512.   *Kinetics and Mechanism of Aromatic Nitration.   Part VI.   The Nitration of Phenols and Phenolic Ethers : the Concomitant Dealkylation of Phenolic Ethers.   The Role of Nitrous Acid.*

By C. A. Bunton, E. D. Hughes, C. K. Ingold, D. I. H. Jacobs, M. H. Jones, G. J. Minkoff, and R. I. Reed.

It has been shown (Parts I—V; *J.*, 1938, 929; 1950, 2400—2467) that the nitration of aromatic compounds in general by nitric acid in organic solvents is retarded by nitrous acid, the " zeroth-order " equation

$$\text{Rate} \infty [\text{ArH}]^0\{a + b[\text{HNO}_2]^{1/2}\}^{-1} \quad . \quad . \quad . \quad . \quad . \quad . \quad (\text{i})$$

applying to sufficiently reactive aromatic compounds, when nitric acid is in constant excess. This law has been interpreted as characteristic of nitration by the free nitronium ion, which, however, may also enter reaction in combined forms, such as the nitric acidium ion, and the dinitrogen pentoxide molecule.   Against this background, a special situation arises in the nitration of phenol and aniline and their derivatives, including the laterally alkylated derivatives. Such nitrations are known to be accelerated by nitrous acid, to involve kinetics that have hitherto defied analysis, to exhibit a tendency to the loss of a lateral alkyl group, and to involve other non-oxidative and oxidative side-reactions.   These phenomena are here examined over the field of phenols and phenolic ethers.

The acceleration by nitrous acid is shown to be due to a special mechanism of nitration governed by the kinetic law

$$\text{Rate} \propto [\text{ArH}]^1[\text{HNO}_2]^1 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (\text{ii})$$

nitric acid being in constant excess.   The complex kinetics are due, generally and essentially, to the superposition of this special process on the general nitration process, which, for compounds as reactive as phenols and phenolic ethers, is governed by the zeroth-order equation (i).

The transition which replaces the special mechanism (ii) by the general mechanism (i) may be effected by increasing the nitric acid concentration, *i.e.*, the availability of nitronium ion, and by decreasing the nitrous acid concentration.   In the nitration of *p*-chloroanisole by nitric acid in acetic acid, it was possible to isolate the pure special mechanism (ii), and to effect, as described, a complete mechanistic conversion to the pure general mechanism (i), rates throughout remaining within the range of magnitudes which allow kinetic measurement.   In some other cases, rates get out of hand when a similarly complete demonstration is attempted : in general the mechanisms are superposed.   For the nitration of *p*-nitrophenol in acetic acid, the pure special mechanism was isolated ; but the transition to the general mechanism was followed only to the stage of giving to the latter a dominating, and not an exclusive, importance.   In the nitration of anisole in acetic acid, neither mechanism could be obtained in a pure condition ; but a shift was demonstrated from a strongly predominating special mechanism to a strongly predominating general mechanism.   In the nitration of phenol in acetic acid, and in water, qualitatively similar shifts were realised.

A theory of the special mechanism is given : in it, the nitrosonium ion plays approximately the same part as the nitronium ion in the general mechanism.   It is assumed that the special mechanism leads primarily to nitrosation, and that the formed nitroso-compounds are rapidly oxidised to nitro-compounds, thereby causing no net loss or gain of nitrous acid.

The nitrosonium ion is assumed to be capable of entering into reaction, not only in the free state, but also in combined forms, such as the nitrous acidium ion and the dinitrogen trioxide molecule.   Changes are demonstrated in the *ortho*/*para*-ratio for the nitration of phenol in water, and in acetic acid, under various conditions, and are interpreted on these lines.

Phenolic ethers may be dealkylated during nitration.   *p*-Chloroanisole is partly dealkylated on nitration by nitric acid in acetic acid, giving 4-chloro-2 : 6-dinitrophenol along with 4-chloro-2-nitroanisole.   This is true for nitration alike by the pure special mechanism and by the pure general mechanism ; but the proportion of dealkylation is greater for the special than for the general mechanism.   For nitration by the special mechanism it was demonstrated that the proportion of dealkylation is characteristic : it remained constant over a 100-fold change in the reaction rate.   These dealkylations involve no oxidation, and do not disturb the kinetic forms of nitration.   Acetic acid being the solvent, the eliminated methyl group was recovered (60% yield) as methyl acetate.

It is assumed that in the course of the nitration an oxonium ion is formed, which loses a carbonium ion, CH_3^+, after the usual heterolytic pattern of 'onium ion decompositions.   Unlike anisole and *p*-chloroanisole, 2 : 6-dichloroanisole and 2 : 6-dimethylanisole were not dealkylated during nitration : this is attributed to steric hindrance in the formation of the assumed oxonium ions.

Although oxidation is thus shown not to be necessary for the detachment of an alkyl group, not all dealkylations are free from oxidation.   Thus the loss of the ethyl group during nitration of *p*-chlorophenetole involves much oxidation, with production of nitrous acid, which complicates the kinetics of the nitration.

Other non-nitrating side-reactions may occur, which depend on condensation through reactive nuclear positions to produce deeply coloured compounds, or on polycondensation to give tars, if there are several such positions.   Such reactions may be non-oxidative or oxidative ; in the latter event they produce autocatalysis or auto-retardation, according as the special

or general nitration mechanism is dominating. The main nuclear side-reaction accompanying the nitration of anisole has been studied. It is a non-oxidative condensation between anisole and nitrous acid, giving, in proportions of the order of 10% under the conditions used, the coloured dianisyloxidoammonium ion, Ar_2NO^+.* This condensation with nitrous acid, like the nitration dependent on nitrous acid, is of first order with respect to anisole.

The only observed nitration mechanisms being the above-described general and special mechanisms, the question has been considered as to why, for phenol and aniline derivatives, the former tends to be replaced by the latter. It is concluded that in principle both mechanisms are universal, but that the special mechanism receives special advantages from the use of highly reactive aromatic compounds. The nitronium ion is a much more reactive substituting agent, but is also much more easily destroyed by bases, than is the nitrosonium ion. In order to secure only mononitration of a highly reactive aromatic compound, it is necessary strongly to restrict the nitronium ion supply by introducing bases such as water; and this leaves the field open for substitution by the nitrosonium ion. From the conclusion that the relevant peculiarity of phenol and aniline derivatives is simply their reactivity, it follows that the special mechanism of nitration should be observable with other kinds of aromatic compound, *e.g.*, hydrocarbons, if sufficiently reactive ones can be found. This has been demonstrated in the example of mesitylene. Complementing what was done with phenol derivatives, the pure general mechanism has, in this case, been made the starting point of a progressive mechanistic change, which has been followed until the special mechanism is in nearly complete control.

(1) *Background and Plan.*

(1.1) *The Special Nature of the Nitration of Phenol and Aniline.*—It has long been apparent that the nitration by nitric acid of phenol and aniline, and of their laterally alkylated derivatives such as anisole and mono- and di-methylaniline, pursues a mechanism which is essentially different from the mechanisms followed by the nitration of aromatic compounds in general.

The existence of the difference is strikingly attested by the effect of nitrous acid. The literature contains many records which show that nitrous acid is a positive catalyst for the nitration of those aromatic compounds of which phenol and aniline are the parents. In certain of these reactions nitrous acid is produced by a concurrent oxidation of the aromatic compound by the nitric acid : when this happens the nitrations are autocatalytic. On the other hand, nitrous acid is in general a negative catalyst for the nitration by nitric acid of aromatic compounds outside the limited class of phenol and aniline derivatives (cf. Part II, Section 4, *J.*, 1950, 2430).

Our study of the general mechanisms of aromatic nitration having developed as described in Parts I—V, we became interested in the nature of the special process operating in the nitration of derivatives of phenol and aniline, and in the reason why this special process appears to replace the ordinary process only for this particular group of aromatic compounds. These are the questions to be considered in Parts VI—VIII.

The previous literature gives two broad indications concerning the special process. The first is that nitrous acid plays a fundamental role. The positive catalysis by nitrous acid is often very strong, in contrast to the negative catalysis of the ordinary process, which is relatively weak, and has been shown (Part II, *loc. cit.*) to be incidental to the mechanism of nitration.

The second indication is of a basic similarity, despite the differences, between the special nitration process and the general one. This follows from the fact that the nitrations of derivatives of phenol and aniline obey the ordinary laws of orientation. This shows that the reagent in the special process, if not the nitronium ion, must at least be electrophilic, like the nitronium ion.

In this paper we describe experiments which were designed to elucidate the nature, and conditions of incursion, of the special process in so far as it applies to the nitration of derivatives of phenol. Derivatives of aniline are treated in the following papers.

(1.2) *Previous Work on the Mechanism of Nitration of Phenols and Phenolic Ethers.*—There is a considerable literature of previous attempts to elucidate the mechanism of nitration of this group of aromatic compounds. The rate of nitration of phenol by nitric acid in water was first examined by Martinsen (*Z. physikal. Chem.*, 1904, **50**, 385), who showed that the reaction was autocatalysed by the nitrous acid it produced, and indeed that, with nitric acid in only moderate concentration, the presence of nitrous acid was essential to the reaction.

Similar observations were made by Klemenc and his collaborators using ether as solvent (Klemenc, *Monatsh.*, 1914, **35**, 85; Klemenc and Ekl, *ibid.*, 1918, **39**, 641; Klemenc and Schöller, *Z. anorg. Chem.*, 1924, **141**, 231). Klemenc and Schöller attempted to analyse the kinetics of nitration in water and in ether. They gave approximate equations such as rate $\propto [HNO_3]^{3.2}[HNO_2]^{0.3}$ for water, and rate $\propto [HNO_3]^{2.5}[HNO_2]^{0.5}$ for ether. They supposed

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* Here and in later parts of this paper, anisyl is used for the radical $MeO \cdot C_6H_4 \cdot$ and not for its benzyl analogue.

that the nitrating agent might be an acid $H_2N_2O_8$, and thought of the nitration process as a modified oxidation.

Arnall studied the nitration of phenol by nitric acid in ethyl alcohol, and again observed autocatalysis by the formed nitrous acid (*J.*, 1923, **123**, 3111; 1924, **125**, 811). Zawidski made similar experiments, and gave the approximate relation, rate $\propto$ [HNO_3][HNO_2] (*Rocz. Chem.*, 1925, **5**, 504). The mechanism of the reaction which Arnall suggested would now be called a homolytic process of nitration :

$$N_2O_4 + C_6H_5 \cdot OH \longrightarrow NO_2 \cdot C_6H_4 \cdot OH + HNO_2$$

Kartaschev studied the nitration of phenol in water and in ethyl acetate (*J. Russ. Chem. Soc.*, 1927, **59**, 813, 833; 1930, **12**, 2129; Kartaschev and Sai-Moiseeva, *ibid.*, p. 385). Using Liebermann's test, he obtained indications of the presence of nitrosophenols in the early stages of nitration, and accordingly supported the theory that nitration proceeds through a nitrosation followed by **an** oxidation :

$$HNO_2 + C_6H_5 \cdot OH \longrightarrow NO \cdot C_6H_4 \cdot OH \xrightarrow{HNO_3} NO_2 \cdot C_6H_4 \cdot OH + HNO_2$$
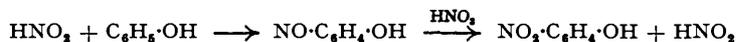
Bunton, Hughes, Minkoff, and Reed have reported (*Nature*, 1946, **158**, 514) the isolation of some *p*-nitrosophenol from the product of an interrupted aqueous nitration of phenol.

Veibel has attempted to deal with the main difficulty which faced the theory that nitration proceeds through nitrosation, *viz.*, that the aqueous nitration of phenol produces a mixture of *o*- and *p*-nitrophenols containing a considerable excess of the former, whereas the nitrosation of phenols leads principally to the *p*-nitroso-compound (*Ber.*, 1930, **63**, 1577; *Z. physikal. Chem.*, 1930, *B*, **10**, 22). Veibel was the first to show that a little *o*-nitroso-compound is formed as well. He dealt with the remaining large discrepancy between the *o/p*-ratios for nitration and for nitrosation by supposing that phenol reversibly forms two intermediate molecular compounds with nitrous acid, one with the latter linked in the *ortho*-position, and the other with it attached to the *para*-position. He assumed that each of these compounds could yield either a nitroso-phenol or a nitrophenol, of corresponding orientation, by alternative parallel modes of decomposition. By assigning suitable relative rates to the different hypothetical stages of reaction, the differing *o/p*-ratios could be accommodated.

Recently, Schramm and Westheimer have reported on the nitration of anisole in aqueous nitric acid (*J. Amer. Chem. Soc.*, 1948, **70**, 1782). They showed that nitrous acid was necessary for the reaction, and made it probable that nitroso-anisoles were intermediates, since *p*-nitroso-anisole gave similar end-products. These contained not only nitroanisoles, but also 2 : 4-dinitrophenols.

Partial dearylation of diaryl ethers during nitration has been reported by Reilly, Drumm, and Barrett (*J.*, 1927, 67). The partial dealkylation observed by Schramm and Westheimer in the nitration of anisole has been found by us to be a somewhat general accompaniment of the nitration of *O*-alkylated phenols. Dealkylation is again observed in the nitration of *N*-di-alkylated anilines (cf. Part VII, *J.*, 1950, paper no. 513). We see in these facts another preliminary indication of major importance, *viz.*, that alkyl displacement from fully *O*- or *N*-alkylated derivatives of phenol or aniline is in some way concerned in the nitration mechanism which we are investigating.

(1.3) *Plan of the Present Work on the Nitration of Phenols and Phenolic Ethers.*—In this investigation much attention has been given to the task of isolating the nitration mechanism we wished to observe, from accompanying phenomena of less immediate interest. Some degree of isolation is necessary if conclusions are to be drawn from a study of reaction products, and a high degree of isolation is required if the method of chemical kinetics is to be used to the best effect. In this preliminary search for a suitable system, we found that some gain resulted from modifying the conditions of nitration, but much more from changing the substance nitrated. Thus we passed in succession from the study of the nitration of phenol, the most complicated case of all, to that of anisole, which is not much simpler, then to that of substituted phenols, and finally to substituted anisoles. We shall report our work in these fields in almost the reverse order, because it was from the investigation of substituted anisoles, the leading example being *p*-chloroanisole, that we obtained most insight into the reaction. With this information, it was possible to interpret kinetic results obtained earlier for substituted phenols, in particular, *p*-nitrophenol, and qualitatively to understand a number of kinetic and other observations which had been made on the nitration of anisole and phenol.

(2) *Products of Nitration of* p-*Chloroanisole.*

(2.1) *The Partial Demethylation accompanying Nitration.*—*p*-Chloroanisole is smoothly nitrated by 4—10M-nitric acid in acetic acid at temperatures between $-15°$ and $+35°$. There is very little, if any, accompanying oxidation. It is possible to account for almost the whole of the introduced aromatic material in the form of two nitro-compounds, *viz.*, 4-chloro-2-nitro-anisole and 4-chloro-2 : 6-dinitrophenol. The production of the latter involves elimination of the methyl group of *p*-chloroanisole. The fate of this group is established in Section 2.2.

We have determined the proportions in which 4-chloro-2-nitroanisole and 4-chloro-2 : 6-di-nitrophenol are produced during the nitration of *p*-chloroanisole under various conditions. In order to understand the significance of the conditions, it is necessary to refer to some of the kinetic findings given in Section 3, especially to those which relate to effects of " nitrous acid " in the presence of different concentrations of nitric acid. Following Benford and Ingold (*J.*, 1938, 929), we shall mean by " nitrous acid " the total material in a nitration medium which, after dilution with water, could be estimated as nitrous acid.

