724. *Some Free-radical Reactions of Chlorobenzene. The Action of the Hydrogen Peroxide–Ferrous Salt Reagent and of X-Rays on Aqueous Solutions of Chlorobenzene.*

By G. R. A. JOHNSON, GABRIEL STEIN, and JOSEPH WEISS.

The reactions of chlorobenzene in aqueous solution with OH and HO_2 radicals, produced by means of Fenton's reagent and by *X*-rays, have been studied. The three chlorophenols were formed in both cases. Their relative proportions have been estimated, and the dependence of this ratio on the pH investigated.

The position occupied by the chlorine atom is also attacked, and dechlorination and formation of diphenyl result. The extent of this reaction is apparently not influenced by pH.

The results indicate that the presence of the chlorine substituent in the aromatic ring has an effect similar to that of the nitro- or carboxy-groups (*J.*, 1949, 2074; 1950, 2704; 1951, 405), but different from that of the hydroxyl group (preceding paper).

Possible reaction mechanisms are discussed. Separation of the chlorophenols by paper chromatography is described.

IN previous papers it has been shown that the action of ionising radiations, *e.g.*, *X*-rays, on dilute aqueous solutions is due to free radicals (Weiss, *Nature*, 1944, **153**, 748; *Brit. J. Radiol.*, Suppl. 1, 1947, etc.). When solutions containing oxygen are irradiated with small doses of radiations, in the presence of suitable acceptors, the reactions are somewhat similar to those obtained by the hydrogen peroxide–ferrous salt reagent (Fenton's), and are due to OH and HO_2 radicals.

The present paper records results for the corresponding reactions with chlorobenzene. In particular, two points seemed of interest. First, whether the directive influence of the chlorine atom would be similar to that of the *meta*-directing nitro- and carboxy-groups (Loebl, Stein, and Weiss, *J.*, 1949, 2074; 1950, 2704; 1951, 405), or the *ortho–para*-directing hydroxyl group (preceding paper). Secondly, whether any dechlorination which occurs is due to the OH and HO_2 radicals, as in the case of nitrobenzene, rather than to the hydrogen atoms, and its dependence on pH.

That dechlorination by *X*-rays takes place in solution has been shown by Minder (cf. Minder and Liechti, *Radiol. Clin.*, 1949, **18**, 108). In the electrolytic oxidation of chlorobenzene in aqueous media (Fichter and Adler, *Helv. Chim. Acta*, 1926, **9**, 279; Fichter, " Organsiche Elektrochemie," 1942, p. 102), the formation of *p*-benzoquinone was observed, and chloride ions were found in the solution. Fichter interprets his results by assuming *p*-chlorophenol to be the main primary product of the reaction.

After reaction of Fenton's reagent with chlorobenzene, Merz and Waters (*J.*, 1949, 2427) isolated *o*-chlorophenol.

In agreement with the principles discussed in the preceding paper, we have employed a saturated aqueous solution of chlorobenzene, and sufficiently small doses of radiation to ensure that the whole of the radiation reaction occurred in the presence of dissolved oxygen in the solution. The solubility of chlorobenzene in water is only 0·05 g./100 ml. at 30° (cf. " Handbook of Chemistry and Physics," Chem. Rubber Publ. Co., 1949, p. 677). However, we have shown previously in the case of benzene (Stein and Weiss, *J.*, 1949, 3245) where the solubility in water is only 0·09 g./100 ml. (at 22°) that as little as 0·02 g. of benzene per 100 ml. will give a yield which is only 10% lower than the maximum yield. In the present case we have also found that the reaction proceeds readily, and gives yields comparable to those obtained in the case of benzene and nitrobenzene. Thus, the concentrations of these substances in aqueous solutions are sufficient to ensure a reaction velocity which prevents the recombination of the primary radicals (cf. Weiss, *loc. cit.*).

The Action of X-*Rays. Determination of the Isomeric Chlorophenols.*—In the present case we combined the results from infra-red spectrum analysis and from paper chromatography, for the determination of the chlorophenols. Thus, from the infra-red spectra the presence and the quantity of the *o*- and especially the *p*-derivative could be established with some certainty; on the other hand, paper chromatography yielded reliable results for the *o*- and, particularly, the *m*-derivative. Combination of these procedures established beyond doubt that all three isomers are formed, their relative proportions depending on the pH. From the quantitative point of view the results obtained from the infra-red spectroscopy (Table) were more accurate. In addition to these products, the presence of phenol was also shown by the infra-red analysis.

