Apart from this hydrogen-for-hydrogen replacement, it is also possible that radiolytically formed hydrogen (tritium) atoms react with an aromatic compound by attachment to a nuclear position already carrying a substituent group, with eventual displacement of that substituent group by hydrogen, as in reaction (1). When the medium contains tritium, a reaction of this type will lead to labelled benzene. The substitution (1) will be in competition with the corresponding hydrogen-exchange reactions at the other nuclear positions, such as that at the *para*-position represented in reaction (2). The replacement of substituent groups of aromatic compounds by hydrogen is known to occur under certain experimenta conditions,[5] especially in acid solutions where protonation of the aromatic system at a substituted carbon atom can lead to heterolytic ejection of the substituent group from the cyclohexadienyl cation.



The present work describes the formation of labelled benzene from benzene derivatives, under the influence of radiation on solutions in tritium-containing water, and the establishment of some features of its mechanism.[6]

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[1] J. R. Adsetts and V. Gold, *Chem. Comm.*, 1968, 915; *J. Chem. Soc.* (*B*), 1969, 1108.

[2] C. L. Brett and V. Gold, *J.C.S. Perkin II*, 1973, **1437**.

[3] M. C. Sauer, jun., and B. Ward, *J. Phys. Chem.*, 1967, **71**, 3971; B. D. Michael and E. J. Hart, *ibid.*, 1970, **74**, 2878; M. H. Studier and E. J. Hart, *J. Amer. Chem. Soc.*, 1969, **91**, 4068.

[4] J. R. Adsetts and V. Gold, *Chem. Comm.*, 1969, 353; *J. Chem. Soc.* (*B*), 1969, 1114; C. L. Brett and V. Gold, *Chem. Comm.*, 1971, 148.

[5] For a review, see R. O. C. Norman and R. Taylor, ' Electrophilic Substitution in Benzenoid Compounds,' Elsevier, Amsterdam–London–New York, 1968.

[6] For a preliminary account, see C. L. Brett and V. Gold, *Chem. Comm.*, 1971, 1426.

EXPERIMENTAL

The general procedures, using triply-distilled water and de-gassed solutions, were the same as in related work.[2] For the measurement of the simultaneously occurring exchange and substituent displacement reactions, the carrier used for the extraction of labelled solute was a mixture of the original substrate and benzene (or *m*-xylene in the case of experiments on mesitylene), sometimes with addition of n-hexane to facilitate handling. After being washed and dried in the usual way, the extracts were separated into the components by preparative g.l.c., on an appropriate column with temperature programming. In the case of mesitylene, the *m*-xylene was gas-chromatographed twice, inactive mesitylene being added before the second pass. The tritium activity of each of the aromatic components was determined in the usual way.[2] For chlorobenzene several determinations were performed under different conditions (Table 1) and for bromobenzene a systematic group of experiments, with varying amounts of added copper(II) sulphate, is recorded (Table 2). For chloro-, bromo-, and iodo-benzene, for the last of which the replacement of iodine is the predominant reaction, experiments at two different tritium concentrations are reported (Tables 1—3). For other substrates (Table 3) the substituent displacement was of very minor importance. Cases in which the resultant activity of benzene (or *m*-xylene) amounted to less than a doubling of the background activity are indicated by parentheses round the experimental values. Values of v_X and v_H are initial rates (5 days, unless stated otherwise) for the replacement by tritium of the substituent group X and of H, respectively, and refer to a temperature of 25 °C. These rates are expressed in the usual practical units: disintegrations per minute (d.p.m.) for solute in 1 dm³ of reaction solution, per day of reaction per (Ci/dm³)² of tritium activity in the medium (d.p.m. day⁻¹ dm³ Ci⁻²).

