

539. *Hydroxylation. Part I. The Oxidation of Benzene and Toluene by Fenton's Reagent.*

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The reactions of benzene and toluene with Fenton's reagent have been investigated. Evidence is presented that the species which initiates the oxidation of benzene is the hydroxyl radical, and that this adds to the benzene nucleus. The resulting adduct gives biphenyl by dimerisation and then dehydration, and phenol by both disproportionation and further oxidation. Toluene undergoes both nuclear hydroxylation and oxidation at its methyl group.

THIS paper is the first of a series in which investigations will be reported of the mechanisms of hydroxylation of aromatic and aliphatic carbon atoms by reagents of both free-radical and ionic type. Since hydroxylation is of wide occurrence in biological systems, particular attention will be given to consideration of the reactions as model systems for the biological processes.

Many aromatic compounds which are foreign to animal organisms are metabolised to phenolic derivatives.¹ Williams and his co-workers^{1,2} have studied the products excreted by rabbits and other animals after administration of substituted benzenoid compounds, and Mitoma *et al.*³ have examined the products of hydroxylation of aromatic compounds by a partially purified enzyme system from liver microsomes. Both groups of workers observed that the hydroxyl group is introduced into the aromatic nucleus at those positions which are normally the most reactive towards electrophilic reagents, and it was suggested that the species responsible for the reaction is an electrophile such as an enzyme-held iron-oxygen complex, (Enzyme-FeO²⁺).⁴ The alternative suggestion, that the process involves a free-radical reaction, has also been made.⁵

Two chemical systems which bring about the hydroxylation of benzenoid compounds, namely, Fenton's reagent (ferrous ion and hydrogen peroxide) and a system consisting of ferrous ion, oxygen, ascorbic acid, and ethylenediaminetetra-acetic acid, have been studied in the hope that comparison with results from biological systems would reveal mechanistic features of the natural processes.⁶ The usefulness of such comparisons requires detailed information about the mechanisms of the model systems. Much is already known about the oxidation of aromatic compounds by Fenton's reagent,^{7,8} and the present work was directed towards quantitative studies which would enable the detailed steps of the process to be discerned. A preliminary report of one aspect of these studies has been published.⁹ Less is known about the second of the model systems, and the results of our investigation will be reported subsequently.

The Oxidation of Benzenoid Compounds by Fenton's Reagent.—There is evidence that

¹ Parke and Williams, *Ann. Reports*, 1958, **55**, 376.

² Parke and Williams, *Biochem. J.*, 1956, **63**, 12P.

³ Mitoma, Posner, Reitz, and Udenfriend, *Arch. Biochem. Biophys.*, 1956, **61**, 431.

⁴ Mason, *Science*, 1957, **125**, 1185.

⁵ Stein and Weiss, *Nature*, 1948, **161**, 650; Dalglish, *Arch. Biochem. Biophys.*, 1955, **58**, 214.

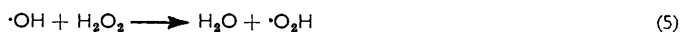
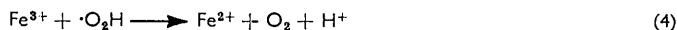
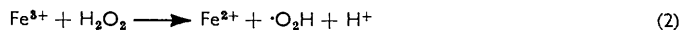
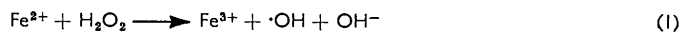
⁶ See, e.g., Boyland and Sims, *J.*, 1953, 2966; Udenfriend, Clark, Axelrod, and Brodie, *J. Biol. Chem.*, 1954, **208**, 731; Breslow and Lukens, *J. Biol. Chem.*, 1960, **235**, 292; Acheson and Hazelwood, *Biochim. Biophys. Acta*, 1960, **42**, 49. For a detailed discussion, see Mason, in "Advances in Enzymology," ed. F. F. Nord, Interscience Publ., Inc., Vol. XIX, 1957, p. 79.