A range of concentrations of nitric acid has been investigated. Over the lower part of the range, *i.e.*, from below 4M- to above 6M-nitric acid, the nitration is strongly catalysed by nitrous acid; but there is no autocatalysis, as there is with some phenol derivatives, and no nitrous acid is produced in the reaction, *i.e.*, there is no oxidation. In the lowest part of the concentration range, near 4M-nitric acid, the presence of nitrous acid is essential to give the reaction an appreciable rate. At higher concentrations, near 6M-nitric acid, there is a detectable reaction in the absence of nitrous acid; but still this material is a powerful catalyst, and the presence of quite a small amount will determine that nearly the whole observed reaction is catalysed. At still higher nitric acid concentrations the importance of the uncatalysed reaction increases, while that of the catalysed process diminishes. In the highest part of the investigated range, from 9M- to 10M-nitric acid, the reaction in the absence of nitrous acid becomes rapid; and now nitrous acid is found to be a negative catalyst. We shall later consider the other kinetic changes that occur concurrently with these, as well as the quantitative aspect of all these effects. The point now to be made is that our investigated range of concentrations includes (*a*) a region in which the reaction is wholly dependent on catalysis by nitrous acid, (*b*) a transitional region, and (*c*) a region in which nitration is, not merely not assisted, but is retarded, by nitrous acid. In region (*a*), the mechanism is obviously the special one, applying to the nitration of derivatives of phenol and aniline, which we are at present concerned to investigate; for the essential character by which we recognise it is its dependence on strong positive catalysis by nitrous acid. In region (*c*), the mechanism is, as we shall later fully confirm, the general mechanism of aromatic nitration, to the study of which Parts I and II were devoted, where the characteristic negative catalysis by nitrous acid was first demonstrated. The present importance of the transitional region (*b*) is simply that it guarantees for us a reasonably complete isolation of the special mechanism in region (*a*), from the general mechanism characteristic of region (*c*).

TABLE I.

Proportions of nitro-products formed by the nitration of p-*chloroanisole by nitric acid in acetic acid.*

Expt. no.	Temp.	HNO_3 (M.).	HNO_2 (M.).	CNA * (mols. %).	CDNP * (mols. %).	$\dfrac{CNA}{CDNP}$.
302	20°	3·81	0·193	59·5	30·2	1·97
304, 311, 312	,,	4·75	high	60·7	29·9	2·03
305	,,	5·70	0·038	60·5	30·5	1·98
313—316	,,		high	66·0	33·2	1·99
307	$-10°$	10·00	none	75·0	24·0	3·12

* CNA = 4-Chloro-2-nitroanisole; CDNP = 4-chloro-2 : 6-dinitrophenol.

The measured proportions of nitro-compounds are given in Table I. The experiments at 20°, with nitric acid in concentrations 3·81, 4·75, 5·70M., involve conditions (*a*), in which the mechanism dependent on catalysis by nitrous acid is dominating. Although the rates of nitration at exactly these concentrations and temperature were not measured, it can be estimated, from the kinetic measurements recorded in Section 3, that in the group of experiments now considered the reaction rates must have varied over a range of the order of 100-fold. The significant result is that, in spite of this, the ratio in which 4-chloro-2-nitroanisole and 4-chloro-2 : 6-dinitrophenol

are produced, *i.e.*, the proportion of demethylation, is practically constant. We conclude that, in the mechanism operating over this range of conditions, the processes of nuclear nitration and lateral demethylation either depend identically on a common reagent, or involve a common intermediate; and that the factors which control the rate of the total reaction affect either the rate, or the equilibrium degree, of formation of this reagent or intermediate, rather than the rate of its conversion into the products.

In the measurements at $-10°$ with nitric acid in concentration $10 \cdot 0$M., the conditions are those labelled (*c*) above, and the mechanism of nitration is the ordinary one, involving attack by the nitronium ion. In this mechanism, nitrous acid is just a complication, and we record in Table I an experiment in which it was excluded. This shows that demethylation also occurs during nitration by the nitronium ion mechanism, although the proportion of demethylation is appreciably different from that applying to the nitration mechanism dependent on nitrous acid.

The following qualitative experiments were carried out in order to determine, or delimit, the reactants involved in demethylation. 4-Chloro-2-nitroanisole was neither demethylated nor further nitrated under the conditions of the experiments noted in Table I. 4-Chloroanisole was not demethylated by a large concentration of sulphuric acid in acetic acid; this makes it clear that no ordinary kind of acidolysis is involved. 4-Chloroanisole was demethylated by a solution of nitrosonium hydrogen sulphate ("nitrosylsulphuric acid") in acetic acid. It was also demethylated by a solution of redistilled dinitrogen tetroxide in acetic acid. In each case the aromatic product gave the reactions of nitrosophenols. With a solution of colourless anhydrous nitric acid, together with urea nitrate, in acetic acid, no reaction at all occurred, unless the concentration of nitric acid was high enough to bring about nitration; and then considerable demethylation accompanied the nitration.

We interpret these results as meaning that there are two demethylating agents, or types of demethylating agent. One is the nitrosonium ion, or a "carrier" of the nitrosonium ion. The other is the nitronium ion, or a "carrier" of the nitronium ion. In either case, the demethylating agent is apparently not effective for demethylation except when it is also effective for nitrosation or nitration. Thus the two processes are closely linked together. The ineffectiveness of sulphuric acid allows us to conclude that the hydrogen ion, and "carriers" of the hydrogen ion (*i.e.*, acids), are not responsible for the observed demethylations.

(2.2) *The Fate of the Eliminated Methyl Group.*—*p*-Chloroanisole was nitrated by a 4M-solution of nitric acid in acetic acid at 35°, these conditions ensuring that the nitration mechanism is the special one, depending on catalysis by nitrous acid. The eliminated methyl group was recovered in the form of methyl acetate (cf. Section 12. 2). No sign of any considerable degree of oxidation was observed.

Experiments on the nitration of *p*-chlorophenetole were carried out, the conditions being as described above; but ethyl acetate could not be isolated, although it was detected by its odour during the attempts which were made to separate it. In contrast to the nitration of *p*-chloroanisole, the nitration of *p*-chlorophenetole involves a considerable amount of oxidation. Blank experiments with added ethyl acetate, and also with added ethyl nitrate, showed that, had either of these esters been produced in any substantial proportion, it could have been isolated by the methods employed. It seemed clear from these results that the eliminated ethyl group had been converted into oxidised forms. Attempts to detect acetaldehyde were unsuccessful. The possible production of acetic acid could not be tested, owing to the use of this substance as solvent.

We conclude from these experiments that, although oxidation may accompany the elimination of an alkyl group during the nitration of a phenolic ether, oxidation is not essential for the detaching of the alkyl group. We consider that the production of methyl acetate in the experiments on the nitration of *p*-chloroanisole by nitric acid in acetic acid makes it certain that the methyl group of the phenolic ether separates as its cation CH_3^+. This cation is sufficiently resistant to the oxidising environment to terminate its existence in the normal way, *viz.*, by combination with the most freely available anion, which, in these experiments, is the acetate ion derived from the acetic acid solvent.

(3) *Kinetics of the Nitration of* p-*Chloroanisole.*

(3.1) *Constancy of the Nitrous Acid Concentration.*—The kinetics of nitration of *p*-chloroanisole by nitric acid in acetic acid, in the presence of what we are calling "nitrous acid," has been studied by our usual technique which employs the dilatometer as the main instrument, with chemical analysis as an occasional check. In this method, the nitrating acid is kept in large

excess (*e.g.*, 50-fold) over the aromatic compound, and the order of reaction with respect to the aromatic compound is established ; it is usually first or zeroth, but may have intermediate values ; if it is first or zeroth, the dependence of the corresponding rate constant on the concentration of the nitrous acid, and on that of the nitric acid, is explored.

This procedure assumes that the concentration of the nitrous acid and of the nitric acid remains steady during a run, a condition which is obviously satisfied to a close approximation in the case of the nitric acid. But the nitrous acid is often present in a concentration of the same order of magnitude as that of the aromatic compound, and hence it is necessary to test for the consumption or production of nitrous acid.

In the kinetic investigations of nitration which were reported in Parts I and II it was always found that the concentration of nitrous acid remained constant during a run. However, a corresponding result could not here be assumed, because we have present a different nitration mechanism. We find, nevertheless, that under the conditions of all the dilatometric runs reported below, the concentration of nitrous acid in the solution expelled from the dilatometer after reaction was the same as the concentration in the initial solution, to within the accuracy of analysis.

FIG. 1.
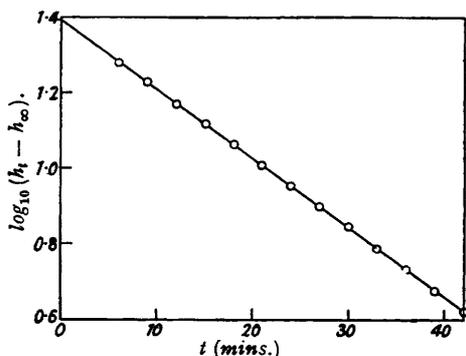
General kinetic form of the nitration of p-chloro-anisole in acetic acid by nitric acid in the concentration range 4—6M.; illustrated by Run No. 353. Temperature 25·01°. Initially, [HNO$_3$] = 4·14M.; [HNO$_2$] = 0·099M.; [Cl·C$_6$H$_4$·OMe] = 0·031M. Finally, [HNO$_2$] = 0·098M. First-order rate constant k$_1$ = 0·000673 sec.$^{-1}$.

FIG. 2.
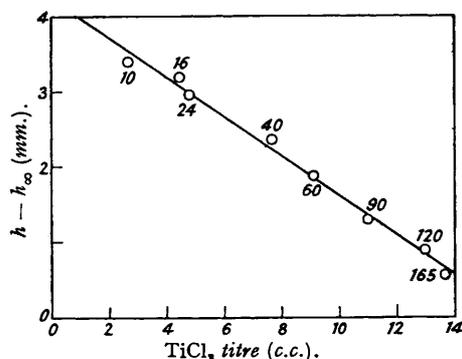
Run No. 412 : Temperature, 34·98°. Initially, [HNO$_3$] = 4·14M.; [HNO$_2$] = 0·052M., [Cl·C$_6$H$_4$·OMe] = 0·020M. The dilatometric readings are plotted against the chemical titres measuring the 4-chloro-2-nitroanisole in samples taken at the same times. The times (in minutes) are given by the figures against the graph. The slope of the curve corresponds to a titrimetric registration of the uptake of 0·67 mol. of nitroxyl per mol. of p-chloroanisole converted (cf. Table I).

The kinetics themselves, as reported below, confirm that nitrous acid is neither produced nor destroyed. For, under most of the conditions used, the rate depends strongly on the concentration of nitrous acid ; and yet no signs were found either of an autocatalysis, or of any growing inhibition of the reaction.

(3.2) *The Nitrous Acid-catalysed Reaction. The Reaction Order with Respect to the Aromatic Compound.*—In this and the immediately following Sections we shall present data relating to the nitration of *p*-chloroanisole in acetic acid by means of nitric acid in the concentration range 4—6M., *i.e.*, under the conditions, labelled (*a*) in Section 2.1, in which the special nitration mechanism, dependent on nitrous acid, is in exclusive, or almost exclusive control.

For this range of concentrations of nitric acid, and, within it, for all investigated concentrations of nitrous acid (with a single exception to be mentioned in Section 3.3), the dilatometer rate followed the first-order rate law with considerable precision. In illustration Fig. 1 is given, in which the course of a run is shown in the form of a logarithmic plot of the variable part of the dilatometric height against the time.

The first-order character of the rate law was confirmed by carrying out two or more runs with the same nitrating solution, but with different initial concentrations of *p*-chloroanisole. Even though these concentrations might differ by several-fold, the first-order constants remained substantially the same. For example, the run, No. 353, illustrated in Fig. 1 was duplicated, and

in the duplicate, No. 354, the initial concentration of *p*-chloroanisole was made 2·7 times larger; however, the rate constant was the same :

> Conditions as under Fig. 1, apart from initial [$Cl \cdot C_6H_4 \cdot OMe$] :
>
> No. 353.   Initial $Cl \cdot C_6H_4 \cdot OMe$ = 0·031M.; k_1 = 0·000673 sec.$^{-1}$.
> No. 354.   ,,   ,,   = 0·082M.; k_1 = 0·000681 ,,

It was necessary to show that the dilatometric contractions are correlated with nitration of the aromatic molecule. This was done by following the same run dilatometrically and by chemical analysis. The analytical method involved separating 4-chloro-2-nitroanisole by solvent extraction from basified samples of the reaction solution, and then estimating nitroxyl in the extracted material by reduction with titanous chloride. The dilatometric and analytical rate constants agreed to within the rather large error of the analytical method, as the following comparison illustrates :

> No. 412.   Conditions as under Fig. 2 :
>
> By dilatometry, k_1 = 0·000206 sec.$^{-1}$.   By analysis, k_1 = 0·00023 sec.$^{-1}$.

The same run can be used to illustrate another form of comparison, which was sometimes made. One starts the same reaction simultaneously in a dilatometer and in a flask, and withdraws samples for analysis from the flask at the times of the dilatometer readings. A plot of the dilatometric heights against the titanous chloride titres should then be linear. It was linear, to within the error of the analytical method, as is illustrated in Fig. 2.

As in this reaction there are two products, we may remind ourselves of the meaning of the measured first-order rate constants in relation to them. This constant defines the rate at which the original substance is converted into its immediate products. If two such conversion processes run concurrently, they must both be of the first order; and the dilatometrically measured constant will be the sum of their rate constants, whether or not they produce similar volume changes. There can be no concurrent conversion process which is not of first order, not even one which happens not to produce a volume change. All reaction steps subsequent to the original step or steps must be fast.

A subsequent reaction step is evidently involved in the introduction of the second nitro-group into the dinitrophenolic product. We assume that the precursor of this product is 4-chloro-2-nitrophenol; and we have directly verified that the nitration of 4-chloro-2-nitrophenol to 4-chloro-2 : 6-dinitrophenol is a much faster reaction than the nitration of *p*-chloroanisole, under the conditions of the measurements.

(3.3) *The Nitrous Acid-catalysed Reaction (continued). The Reaction Order with Respect to Nitrous Acid.*—This was investigated by carrying out " blocks " of runs at a common temperature, with the same concentration of nitric acid in the acetic acid solvent, but with different concentrations of nitrous acid, the object being to find a relationship between the first-order rate constants and the nitrous acid concentrations. The results obtained in such a block of runs, applying to one of the lowest of the investigated concentrations of nitric acid, are given in Table II. It will be noticed that, with this concentration of nitric acid, when the content of nitrous acid is too small to be measured, then the reaction rate is too small to be observed. The empirical relation between the rate constant and the nitrous acid content is shown graphically in Fig. 3.

TABLE II.

Nitration of p-*chloroanisole in acetic acid by nitric acid in relatively low concentration. Dependence of the first-order rate constants* (k_1 *in sec.*$^{-1}$) *on the concentrations of nitrous acid.*

Temp. : 25·01°.   [HNO_3] = 4·14M.   Initially [$Cl \cdot C_6H_4 \cdot OMe$] $\approx$ 0·05M.

Run no.	358	357	355	363	361	364	367	366	365
[HNO_2]	0·000	0·041	0·073	0·110	0·133	0·165	0·237	0·278	0·338
$10^4 k_1$	0·00	1·70	3·6	5·4	8·0	9·8	12·8	15·0	17·4

The results for another block of runs are given in Table III. They apply to a concentration of nitric acid which is near the upper limit, above which it would not be possible to say that only the nitration mechanism dependent on nitrous acid is under observation. Indeed, we see the first signs here that this mechanism is going to be superseded at still higher concentrations of nitric acid. For in this series, when the concentration of nitrous acid is reduced below the limits of detection, the reaction still has a measurable rate; and, moreover, this residual reaction is

not of first order with respect to the aromatic compound. In most of the experiments, however, the residual reaction is overlaid by the much faster catalysed reaction, which certainly is of first order with respect to the aromatic compound. Its rate constants are graphically compared with the corresponding nitrous acid concentrations in Fig. 4.