TABLE 1

Chlorobenzene results

10^3 [PhCl]/M	[HTO]/ Ci dm^{-3}	v_X	v_H	v_X/v_H
2·16	6·43	58	454	0·11
1·54	7·32	58	394	0·13
1·54	7·32	28 [a]	309 [a]	0·08
1·54	14·64	56	459	0·11
1·13	7·32	57 [b]	350 [b]	0·14
1·13	7·32	47	350	0·12
			Mean [c]	$0·11_5$

[a] With 0·05M-$NiSO_4$. The pronounced reduction of both reactions in this experiment runs counter to our experience with nickel(II) ions in the hydrogen exchange reaction where its effect is normally small. For this reason we now suspect that the solution in this experiment was imperfectly de-gassed, perhaps owing to an undetected air leak. [b] Reaction time 2 days (others 5 days). [c] Excluding result in the presence of $NiSO_4$.

TABLE 2

Bromobenzene results

[PhBr] = 1·72 × 13⁻³M; tritium activity of water = 7·75 Ci dm⁻³; reaction time = 11 days

10^3[$CuSO_4$]	v_X	v_H	v_X/v_H
	168		
a	166		
b	152	480	0·32
	137	435	0·31
2·5	50	274	0·18
5	29	232	0·13
7·5	18	190	0·10
10	12	187	0·07
20	7	141	0·05
35	5	91	0·06
50	3	70	0·04

[a] With 0·05M-$NiSO_4$. [b] Tritium activity of water = 14·6 Ci dm⁻³.

TABLE 3

Results for all substrates

Substrate	10^3[Substrate]/ M	Tritium activity/ Ci dm^{-3}	Reaction time/ day	v_X	v_H	v_X/v_H
Iodobenzene		7·31	7	301	37	8·1
		14·62	7	292	36	8·1
Bromobenzene	1·72	7·75	11	137	435	0·31
Chlorobenzene						0·12 [a]
Anisole	2·7	7·31	5	18	662	0·03
t-Butylbenzene [b]	0·08	7·83	5	19	376	0·05
Toluene	1·1	7·31	5	(3)	557	(0·005)
Trifluoromethylbenzene	1·63	7·73	5	(1)	304	(0·003)
Benzonitrile	1·95	7·75	7	(1)	460	(0·002)
Mesitylene	0·5	14·64	10	(2)	560	(0·004)

[a] Mean value, see Table 1. [b] Radiation damage not negligible at the unavoidably low substrate concentration; in the absence of information, no correction applied to results.

DISCUSSION

The observations summarised in Table 3 show that the hydrogen exchange reaction of aromatic compounds, brought about in aqueous solution by the agency of β-radiation, is accompanied in certain cases by loss of a substituent group attached directly to the aromatic ring and attachment of solvent-derived hydrogen (*i.e.* carrying the tritium label introduced into the solvent in the form of tritiated water) in its place. This reaction is negligible for all substituents studied with the exception of the halogens, iodine, bromine, and chlorine, in decreasing order of importance. For iodobenzene, iodine loss and formation of labelled benzene is eight times more important than the parallel tritium exchange into iodobenzene; for chlorobenzene the reverse relationship holds. The case of fluorobenzene could not be examined as we were unsuccessful in achieving adequate separation of benzene from fluorobenzene on the required scale.

It was ascertained, for the case of *p*-iodoanisole, that the hydrogen (tritium) atom enters (at least predominantly) at the position originally occupied by the halogen atom. The determination of the tritium distribution in the anisole produced indicates that 75% of the labelling is at the *para*-position.[7] However, this result must be an underestimate. The introduction of tritium at the other nuclear positions occurs almost certainly subsequently to the formation of anisole, as a result of the further exposure of anisole to radiation and hence the occurrence of radiation-induced tritium exchange in anisole, which is known to favour the two *ortho*-positions adjacent to the methoxy-group.[7]

Apart from the halogenobenzenes only t-butylbenzene

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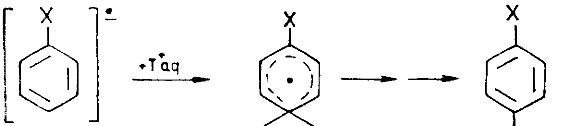
[7] C. L. Brett, V. Gold, and G. Perez, preceding paper.

and anisole led to tritiated benzene in amounts which we consider to be outside the limits of the error of separation and radioactivity assay. Even in these two cases, the proportion of the substituent replacement reaction was so small that the value of the rate ratio quoted in Table 3 can only be regarded as an approximate upper limit. A consideration of reaction mechanisms must therefore remain confined to the case of the halogenobenzenes.