⁷ (a) Baxendale and Magee, *Discuss. Faraday Soc.*, 1953, **14**, 160; (b) Ono, Oyamada, and Katsuragi, *J. Soc. Chem. Ind., Japan*, 1938, **41**, Suppl. 209; (c) Loebel, Stein, and Weiss, *J.*, 1949, 2074; Johnson, Stein, and Weiss, *J.*, 1951, 3275.

⁸ Merz and Waters, *J.*, 1949, 2427; Stein and Weiss, *J.*, 1949, 3245.

⁹ Norman and Radda, *Proc. Chem. Soc.*, 1962, 138.

the ferrous ion-catalysed decomposition of hydrogen peroxide may be represented by the following modification¹⁰ of the original proposal by Haber and Weiss:¹¹



Other mechanisms, involving two-electron steps, have also been suggested.^{12,13} One of these¹² has been ruled out on the basis of kinetic data.¹⁴ The second was based on results from which it was concluded that, while the reaction occurs mainly through two-electron transfers, the one-electron process may be concurrent with it.¹³ Further support for the intermediacy of radicals is derived from two studies. First, Fenton's reagent initiates a radical-chain polymerisation.¹⁵ Secondly, the isomer ratios obtained in the hydroxylation of nitrobenzene and chlorobenzene^{7c} are similar to those obtained when the hydroxylating species is produced by the irradiation of water with X-rays,¹⁶ while the ratios in the hydroxylation of anisole and fluorobenzene are similar to those when hydroxyl radicals are generated by ultraviolet irradiation of hydrogen peroxide.⁹ There is therefore convincing evidence that the hydroxylation of benzenoid compounds by Fenton's reagent involves the hydroxyl radical. It has also been observed that, in its aromatic substitutions, this radical displays marked electrophilic character.⁹

The main products from the oxidation of benzene by Fenton's reagent are phenol and biphenyl. Their relative proportions vary with the conditions of the reaction.^{7a,b} although no systematic study of the variations has been carried out quantitatively. Further, it has not been ascertained whether the interaction of the hydroxyl radical with benzene involves addition of the radical to the nucleus or abstraction of a hydrogen atom from it, although the latter has been suggested to account for the formation of biphenyl.⁸ We therefore studied quantitatively the effects both of replacing benzene by hexadeuterobenzene and of varying the conditions of the reaction, in the hope of elucidating the nature both of the initial step of the reaction and of the subsequent processes leading to phenol and biphenyl.

RESULTS

When hydrogen peroxide was added dropwise to a vigorously stirred suspension of benzene in dilute sulphuric acid containing ferrous sulphate, phenol and biphenyl were formed in low yield. Their relative amounts depended on the rate of addition of the peroxide: the proportion of biphenyl was increased from 8.5% to 39.0% by increasing the rate of addition by a factor of 60. With given rates of mechanical stirring and addition of peroxide the ratio of the products was constant and reproducible, and the fast rate of addition was used in subsequent work.

In the experiments described below, reaction was always carried out in heterogeneous conditions except in the isotope-effect measurements where homogeneous conditions were employed, with aqueous acetone as the solvent. It has previously been shown that the mechanism of oxidation is essentially unchanged when homogeneous instead of heterogeneous conditions are used.⁹

Isotope Effects.—(a) Benzene and hexadeuterobenzene were oxidised separately under identical conditions. The yields of phenol and deuterated phenol, and of biphenyl and deuterated biphenyl, measured by gas chromatography relative to an external standard, were

¹⁰ Uri, *Chem. Rev.*, 1952, **50**, 375.

¹¹ Haber and Weiss, *Proc. Roy. Soc.*, 1934, *A*, **147**, 332.

¹² Bray and Gorin, *J. Amer. Chem. Soc.*, 1932, **54**, 2124.

¹³ Cahill and Taube, *J. Amer. Chem. Soc.*, 1952, **74**, 2312.

¹⁴ Medalia and Kolthoff, *J. Polymer. Sci.*, 1949, **4**, 377.

¹⁵ Baxendale, Evans, and Park, *Trans. Faraday Soc.*, 1946, **42**, 155.