TABLE III.

Nitration of p-chloroanisole in acetic acid by nitric acid at an intermediate concentration.
  Dependence of the first-order rate constants (k_1 in sec.$^{-1}$) on the concentrations of nitrous acid.

Temp.: 25·01°. [HNO$_3$] = 5·94M. Initially [Cl·C$_6$H$_4$·OMe] $\approx$ 0·05M.

Run no.	375	374	371	370	373	361	372
[HNO$_2$]	0·000	0·0057	0·032	0·046	0·080	0·097	0·141
$10^4 k_1$	(1·8) *	8·8	18·7	31·6	50·2	58·1	79·3

 * This was not a first-order reaction, but was a somewhat imperfect zeroth-order reaction. The figure in parentheses is its initial value, calculated as for a first-order reaction, *i.e.*, expressed as the mol.-fraction converted per second. It is included in the Table only for the purpose of conveying a rough idea of how fast the uncatalysed reaction proceeds in these conditions, relatively to the truly first-order catalysed reactions.

The most significant result of this group of experiments will be obvious from Figs. 3 and 4 : within the range of nitric acid concentrations 4—6M., the first-order rate constant for the

FIG. 3.   FIG. 4.

Dependence on nitrous acid concentration of the first-order rate constants for the nitration of p-chloroanisole in acetic acid by nitric acid in two concentrations at 25·0°.
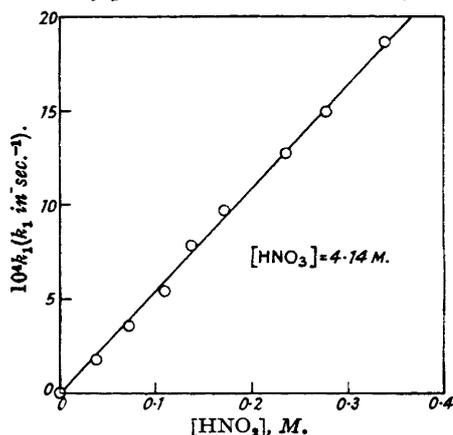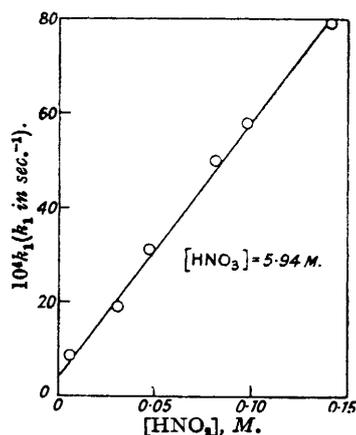
nitration of *p*-chloroanisole is proportional to the first power of the concentration of nitrous acid.

For a given nitrous acid concentration, the rate increases as the sixth-to-seventh power of the nitric acid concentration, within the range of concentrations now considered. Of course, the precise power has no simple chemical significance at these high concentrations.

We may summarise the above kinetic results for the nitration of *p*-chloroanisole by 4—6M-nitric acid in acetic acid. Writing ArH for *p*-chloroanisole and HNO$_2$ for what we have been calling " nitrous acid," the conclusion is as follows :

$$\begin{cases} \text{Rate} \propto [\text{ArH}][\text{HNO}_2] \\ \text{Rate increases steeply with } [\text{HNO}_3] \end{cases} \quad (\text{HNO}_3 \text{ in excess})$$

Near 6M-nitric acid it is a necessary condition for these kinetics that the concentration of nitrous acid shall not be too small.

In Section 6 we shall again illustrate the law Rate $\propto$ [ArH][HNO$_2$], this time for the nitration of a free phenol, rather than a phenolic ether. However, an exploratory kinetic examination of the nitration of a number of phenolic ethers and free phenols has convinced us that *this is a limiting law*. We have never observed the rate to vary as a higher power of the nitrous acid concentration than the first power (and neither has any previous investigator),

though it has often been found to vary as lower and non-constant powers, even negative powers. Furthermore, when the order with respect to nitrous acid falls below first-order, then the order with respect to the aromatic compound may also fall below first-order. The general kinetic picture is therefore complicated, but we can most easily discover the elements of which it is composed by progressively changing the conditions so that we pass from the domain of control by the limiting law already illustrated, through the region of complicated kinetics, to a situation in which a *second limiting law* is in control. The elucidation of this second law is the subject of the next two Sections.

(3.4) *The Nitrous Acid-anticatalysed Reaction. Reaction Order with Respect to the Aromatic Compound.*—In the example of the nitration of *p*-chloroanisole, the transition from the first limiting law to the second is made essentially by increasing the concentration of nitric acid. With nitric acid in 6—9M-concentration we encounter complicated kinetics with fractional, non-constant reaction orders. In the range 9—10M-nitric acid, simple kinetics are again observed. Near 9M-nitric acid, it is a condition that the concentration of nitrous acid shall not be too large. Above 10M-nitric acid, the reactions are too fast to be conveniently studied by our methods.

These nitrations were found to be of zeroth order with respect to the aromatic compound. A typical reaction–time curve, as observed dilatometrically, is shown in Fig. 5.

Hughes, Ingold, and Reed (cf. Part II) measured the zeroth-order rates of nitration of toluene, ethylbenzene, *p*-xylene, and mesitylene by nitric acid in acetic acid. It is readily possible to establish that the reaction mechanism which is yielding the zeroth-order nitration of *p*-chloroanisole by 9—10M-nitric acid in acetic acid is identical with that from which Hughes, Ingold, and Reed obtained zeroth-order kinetics, and proved to be the nitronium ion mechanism. One has simply to make a comparison of the absolute rates of nitration of *p*-chloroanisole and one of the other group of substances, say, toluene ; all those aromatic compounds that obey the zeroth-order law, should, provided that that law always arises from the same mechanism, nitrate at the same rate under the same conditions. The results of such a comparison, which are given in Table IV, make it clear that the mechanism which is producing the zeroth-order kinetics is the same for *p*-chloroanisole as for toluene; *i.e.*, it is the nitronium ion mechanism.

TABLE IV.

Comparison of rates (k_0 in g.-mol. l.$^{-1}$ sec.$^{-1}$) of zeroth-order nitration of p-chloroanisole and of toluene by nitric acid in acetic acid at $-14 \cdot 93°$.

Run no.*	ArH.	[HNO_3].	[HNO_2].	$10^6 k_0$.
⎰ 648	*p*-Chloroanisole	*ca.* 9·05	*ca.* 0·00035	9·12
⎱ 649	Toluene	,,	,,	9·19
⎰ 650	*p*-Chloroanisole	9·05	0·00070	9·95
⎱ 651	Toluene	,,	,,	9·67
⎰ 652	*p*-Chloroanisole	9·05	0·00077	9·26
⎱ 653	Toluene	,,	,,	9·98
⎰ 654	*p*-Chloroanisole	9·05	0·00076	9·65
⎱ 655	Toluene	,,	,,	9·78

* The braces indicate pairs of runs with the same nitration medium.

It will already be clear that *p*-chloroanisole is reacting, in the conditions described, by the nitronium ion mechanism, which was elucidated, for aromatic nitration in general, in Part II. In organic solvents, and with nitric acid in constant excess, this mechanism led to two limiting forms of kinetics : sufficiently reactive aromatic compounds nitrated according to a zeroth-order law, this being one of the most characteristic kinetic features of the mechanism; and sufficiently unreactive aromatic compounds nitrated according to a first-order law. Since the methoxyl group is strongly activating in electrophilic substitution, while the chlorine substituent is only moderately deactivating, it is entirely consistent that *p*-chloroanisole should take its place with the group of reactive aromatic compounds which exhibit zeroth-order kinetics under the conditions specified.

With nitric acid in concentrations near 9M., the zeroth-order kinetic form of nitration is not sensibly disturbed by the presence of nitrous acid in concentrations up to 0·001M., although the actual rate of nitration is appreciably changed. However, large concentrations of nitrous acid, *e.g.*, 0·1M., disturb the kinetic order as well as increasing the reaction rate. This is obviously due to the incursion of the nitrous acid-catalysed mechanism, with its different form of dependence of the rate on the concentration of the aromatic compound. With somewhat

higher concentrations of nitric acid the faster zeroth-order reactions will tolerate more nitrous acid before they begin to lose their simple kinetic form.

(3.5) *The Nitrous Acid-anticatalysed Reaction (continued). Dependence of the Rate on Nitrous Acid.*—One of the characteristic features of nitration by the nitronium ion mechanism is that the rate of reaction is depressed by nitrous acid. Benford and Ingold (Part I) gave a law for the depression, *viz.*, that the reciprocal of the rate increases linearly with the square-root of the concentration of nitrous acid; and Hughes, Ingold, and Reed (Part II) confirmed the law, showing that it applied alike to zeroth-order and first-order reactions, and to the solvents nitromethane and acetic acid.

The effect of nitrous acid on the zeroth-order rate of nitration of *p*-chloroanisole by approximately 9M-nitric acid in acetic acid has been investigated within the range of concentrations of nitrous acid over which the zeroth-order law is preserved. The figures for a block of runs are given in Table V.

TABLE V.

Nitration of p-*chloroanisole in acetic acid by nitric acid in one of the higher concentrations. Dependence of the zeroth-order rate constant* (k_0 *in sec.*$^{-1}$ *g.-mol. l.*$^{-1}$) *on the concentration of nitrous acid.*

Temp. $-5.10°$. $[HNO_2] = 9.05$M. Initially $[Cl \cdot C_6H_4 \cdot OMe] \approx 0.02$M.

Run no.	392	385	391	386	389	388	387
$[HNO_2]$	0.0000	0.00025	0.00035	0.00055	0.00060	0.00075	0.00095
$10^4 k_0$	0.35	0.24	0.22	0.20	0.21	0.19	0.17

A plot of the reciprocal of the zeroth-order rate constant against the square root of the concentration of nitrous acid is shown in Fig. 6, from which it is clear that the law characteristic

FIG. 5.
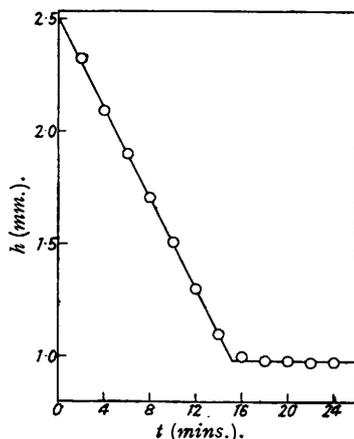
General kinetic form of the nitration of p-chloroanisole *in acetic acid by* 9—10M-*nitric acid and in the absence of too large amounts of nitrous acid : illustrated by Run No.* 382. *Temperature* $-11.21°$. $[HNO_3] = 9.05$M. $[HNO_2] = 0.000$M. *Initially,* $[Cl \cdot C_6H_4 \cdot OMe] = 0.020$M. *Zeroth-order rate constant* $k_0 = 0.22 \times 10^{-4}$ *sec.*$^{-1}$ *g.-mol. l.*$^{-1}$.

FIG. 6.

$[HNO_3] = 9.05$ M.
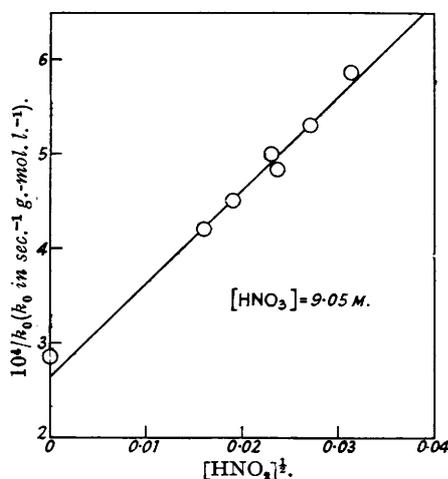
Dependence on nitrous acid concentration of the zeroth-order rate constants for the nitration of p-chloroanisole *by* 9.05M-nitric acid *in acetic acid at* $-5.10°$.

of aromatic nitration by the nitronium ion mechanism is obeyed. This confirms the already drawn conclusion that the general mechanism of aromatic nitration is under observation in these experiments. This general mechanism provides the second limiting kinetic law :

$$\text{Rate} = [\text{ArH}]^0 (a + b[HNO_2]^{1/2})^{-1}$$

The kinetic complications to which reference was made earlier arise from the superposition of

the special and the general mechanism, and from their very different forms of dependence of the rate on the concentrations of the aromatic compound, and also of the nitrous acid.

(3.6) *The Nitrous Acid-catalysed Reaction* (*continued from Section* 3.3). *Dependence of the Rate on Added Alkali-metal Nitrates and on Added Water.*—A short investigation has been made of the effect of the added substances mentioned on the rate of nitration of *p*-chloroanisole by the special mechanism, which acts to the exclusion of the general mechanism at the lower concentrations of nitric acid. In these experiments, nitrous acid has to be present. It is difficult to standardise its concentration over a series of runs intended to be comparative. However, a basis for measuring and comparing the kinetic effects of the added substances exists in the second-order constants, k_2 in the equation, rate $= k_2[\text{ArH}][\text{HNO}_2]$. These second-order constants are obtained by dividing the dilatometrically measured first-order constant, k_1, of each run by the concentration of nitrous acid which was present during that run.

Data showing the kinetic effect of added lithium nitrate, potassium nitrate, and water on the nitration of *p*-chloroanisole by approximately 4M-nitric acid in acetic acid are given in Table VI.

TABLE VI.

Effect of added substances ("AS") *on the second-order rate constants* (k_2 *in sec.*$^{-1}$ *g.-mol.*$^{-1}$ *l.*) *for the nitration of* p-*chloroanisole by* 4M-*nitric acid in acetic acid in the presence of nitrous acid at* 34·98°.

Run no.	[AS].	[HNO$_2$].	$10^4 k_1$.	$10^3 k_2$.	Run no.	[AS].	[HNO$_2$].	$10^4 k_1$.	$10^3 k_2$.
Added lithium nitrate :									
		([HNO$_3$] $= 4\cdot2$M.		Initially,	[Cl·C$_6$H$_4$·OMe] $\approx 0\cdot06$M.)				
453	none	0·079	12·6	15·9	456	0·162	0·074	9·2	12·4
458	0·040	0·067	8·9	13·3	455	0·244	0·071	10·3	14·5
460	0·081	0·041	4·2	10·3	454	0·385	0·065	11·5	17·7
Added potassium nitrate :									
		([HNO$_3$] $= 4\cdot1$M.		Initially	[Cl·C$_6$H$_4$·OMe] $\approx 0\cdot06$M.)				
443	none	0·158	22·0	14·0	445	0·114	0·134	15·0	11·2
446	0·055	0·131	16·7	12·7	448	0·152	0·119	13·0	10·9
447	0·076	0·108	13·3	12·2	450	0·228	0·102	12·0	11·8
Added water :									
		([HNO$_3$] $= 4\cdot0$M.		Initially	[Cl·C$_6$H$_4$·OMe] $\approx 0\cdot06$M.)				
496	none	0·148	19·4	13·1	500	0·44	0·090	9·1	10·1
497	0·11	0·141	17·0	12·1	507	0·67	0·141	13·1	9·3
498	0·22	0·134	14·7	11·1	509	0·89	0·132	12·3	9·3
499	0·33	0·131	13·4	10·2	510	1·11	0·131	12·2	9·4

The results are compared graphically in Fig. 7. For the purposes of the graphical comparison, some small adjustments have been made to the rate constants of the blocks of runs concerned

FIG. 7.