The results obtained from the paper chromatography confirmed the presence of the three isomers, and of phenol, and have shown that apparently chlorodihydroxybenzenes are not present in comparable amounts.

The relative ratios of the three isomeric chlorophenols are similar to those obtained in the cases of nitrobenzene and of benzoic acid (Loebl, Stein, and Weiss, *loc. cit.*) but differ from those obtained with phenol, where no *m*-derivative was found (see Table).

Action of X-*rays on aqueous solutions of chlorobenzene* (200 ml. of solution irradiated with a dose of $3{\cdot}25 \times 10^4$ E.U.).

pH:	2	6	12
Total solid residue (including phenol and diphenyl) (mg.) ...	2·4	2·0	2·3
Relative ratios (%):			
ortho	25—30	15—20	35—40
meta	30—35	20—25	20—25
para	35—40	50—60	35—40

The Action of Fenton's Reagent.—The hydrogen peroxide–ferrous salt reagent was used in acid solution, at pH ~1. Under these conditions, the procedure described for nitrobenzene being used, only a slow and mild attack takes place, resulting in the formation of small amounts of chlorophenols, the solution at the end of the reaction being pale yellow. Infra-red analysis showed *ortho* 40—45, *meta* 20—25, and *para*-isomer 20—25%. The relatively large proportion of the *o*-derivative was confirmed in several experiments. Paper chromatography yielded results similar to those obtained in the case of *X*-rays, and secondary products were again absent.

In view of the relative inaccuracy of these determinations, it is impossible to draw conclusions beyond the fact that all three isomeric chlorophenols are formed, their ratios not differing materially from those obtained by the use of *X*-rays, and in qualitative agreement with those obtained in the case of nitrobenzene and benzoic acid.

The Dechlorination of Chlorobenzene.—The formation of the chlorophenol is the result of a sequence of reactions:

$$H_2O \rightsquigarrow H + OH \quad \dots\dots\dots \quad (1)$$

$$H + O_2 \longrightarrow HO_2 \quad \dots\dots\dots \quad (1a)$$

$$C_6H_5Cl + OH \longrightarrow C_6H_4Cl + H_2O \quad \dots\dots\dots \quad (2)$$

$$C_6H_4Cl + OH \longrightarrow C_6H_4Cl{\cdot}OH \quad \dots\dots\dots \quad (3)$$

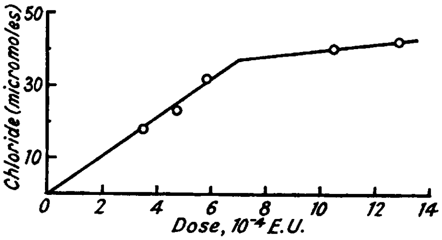
or of the equivalent reactions of the aryl radical with HO_2. Furthermore, the chlorine atom could behave in the same way as a hydrogen atom, and thus be removed:

$$C_6H_5Cl + OH \longrightarrow C_6H_5 + HOCl \quad \dots\dots\dots \quad (4)$$

A similar reaction (denitration) has been observed in the case of nitrobenzene (Loebl, Stein, and Weiss, *loc. cit.*). In the present case dechlorination occurs and chloride ions are present in the solution after the irradiation. Irradiation of 200 ml. of a solution with a dose of $5{\cdot}85 \times 10^4$ E.U. produced $3{\cdot}2 \times 10^{-5}$ mole of chloride ion at pH 2 or 6 and $3{\cdot}3 \times 10^{-5}$ mole at pH 12 (determined turbidimetrically). The dechlorination reaction is thus apparently not influenced by the pH. Moreover, the figure shows that it is more rapid in the presence of oxygen, indicating that the removal of chlorine proceeds more readily by means of OH or HO_2 than of hydrogen atoms. The analytical accuracy in the present case is very good and lends further support to the less accurately established but similar conclusions for nitrobenzene. The favourable effect of oxygen is remarkable, since reductive dechlorination of chlorobenzene is known to proceed fairly readily (Kelber, *Ber.*, 1917, **50**, 309; Busch and Schmidt, *Ber.*, 1929, **62**, 2617). Our findings are supported, however, by those of Fichter (*loc. cit.*) that an extremely ready dechlorination of chlorobenzene occurs in anodic oxidation processes.