¹⁶ Loebel, Stein, and Weiss, *J.*, 1950, 2704.

the same. (b) When these experiments were repeated with the addition of chlorobenzene to each, the ratios of the peak areas on gas-chromatographic analysis were: phenol : *o*-chlorophenol, 0.66; deuterated phenol : *o*-chlorophenol, 0.475. Isotopic discrimination is therefore occurring, but the values have only qualitative significance since benzene gives some benzyl methyl ketone under these conditions and this had the same retention time as *o*-chlorophenol on our column. The isotope effect was confirmed, however, when reaction was carried out under conditions in which benzyl methyl ketone is not formed (by using a neutral solution of aqueous acetone in the presence of ascorbic acid): the corresponding ratios were 0.75 and 0.47.

Since the total yield of oxidation products in each set of experiments was very low (<5%), the ratios of the yields of the products are measures of the relative reactivities of the aromatic compounds.

The oxidation of chlorobenzene by Fenton's reagent gave phenol in small yield. It was shown that this was negligible compared with the yields of phenol and deuterated phenol from benzene and hexadeuterobenzene in (b).

Variation of Reaction Conditions.—The combined yields of phenol and biphenyl, and the proportion of phenol in the product, were measured under the following conditions:

(a) The initial concentration of ferrous ion was increased. The total yield passed through a maximum and the proportion of phenol increased (Table).

(b) Increasing amounts of ferric alum were added. The total yield remained constant but the proportion of phenol increased (Table).

(c) Ferrous sulphate was replaced by an equivalent quantity of ferric alum and then ceric sulphate. Traces of the oxidation products were detected but their yields were negligible compared with those using ferrous ion.

(d) Sodium fluoride (40 g. l.⁻¹) was added to the ferrous sulphate (13.4 g. l.⁻¹). The total yield was unchanged, but the proportion of phenol decreased from 61 to 30%.

(e) Reaction was carried out, in the presence of fluoride ion, first under nitrogen (in deaerated distilled water) and then while oxygen was bubbled through the solution. The proportions of phenol formed were 20% and 43%, respectively.

Products from the oxidation of benzene.

(a) Initial ferrous sulphate concentration (g. l.⁻¹).

	1.25	1.34	2.5	10.0	13.4	16	20	24	40	80	134	160
Total yield *	0.17		0.28	0.86	1.00	1.04	1.23	0.98	0.67	0.38		0.10
Phenol (%)		46.5			61.0						77.0	

(b) Ferric alum (g. l.⁻¹) added to ferrous sulphate (13.4 g. l.⁻¹)

	0	10	25	40	50	75	100
Total yield *	1.00	1.05	1.03	0.98	0.93	1.05	1.07
Phenol (%)	61.0	68.5	75.6	78.5	81.0	87.7	90.0

* Relative to that obtained when using ferrous sulphate (13.4 g. l.⁻¹).

(f) Ferrous was replaced by an equivalent concentration of titanous ion. Only traces of the oxidation products were detected when hydrogen peroxide was added to a suspension of benzene in acidified titanous chloride solution. The yields were increased when titanous chloride solution was added to a suspension of benzene in acidified hydrogen peroxide, phenol and biphenyl being formed in a ratio of about 1 : 4. Fluorobenzene and chlorobenzene, when oxidised in the same way, gave the three phenolic derivatives in each case, in relative amounts similar to those obtained by oxidation with Fenton's reagent⁹ (fluorobenzene: *o*-, 35.3; *m*-, 24.7; *p*-, 40.0%; chlorobenzene: *o*-, 47.1; *m*- + *p*-, 52.9%).

Oxidation of Toluene.—Toluene was oxidised by Fenton's reagent in the heterogeneous conditions used for benzene. The following products were obtained, the relative molar proportions being given in parentheses: benzyl alcohol and benzaldehyde (38.3, combined), benzoic acid (18.0), bibenzyl (30.5), phenol (2.9), *o*-cresol (3.0), *m*-cresol (0.2), *p*-cresol (1.0), *o*-hydroxybenzaldehyde (3.2), diphenylmethane (1.0), and 2,2'-bitolyl (2.1).

The same products were formed when the reaction was carried out under nitrogen. The relative amounts of the following products decreased slightly: benzaldehyde and benzyl alcohol (36.8), benzoic acid (16.3), phenol and *o*-cresol (3.0, combined), *m*- and *p*-cresol (0.5, combined), while those of bibenzyl (39.3), and *o*-hydroxybenzaldehyde (4.4) increased.