Effect of nitrates and of water on the rate of the nitrous acid-catalysed nitration of p-*chloroanisole by* 4M-*nitric acid in acetic acid at* 35°.
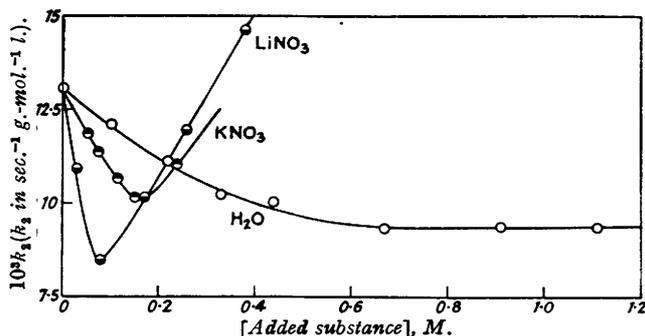
with the effect of salts, in order to bring them into correspondence, as regards the exact concentration of nitric acid, with the block of runs concerned with the effect of water.

Because of our lack of detailed knowledge concerning the condition of the added solutes in this type of medium, it is possible to offer only a qualitative and general interpretation of these results. The alkali-metal nitrates would appear to have two qualitatively opposite kinetic effects, which work according to different mathematical laws, and thus, by superposition, produced rate minima. The retarding effect, which dominates at the lower concentrations, we take to be a specific nitrate ion effect, and we suggest that it operates by repressing the dissociation of dinitrogen tetroxide into nitrosonium and nitrate ions (cf. Section 10). If this is true, it would seem to follow that the salts can be only partly ionised, since lithium and potassium nitrates give different depressions of reaction rate. The accelerative effect of the salts, which is the predominating effect at the higher salt concentrations, we believe to be a general salt effect, *i.e.*, an effect of ions or ion-pairs acting mainly electrostatically on some critical reaction stage, which again may be the ionisation of dinitrogen tetroxide.

The retarding effect of water is weaker than that of the salts; and most of the observed effect is exerted in the early stages of the progressive addition of water. We know that when a small amount of water is added to an excess of nitric acid, it combines, first, with any nitronium ion present to form nitric acidium ion, secondly, with nitric acid molecules to form a non-ionised hydrate, and thirdly, with protons from nitric acid to leave free nitrate ions (Gillespie and Millen, *Quart. Reviews*, 1948, **2**, 277; Part II, *J.*, 1950, 2400; Gillespie, Hughes, and Ingold, *J.*, 1950, 2473; Ingold and Millen, *J.*, 1950, 2612). In organic solvents such as acetic acid, the proportion of free nitronium ion is small (Part II, *loc. cit.*); and so we suppose that the main kinetic effects of water, in so far as they are exerted on the nitrosonium ion indirectly through their action on the nitric acid, are due to the second and third of the processes mentioned. The hydration of nitric acid molecules is certain to affect their power of promoting the ionisation of dinitrogen tetroxide; and the production of any free nitrate ion will repress nitrosonium ion formation as already described. Apart from these indirectly exerted effects, water may act directly on what we call " nitrous acid " by combining with its most reactive component, the nitrosonium ion, to give less reactive entities, such as the nitrous acidium ion and the nitrous acid molecule (cf. Part II, *loc. cit.*).

(4) *Products of Nitration of Simple and Substituted Anisoles.*

In this Section we shall note the products obtained by the nitration of four phenolic ethers under conditions of positive catalysis by nitrous acid. The results present contrasts which we believe to be theoretically significant.

Schramm and Westheimer have shown that anisole, on nitration by nitric acid containing nitrous acid in water as solvent, undergoes partial demethylation (*loc. cit.*). In our experiments, which have been conducted with acetic acid as the solvent, considerable amounts of deeply coloured and tarry by-products were formed ; our recoveries of simple nitro-compounds seldom exceeded 80% (cf. Section 12.4).

p-Chloroanisole is nitrated more slowly than anisole by nitric acid in the lower of the investigated concentrations, *e.g.*, 4M., in acetic acid solutions containing nitrous acid. As we have shown, a considerable amount of demethylation occurs (Section 2). The total nitration is much more nearly quantitative than that of anisole. Coloured by-products are formed in small amount.

2 : 6-Dichloroanisole nitrates much more slowly still under similar conditions. In this case, scarcely any demethylation accompanies the nitration, the sole product of which is 2 : 6-dichloro-4-nitroanisole. Strongly coloured by-products are not formed at all.

2 : 6-Dimethylanisole nitrates more rapidly than any of the above compounds in similar conditions. Again, scarcely any demethylation takes place, the uniform product being 4-nitro-2 : 6-dimethylanisole. Again, deeply coloured by-products do not appear.

We conclude from these results that 2 : 6-disubstitution in a phenolic ether suppresses the dealkylation which otherwise would be liable to accompany nitration. The effect is not correlated with the general vigour of the reaction. It is not an indirect effect, arising from an increased tendency to reaction in the aromatic nucleus. We shall suggest (Section 10) that it is to be interpreted as an effect of the steric inhibition of an addition process essential to the demethylation. The formation of coloured products is discussed in Section 8.

(5) *Nitration of Anisole. Kinetics.*

The nitration of anisole by nitric acid in acetic acid containing nitrous acid has been investigated at temperatures near 20°, with nitric acid concentrations in the range 3—8M., and nitrous

8 G

acid concentrations varying in order of magnitude from 0·01 to 1·0M. The dilatometric method was again employed; and it was checked as usual by chemical analysis.

The kinetics are very complicated, and only the salient qualitative features will be described. However, these will be sufficient to enable us, in the light of our already gained knowledge, to recognise the principal elements which compose the complex situation. We might have expected complicated kinetics for the understood reason that the general and the special mechanism of nitration, which have completely different kinetics, are likely to be superposed. We shall find that the superposition of mechanisms does, indeed, dominate the kinetic picture. Moreover, some special sources of complication arise additionally to any encountered hitherto.

We are forewarned of such special effects by our knowledge that anisole, unlike *p*-chloroanisole, is not converted nearly quantitatively into simple nitration products, proportions of the order of 10% being simultaneously transformed into complex substances. Probably in part, though certainly not wholly, the production of these complex materials involves oxidation. From the point of view of reaction kinetics, the main extra complication appears in the form of an auto-catalysis, or in some cases an auto-retardation; such effects were never observed with *p*-chloroanisole. Under many of the conditions employed in the present nitrations of anisole, a proportion of this substance becomes oxidised, with the production of nitrous acid often in quantity much greater than that which was present initially; and this leads to autocatalysis, if the concentration of nitric acid is not too high, or to an auto-retardation, if the concentration of nitric acid is sufficiently high.

Autocatalysis has been observed in nitrations of anisole in acetic acid by nitric acid in the range of concentrations 3·0—6·0M. The chief additional condition for autocatalysis seems to be that the initial concentration of nitrous acid shall be low : usually it must be below 0·01M. This is not merely in order that the produced nitrous acid shall not be negligible in comparison with the initially present nitrous acid. The curious observation was repeatedly made that, once autocatalysis sets in, the nitrous acid may rise to considerably higher concentrations than those which, if they had been present initially, would have prevented any development of autocatalysis. The cause of this phenomenon is not known. Auto-retardation, again associated with the production of nitrous acid by oxidation, arises in the presence of higher concentrations of nitric acid, again provided that the initial concentration of nitrous acid is low.

For the next few paragraphs, we shall restrict description to those experiments in which a sufficient initial concentration of nitrous acid was employed to avoid the onset of autocatalysis or auto-retardation. In such cases the concentration of nitrous acid remained substantially constant during any one run. As usual, the nitric acid was in large and constant excess, so that the only reactant whose concentration varied during a run was the anisole.

The order of reaction with respect to the anisole was not observed to have any exact and universal value; but it can fairly be described as being nearer to unity than to any other integral value over most of the conditions of the present survey. It is close to unity at the lower end of the investigated range of concentrations of nitric acid; it tends to fall, and to deviate more from constancy, at the upper end of the range. It is also very much closer to unity when the concentration of nitrous acid is high than when it is relatively low. The logarithmic plot of the course of a run with a high concentration of nitrous acid, and a relatively low concentration of nitric acid, is shown in Fig. 8.

We have calculated mean first-order rate constants for most of the runs carried out with anisole, even when the first-order law is not accurately obeyed. When it is not, the derived constants naturally have no exact meaning ; but they do enable the rates of different runs to be compared in an approximate way : and such a comparison is necessary if we are to make even a qualitative appraisal of the main features of the effect of nitrous acid on the reaction rate. We shall now describe this effect in outline.

Over the range 3—6M. of nitric acid concentrations, the nitration is positively catalysed by nitrous acid. This is illustrated in Fig. 9 by reference to a block of nitrations in 4·93M-nitric acid. The diagram is a plot of the logarithm of the mean, first-order rate constant against the logarithm of the concentration of nitric acid. The points are seen approximately to define a straight line of positive slope. If the rate were proportional to the concentration of nitrous acid the slope would be unity; but in fact it is smaller, and corresponds to a rate proportional to the square-root of the concentration of nitrous acid. However, it is only accidental that the relevant power of the concentration of nitrous acid has in this case the simple value one-half.

If, over the range 3—6M. of nitric acid concentrations, we represent the dependence of the rate on the nitrous acid concentration by an approximate power of the latter, as has just been

Fig. 8.
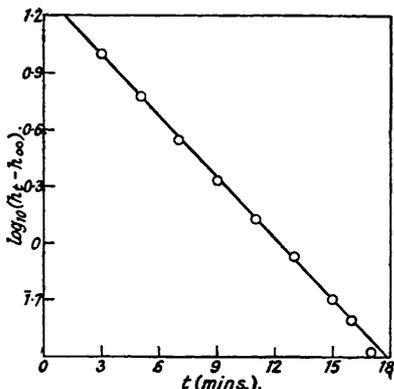
First-order nitration of anisole by nitric acid in acetic acid containing a high concentration of nitrous acid : illustrated by Run No. 145. Temperature 20·87°. [HNO$_3$]=4·93M. [HNO$_2$]= 0·691M. Initially [PhOMe]=0·026M. Rate constant $k_1 = 0·00414$ sec.$^{-1}$.

Fig. 9.
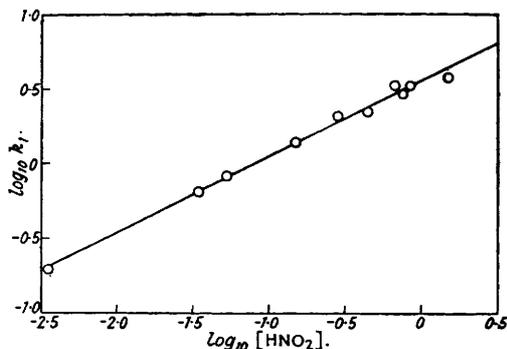
Positive catalysis in the nitration of anisole by 4·93M-nitric acid in acetic acid containing nitrous acid at 19·97°. Dependence of the rate on the concentration of nitrous acid. The logarithms of the mean first-order rate constants are plotted against the logarithms of the nitrous acid concentrations. The slope of the line is +0·50.

Fig. 10.

Negative and positive catalysis by nitrous acid of the nitration of anisole by 6·30M-nitric acid in acetic acid at 19·97°. The mean first-order rate constants are plotted against concentrations of nitrous acid.
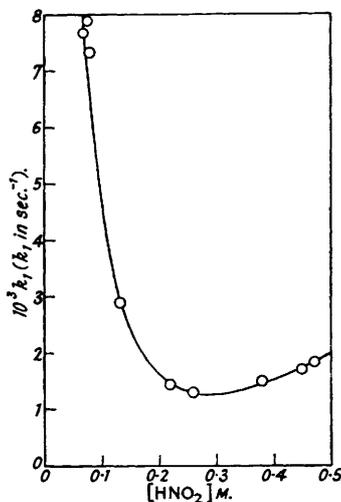
Fig. 11.

Negative catalysis by nitrous acid of the nitration of anisole by 8·0M-nitric acid in acetic acid at 19·97°. The reciprocals of the mean first-order rate constants are plotted against the square-roots of the nitrous acid concentrations.
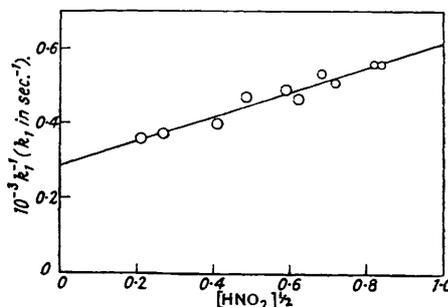
illustrated for nitrations in 4·93M-nitric acid, then this power drops throughout the concentration range as follows :

[HNO$_3$]	3·00	4·93	5·20	6·00
Power of [HNO$_2$]	0·65	0·5	0·35	0·2

Even in 3M-nitric acid there is no close approach to a reaction of unit order with respect to nitrous acid, such as would indicate an isolation of the special mechanism of nitration. And it is clear

from the trend of the figures that, in nitric acid of concentrations above 6M., positive catalysis by nitrous acid, the main characteristic of the special mechanism, is going to disappear altogether.

In the range 6·3—6·7M. of nitric acid concentrations, there is a transitional situation : positive catalysis is disappearing, but has not quite completely disappeared; and negative catalysis is setting in. Naturally, the negative catalysis appears first at the lower nitrous acid concentrations, and the last of the disappearing positive catalysis is seen at the highest nitrous acid concentrations. As we progressively increase the nitrous acid concentration in 6·3M-nitric acid, the mean first-order rate constant for the nitration of anisole drops, passes through a minimum, and then rises slowly, as is illustrated in Fig. 10. As we do the same in 6·72M-nitric acid, the rate at first drops, and then remains roughly constant.

At the nitric acid concentration 8·0M., there is only negative catalysis by nitrous acid. Because the order of reaction with respect to the aromatic compound is not well defined in these experiments, the law of the anticatalysis cannot be given with precision. However, if we plot the reciprocals of the mean first-order rate constants against the square-roots of the nitrous acid concentrations, the points obtained roughly define a straight line, as is shown in Fig. 11. We conclude that the form of the anticatalysis can be regarded as approaching the reciprocal-square-root law, which characterises the anticatalysis of the general mechanism of aromatic nitration.

TABLE VII.

Summary of the main features of the kinetics of the nitration of anisole by nitric acid in acetic acid containing nitrous acid at 20°.

Run no.	[HNO$_3$].	[HNO$_2$] $= n$.	Type of catalysis by HNO$_2$.	Rate approx. propl. to :
189—196 205 }	3·00	{ Initial $n<0·01$ 0·02$<n<$0·25	+ Auto. (n rises) + ve	— $n^{0·65}$
137—147	4·93	0·01$<n<$1·25	+ ve	$n^{0·5}$
198—204 206, 207 }	5·20	{ Initial $n<0·01$ 0·02$<n<$0·50	+ Auto. (n rises) + ve	— $n^{0·35}$
220—228	6·00	0·02$<n<$0·25	+ ve	$n^{0·2}$
229—248	6·30	{ Initial $n<0·02$ 0·05$<n<$0·25 0·25$<n<$0·50	± Auto. (n rises) − ve + ve	— (complicated) (weak effect)
159—167	6·72	{ Initial $n<0·20$ 0·05$<n<$0·50 0·05$<n<$1·25	− Auto. (n rises) − ve (practically no effect)	— (complicated)
178—187 266, 268 }	8·00	0·04$<n<$0·75	− ve	$(a + bn^{1/2})^1$

Table VII is offered as a summary of these findings. It seems to us that they leave little doubt about the main elements which compose the total kinetic picture presented by the nitration of anisole. In particular, we conclude that the same two nitration mechanisms are in operation, *viz.*, the special nitrous acid mechanism, and the general nitronium ion mechanism, which we found, and were able to isolate, in the course of our study of the nitration of *p*-chloro-anisole. However, in the present study of anisole we have not been able completely to isolate either of those mechanisms, though we have succeeded in making either strongly dominating by suitably changing the conditions. Superposed on the normal operation of these two mechanisms, we find kinetic auto-effects arising from the oxidation of a portion of the anisole. Furthermore, appreciable amounts of by-products are formed, including some polycondensation products. These are extra complexities; but in spite of them, we recognise in the kinetics only the two mechanisms of nitration specified above.