Results for all three halogenobenzenes indicate that, as for the tritium exchange reaction,[1,2,4] the rate of tritiodehalogenation is proportional to the square of the tritium activity of the solvent. This square dependence has previously been discussed for the exchange reaction and it implies the occurrence of a radiation-induced process (the rate being dependent on the tritium concentration first by virtue of its function as a tracer in the reaction and, secondly, because of its role as a radiation source). At the low concentrations of substrate employed in these experiments (all of which relate only to homogeneous solutions) the radiation must act on the solvent molecules, and the reaction must be due to interaction of radiolysis products of water and the solute. As for the isotope exchange, both the hydrogen (tritium) atom [reaction (2)] and the solvated electron [reaction (3)] are conceivably the radiolytic species

$$\mathrm{ArX} + e^-_{aq} \longrightarrow \mathrm{ArX}^- \xrightarrow{+\mathrm{T}^+_{aq}} \mathrm{ArTX}\cdot \longrightarrow \longrightarrow \mathrm{ArT} \quad (3)$$

responsible for initiating the substitution. It is assumed that the addition of a proton (triton) to the halogenobenzene radical anion, formed in the first step, results in the formation of a cyclohexadienyl radical containing a $>$CHX grouping [reaction (3)]. Alternative reactions of the radical anion are (i) proton (triton) addition at a hydrogen-carrying carbon atom, which could lead to aromatic hydrogen exchange by a reaction such as (4), and (ii) halide ion loss, giving rise to a phenyl radical, an intermediate which is not likely to result in tritiated benzene as the final product.



(4)

It has been shown for hydrogen exchange reactions that reaction (4) does not represent an important exchange route provided an electron scavenger, even in quite low concentration, is present in the system. Residual oxygen in imperfectly degassed solutions or low concentrations of nickel(II) or copper(II) ions appear to suppress this route so that only the mechanisms typified by equation (2) are operative. However, in the absence of such electron scavengers, the electron-induced reaction does to some extent occur side-by-side with reaction (2).

In the dehalogenation experiments we find that traces of electron scavengers do not entirely suppress the reaction. Some reduction appears for solutions containing 0·05M-nickel sulphate in the case of chlorobenzene but this result is somewhat suspect (see footnote *a* to Table 1) and with bromobenzene there is no corresponding effect at all. However, it is apparent that 0·05M-$\mathrm{NiSO_4}$ does not suppress the dehalogenation in either case, which points to the importance of the hydrogen (tritium) atom-induced reaction (2). By contrast, 0·05M-copper(II) sulphate suffices to reduce both exchange and dehalogenation of bromobenzene to a small fraction of the value in the scavenger-free solution. This is qualitatively consistent with the additional function of copper(II) ion as a hydrogen atom scavenger.

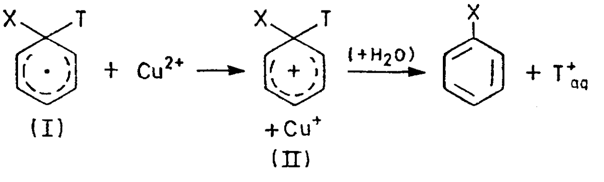
However, the role of copper(II) ions must be even more complex. As the results in Table 2 show, the two reactions are not subject to copper(II) inhibition to the same extent, and there is a progressive fall in the debromination/exchange ratio as the copper(II) concentration is raised. In 0·05M-copper(II) sulphate the debromination is almost completely suppressed, whereas the exchange reaction is still observable.