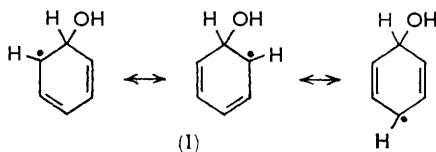
DISCUSSION

The Attacking Species.—Evidence was quoted earlier that the hydroxylation of benzenoid compounds by Fenton's reagent is a homolytic process. The isolation of biphenyl and bibenzyl from benzene and toluene, respectively, is also indicative of a free-radical reaction. Further, since with certain variations of the conditions used for oxidising benzene the phenol : biphenyl ratio changes while their combined yield remains constant, it is probable that both are formed from a common intermediate.

According to the modified Haber-Weiss mechanism the two oxygen-containing radicals which may initiate oxidation are $\cdot\text{OH}$ and $\cdot\text{O}_2\text{H}$. The following evidence shows that it is the former which reacts with benzene. (a) Ceric ion reacts with hydrogen peroxide to give $\cdot\text{O}_2\text{H}$, identified by electron-spin resonance spectroscopy,^{17,18} but this system is barely effective in oxidising benzene. (b) The $\cdot\text{O}_2\text{H}$ radical should be formed in higher concentration, according to reaction (2), by the addition of ferric ion to Fenton's reagent. However, the yield of oxidation products was not increased by the addition of ferric ion, nor did the system of ferric ion and hydrogen peroxide give oxidation products in significant yield. (c) The system, titanous ion and hydrogen peroxide, hydroxylates chlorobenzene and fluorobenzene in a similar manner to Fenton's reagent, and oxidises benzene to phenol and biphenyl. The hydroxyl radical has been identified as an intermediate in this system by electron-spin resonance spectroscopy, whereas $\cdot\text{O}_2\text{H}$ is not present.¹⁸

It is concluded that $\cdot\text{O}_2\text{H}$ is not the attacking species. This may be either because it is too rapidly destroyed by further oxidation [reaction (4)] or because it is much less reactive than $\cdot\text{OH}$ towards benzene. There is evidence that $\cdot\text{O}_2\text{H}$ is less reactive than $\cdot\text{OH}$ towards olefinic monomers.¹⁹

The Interaction of Benzene and $\cdot\text{OH}$.—It has been suggested that the hydroxyl radical abstracts a hydrogen atom from benzene to give a phenyl radical, and that this gives phenol by further oxidation and biphenyl by dimerisation.⁸ The absence of a hydrogen isotope effect in the formation of both phenol and biphenyl when benzene and hexa-deuterobenzene are separately oxidised is not consistent with this suggestion. It is, however, compatible with the addition of $\cdot\text{OH}$ to the aromatic nucleus to give the resonance-stabilised adduct (I).



There is evidence from electron-spin resonance studies that this adduct is formed when benzene is oxidised by titanous ion and hydrogen peroxide,²⁰ and also evidence from spectroscopic studies that it is formed during the pulse-irradiation of benzene in water.²¹ Further, species (I) is analogous to the intermediate postulated in the homolytic phenylation of benzenoid compounds on the basis of the absence of a kinetic isotope effect²² and product studies.²³

Ferrous ion should compete with benzene for the hydroxyl radical, according to reaction (3). This is confirmed by the results in the Table. As expected, the yield of oxidation

¹⁷ Saito and Bielski, *J. Amer. Chem. Soc.*, 1961, **83**, 4467.

¹⁸ Dixon and Norman, *Nature*, 1962, **196**, 891.

¹⁹ Barb, Baxendale, George, and Hargrave, *Trans. Faraday Soc.*, 1951, **47**, 462.

²⁰ Dixon and Norman, *Proc. Chem. Soc.*, 1963, 97.

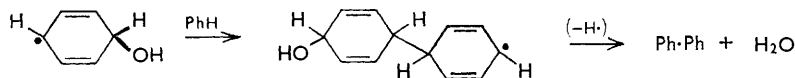
²¹ Dorfman, Bühler, and Taub, *J. Chem. Phys.*, 1962, **36**, 549.

