175. *Influence of Directing Groups on Nuclear Reactivity in Oriented Aromatic Substitutions. Part III. Nitration of Ethyl Benzoate.*

By CHRISTOPHER K. INGOLD and MARGARET S. SMITH.

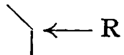
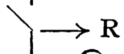
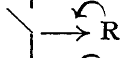
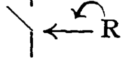
In the discussion of aromatic substitution in Part I it was shown that directing substituents could be divided into four broad classes, differing in the mechanism of electronic interaction between the substituent and the ring, and observably distinguished by their effects on both the orientation and the velocity of substitution. The four classes are typically represented by toluene, ethyl benzoate, chlorobenzene and the phenoxide ion, severally : the substituent in each of these compounds modifies the reactivity of the available nuclear positions in a characteristic way. For a given substitution process, the effect of the original group can be represented by a set of factors expressing the ratios in which, for each nuclear position, the probability of substitution has been changed by the group.

In Part II such sets of factors were determined for the nitration of toluene, by reagents including acetyl nitrate in acetic anhydride, at 0° and at 30°. In this paper the same factors are determined for the nitration of ethyl benzoate by acetyl nitrate in acetic anhydride at 18°. In Part IV the work is extended to the halogenobenzenes.

The reported experiments include a determination by the competition method (the theory of which is discussed) of the ratio of the rates of nitration of benzene and of ethyl benzoate. The latter is nitrated 272 ± 6 times more slowly than the former. Another series of experiments is concerned with the determination of the proportions in which *o*-, *m*-, and *p*-nitro-isomerides are formed in the nitration of ethyl benzoate, with the reagent and temperature used in the rate experiments. The respective proportions are 24·1 ± 0·1, 72·0 ± 0·1, and 4·0 ± 0·1%.

From these results the factors referred to can be calculated. The carbethoxyl group in ethyl benzoate reduces the probability of substitution of each *o*-position by the factor 0·0026, of each *m*-position by the factor 0·0079, and of the *p*-position by the factor 0·0009. Thus just as the methyl substituent activates all positions, the *o*- and *p*-positions more than the *m*-, so the carbethoxyl group deactivates all positions, *o*- and *p*- more than *m*-. These relations are shown schematically at the end of the paper.

PART I of this series (Ingold and Shaw, J., 1927, 2918) was devoted to a general discussion of the laws of aromatic substitution by electrophilic reagents, and it was there pointed out that directing substituents can be divided into four broad classes, differing from one another in the mechanism of the electronic interaction between the group and the nucleus :

Class 1.		Mechanism	$+I$	Example :	Toluene
,, 2.		,,	$-I$	,,	Ethyl benzoate
,, 3.		,,	$-I+T$	,,	Chlorobenzene
,, 4.		,,	$+I+T$	,,	Phenoxide ion

It was shown both theoretically and practically that these four classes are distinguishable with respect to the observable phenomena of substitution if one takes account, not only of orienting action, but also of effects on rate of substitution. When we know the effect of a group, not only on the proportions in which isomeric substitution products are formed, but also on the speed of the total substitution, we have a measure of the extent to which that group has modified the reactivity of each of the available nuclear positions with respect to the substitution.

The next step was to obtain quantitative orientational and velocity data for a few important members of each of the four classes. For this purpose we considered the substitution of monosubstituted benzenes only, in order not to have to take account of the superposed effects of several groups. We selected nitration as the substitution to be studied, owing to its wide applicability, and the circumstance that monosubstitution can be realised with less disturbance from polysubstitution in this than in most other reactions. An extensive mass of orientational data for the nitration of monosubstituted benzenes already exists, although we have had to supplement it. Our main task, however, was to supply the complementary velocity data.

This experimental programme was commenced with the work described in Part II (Ingold, Lapworth, Rothstein, and Ward, J., 1931, 1959). The example studied was toluene (Class 1). In this paper it is ethyl benzoate (Class 2). In Part IV it is the group of halogenobenzenes (Class 3).