We have previously noted [2] that the oxidising action of the copper(II) ion which is responsible for the scavenging of hydrogen atoms by reaction (5) is also effective towards organic radicals and that it is likely to constitute the essential step in the sequence (6) by which a cyclohexadienyl radical is converted to an aromatic compound under conditions where the radical concentration is low so that radical–radical reactions are unimportant.

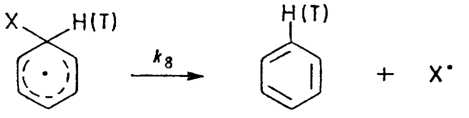
$$\mathrm{H}^\cdot + \mathrm{Cu}^{2+} \xrightarrow{k_{\mathrm{Cu}}} \mathrm{H}^+ + \mathrm{Cu}^+ \quad (5)$$

$$\mathrm{ArH_2}^\cdot + \mathrm{Cu}^{2+} \xrightarrow{k_6} \mathrm{Cu}^+ + \mathrm{ArH_2}^+ \longrightarrow \mathrm{ArH} + \mathrm{H}^+ + \mathrm{Cu}^+ \quad (6)$$

It should be noted that an oxidation step of this kind is unlikely to be equally effective in a dehalogenation sequence of reactions (1). Oxidation of the corresponding radical (I) would form a cation, the natural mode of decomposition of which would be loss of tritium by triton transfer to water, as shown in equation (7). The corresponding ejection of a halogen cation from (II) is inherently a much less likely event. The result of reaction (7) is the regeneration of the substrate halogenobenzene. On the other hand, it is possible for the intermediate radical (I) to lose a halogen atom by homolysis (8), and it is this reaction which presumably

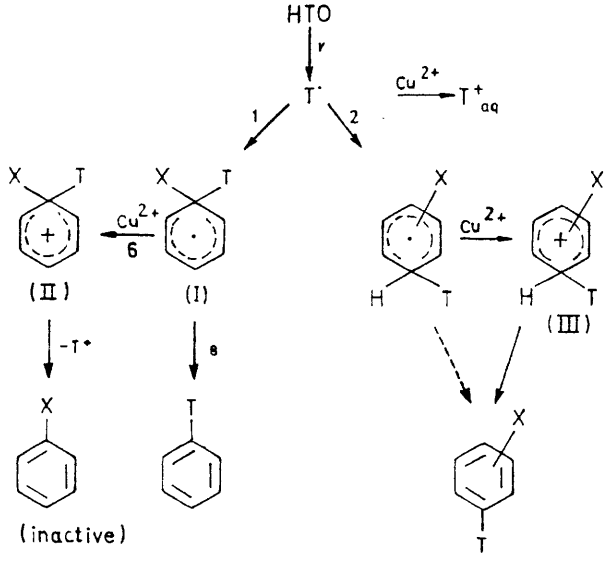


(7)



(8)

causes the conversion of (I) to benzene. Thus copper(II) ions have an additional inhibitory effect on the dehalogenation process by diverting the intermediate radical (I) into an unprofitable route. The Scheme sets out the steps involved.



SCHEME

The rate of formation of tritium atoms (v) must equal their rate of destruction. On the basis of earlier evidence it seems reasonable to assume that the only processes of destruction to be considered in our system are the initial steps in reactions (1) and (2), characterised by rate constants k_1 and k_2, and the scavenging reaction (5), *i.e.* equation (9). The intermediate (III) leads only

$$v/[\mathrm{T}^\cdot] = (k_1 + k_2)[\mathrm{PhX}] + k_{\mathrm{Cu}}[\mathrm{Cu}^{2+}] \qquad (9)$$

to XC_6H_4–H and XC_6H_4–T, the latter predominating by a factor of the order of 10 by virtue of the primary kinetic isotope effect. The intermediate (I) will lead to C_6H_5T or to C_6H_5X (inactive), the fraction of the former product being given by the ratio $k_8 : (k_8 + k_6[\mathrm{Cu}^{2+}])$. Accordingly, the fraction of tritium atoms which finish up as labelled PhX(f_{PhX}) is given by (10) whereas the