(6) *Nitration of* p-*Nitrophenol. Kinetics.*

(6.1) *Preliminary Observations.*—The rate of nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid has been studied at temperatures near 20° over the range of concentrations 1·4—10·0M. of nitric acid, and with nitrous acid concentrations varying from values of the order of 0·01M. to values of the order of 1·0M.

Our usual dilatometric technique has been employed. It was proved by chemical examination that the reaction measured by the dilatometric contraction in these experiments consists in the conversion of the *p*-nitrophenol into the single product 2 : 4-dinitrophenol. No

by-products of any kind are formed in appreciable quantity, and the produced 2 : 4-dinitrophenol undergoes no further nitration under the conditions used.

The presence of nitrous acid markedly affects the rate of nitration of *p*-nitrophenol. However, it was found that, over the whole range of these experiments, nitrous acid is neither produced nor destroyed in the course of nitration. No autocatalysis was observed.

The kinetic results are conveniently presented in two parts, one relating to runs with nitric acid concentrations in the range 1·4—6·0M., a range in which positive catalysis by nitrous acid is dominant, and the other referring to nitric acid concentrations in the range 7·0—10·0M., where negative catalysis by nitrous acid supervenes.

FIG. 12.
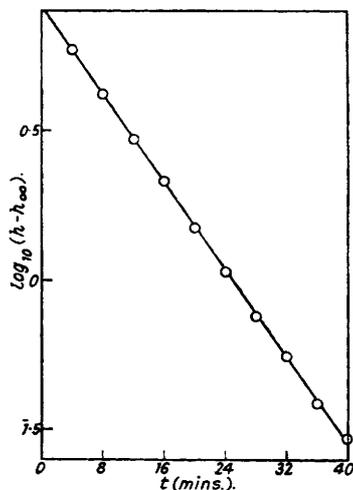
General kinetic form of the nitration of p-nitrophenol in acetic acid by nitric acid in the concentration range 1·4—6·0M. in the presence of nitrous acid: illustrated by Run No. 324. Temperature 20·87°. [HNO₃] = 4·60M. [HNO₂] = 0·627M. Initially [NO₂·C₆H₄·OH] = 0·025M. First-order rate constant, k_1 = 0·00134 sec.⁻¹.

FIG. 13.
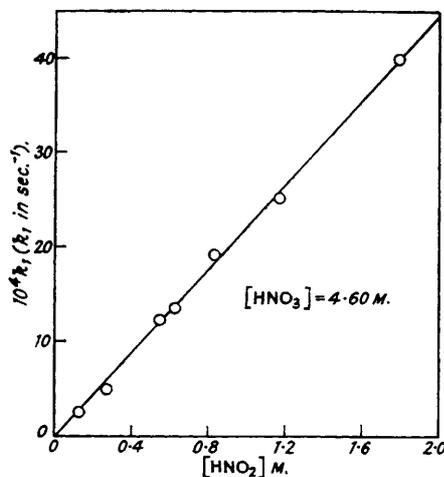
Dependence on nitrous acid concentration of the first-order rate constants of nitration of p-nitrophenol by 4·60M-nitric acid in acetic acid at 20·87°.

(6.2) *The Nitrous Acid-catalysed Reaction. Reaction Order with Respect to the Aromatic Compound.*—The course of a typical kinetic run, as observed in nitrations with nitric acid concentrations in the range 1·4—6·0M., is illustrated by the logarithmic plot in Fig. 12. It shows that the run obeys the first-order law very accurately. Throughout the stated range of concentrations of nitric acid, first-order reactions are observed, except when, near the upper end of the range, the concentration of nitrous acid is very small.

The first-order nature of these reactions was confirmed in a few cases by conducting pairs of runs with the same nitration solution, and at the same temperature, but with different initial concentrations of *p*-nitrophenol. In all such pairs of experiments consistent first-order rate constants were obtained, as the following example illustrates :

Common solution : [HNO₃] = 3·0M.; [HNO₂] = 0·2M. Temp. 19·98°.
        No. 311. Initial [C₆H₅O₃N] = 0·0225M. k_1 = 0·00140 sec.⁻¹
        No. 312.   ,,   ,, = 0·0450M. k_1 = 0·00138 ,,

(6.3) *The Nitrous Acid-catalysed Reactions (continued). Reaction Order with Respect to Nitrous Acid.*—Blocks of runs were carried out at several nitric acid concentrations within the range 1·4—6·0M., in order to determine how the first-order rate constants vary with the concentration of nitrous acid. The record of a block, one relating to the nitric acid concentration 4·6M., is given in Table VIII.

TABLE VIII.

Nitration of p-*nitrophenol in acetic acid by nitric acid in the concentration range* 1·4—6·0M.
Example showing the dependence of the first-order rate constant (k_1 *in sec.*$^{-1}$) *on the concentration
of nitrous acid.*

Temp. 20·87°. $[HNO_3]$ = 4·60M. Initially $[C_6H_5O_3N]$ = 0·025M.

Run no.	327	323	325	324	329	328	322
$[HNO_2]$	0·135	0·276	0·553	0·627	0·816	1·188	1·787
10^4k_1	2·34	4·87	12·2	13·4	19·5	24·7	39·9

The nature of the result here illustrated will be clear from Fig. 13. It is typical of the nitrations of *p*-nitrophenol in acetic acid by nitric acid, within the range of concentrations now under discussion, that the first-order rate constants are directly proportional to the concentration of nitrous acid. There is no residual rate, or at most a very small one, in the absence of nitrous acid.

The results presented so far concerning the nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid may be summarised in the equation

$$\text{Rate} = k_2[\text{ArH}][\text{HNO}_2]$$

It applies to nitric acid concentrations below 6M. The same kinetic formula was obtained for the nitration of *p*-chloroanisole. In this case also it applied to nitric acid concentrations below 6M.

(6.4) *The Nitrous Acid-catalysed Reaction* (*continued*). *Dependence of the Rate on the Concentration of Nitric Acid.*—Up to this point, the analogy between the kinetics of nitration of *p*-nitrophenol and those of the nitration of *p*-chloroanisole holds perfectly. But in the next effect we shall describe, the analogy breaks down. It will be recalled that, for nitric acid concentrations below 6M., the first-order rate constant for the nitration of *p*-chloroanisole with a fixed concentration of nitrous acid, or, alternatively, the second-order constant, k_2, in the above equation, increases steeply with the nitric acid concentration—a sixth-to-seventh power of the latter being required to express the dependence. On the contrary, for nitric acid concentrations below 6M., the second-order constant, k_2, for the nitration of *p*-nitrophenol actually decreases as the concentration of nitric acid increases. This is established by the figures in Table IX.

TABLE IX.

Effect of nitric acid concentration on the second-order rate constants (k_2 *in sec.*$^{-1}$ *g.-mol.*$^{-1}$ *l.*) *for the
nitration of* p-*nitrophenol in acetic acid by nitric acid in the presence of nitrous acid.*

Temp. : 20·87°. Initially $[C_6H_5O_3N]$ = 0·025M.

Run no.	$[HNO_3]$	$[HNO_2]$	10^4k_1	10^4k_2	Run no.	$[HNO_3]$	$[HNO_2]$	10^4k_1	10^4k_2
334	1·38	0·380	13·8	36·3	332	3·35	0·556	15·3	27·5
330	1·68	0·495	17·1	34·9	325	4·60	0·553	12·2	22·0
335	2·70	0·555	17·3	31·2	333	5·83	0·703	11·5	16·3

FIG. 14.

*Effect of the concentration of nitric acid on the second-order rate of
the nitrous acid-catalysed nitration of* p-*nitrophenol in acetic
acid at* 20·87°, *the nitric acid being always in constant excess.*
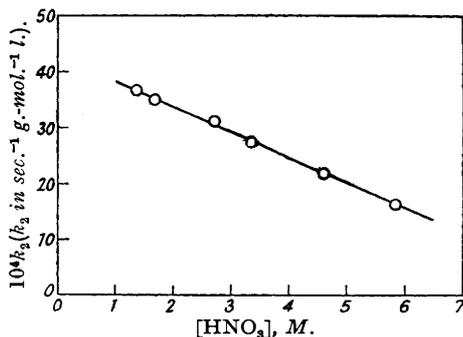
The form of the effect is exhibited in Fig. 14. Over a four-fold increase in the concentration of nitric acid, the second-order rate constant drops linearly to about one-half its initial value.

The form of the relationship appears simple, and the whole effect seems mild, having regard to the usually great sensitivity of nitration rates to nitric acid concentration.

We think that the mild effect results from the approximate cancellation of two opposing strong effects, and that the apparent simplicity is deceptive. There is much evidence that the ability of nitric acid to donate protons, and to produce nitronium ions, and, in suitable circumstances, to produce other active cations, such as nitrosonium ions, increases steeply with the concentration of nitric acid. We must expect, therefore, that the ability of nitric acid to suppress, by proton donation, the last traces of a weak base will increase steeply with the acid concentration. If we assume that the aromatic attack, which leads to nitration, is the attack, say, of a nitrosonium ion on a *p*-nitrophenoxide ion, *i.e.*, of an active cation on a weak base, then the mildness of the effect on rate can be understood as representing the result of an approximate balance between opposing strong effects on the concentrations of the separate reactants.

(6.5) *The Existence of a Nitrous Acid-anticatalysed Reaction*—The kinetics of the nitration of *p*-nitrophenol by nitric acid in acetic acid containing nitrous acid become quite complicated if the nitric acid concentration is above 7M. The closest analogy now seems to be with anisole, rather than with *p*-chloroanisole. Runs with 8M-nitric acid still showed positive catalysis by nitrous acid; but the individual runs were no longer accurately of first-order. When, ignoring

Fig. 15.

Diminished positive catalysis by nitrous acid in the nitration of p-*nitrophenol by* 8·0M-*nitric acid in acetic acid at* 19·97°. *The logarithms of the mean first-order rate constants are plotted against those of the nitrous acid concentrations. The slope of the line is* 0·52.
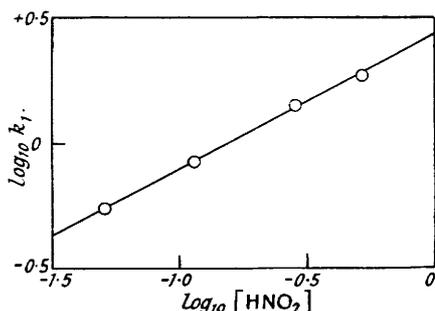
Fig. 16.

Negative catalysis by nitrous acid in the nitration of p-*nitrophenol by* 10·0M-*nitric acid in acetic acid at* 19·97°. *Mean first-order rate constants are plotted against concentrations of nitrous acid.*
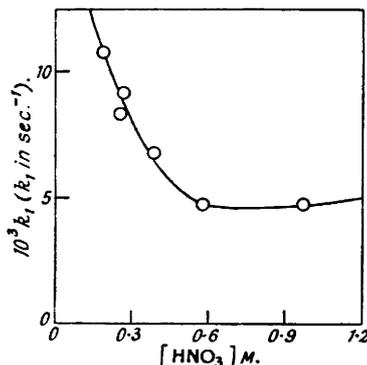
the deviations, we calculated mean first-order constants, these constants were found to increase with the nitrous acid concentration much less steeply than corresponds to proportionality. As a rough expression of the connexion, we may say that the rate is proportional to the power 0·5 of the nitrous acid concentration. This is illustrated by the logarithmic plot in Fig. 15. However, the law stated is not exactly obeyed. In particular, the experiments indicate a definite residual rate in the absence of nitrous acid.

When the concentration of the nitric acid is increased to 10M., a substantial negative catalysis by nitrous acid is observed. The runs depart considerably from the first-order form,

TABLE X.

Variation in the rate of nitration of p-*nitrophenol in acetic acid with changes in the concentration of nitric acid at various fixed concentrations of nitrous acid.*

		$10^4 k_1$ at 20·8°.		
[HNO₃]		2·0M.	5·0M.	10·0M.
	0·1M.	3·4	2·0	130
[HNO₂] {	0·5M.	17	10	50
	1·0M.	34	20	50

but are not even approximately of zeroth-order. When we calculate mean first-order constants and plot them against the nitrous acid concentrations, we obtain the curve in Fig. 16. This

shows that negative catalysis enters fairly strongly at the lower nitrous acid concentrations, leaving only a vestigial positive catalysis at the higher concentrations. The experiments indicated a considerable reaction rate in the absence of nitrous acid.

Although the first-order rate constants, for a fixed concentration of nitrous acid, fall as the concentration of nitric acid is increased from 1·4 to 5·8M., the mean, first-order, rate constants rise again as we continue to increase the nitric acid concentration up to 10·0M. The general character of the variation is indicated in Table X, in which the figures relating to 10M-nitric acid must be considered as only approximate. These changes can be understood on the lines already indicated.

Table XI contains, in a summarised form, the main results, described in this Section, concerning the incursion of negative catalysis by nitrous acid in the nitration of *p*-nitrophenol in the higher concentrations of nitric acid in acetic acid. Some results, given in previous Sections, for the positive catalysis of the reaction by nitrous acid in the lower concentrations of nitric acid in acetic acid are similarly summarised for comparison.

TABLE XI.

Summary of the main features of the kinetics of the nitration of p-*nitrophenol by nitric acid in acetic acid containing nitrous acid at 20°.*

Runs no.	[HNO$_3$.]	[HNO$_2$] = n.	Type of catalysis by HNO$_2$.	Rate approx. propl. to :
53—60	2·89	0·04 < n < 0·25	+ ve	$n^{1·00}$
322—329	4·60	0·10 < n < 1·75	+ ve	$n^{1·00}$
460—469	8·00	0·04 < n < 0·50	+ ve	$n^{0·5}$
549—558	10·00	{ 0·01 < n < 0·50 0·50 < n < 1·00	− ve (practically no effect)	(complicated)

The analogy between these phenomena as a whole, and those which were observed in connexion with the nitration of anisole and of *p*-chloroanisole, will be obvious. It cannot be doubted that the same two mechanisms of nitration, the special mechanism positively catalysed by nitrous acid, and the general mechanism negatively catalysed by nitrous acid, are operative in all three cases. In our examination of the nitration of *p*-chloroanisole we isolated both mechanisms. In the case of anisole, we did not succeed in completely isolating either; but we did separate them sufficiently to recognise them. The present study of the nitration of *p*-nitrophenol is in the intermediate position that we have isolated the special mechanism, though we have only recognised, without fully isolating, the general mechanism.

(7) *Nitration of Phenol.*

(7.1) *Kinetics in Acid–Aqueous Solutions, and in Acetic Acid Solutions.*—We shall make no detailed report of our kinetic experiments on the nitration of phenol, partly for the reason that a number of reports on this complicated subject have already appeared. They relate both to aqueous solvents and to organic solvents (cf. Section 1.2). Catalysis by nitrous acid is the rule; but the power of the nitrous acid concentration to which the nitration rate is proportional is never higher, and is almost always considerably lower, than the first power. Autocatalysis, arising from the production of nitrous acid by oxidation of some of the phenol, has been observed. In water, complex by-products are formed extensively.

The general picture presented by the kinetics of the nitration of phenol in acetic acid has close analogies with that of the nitration of anisole in that solvent (Section 5). It is not difficult to recognise that the same two mechanisms of nitration are in operation. There is catalysis by nitrous acid, which diminishes in intensity with increasing concentration of nitric acid. There is also autocatalysis, and an appreciable formation of complex by-products.