With a dose of $3{\cdot}25 \times 10^4$ E.U. approximately 18 micromoles of chloride ion were produced (see figure) under conditions in which the total production of chlorophenols was of the order of 5 micromoles (Table I). We have no reliable quantitative data regarding products of the dimerisation of the aryl radical, but one may conclude that on the whole the dechlorination reaction seems to be favoured. This view is supported by the fact that apparently very little dichlorodiphenyl is formed in the reaction, whilst diphenyl was found in relatively large quantities. The results, therefore, seem to establish definitely the following salient points: the removal of the existing substituent occurs in a process which is apparently independent of the pH, whilst the introduction of the hydroxyl group occurs in a reaction which is influenced by the pH. In the case of benzene, quantitative evidence has been produced (Stein and Weiss, *J.*, 1949, 3256) in favour of a reaction mechanism involving two distinct steps, namely, those equivalent to reactions (2) and (3), and *not* a reaction mechanism involving a direct displacement, in which the total process coalesces into a single step. The evidence obtained in the present paper supports this view. Moreover the results indicate strongly that in the present reaction the chlorine atom has a directive influence similar to that of the nitro- or carboxy-group. The influence of chlorine in aromatic substitution (cf. Ingold and Shaw, *J.*, 1949, 575; Bird and Ingold, *J.*, 1938, 918) is composed of a " $-I$ " and a " $+T$ " effect. Our results seem to indicate the preponderence of the " $-I$ " effect in the particular step in which the OH radical enters into the molecule. Regarding the predominantly *para*-type of substitution, our results are in agreement with the results and views of Hey (*J.*, 1934, 1957; Augood, Hey, Nechvatel, and Williams, *Nature*, 1951, **167**, 725) on homolytic aromatic substitution by free radicals in solution.

These results also seem to support De la Mare's views (*J.*, 1949, 2871) on the importance of electromeric polarisability in some reactions which may perhaps have some bearing on the present case. In particular, it is possible that the increased formation of the *ortho*-derivative in the case of Fenton's reagent is due to the ionic nature of one of the reactive entities. In the preceding paper we have already described some possible effects of the $Fe(OH)^{2+}$ complex.



Formation of chloride by the action of X-*rays on chlorobenzene in aqueous solutions, in the presence of air* (*showing the diminished rate of formation on exhaustion of the oxygen in the solution*).

Our results seem to be in general agreement with the results of other workers regarding free-radical reactions of similar type in solutions. It is inadmissible to conclude, however, without establishing first a complete identity of the reaction mechanisms and of the type of reactants, that other free-radical reactions must yield very similar results or that reactions giving somewhat similar results are necessarily free-radical reactions.

EXPERIMENTAL.

Materials.—The water used in the present experiments was of the quality described in the preceding paper. The chlorobenzene (B.D.H.) was shaken with aqueous potassium hydroxide, washed with water, dried, and distilled at atmospheric pressure. The *o*-chlorophenol (B.D.H.) was freed from phenol by shaking it with 10% aqueous potassium carbonate, the alkaline solution being extracted with ether and then acidified, and the separated *o*-chlorophenol dried ($CaCl_2$) and distilled at atmospheric pressure. *m*-Chlorophenol was prepared according to Holleman and Rinkes's procedure (*Rec. Trav. chim.*, 1911, **30**, 81) and recrystallised from light petroleum; it had m. p. 26—28°. The *p*-chlorophenol (B.D.H.) was not further purified.