²² Convery and Price, *J. Amer. Chem. Soc.*, 1958, **80**, 4101; Chang Shih, Hey, and Williams, *J.*, 1959, 1871.

²³ DeTar and Long, *J. Amer. Chem. Soc.*, 1958, **80**, 4742.

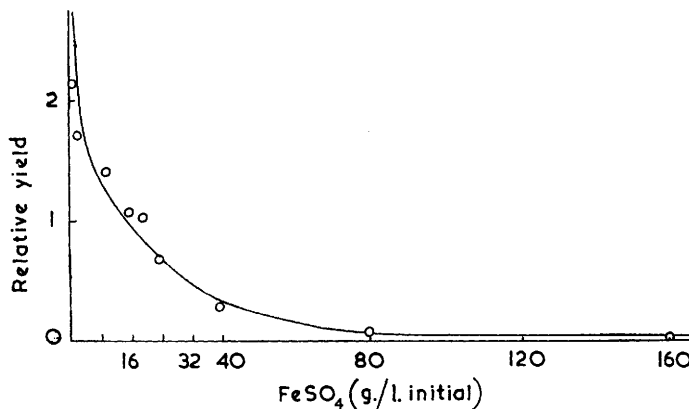
products per gram of ferrous sulphate rises towards a theoretical maximum at zero concentration of ferrous sulphate (Figure). The maximum yield of oxidation products occurs when $[\text{Fe}^{2+}] = [\text{H}_2\text{O}_2]$.

Reactions of Species (I).—(a) *Formation of biphenyl.* The two simplest paths by which the species (I) could give biphenyl are (i) attack on benzene followed by loss of a hydrogen atom and dehydration:



(ii) dimerisation followed by dehydration. Increase in the amount of benzene does not increase the relative yield of biphenyl, contrary to expectation if (i) were followed.²⁴ That course (ii) is followed is consistent with two sets of observations. First, the proportion of biphenyl is increased by increasing the rate of addition of hydrogen peroxide. This

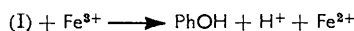
Dependence of total yield of oxidation products per gram of ferrousulphate on ferrous sulphate concentration.



increases the rate of production of $\cdot\text{OH}$ and hence of species (I), thereby promoting the formation of biphenyl which, according to (ii), is dependent on the square of the concentration of (I). Secondly, increasing the concentration of ferrous ion reduces the concentration of species (I), and therefore the proportion of biphenyl, by providing greater competition for $\cdot\text{OH}$.

The formation of biphenyl through dimerisation is analogous to the formation of 1',4',4''-tetrahydro-*p*-quaterphenyl from the intermediate corresponding to (I) in the homolytic phenylation of benzene.²³

(b) *Formation of phenol.* (i) The increased proportion of phenol caused by the addition of ferric ion and by carrying out the reaction under oxygen shows that species (I) can be oxidised to phenol both by ferric ion:



and by oxygen. It has been shown that the phenylcyclohexadienyl radical [the analogue of (I)] also reacts with oxygen.²⁵

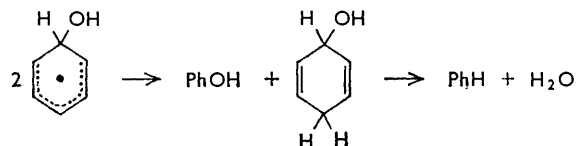
The reduction in the proportion of phenol formed when fluoride ion is present may be attributed to the removal of ferric ion as it is formed by complex-formation. Finally, the lower proportion of phenol formed when ferrous is replaced by titanous ion follows from the weak oxidising power of titanous relative to ferric ion.