As in the previous work on toluene, two groups of experiments are here recorded. In the first we measure by a competition method the ratio of the rates of mononitration of ethyl benzoate and of benzene. The reagent must be one which will form a homogeneous reaction mixture, since otherwise observed rates have no simple significance: we have employed as nitrating agent acetyl nitrate in acetic anhydride, *i.e.*, mixtures made from nitric acid and excess of acetic anhydride. It is this circumstance which necessitated the second group of experiments. Holleman determined the proportions in which isomerides are formed when ethyl benzoate is nitrated with nitric acid: we have carried out similar determinations for the reagent used in the rate experiments.

(1) *Relative Rates of Nitration of Ethyl Benzoate and of Benzene with Acetyl Nitrate in Acetic Anhydride at* 18°.

The immediate object of the experiments was to determine the ratio in which ethyl nitrobenzoates (total) and nitrobenzene are formed when the nitrating agent competes for ethyl benzoate and benzene originally present in known proportions and both in large excess. In the present work the two aromatic compounds were always initially in equivalent proportions. For this case, the experimental ratio, R, in which the compounds are found to have undergone nitration is equal to the ratio of their specific rates of reaction k_y/k_x, in the limit of small amounts of nitration. If the quantity of either compound nitrated is not small in comparison with the amount originally present, then R is only a first approximation to k_y/k_x, because, after the commencement of reaction, the two aromatic compounds get out of equivalence; the ratio R can, however, be corrected to give k_y/k_x. The formula we use for this purpose is $k_y/k_x = \log(y/y_0)/\log(x/x_0)$, to which the first approximation is clearly $R = (y_0 - y)/(x_0 - x)$, where x_0 and y_0 are the initial concentrations of the aromatic compounds and x and y their concentrations when the reaction is stopped.

It is important to consider the conditions under which the correction formula is valid, because it cannot, of course, be derived without any kinetic assumptions. In Part I we cited the conclusions of other workers to the effect that nitration is of the second order, being of the first with respect both to the compound nitrated and to the nitrating agent. On account of the experiments described in Part IV, we doubt if the matter can in general be represented so simply. It is, however, unnecessary to assume such simplicity in order to derive our correction formula. The one essential assumption is that the *attack of the active nitrating entity* (whatever that may be) *on the aromatic compound is unimolecular with respect to the aromatic compound.* Nothing else matters: the active agent may be unknown and its attack may be of any total order; it may be produced in some preliminary change—

possibly slow, possibly reversible; it, or some material essential to it, may be simultaneously concerned in a dozen independent, or mutually interdependent, side reactions; all circumstances which would render hopeless any direct kinetic attack on the problem of relative rates of nitration: yet the competition method will give the right result. It will do so because, if the italicised assumption is fulfilled (as it almost certainly is) our logarithmic formula for k_y/k_x is rigorous, and if it is not, we can still make R as close an approximation as we please to k_y/k_x by approaching the limit of small nitration. The one condition which *is* essential to the success of the competition method is that the reaction should be homogeneous. These matters are more fully illustrated in Part V, which describes a detailed kinetic investigation of nitration. The point to be made now is simply that the competition, not the kinetic, method is the correct one for solving the problem we are concerned to solve.

Methods.—Ethyl benzoate is only rather slowly nitrated, and therefore we used what, so far as we knew, was the most active nitrating agent that would give the necessary homogeneous solution, *viz.*, acetyl nitrate, prepared by mixing nitric acid and excess of acetic anhydride. With this reagent in excess, ethyl benzoate was considerably, though incompletely, mononitrated in, *e.g.*, 24 hours at room temperature (product analysed). Aromatic acid products were not formed in appreciable amount, a point of significance in relation to the methods of analysis. Benzene was rather easily nitrated with the same reagent, and little if any acid products were formed.

The task of analysing the mixture of nitrobenzene and ethyl nitrobenzoates arising in the competitive nitration of benzene and ethyl benzoate has presented unusual difficulty, essentially on account of the large difference in the speeds of the simultaneous reactions. The amount of ethyl nitrobenzoates formed was of the order of 1/200th of the amount of nitrobenzene; and for reasons already indicated the quantity of the latter was kept rather small in comparison with the excesses of initial materials. Thus the most difficult part of our task was to estimate a material constituting not much more than 1/2000th of the final mixture of aromatic compounds, and to do this with accuracy of a few units per cent. The result has been that minor side reactions and other disturbances, which would have been small enough to pass unnoticed had the proportions of materials been more normal, have in our case assumed such importance that each in turn had to be tracked down and eliminated. The interest of the chemistry involved is independent of the main subject of the paper, but this chemistry has been largely elucidated by survey of preliminary results and is inextricably concerned in the elaboration of method. Therefore we report these matters collectively in the following section in small type, and afterwards give in ordinary type a summary of those results which are of importance for the subsequent discussion.