(7.2) *Products in Acid–Aqueous Solutions.*—It has been shown (Bunton, Minkoff, and Reed, *J.*, 1947, 1416) that the mononitration product of phenol consists of *o*- and *p*-nitrophenols only, the proportion of *m*-isomeride constituting less than 0·1% of the mixture. We have made some experiments to determine how the proportions of these products vary with the nitrous acid content of an aqueous acidic nitration medium.

We used strongly acidified aqueous media in these experiments having in mind the possibility of attack on the aromatic nucleus by hydrated forms of the nitronium ion or the nitrosonium ion, *i.e.*, by the nitric acidium ion, $H_2NO_3^+$, or the nitrous acidium ion, $H_2NO_2^+$. Our guide in this part of our work was the series of experiments, described by Halberstadt, Hughes, and Ingold in Part III (*J.*, 1950, 2441), on ordinary aromatic nitration in acidified aqueous media. Here it is

shown that aromatic nitration in aqueous solution depends on the presence of a strong proton-donor.

We employed sulphuric acid as the acidifying acid. The nitration solution also contained salts, since our method of making them up was to dissolve potassium nitrate and potassium nitrite in water, and then add the requisite excess of sulphuric acid. We have assumed that the dissolved potassium hydrogen sulphate made no difference to the proportions of the products.

The results are in Table XII. Errors of several units % are possible in the proportions of the products, especially since the yields of mononitro-products were in the neighbourhood of 70—80% only. However, the change in the product proportions, with the increase of nitrous acid content, is so large that there can be no doubt about its reality.

As to the cause of this effect, we assume that the reagent which attacks the aromatic molecule is different, according to whether nitrous acid is absent (Runs 1, 2), or an excess of nitrous acid is present (Run 5). In view of all we know concerning aromatic nitration in general, and phenolic nitration in particular, it seems an obvious suggestion that, in the absence of nitrous acid, the reagent is either NO_2^+ or $H_2NO_3^+$, whilst, in the presence of excess of nitrous acid, it is either NO^+ or $H_2NO_2^+$. Support for this idea may be derived from the fact that the proportion, 9% : 91%, in which *o*- and *p*-nitrophenols are found in the product of the acid-aqueous mononitration of phenol by nitric acid in the presence of an excess of nitrous acid is exactly the same as the proportion in which Veibel (*loc. cit.*) found *o*- and *p*-nitrosophenols in the product of the acid-aqueous mononitrosation of phenol by nitrous acid in the absence of nitric acid.

The question of whether dehydrated or hydrated cations act is a difficult one. Halberstadt, Hughes, and Ingold, dealing in Part III with general aromatic nitration, attempted to make

TABLE XII.

Effect of nitrous acid on the proportions of o- *and* p-*nitrophenols in the product of the mononitration of phenol by nitric acid in strongly acidified aqueous solutions.*

Temp.: 20°. Initially: [PhOH] = 0·45M.; [HNO$_3$] = 0·50M.; [H$_2$SO$_4$] = 1·75M.
(KHSO$_4$ was also present in quantity equivalent to the total [HNO$_3$] + [HNO$_2$].)

Run no.	1	2	3	4	5
[HNO$_2$]	0·00	0·00	0·25	0·25	1·00
o-Nitrophenol, %	73	72	55	52	9

plausible the theory that aromatic attack, in highly aqueous acidified solutions, is by the nitric acidium ion, $H_2NO_3^+$. The corresponding conclusion for special phenolic nitration would be that, in such solutions, the effective agent is the nitrous acidium ion, $H_2NO_2^+$. The experiments of this Section can be considered to bear the same relation to the wider study of phenolic nitration reported in this paper, as do the experiments of Part III to the study of general aromatic nitration as reported in Parts I—V of this series.

(7.3) *Products in Acetic Acid Solution.*—We have made some experiments to determine how the proportions, in which *o*- and *p*-nitrophenols occur in the product of the mononitration of phenol by nitric acid in acetic acid, depend on the nitrous acid content of this medium.

We were interested to detect if possible the activity of another conceivable " carrier " of the nitrosonium ion, *viz.*, the dinitrogen tetroxide molecule. Therefore, in the present experiments, we kept the nitric acid concentration in the nitration solutions sufficiently low substantially to exclude nitration by a nitronium ion mechanism. We know (Part II, *J.*, 1950, 2400) that what we here call " nitrous acid " exists in acetic acid mainly in the form of dinitrogen tetroxide. Therefore, we prepared the nitration mixtures by adding known quantities of freshly distilled dinitrogen tetroxide to a solution of nitric acid in acetic acid. This procedure is particularly convenient when large proportions of " nitrous acid " are required.

The main series of results, applying to the temperature 0°, are reported in Table XIII. They are confirmed by two shorter series which were obtained for the temperatures −10° and +20°. The figures can probably be trusted to a few units %. The proportions in which dinitration took place under the conditions used were never more than a few units %, and the proportions in which complex products were formed were comparably small.

Table XIII shows that, so long as the concentration of " nitrous acid," *i.e.*, of dinitrogen tetroxide, remains small in comparison with that of the nitric acid—as it was in all our kinetic experiments—the proportion of *o*-nitrophenol in the mononitrophenols remains fairly constant at about 46%; but that, as the concentration of dinitrogen tetroxide becomes comparable to that of the nitric acid, the proportion of *o*-nitrophenol increases, rising to more than 70% when the concentration of dinitrogen tetroxide exceeds that of the nitric acid.

TABLE XIII.

Effect of dinitrogen tetroxide on the proportions of o- and p-nitrophenols in the product of mononitration of phenol by nitric acid in acetic acid.

Temp. : 0°.   Initially, [PhOH] = 0·6M.; [HNO₃] = 3·2M.

Run no.	8	9	10	11	12	13	14	15
[N₂O₄]	small	small	0·030	0·27	1·8	3·2	3·5	4·5
o-Nitrophenol, % ...	44	49	45	46	64	68	70	74

Our main guide in the interpretation of these results is analogy with the work, reported in Part IV (*J.*, 1950, 2452), on ordinary aromatic nitration with dinitrogen pentoxide as the reagent. It was shown that the nitrating properties of this substance differ according to whether, as in the presence of nitric acid, it is ionised to give the nitronium ion, or whether, as in the absence of nitric acid, it remains covalent in an organic solvent. In the former case the free nitronium ion attacks the aromatic compound. In the latter, the dinitrogen pentoxide molecule itself is the attacking reagent, acting as a " carrier " of the nitronium ion into the aromatic molecule.

Goulden and Millen have shown (*J.*, 1950, 2620) that, just as dinitrogen pentoxide is ionised by nitric acid to give the nitronium ion, so dinitrogen tetroxide is ionised in nitric acid to give the nitrosonium ion. But in the absence of nitric acid, or of a sufficient excess of nitric acid, dinitrogen tetroxide remains largely covalent in an organic solvent.

The general view which we shall develop concerning those nitration mechanisms which are especially applicable to the nitrations of phenols and phenolic ethers will involve the conclusion that, in ionising conditions, the entity which attacks the aromatic molecule is the nitrosonium ion, NO⁺. This should be the effective reagent when (as in Runs 8—11) the nitric acid is in sufficiently large excess over the dinitrogen tetroxide to secure extensive ionisation of the latter. But when the concentration of dinitrogen tetroxide is large, and when the proportion of nitric acid is insufficient to secure its adequate ionisation (as in Runs 12—15), then we might expect the covalent dinitrogen tetroxide molecule, N₂O₄, itself to become the attacking reagent, acting as a " carrier " of the nitrosonium ion into the aromatic molecule. The fact that the proportions of products alter as they do shows that some significant change of reagent occurs in these circumstances; and the change that we have suggested seems plausible, having regard to the known ionising properties of dinitrogen tetroxide. Thus the experiments of this Section can be considered to bear the same relation to the wider study of phenolic nitration reported in this paper, as do the experiments of Part IV to the study of general aromatic nitration as reported in Parts I—V of this series. Just as we envisage a series of " carriers " of the nitronium ion, *e.g.*, NO₂⁺, H₂NO₃⁺, N₂O₅, NO₃Bz, in order of diminishing activity, so we contemplate a series of possible " carriers " of the nitrosonium ion, *e.g.*, NO⁺, H₂NO₂⁺, N₂O₄, etc.

(8) *Coloured By-products of Nitration, particularly of Anisole.*

We have now described our observations on the mechanisms of *nitration* of phenolic ethers and phenols; but there remain for consideration the non-nitrating side reactions. These side reactions are partly non-oxidative, giving coloured, and in some cases polycondensed, compounds. They are also partly oxidative, producing the already discussed kinetic auto-effects.

We have attacked only the more tractable part of this problem, *viz.*, the non-oxidative formation of non-polycondensed by-products. The chief of the encountered examples in which the total formation of by-products may assume large proportions (*e.g.*, 10%) are the nitration of anisole, which gives a coloured binuclear by-product, as well as polycondensed products, and the nitration of phenol, which, as is well known, gives polycondensed products. We have studied particularly the example of anisole. It is only a conjecture that the polycondensations are elaborations of the relatively simple condensation illustrated in the case of anisole.

The formation of coloured by-products during nitration is not peculiar to the nitration of phenolic ethers and phenols. What is peculiar is that the coloured compounds derived from phenolic ethers and phenols exhibit greater stability, and in particular survive nitration conditions better, than do those derived from aromatic hydrocarbons or halogeno-hydrocarbons. Benford and Ingold studied the unstable crimson colours that appear during the nitration of aromatic hydrocarbons and halogeno-hydrocarbons in organic solvents (*J.*, 1938, 947). They showed that the reagents necessary to produce the coloured substances were the aromatic compound, some form of " nitrous acid," and some strong acid, which in nitration conditions was nitric acid, though this could be replaced by other strong acids. The same authors showed that

the coloured compounds were formed reversibly, in equilibrium with their factors; one result of this was that, as the aromatic compounds became consumed in the nitration process, the colours disappeared. Finally, these authors found that, although the equilibrium proportions in which the coloured compounds were produced were small, they tended to increase with the general reactivity of the aromatic compound. Benford made the acute suggestion (Thesis, London, 1938, p. 139) that the coloured substances might be radicals of the diarylaminyl oxide type, Ar_2NO, though he was not able at that time firmly to establish this idea.

During the nitration of anisole in acetic acid in the presence of nitrous acid, a deep purple colour is produced. The colour does not disappear as the anisole becomes consumed in nitration. This coloured substance has been definitely identified as the dianisyloxidoammonium ion, $\{(MeO \cdot C_6H_4)_2NO\}^+$, by a direct comparison of its absorption spectrum with that of the salt, dianisyloxidoammonium perchlorate, prepared from anisole and nitric acid by K. H. Meyer and Gottlieb-Billroth (*Ber.*, 1919, **52**, 1476).

The proportions in which this cation is produced during the nitration of anisole in acetic acid have been measured colorimetrically for a number of different conditions. These proportions may be quite large, and are frequently in the range 5—15%.

The diarylaminyl oxides are odd-electron radicals. But the more basic of them form non-radical salts with loss of an electron. This means that some substance, which may be the substance supplying the anion of the salt, or a portion of the free radical, or some foreign substance, becomes reduced. The salt-forming reaction with elemental bromine can be represented as follows (here the halogen is reduced) :

$$R_2NO + \tfrac{1}{2}Br_2 = (R_2NO)^+Br^-$$
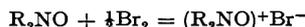
The formation of dianisylaminyl oxide from anisole and " nitrous acid," under the influence of an acid condensing agent, can be formally represented as a condensation between anisole and the free-radical nitrogen dioxide :

$$2MeO \cdot C_6H_5 + NO_2 = (MeO \cdot C_6H_4)_2NO + H_2O$$
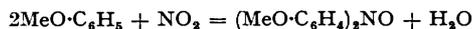
This equation may not be mechanistically correct, but it at least expresses the need for " nitrous acid." Dianisylaminyl oxide is a moderately strongly basic radical; and it is converted by excess of nitric acid into the non-radical salt, dianisyloxidoammonium nitrate. The conversion must involve a reduction of some nitric acid, and therefore a restoration of some " nitrous acid." We can formally represent the restored " nitrous acid " as nitrogen dioxide :

$$(MeO \cdot C_6H_4)_2NO + 2HNO_3 = \{(MeO \cdot C_6H_4)_2NO\}^+NO_3^- + H_2O + NO_2$$

It is then seen, by addition of the last two equations, that the over-all reaction is non-oxidative.

The diaminyloxidoammonium ion doubtless owes much of its stability to a partial mesomeric conversion into oxonium ionic forms :
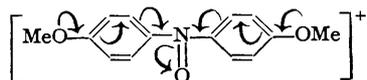
This is only a modernisation of the quinonoid theory of the structure of the ion, which was originally put forward by Meyer and Gottlieb-Billroth (*loc. cit.*).

(9) *Catalysis by Nitrous Acid outside the Field of Phenol and Aniline Derivatives. Nitration of Mesitylene.*

We have given our results relating to the special mechanism operating in the nitration of derivatives of phenol. We shall show in Part VII that it also operates in the nitration of derivatives of aniline. One further matter required experimental examination. This was the question of why the special mechanism has always appeared to be peculiar to derivatives of phenol and aniline; why it supplants the general mechanism of nitration in these particular cases; and why, if it can do that, it does not take some notable part in aromatic nitration universally.

For a long time we have had a hypothetical answer to this question. It is that, in principle, the special, nitrous acid mechanism *is* universal, just as is the general, nitronium ion mechanism; but that the special mechanism receives special advantages from the use of an aromatic compound of high nuclear reactivity, independently of what particular substituents confer such

reactivity on the nucleus. We think that the special mechanism supplies a reagent—the nitrosonium ion—which is more stable and less reactive than the reagent—the nitronium ion—which is furnished by the general mechanism. If only the general mechanism of nitration existed, we should inevitably have greatly to milden the conditions of nitration, *i.e.*, restrict the nitronium ion supply, whenever we attempted to study the *mono*nitration of such a highly reactive substance as anisole or phenol. Actually, such a reduction in the opportunities for the general mechanism simply leaves the field open for the special mechanism; for this is not necessarily impeded by those changes of conditions which are made for the purpose of repressing the nitronium ion (cf. Millen, *J.*, 1950, 2600). And if only the special mechanism existed, many aromatic compounds would not, or would only with difficulty, be nitrated; for the active reagent is less electrophilic than is that provided by the general mechanism (*idem, ibid.*). But the special mechanism is quite adequate to cope with the nitration of such highly reactive nuclei as those present in derivatives of phenol and aniline.

It was clear to us that in order to establish this assumed universality of both mechanisms, two things had to be done. First, we had to show that the general mechanism does not become abrogated in the nitration of derivatives of phenol and aniline, but applies to these as to other aromatic compounds. This has been done for derivatives of phenol, inasmuch as we show (Sections 3.4, 3.5, 5, 6.5, and 7.1) that the much-discussed complications applying to the nitration of phenolic ethers and phenols arise, not from the suppression of the general mechanism of nitration, but from the adding to it of the special mechanism (and the adding also, in some cases, of non-nitrating side reactions). Our second task was the complement of this : we had to show that the special mechanism of nitration was not peculiar to derivatives of phenol and aniline, but could be observed outside that field, for instance, in the nitration of a hydrocarbon. That is the theme of the work now to be reported.

According to our view of the facility of occurrence of the two nitration mechanisms, an aromatic hydrocarbon of high nuclear reactivity should offer a comparatively good chance for an observation of the incursion of the special mechanism of nitration. Therefore, we selected for this study one of the more reactive of the aromatic compounds previously investigated by us, namely, mesitylene.

The nitration of mesitylene by the general, nitronium ion mechanism in acetic acid as solvent has been described in Part II (*J.*, 1950, 2400). With nitric acid in constant excess, the reaction seems to be weakly anticatalysed by nitrous acid. The conditions in which these statements have been illustrated are relevant to the comparison now to be made. They are as follows : temperature, 20°; [HNO_3], 5—7M.; [HNO_2], below 0·014M.