(ii) Whereas there is no kinetic isotope effect when benzene and hexadeuterobenzene are oxidised separately, the presence of chlorobenzene as a competitor in each case

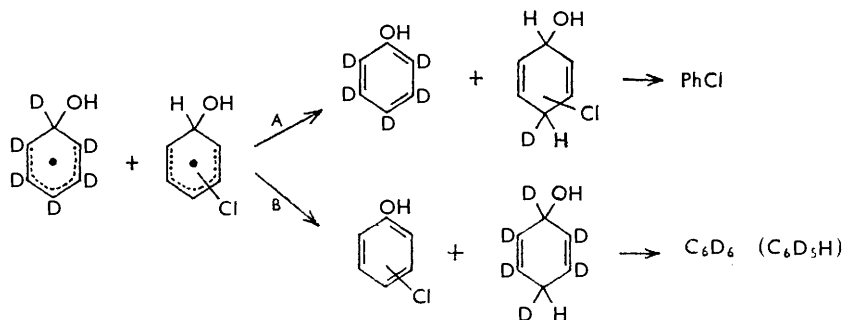
²⁴ Baxendale and Magee, *Trans. Faraday Soc.*, 1955, **51**, 205.

²⁵ Eberhardt and Eliel, *J. Org. Chem.*, 1962, **27**, 2289.

introduces a significant positive isotope effect. This may be attributed to the formation of phenol by the disproportionation of the initial adduct, *e.g.*:

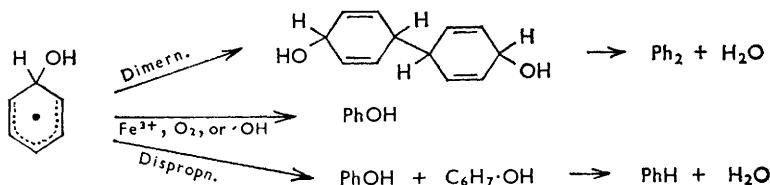


In the absence of chlorobenzene, there is only one possibility for this disproportionation, a hydrogen atom being transferred from one adduct to the other when benzene is the reactant, and a deuterium atom being transferred when hexadeuterobenzene is the reactant. In the presence of chlorobenzene, however, the possibility of a "crossed" disproportionation arises, especially as benzene and chlorobenzene have closely similar reactivities in these hydroxylations.⁹ The two crossed reactions when hexadeuterobenzene and chloro-



benzene are used together are as shown in (A) and (B). The second, involving transfer of a hydrogen atom, should occur more readily than the other, in which deuterium is transferred. This could lead to the observed decrease in the ratio of phenol : *o*-chlorophenol when hexadeuterobenzene is substituted for benzene.

This disproportionation mechanism is similar to that involved in the formation of biaryls by the phenylation of benzene for which evidence has been obtained from studies of the isotopic composition of the products.²⁶



The reactions of species (I) may be set out in the annexed summary. It is difficult to assess quantitatively the relative importance of the various processes, but it is notable that, when ferric ion and oxygen are excluded, the ratio phenol : biphenyl is only 1 : 4. Evidently dimerisation of species (I), involving no bond-breaking step, occurs more readily than disproportionation.

Oxidation of Toluene.—Toluene undergoes both nuclear hydroxylation and oxidation at its methyl group. The isomer distribution of the three cresols (*o*-, 71; *m*-, 5; *p*-, 24%) is similar to that observed in the homolytic phenylation²⁷ and methylation²⁸ of toluene

²⁶ Eliel, Meyerson, Welvert, and Wilen, *J. Amer. Chem. Soc.*, 1960, **82**, 2936.

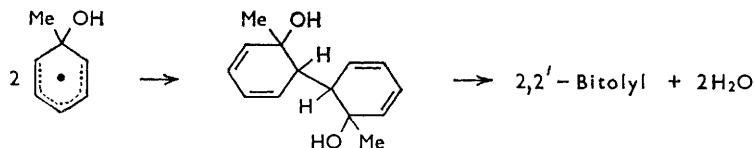
²⁷ Walling, in "Free Radicals in Solution," John Wiley and Sons, Inc., New York, 1957, p. 484.

²⁸ Cowley, Norman, and Waters, *J.*, 1959, 1799.

in that the *ortho*-isomer is the major component, but differs in that the *para*-position is here more reactive than the *meta*-position. This is a further example of the electrophilic properties of $\cdot\text{OH}$.⁹

The formation of bibenzyl is indicative of the presence of the benzyl radical as an intermediate in oxidation at the side-chain. Even in the absence of oxygen this gives benzyl alcohol and further oxidation products, and these are increased at the expense of bibenzyl when the reaction is carried out in air, evidently because the benzyl radical reacts with oxygen.