Experiments with Fenton's Reagent.—Ferrous sulphate (AnalaR, Messrs. Hopkins and Williams) and hydrogen peroxide (Laporte, 90%, stabiliser-free) were used, the experimental procedure being as for nitrobenzene (*loc. cit.*). Separate solutions of the ferrous salt and the dilute hydrogen peroxide were run simultaneously into the acidified (pH approx. 1) saturated, aqueous solution of chlorobenzene. The acid solution was extracted with ether, the organic layer treated with 10% sodium hydroxide solution, and this extract washed with ether, acidified, and extracted with ether. The last ethereal extract was evaporated and the residue submitted either to infra-red analysis or to paper chromatography. From the neutral fraction of the products, which remained in the ethereal extract of the acid reaction mixture, after treatment with alkali, there was obtained by elution chromatography diphenyl (m. p. 67°, not depressed on admixture with authentic specimen) and a second small fraction of a crystalline material (possibly some dichlorodiphenyls).

Irradiations.—These were carried out as described previously (cf. preceding paper, and Farmer, Stein, and Weiss, *J.*, 1949, 3241), the dose being measured by Day and Stein's method (*Nature*, 1949, **164**, 671; *Nucleonics*, 1951, **8**, No. 2, 34), in terms of the Gray–Read Energy Unit (E.U.), which is approximately equal to the roentgen. Their radiated solutions were treated similarly to those resulting from experiments with Fenton's reagent. In these cases the quantities of diphenyl and of dichlorodiphenyl were too small for definite identification. The products of six irradiations were combined for analysis by either method.

Infra-red Analysis.—These were carried out with a Hilger D.209 single-beam instrument with nitromethane as solvent. With this method, reliable and reproducible results could be obtained for *p*-chlorophenol, and, in the case of experiments with Fenton's reagent where larger yields were obtained, also for *o*-chlorophenol. The results for the *m*-derivative were, however, not very accurate. The presence of phenol was clearly indicated in all the spectra.

Paper Chromatography.—It was not possible to separate the isomeric chlorophenols themselves by paper chromatography. Coupling with diazotised *p*-nitroaniline, which yields strongly coloured derivatives, and subsequent paper chromatography, was no better. Since it was possible to separate the isomeric hydroxybenzoic acids by paper chromatography (*loc. cit.*), we attempted coupling with derivatives which would introduce an acid group into the molecule; *p*-aminobenzoic acid was tried unsuccessfully. Finally, coupling with sulphanilic acid gave a separation of the isomers which could be used for the qualitative identification of, especially, the *m*-derivative. Thus, the mixture of the three isomeric chlorophenols (containing also some phenol) was coupled with diazotised sulphanilic acid at 0° according to Snell's procedure (" Colorimetric Methods of Analysis," 1937, Vol. 2). The solution of the diazoates was kept at 0°, acidified, and extracted with *iso*butyl alcohol, the resulting extract was run on Whatman paper No. 1, in a mixture of *iso*butyl alcohol 70, ammonia solution (*d* 0·88) 25, water 80, and ethanol 25 parts by vol., the non-aqueous layer being used. Chromatograms were run upward in a constant-temperature room. The *m*- is separated well from the *o*- and the *p*-isomer and also from the phenol, but the *o*- and *p*-derivatives are not separated well from each other. From the *o*-chlorophenol two spots were obtained in the chromatogram due, perhaps, to coupling in two alternative positions. One of these spots coincides with that obtained from the *p*-derivative. The other is unique, and can be used for the identification of the *o*-derivative. The *p*-derivative does not, in the presence of *o*-isomer, produce a unique spot, and cannot be identified with certainty from the chromatogram alone. This method thus confirmed the presence of the *o*- and the *m*-derivative, which have been established also be infra-red analysis.

Determination of Chloride.—This was carried out according to the method of Luce, Denis, and Akerlund (*Ind. Eng. Chem. Anal.*, 1943, **15**, 365) with a Spekker Colorimeter and a neutral grey filter.

The infra-red determinations were carried out in the Infra-red Spectroscopy Section of Imperial Chemical Industries Limited, Billingham; we are grateful to Dr. R. Holroyd and Dr. B. W. Bradford for permission to carry out the measurements, and to Mrs. M. Broomfield for the analyses. We thank Dr. Hanna Loebl for assistance, Dr. F. T. Farmer and Mr. M. J. Day of the Radiotherapy Department, Royal Victoria Infirmary, for help with the *X*-ray irradiations, and the North of England Council of the British Empire Cancer Campaign for financial assistance.

UNIVERSITY OF DURHAM, KING'S COLLEGE,
NEWCASTLE-ON-TYNE, 1.

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