Now we have seen that the special, nitrous acid mechanism, when in isolation, produces a reaction which is of first order with respect to the aromatic compound, and of first order with respect to nitrous acid. It follows that, if, by increasing the nitrous acid content of the nitration solutions considerably above 0·014M., we should succeed in realising a substantial incursion of the special mechanism of nitration, then two kinetic effects should be observed. First, the absolute rates, with all concentrations fixed except that of nitrous acid, should increase with increasing concentration of nitrous acid; and the increase should be approximately linear, or at least asymptotically linear. Secondly, the zeroth-order law should break down, giving place, at first, to a mixed, zeroth-to-first order kinetic form, and eventually, if the special mechanism can be made sufficiently dominating, to an approximate first-order form.

TABLE XIV.

Dependence of the initial nitration rate of mesitylene in acetic acid at 25·0° on the concentration of nitrous acid.

Initially, [HNO_3] = 5·7M., [$C_6H_3Me_3$] = 0·08M. (the same throughout).

Run no.	586	587	585	584	583
[HNO_2], M.	0·018	0·055	0·084	0·210	0·317
dh/dt in mm. sec.$^{-1}$	0·0033	0·0040	0·0046	0·0070	0·0088

A dilatometric study of the influence of nitrous acid on the kinetics of nitration of mesitylene has been made, and both the expected effects have been observed. A convenient way of comparing absolute rates at standardised concentrations is to measure initial rates in runs conducted under standardised initial conditions. Such a set of initial rates, obtained for a block of runs in which all initial concentrations were the same, except the concentration of nitrous acid, is given in Table XIV. It will be noticed that the lowest of the nitrous acid concentrations, 0·018M., is

higher than the upper limit of those used in the above-mentioned experiments recorded in Part II; and that, in the present block of runs, the concentration of nitrous acid is increased to more than 20 times that limit. One sees that the rates increase considerably with increasing concentration of nitrous acid. The form of the increase is simple, as is shown in Fig. 17.

From this result it is clear that we are observing, superposed on a reaction which does not require nitrous acid, and is evidently the nitronium ion reaction, a second reaction, the rate of which is proportional to the concentration of nitrous acid. Thus we identify one of the two main kinetic criteria of the nitrous acid mechanism.

FIG. 17.

Initial rates of nitration (expressed as rates of fall of height in the same dilatometer) of mesitylene (in the same initial concentration, about 0·08M.), by 5·7M-nitric acid in acetic acid at 25°, are plotted against the concentrations of nitrous acid. The linear curve shows that a reaction catalysed by nitrous acid is present, as well as a reaction which does not depend on nitrous acid.
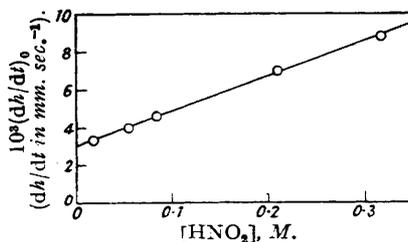
FIG. 18.
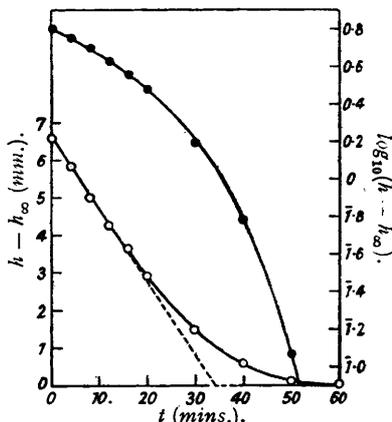
FIG. 19.

Run no. 586 : ordinary plot and logarithmic plot of the course of the nitration of mesitylene by 5·71M-nitric acid in acetic acid at 25·0° in the presence of 0·018M-nitrous acid.
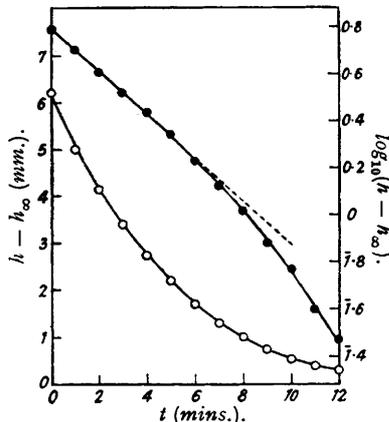
Run no. 580 : ordinary plot and logarithmic plot of the course of the nitration of mesitylene by 5·71M-nitric acid in acetic acid at 30·0° in the presence of 0·56M-nitrous acid.

It will be clear from Fig. 17 that we can scarcely expect to isolate the nitrous acid mechanism in a pure form, and thus to observe a pure first-order reaction with respect to the mesitylene, within the permissible range of concentrations of nitrous acid. (The concentration of nitrous acid has always to be low in comparison with the concentration of nitric acid : otherwise the " nitrous acid " would not retain the same properties—see Section 7.3.) With 0·3M-nitrous acid the special mechanism is about twice as important as the general one. Overall in these experiments, we have used concentrations of nitrous acid up to 0·6M., which seemed about as far as it was wise to go. However, this suffices to give a considerable degree of domination to the nitrous acid mechanism, and therefore it allows us to observe a moderately close approach to first-order kinetics, though not a pure first-order reaction.

Figs. 18 and 19 will establish that the reaction order with respect to mesitylene does indeed rise from a little above zero to a little below unity over the range of nitrous acid concentrations stated. Each figure shows, for the kinetic run to which it refers, both a plot of the variable part of the dilatometric height, and a plot of its logarithm, each against time. Fig. 18 relates to a run in which the concentration of nitrous acid was only 0·018M. One sees that about the first half of the reaction proceeds at a practically constant rate, whilst the logarithmic plot is curved throughout its length. Evidently the reaction order is here approximating to zeroth order. Fig. 19 refers to a run in which the concentration of nitrous acid was 0·56M. In this case the whole of the reaction–time graph is curved, whilst a considerable portion of the reaction yields a linear logarithmic plot. Obviously this reaction is approaching a first-order form. Thus we recognise in our results the second of the two main kinetic characteristics of the nitrous acid mechanism.

As the first kinetic property by which we recognise the special mechanism is the acceleration of nitration by nitrous acid, it was necessary to prove that this did not arise from the simultaneous incursion of a form of side-chain nitration induced by nitrous acid. And as the recognition of the second characteristic, *viz.*, the increased kinetic order, depends on the observation, not of initial rates, but of the general course of the reaction, it was necessary to show that the relatively lower rate in the later part of the reaction, which is observed in the presence of much nitrous acid, does not result from the incursion of a second stage of nitration. Both these points were covered in the course of our chemical checks. The main product obtained in preparative experiments carried out under conditions comparable as to temperature, time, and the concentrations of reagents with those of the kinetic runs, including runs with a low (*e.g.* 0·01M.) and with a high (*e.g.*, 0·3M.) content of nitrous acid, in solution of nitric acid (5·7M.) in acetic acid, was always the nuclear mononitration product. Its accelerated production in presence of nitrous acid was qualitatively confirmed by the larger amounts isolated, and the smaller quantities of mesitylene recovered (after equal nitration times at the same temperature) in the presence, than in the absence, of much nitrous acid. As far as could be ascertained, no substantial amount of side-chain nitration, or of dinitration, took place under the conditions of the kinetic experiments.

(10) *Summary of Conclusions : Nitration through the Nitrosonium Ion.*

We have concluded that the complexities which arise in the nitration of phenolic ethers and phenols are due essentially to the simultaneous effectiveness of two mechanisms of nitration, though non-nitrating side reactions, oxidative or otherwise, sometimes contribute further complications. One of the two nitration mechanisms is identified as the nitronium ion mechanism elucidated in Part II (*J.*, 1950, 2400). The other is concluded to be a similar mechanism in which the nitrosonium ion combines with the aromatic electrons : thus a nitroso-group is introduced, which rapidly becomes oxidised to a nitro-group. Both the nitronium ion mechanism and the nitrosonium ion mechanism are assumed to be in principle of universal application to aromatic nitration; but the latter mechanism is relatively favoured in the nitration of highly reactive aromatic molecules (cf. Sections 3, 5, 6, 7, and 9).

The equilibria involved in the production of the free nitrosonium ion are presumed to be as follows :

$$\text{HNO}_2 + \text{HNO}_3 \rightleftharpoons \text{H}_2\text{NO}_2^+ + \text{NO}_3^- \quad . \quad . \quad . \quad . \quad . \quad . \quad (1)$$
$$\text{H}_2\text{NO}_2^+ \rightleftharpoons \text{NO}^+ + \text{H}_2\text{O} \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (2)$$
$$\text{NO}^+ + \text{NO}_3^- \rightleftharpoons \text{N}_2\text{O}_4 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$
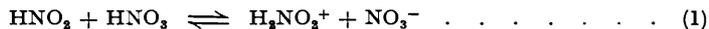
Equations (1) and (2), which show the nitrous acidium ion as an intermediate, are hypothetical, but are supported by analogy with the well-established equilibria leading to the nitric acidium ion, and thence to the nitronium ion (cf. Part II, Section 2.4.1, *J.*, 1950, 2419). Equation (3) has to be added because dinitrogen tetroxide is a weak electrolyte in solutions of nitric acid in organic solvents, whereas the corresponding ionic equilibrium involving dinitrogen pentoxide could be neglected in the considerations of Part II concerning the production of the nitronium ion because dinitrogen pentoxide is a strong electrolyte in such solutions (cf. Part II, Section 4.2.1, *J.*, 1950, 2419; Goulden and Millen, *J.*, 1950, 2620; Millen and Reed, forthcoming papers).

No doubt the free nitrosonium ion is a more effective substituting group than any covalent structure (" carrier ") from which it can be liberated on interaction with the aromatic nucleus. But we have tried to make plausible the view that, just as the nitronium ion may be carried into reaction in combined forms, such as H_2NO_3^+, N_2O_5, and NO_3Bz (Parts III, IV, and V, *J.*, 1950, 2441, 2452, 2467), so also the nitrosonium ion can in forms such as H_2NO_2^+ and N_2O_4, and perhaps N_2O_3 and NOCl (Sections 7.2 and 7.3).

The simplest view that can be taken of the reaction of the nitrosonium ion with the aromatic nucleus applies when no point of attachment for the ion is presented by any side chain. We assume that a rate-determining addition of the nitrosonium ion is succeeded by a fast ejection of the aromatic proton, and a fast oxidation of the nitroso-compound to a nitro-compound :

$$ArH + NO^+ \xrightarrow[\text{slow}]{} ArHNO^+ \quad \text{.......} \quad (4)$$

$$ArHNO^+ \xrightarrow[\text{fast}]{} ArNO + H^+ \quad \text{.......} \quad (5)$$

$$ArNO + HNO_3 \xrightarrow[\text{fast}]{} ArNO_2 + HNO_2 \quad \text{.......} \quad (6)$$
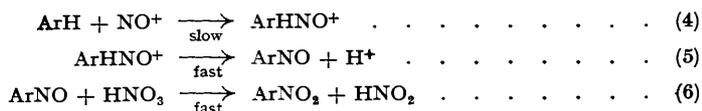
Reactions (4) and (5) are assumed, and are supported by analogy with the proved course of nitronium ion nitration (Part II, Section 3.2, *J.*, 1950, 2426). Reaction (6) has necessarily to be assumed in order to account for the stoicheiometry of the process.

Having recognised the general character of the mechanisms operating in the nitration of phenols and phenolic ethers,* we shall endeavour to secure direct kinetic evidence for those detailed steps in the special mechanism, which at present rest only on arguments of analogy (*viz.*, those of equations 1, 2, 4, and 5).

The nitration of phenolic ethers and phenols presents the complication that there is, in the side chains of these molecules, a point of attachment for a reactive cation, be it a nitronium ion or a nitrosonium ion. A possible chemical consequence of this is recognised in the observation that phenolic ethers are partly dealkylated during nitration, by either the nitronium ion mechanism or the nitrosonium ion mechanism (Section 2.1). The assumed dealkylation mechanisms may be illustrated for demethylation as follows :
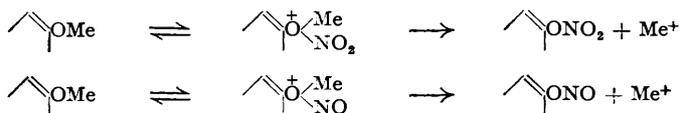
The aryl nitrate, or nitrite, will undergo rapid acidolysis, and will be isolated as a phenol. The methyl cation will combine with the most accessible anion, *e.g.*, an acetate ion if the solvent is acetic acid.

A second possibility was suggested to us independently by Professor J. F. Bunnett and by Professor J. W. Cook, whom we thank for permission to quote their ideas. These are that the slow stage of nitration·(as in equation 4, or in the analogous equation of the nitronium-ion reaction) leads to an almost fully quinonoid oxonium ion, and that then the proton loss (as in equation 5), and the loss of a methyl cation, have comparable (fast) rates :
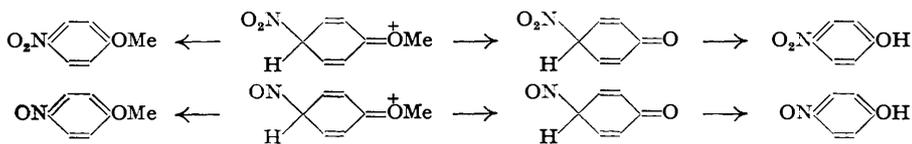
We offer three arguments which support either of these suggestions. First, there is evidence (Section 2.1) that the proportion of dealkylation under a single nitration mechanism is independent of the absolute rate of nitration; this indicates that the processes of dealkylation and of normal nitration have kinetics of the same form. Secondly, dealkylation during nitration is suppressed (Section 4) in 2 : 6-dichloro- and 2 : 6-dimethyl-anisole ; this suggests steric hindrance in the formation, either of a branched side-chain, as in the first of the postulated mechanisms, or of the fully quinonoid structure (with the methyl group sideways to the oxygen double bond, and fixed in the plane of the ring), as in the second. Thirdly, the methyl group eliminated during the nitration of *p*-chloroanisole in acetic acid as solvent has been recovered as methyl acetate ; this makes it practically certain that the group is indeed eliminated as a methyl cation (Section 2.2).

We need not deal further with effects due to ion-formation by proton transfer in phenol derivatives; for the theory of such effects in aromatic substitution is today a commonplace.

However, the effects may be chemically very significant, as has been illustrated in the example of p-nitrophenol, which almost certainly nitrates largely through its anion (Section 4.6).

Finally, as to non-nitrating side reactions, we have identified the principal one which anisole undergoes in our conditions : it involves condensation of the anisole with nitrous acid (or a lower oxide of nitrogen), and produces the coloured dianisyloxidoammonium cation, derived from the radical dianisylaminyl oxide. This makes it probable that the unstable coloured products, which commonly appear (Part I, *J.*, 1938, 947) during the nitration of aromatic compounds with nitric acid containing nitrous acid, are derivatives of diphenylaminyl oxide, as Benford first suggested (Section 8).

(11) *General Experimental Methods.*

(11.1) *Materials.*—Nitric acid, acetic acid, and dinitrogen tetroxide were purified as noted in Part II (*J.*, 1950, 2400). When nitrating solutions containing considerable concentrations of so-called nitrous acid were required, the " nitrous acid " was added in the form of freshly distilled dinitrogen tetroxide. Solutions containing small concentrations of nitrous acid were usually made by mixing solutions free from nitrous acid with solutions relatively rich in nitrous acid. The various phenols and phenol ethers were prepared or purified by well-known methods.