$$f_{\mathrm{PhX}} = \frac{k_2[\mathrm{PhX}]}{(k_1 + k_2)[\mathrm{PhX}] + k_{\mathrm{Cu}}[\mathrm{Cu}^{2+}]} \qquad (10)$$

fraction of tritium atoms resulting in labelled benzene (f_{PhT}) is given by (11). The experimental ratios $v_{\mathrm{H}} : v_{\mathrm{X}}$

$$f_{\mathrm{PhT}} = \frac{k_1[\mathrm{PhX}]}{(k_1 + k_2)[\mathrm{PhX}] + k_{\mathrm{Cu}}[\mathrm{Cu}^{2+}]} \cdot \frac{k_8}{k_8 + k_6[\mathrm{Cu}^{2+}]} \qquad (11)$$

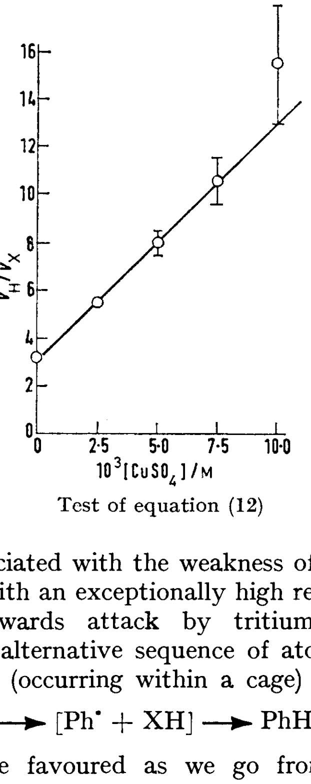
$$\frac{f_{\mathrm{PhX}}}{f_{\mathrm{PhT}}} = \frac{v_{\mathrm{H}}}{v_{\mathrm{X}}} = \frac{k_2}{k_1}\left(1 + \frac{k_6}{k_8}[\mathrm{Cu}^{2+}]\right) \qquad (12)$$

for bromobenzene given in Table 2 show the implied linear dependence on the concentration of copper(II) ions over the range where the replacement rate is sufficiently high to be reliably measurable (see Figure). The intercept of the graph corresponds to $k_2/k_1 \simeq 3$ and the slope to $k_6/k_8 = 1000$ mol^{-1} dm^3, the former result having the implication that tritium atom attack at the 1-position of bromobenzene is one-third times as likely as attack at all the other aromatic positions taken together.

Since radiation-induced hydrogen exchange in chlorobenzene and fluorobenzene appears to show no strong discrimination between *ortho*-, *meta*-, and *para*-positions,[7] the same is probably also true for bromobenzene. On this basis, attack of tritium atoms at the 1-position of bromobenzene is *ca.* 1·6 times more rapid than attack at each one of the other nuclear positions. However, in the absence of a more thorough mechanistic investigation, it is not certain that this line of reasoning and its extension to the other halogenobenzenes (with the implication that tritium atom attachment to the 1-position of iodobenzene is *ca.* 40 times more rapid than reaction at each of the other nuclear positions) is quite justified. At the present time it is impossible to dismiss the incursion of additional mechanisms, especially for iodobenzene, where the importance of deiodination, could be associated with the weakness of the C–I bond rather than with an exceptionally high reactivity of the 1-position towards attack by tritium atoms. For instance, the alternative sequence of atom abstraction reactions (13) (occurring within a cage) becomes ener-

$$\mathrm{PhX} + \mathrm{H}^\cdot \longrightarrow [\mathrm{Ph}^\cdot + \mathrm{XH}] \longrightarrow \mathrm{PhH} + \mathrm{X}^\cdot \qquad (13)$$

getically more favoured as we go from chlorine to bromine to iodine.



Test of equation (12)

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