Three other products which are formed in very small quantities are *o*-hydroxybenzaldehyde, diphenylmethane, and 2,2'-bitolyl. The first probably arises by hydroxylation of benzaldehyde. Its *meta*- and *para*-isomers were not detected, and by analogy with other homolytic aromatic substitutions²⁷ they should be formed in smaller quantities. Diphenylmethane may arise from the attack of benzyl radicals on benzoic acid, followed by decarboxylation.



The mechanism of formation of 2,2'-bitolyl is not clear. It could result from the abstraction of a hydrogen atom from the *ortho*-position of toluene followed by dimerisation, but there is no other evidence that a hydrogen atom is abstracted from the benzene ring in this way. We therefore tentatively suggest that it arises from addition of $\cdot\text{OH}$ to C-1 of toluene, followed by dimerisation and dehydration, as illustrated. This suggestion is consistent with the formation of phenol from both toluene and chlorobenzene for these also may result from initial addition of $\cdot\text{OH}$ to the C-1.

EXPERIMENTAL

Materials.—Benzene, toluene, phenol, acetone, ferrous sulphate, ferric alum, and sodium fluoride were "AnalaR" reagents. Commercial chlorobenzene and biphenyl were purified by distillation and recrystallisation, respectively. Hexadeuterobenzene was supplied by Koch Laboratories. Oxygen and nitrogen were British Oxygen white-spot grade. 15% Titanous chloride solution (B.D.H., iron-free) was used.

Oxidations.—Reactions were carried out in air at room temperature except where stated otherwise. The yield of oxidation products was always less than 5%, disubstitution thereby being minimised.

A suspension of benzene (5 ml.) in 0.4N-sulphuric acid (100 ml.) containing ferrous sulphate (1.34 g.) was vigorously stirred while diluted (1 : 15) 100-volume hydrogen peroxide (12.5 ml.) was added at a controlled rate from a burette. After 15 min. the reaction mixture was extracted with ether (4 × 100 ml.), and the ethereal solution was dried (Na_2SO_4), evaporated to 1–2 ml., and analysed by gas chromatography. After initial experiments in which the rates of mechanical stirring and of addition of peroxide were varied, a constant rate of stirring was employed and the peroxide was added during 15 sec. Toluene (5 ml.) was oxidised similarly. The other variations in the reaction conditions are recorded in the Results.

Oxidations with titanous ion. A mixture of benzene (5 ml.) and 0.4N-sulphuric acid (500 ml.) containing hydrogen peroxide (2 ml.) was stirred vigorously while a solution of aqueous titanous chloride (5 ml.) in 0.4N-sulphuric acid (500 ml.) was added at a steady rate during 30 min. Fluorobenzene and chlorobenzene were oxidised similarly.

Isotope-effect Experiments.—Reactions were carried out at 25° with thermostat control. (a) Benzene (0.50 g.) and ferrous sulphate (1 g.) were dissolved in a mixture of acetone (100 ml.) and 0.4N-sulphuric acid (100 ml.). Hydrogen peroxide (1 ml.) was added. After 30 min. the mixture was extracted with ether (4 × 100 ml.), and the ethereal solution was treated as

described earlier before analysis. The experiment was repeated with hexadeuterobenzene (0.54 g.). The ratios of phenol and biphenyl to the external standard (diphenylmethane) were 0.69 ± 0.03 and 0.16 ± 0.01 , respectively, and those of the deuterated products were 0.74 ± 0.04 and 0.17 ± 0.01 , respectively.

(b) Reactions were carried out under the same conditions with the addition of chlorobenzene (0.72 g.) in each case.