(11.2) *Kinetics.*—Tapless dilatometers, essentially of Benford and Ingold's " type C," were again employed. The use of such dilatometers with a detachable upper bent portion, as described in Part II (*loc. cit.*), was developed in the course of the work. The significance of dilatometric indications was frequently checked by chemical analysis, usually at the ends of the runs, but sometimes also throughout the course of a run, as illustrated in Section 3.2.

(11.3) *Analysis.*—Organic nitro-compounds in isolated, or in solvent-extracted, samples were determined by titration with titanous chloride in a sodium citrate buffer, the excess of reducing agent being back-titrated with ferric alum. The latter was used to standardise the titanous chloride, and the whole process was standardised by application to pure p-nitroaniline. Nitrous acid in the nitration solutions at the beginning and the end of kinetic runs was determined by the chloramine-T method, when in concentration above 0·005M., and by the absorptiometric method, when in lower concentration (cf. Part II, *loc. cit.*).

(12) *Particulars concerning Products.*

(12.1) *Nitro-products from the Nitration of* p-*Chloroanisole in Acetic Acid.*—In a preliminary qualitative experiment, p-chloroanisole (5 g.) was nitrated at 25° with nitric acid (15 g.) containing nitrous acid, in acetic acid (50 c.c.) as solvent. After 24 hours, the solution was cooled at 0°. The yellow crystals were collected, crystallised from methyl alcohol, and identified as 4-chloro-2-nitroanisole by their m. p., 96°, and by mixed m. p. with a sample prepared by methylation of 4-chloro-2-nitrophenol (Found : C, 45·0; H, 3·4. Calc. : C, 44·8; H, 3·2%). The remaining acetic acid solution was added to excess of 2N-aqueous sodium hydroxide, and the deep-red precipitate was collected and washed with ether. The filtrate was extracted with ether. The precipitate and the residual aqueous solution were then recombined, acidified, and extracted with benzene. The product derived from this extract was identified as 4-chloro-2 : 6-dinitrophenol by its m. p., 80°, and by mixed m. p. with a sample prepared by nitration of p-chlorophenol (Found : C, 32·9; H, 1·3. Calc. : C, 33·0; H, 1·4%).

In quantitative determinations of these two products, amounts of about 1 g. of p-chloroanisole were nitrated in solutions made up to 25 c.c., and portions of 5 c.c. were withdrawn for analysis. Each sample was run into 50 c.c. of dilute aqueous sodium hydroxide. The solution was extracted with benzene, acidified, and similarly extracted. The residues from the evaporated extracts were each taken up in 10 c.c. of methyl alcohol, and analysed by titration with titanous chloride as noted above.

(12.2) *Methyl Acetate from the Nitration of* p-*Chloroanisole in Acetic Acid.*—This experiment was done a number of times, with like results, and, on the final occasion, care was taken to prove that the originally taken p-chloroanisole contained no trace of methyl alcohol, or of a methyl ester, as impurity. A sample prepared from crystalline p-chlorophenol, m. p. 42—43°, by methylation with methyl sulphate and alkali, was fractionated through a 1-metre column packed with glass helices. The p-chloroanisole had b. p. 198·2—198·4°/765 mm. (Found : C, 59·3; H, 5·2; Cl, 24·4. Calc. : C, 59·0; H, 5·0; Cl, 24·9%). The acetic acid, similarly fractionated, after the usual pre-treatment at its b. p. with chromic oxide, had m. p. 16·55°. The nitric acid was absolute material, prepared as usual by non-ebullient distillation from sulphuric acid at a low pressure and temperature. When used, it contained a small concentration of nitrous acid.

A mixture of p-chloroanisole (36·5 g.), nitric acid (63 g.), and acetic acid (200 c.c.) was kept at 35° for 24 hours. It was then cooled, treated with powdered anhydrous sodium acetate (65 g.), and warmed again to 33—35° while connected to the vacuum line through a series of traps cooled at 0° and —80°. The mixture was allowed to boil briskly under the reduced pressure, and the first 100 c.c. of distillate were fractionated through a vacuum-jacketed micro-column of Vigreux type to yield 2·8 g. of methyl acetate, b. p. 56·0—57·0° (Found : C, 47·6; H, 8·4. Calc. : C, 48·6; H, 8·1%). A determination of the saponification equivalent-weight gave the value 75·1 (Calc. : 74), whilst from an authentic sample of methyl acetate the figures 74·1, 75·5 were obtained; this slight inconsistency was attributed to evaporation during transfer. The material from the nitration had $n_D^{19·5}$ 1·3619, and the authentic sample also had $n_D^{19·5}$ 1·3619.

The residue from the distillation under reduced pressure was made alkaline with sodium hydroxide, made up to about 3 l. with water, shaken with 0·5 l. of benzene, and filtered. The solid material was washed with benzene, and the combined benzene extracts were washed with water until the washings were colourless, dried (CaCl₂), and distilled. The residue was crude 4-chloro-2-nitroanisole, m. p.

94·5—95·5° (30·8 g., *i.e.*, 66 mols. %). After crystallisation from aqueous alcohol, it had m. p. 96·0—96·5° (Found : C, 45·3 ; H, 3·3 ; N, 7·5 ; Cl, 18·9. Calc. : C, 44·8 ; H, 3·2 ; N, 7·5 ; Cl, 18·9%). The solid residue and aqueous liquors were combined, acidified with concentrated hydrochloric acid, and extracted with benzene. In this way 4-chloro-2 : 6-dinitrophenol in a yield of 14·0 g. was recovered, *i.e.*, 25 mols. %. After crystallisation from light petroleum, it had m. p. 79° (Found : C, 32·9 ; H, 1·3 ; N, 13·3. Calc. : C, 33·0 ; H, 1·4 ; N, 12·8%). The recovered pure methyl acetate (2·8 g.) is equivalent to 15 mols. %, and therefore accounts for 60 % of the weight of methyl group eliminated during the formation of the aromatic demethylation product.

(12.3) *Products of Nitration of* 2 : 6-*Disubstituted Anisoles in Acetic Acid.*—2 : 6-Dichloroanisole was allowed to be nitrated during 7 days at 20° in a 4M-solution of nitric acid in acetic acid, which was about 0·2M. with respect to nitrous acid. The solution was slowly poured into excess of aqueous sodium hydroxide at 0°, and the crystalline precipitate was collected, washed with water, dried, and weighed. It represented a 94% yield of almost pure 2 : 6-dichloro-4-nitroanisole. Crystallised from methyl alcohol, this substance had m. p. 97°. It was identified by mixed m. p. with an authentic specimen.

In contrast to the nitration of *p*-chloroanisole, very little demethylation accompanied the nitration of 2 : 6-dichloroanisole. The formation of free nitrophenols could be observed qualitatively as a red colour in alkaline solution, but the quantity of nitrophenols produced was too small for isolation under our conditions. In contrast to the nitration of anisole in particular, no purple colour appeared during the nitration of 2 : 6-dichloroanisole.

2 : 6-Dimethylanisole (2-methoxy-*m*-xylene) was nitrated under the conditions described above, except that, since the reaction was relatively rapid, only 3 hours were allowed. The neutral product, isolated in the same way, constituted a 96% yield of 4-nitro-2 : 6-dimethylanisole (5-nitro-2-methoxy-*m*-xylene). Crystallised from methyl alcohol, it had m. p. 92°, which was not depressed by admixture with an authentic specimen.

Again a trace, but no more than a trace, of free nitrophenols was produced, as was qualitatively observed by the red colour which was formed in alkaline solution. No purple colour was produced during the nitration of the anisole derivative.

(12.4) *Nitro-products from the Nitration of Anisole in Acetic Acid.*—Anisole was nitrated at 20° in 5M-nitric acid in an acetic acid solution, which was about 0·1M. with respect to nitrous acid. The solution was poured into excess of aqueous sodium hydroxide. The aqueous solution was extracted with ether, acidified, and again extracted. Both ether extracts were red-brown, and the residual aqueous solution was red. Most of the neutral product could be distilled without decomposition at 123—128°/3 mm. ; but there was a tarry residue. The acid extract yielded a small amount of 2 : 4-dinitrophenol mixed with an acid tar. As to quantities, the distilled neutral product, consisting of mononitroanisoles (Found : C, 54·6 ; H, 4·7 ; NO_2, by titanous chloride, 29·9. Calc. : C, 54·9 ; H, 4·6 ; NO_2, 30·1%), constituted a 75% yield. The neutral tar amounted to 10% of the weight of the employed anisole, and the 2 : 4-dinitrophenol and acid tar taken together to about 3% of the weight of the anisole. Thus, more than 12% of material was not recovered, but it will be shown in Section 12.5 that amounts of this order can be accounted for as dianisyloxidoammonium salts.

In a nitration at 20° with 7M-nitric acid in an acetic acid solution, which was about 0·2M. with respect to nitrous acid, much less neutral tar was formed. The yield of mononitroanisoles (Found : C, 54·5 ; H, 4·8 ; NO_2, by titanous chloride, 30·0%) was 83%. The neutral tar amounted to about 1%, and the 2 : 4-dinitrophenol and acid tar taken together to about 3%, of the weight of the original anisole. More than 13% of material was not recovered, but, as is shown below, this probably consisted of dianisyloxidoammonium salts.

(12.5) *Formation of Dianisyloxidoammonium Salts in the Nitration of Anisole in Acetic Acid.*—When the purple solution, obtained by nitrating anisole by nitric acid in acetic acid containing nitrous acid, was diluted with ice-cold water, filtered, and extracted with ether, much of the purple colour passed into the ether. This colour was changed to red-brown on drying the ether with sodium sulphate ; but the purple colour was restored by passing dry hydrogen chloride into the solution. Purple crystals, believed to consist of dianisyloxidoammonium chloride, were obtained ; and the corresponding perchlorate was precipitated by the use of concentrated aqueous perchloric acid. This salt was identified with Meyer and Gottlieb-Billroth's salt, prepared as they describe (*loc. cit.*), by a direct comparison of their properties, and in particular of their optical absorption in the visible region of the spectrum.

A Hilger visual spectrophotometer was used. Samples of perchlorate were prepared for optical measurements by dissolving them in a 4M-solution of hydrogen chloride in acetic acid. The main absorption band has its maximum of intensity at 5750 A. The general form of the band is indicated by the following measurements of optical density (*d*) :

λ, A.	5000	5200	5400	5600	5700	5800	5900	6000	6200	6400
d	0·22	0·19	0·22	0·29	0·32	0·32	0·27	0·20	0·11	0·08

The wave-length of the absorption maximum being used, the spectrophotometer was calibrated for the measurement of concentration of dianisyloxidoammonium ion. Solutions containing different weighed amounts of the perchlorate were made up in acetic acid containing hydrogen chloride, and the optical densities were measured in a 1-mm. cell. An approximately linear relationship between concentration and optical density was obtained, as is illustrated by the following figures (the concentrations, *c*, are in 10^{-6} g./c.c.) :

c	58	114	240	750	1110	1600
d	3·2	12·0	21·3	68·0	109	176

8 H

These data were used in order to estimate the amounts of dianisyloxidoammonium salts, which were formed during the nitration of anisole by nitric acid containing nitrous acid in acetic acid under various conditions. The proportions in which anisole was converted into the coloured cation during nitration were observed to vary from less than 1% to more than 20%, depending on the conditions.

For nitric acid concentrations in the range 3—7M., and nitrous acid concentrations in the range 0·01—0·50M., the proportion of anisole converted into the coloured ion during nitration, with fixed concentrations of nitric and nitrous acids, was found to be nearly independent of the initial concentration of anisole. This is an indication that nitration, and the condensation leading to the coloured cation, are reactions of the same order with respect to the anisole. The result is illustrated, for two blocks of runs, by the figures in Table XIV.

TABLE XIV.

Proportion of dianisyloxidoammonium ion formed during the nitration of anisole by nitric acid containing nitrous acid in acetic acid at 20°.

| | [HNO₃] = 3M. | | [HNO₂] = 0·0125M. | | [HNO₃] = 7M. | [HNO₂] = 0·100M |

	$[HNO_3] = 3M.$		$[HNO_2] = 0.0125M.$		$[HNO_3] = 7M.$		$[HNO_2] = 0.100M$
Run no.	607	608	609	610	615	616	617
Initial [PhOMe] ...	0·027	0·054	0·073	0·107	0·026	0·055	0·078
% Ion formed ...	23·4	22·6	24·2	27·8	4·8	5·8	6·9

(12.6) *Nitro-products from the Nitration of Phenol in Water and in Acetic Acid.*—The nitration solutions were poured into an excess of cold dilute aqueous sodium hydroxide, and the alkaline solutions were first shaken with salicylic acid until no more of the latter would dissolve, and then extracted with *iso*butyl acetate. This procedure produced solutions which contained all the formed *o*- and *p*-nitrophenols but were almost entirely free from 2 : 4-dinitrophenol, often simultaneously produced in small amount. The nitrophenols were collected from the ester solution by extraction with 4N-aqueous sodium hydroxide, and this aqueous solution was acidified, filtered from salicylic acid, and extracted three times with one-tenth of its volume of carbon tetrachloride. The *p*-nitrophenol remaining in the aqueous solution was then determined by titration with titanous chloride in a sodium citrate buffer. The *o*-nitrophenol extracted by the carbon tetrachloride was passed back into an alkaline aqueous solution, which was then neutralised, and similarly analysed by titration with titanous chloride.

This method of estimating the proportions in which *o*- and *p*-nitrophenols are present in the mono-nitration product of phenol gives values for the proportion of *o*-nitrophenol, which are too large when the actual proportion of *o*-nitrophenol is small. Deviations of this type can be calculated from recorded solubility and partition data; but the observed deviations were greater than those calculated, and the necessary corrections were therefore empirically evaluated. They are as follows :

Observed *o*-nitrophenol (%)	20	40	53	63	70	75
Subtract (%)	6	5	4	3	2	1

These corrections have already been applied to the results recorded in Sections 7.2 and 7.3.

(12.7) *Products of Nitration of p-Nitrophenol in Acetic Acid.*—Routine chemical checks, under conditions comparable to those of the dilatometrically followed nitrations described in Section 6, showed that 2 : 4-dinitrophenol was substantially the sole nitration product. It was identified by m. p. and mixed m. p. with genuine material.

(12.8) *Products of Nitration of Mesitylene in Acetic Acid.*—Preparative experiments were carried out under conditions comparable with those of the kinetic runs reported in Section 9. The only change made was to use mesitylene in 0·3M-concentration, instead of 0·1M., in order to provide more material for isolation, and, correspondingly, to employ 5·8M-nitric acid, instead of 5·7M, in order that the average concentration over the course of the run would be the same as before. Proportions of nitrous acid, temperatures, and times were as for the kinetic runs. The products were poured into aqueous sodium hydroxide, and steam-distilled, and the residues were extracted with ether, acidified, and again steam-distilled, and extracted with ether. The general nature of the results has been indicated in Section 9. The bulk of the product appeared in the first steam-distillate ; it consisted of a mixture of unchanged mesitylene, together with the main product, nuclear mononitromesitylene. The proportions varied, *inter alia*, with the nitrous acid content of the nitration solution. Thus, after 30 minutes at 25°, only about 50—60% of the mesitylene was nitrated in the presence of 0·01M-nitrous acid, whilst 80—90% was nitrated in the presence of 0·3M-nitrous acid (added as dinitrogen tetroxide). The mesitylene and nitromesitylene were separated by distillation, and the latter substance, distilled samples of which had m. p.s about 40°, and, after crystallisation from methyl alcohol, 42—43°, was identified by mixed m. p. with a genuine specimen. Small amounts of impure alkali-soluble nitro-compound were obtained by extraction with ether from the second steam-distillate ; and the residues from the two steam-distillations, on extraction with ether, yielded traces of an impure solid which was acidic, and small amounts of a gummy neutral material. It appeared that, although the nuclear mononitration is accompanied by side reactions, the amounts of the by-products are only of the order of 1%—too little to have any bearing on the interpretation of the kinetic results.

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