(c) Chlorobenzene (2.88 g.), benzene (0.50 g.), ferrous sulphate (1 g.), and ascorbic acid (1 g.) were dissolved in a mixture of acetone (50 ml.) and an aqueous buffer solution (pH 7) (50 ml.). Hydrogen peroxide (1 ml.) was added. After 30 min. the mixture was extracted and analysed as above. The experiment was repeated with hexadeuterobenzene (0.54 g.) in place of benzene. Under these conditions benzene did not give benzyl methyl ketone. The ratios of the peak areas on gas-chromatographic analysis were: phenol: *o*-chlorophenol, 0.75 ± 0.04 ; deuterated phenol: *o*-chlorophenol, 0.47 ± 0.04 ; phenol: biphenyl, 7.6 ± 0.8 ; deuterated phenol: deuterated biphenyl, 5.2 ± 0.6 . Hence the yield of phenol relative to that of *o*-chlorophenol is reduced by a factor of 1.6 by deuteration, and the yield of phenol relative to that of biphenyl is similarly reduced by a factor of 1.5.

Product Identification.—Products were identified first by comparison of retention times with those of known compounds and, secondly, where possible, by collection of the material corresponding to a particular peak at the outlet of the gas chromatography unit and the comparison of its infrared spectrum with that of the suspected compound. In this way it was shown that the main oxidation products from toluene were benzaldehyde, bibenzyl, phenol, the cresols, and benzoic acid. Benzyl alcohol was eluted at the same time as benzaldehyde and was not estimated separately. The peak corresponding to bibenzyl was shown by infrared analysis not to be due, in whole or part, to any of the phenyltolylmethanes, which had the same retention times. Benzyl methyl ketone was identified as a product from the oxidation of benzene in aqueous acetone in acidic conditions.

The amounts of *o*-hydroxybenzaldehyde, diphenylmethane, and 2,2'-bitolyl were too small for collection of samples after gas-chromatographic separation. Evidence for their presence was that their retention times corresponded to those of the authentic materials and that the first was alkali-soluble while the others were not.

Gas Chromatography.—(a) The column (200 cm. \times 4.5 mm.) was packed with diethylene glycol adipate polyester (Lac-2.R.446; Cambridge Industries, Inc., Massachusetts, U.S.A.) (25% w/w) and 85% phosphoric acid (2% w/w) on Embacel (60—100 mesh) and was operated at 160°. The carrier-gas was nitrogen (65 ml./min.) at an inlet pressure 28 cm. Hg above atmospheric and with atmospheric pressure at the outlet. A hydrogen-inject flame ionisation detector coupled to a Sunvic recorder gave a linear response. This column was used for the analysis of all reaction mixtures except that from fluorobenzene and except for analysis of the cresols. Retention times (min.) were: benzyl alcohol and benzaldehyde, 7 (not resolved); *o*-hydroxybenzaldehyde, 12; *o*-chlorophenol, 14; 2,2'-bitolyl, 16; phenol, 19; *o*-cresol, 20; *m*- and *p*-cresol, 26 (not resolved); biphenyl, 26; diphenylmethane, 28; bibenzyl, 34; benzoic acid, 58; *m*- and *p*-chlorophenol, 95 (not resolved).

(b) The column (100 cm. \times 4.5 mm.) was packed with 2,4-xylylene phosphate (5% w/w) on Embacel (60—100 mesh), and was operated at 125° with argon (7 lb. sq. in.) as the carrier-gas and a Pye Argon detector. It was used for analyses of the fluorophenols and cresols, and also for confirming results from the oxidation of benzene. Retention times (min.) were: (i) fluorophenols: *o*-, 12; *p*-, 47; *m*-, 51; (ii) cresols: *o*-, 42; *p*-, 55; *m*-, 59; (iii) pentamethylbenzene, 23; phenol, 38; biphenyl, 60; diphenylmethane, 78.

Relative amounts of materials were determined by constructing triangles made up of tangents to the Gaussian curves of the chromatogram peaks and the intercepts on the base line. For non-isomeric materials equimolar quantities did not give peaks of equal area, and the relationship between the peak area and the amount of the substance injected was determined by using synthetic mixtures. It was shown by subjecting synthetic mixtures of products to the same extraction procedure as that used for the reaction mixtures that no preferential loss of any product occurred.

Relative yields from oxidations were measured by the addition of a known amount of an external standard to the product mixture before analysis. Both pentamethylbenzene and diphenylmethane were used as standards.

The results quoted are mean values from at least two analyses of each of two or more reaction

mixtures obtained in each set of conditions. The analytical technique was shown to be accurate to within $\pm 3\%$.

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