Analysis—In outline, the method of analysis was to digest the mixture with sodium hydroxide, and separate the neutral benzene and nitrobenzene from the hydrolytically-formed benzoic and nitrobenzoic acids by means of ether and alkali; then to estimate the nitrobenzene by a combination of distillation and reduction, and the nitrobenzoic acids by reduction (subsequent bromination was also considered).

The hydrolysis was checked by using purified ethyl benzoate and ethyl *o*-nitrobenzoate. Either ester was found to be hydrolysed practically completely after treatment at 100° for 20—23 hours with twice the calculated quantity of N-aqueous sodium hydroxide; but the addition of benzene and nitrobenzene decreased the rate of the hydrolysis, which could, however, be completed in 28 hours. No resinification or other noticeable change occurred when nitrobenzene alone was placed under these conditions, and there was no perceptible disappearance of alkali. The figures are not here reproduced, but the above statements can be attested with the accuracy to which titres of 20 c.c. can be read.

Nitrobenzene, in quantities of about 5 g., could not be estimated in mixtures with benzene, solely by distillation through Dufton columns, with an accuracy better than 2—3%; but by the use of such columns it was possible to remove most of the benzene without any detectable loss of nitrobenzene. The residue could then be weighed and portions taken for the estimation of nitrobenzene by reduction, a process which gains in convenience from the preliminary distillation.

Difficulty was experienced in the estimation by published methods of nitrobenzene by reduction with titanous chloride: probably owing to the volatility of nitrobenzene and its limited solubility in aqueous solvents, low results, about 98%, were usually obtained. Therefore the following method was evolved. Alcohol (50 c.c.) was boiled (500 c.c. flask) under reflux for 5 mins. in a slow stream of carbon dioxide, which was greatly increased during the subsequent cooling by means of ice-water, and then reduced to 2 bubbles per sec., whereupon a small tube containing the weighed nitrobenzene together with a little benzene was introduced. A known excess of 0·25N-titanous chloride was added, and the mixture gently boiled for 30 mins. It was cooled, treated with 20% potassium thiocyanate solution (10 c.c.), and titrated with standard ferric alum (0·1N). The stream of carbon dioxide was continued throughout the process, and, near the end-point, the sides of the flask were washed down with water that had been boiled till free from air and cooled in carbon dioxide. This experiment was immediately followed by a " blank," in which the whole of the above procedure was followed except, first, that the nitrobenzene was omitted from the small tube, and secondly, that the amount of titanous chloride was equal to the former excess, the balance of the volume of liquid being made up with boiled-out, carbon dioxide-saturated water. In 11 experiments with purified nitrobenzene the errors were all negative, and the mean error was 0·22% ; whilst for 8 of the experiments the individual errors were not more than this.

Purified samples of *o*-, *m*-, and *p*-nitrobenzoic acids were reduced, sometimes in the presence of added benzoic acid, by the same method, except that water was used in place of alcohol. All the errors were negative, the mean for 11 experiments being 0·08%.

Francis and Hill (*J. Amer. Chem. Soc.*, 1924, **46**, 2498) have developed a technique for the quantitative bromination of aromatic amines by means of bromide–bromate solution, and Flürscheim and Holmes (J., 1928, 448) have shown that, on treatment by this method at 30° for a suitable time, *o*-, *m*-, and *p*-aminobenzoic acids all give tribromination products (with loss of the carboxyl group in two cases). With purified samples of the three aminobenzoic acids this method gave satisfactory results (errors negative, average error in 7 experiments 0·21%), but when combined with a previous reduction of nitro-acids the results were very poor. We could discover no conditions in which an excess of titanous chloride could be destroyed by treatment with air or oxygen in such a way that subsequently added bromide–bromate solution could be titrated with potassium iodide and thiosulphate to give a stable end-point. In 15 experiments with purified nitrobenzoic acids the errors of estimation on the basis of bromine uptake varied from + 8·0 to − 7·1%, the average of the magnitudes of the errors being 3·9%. It therefore appears that the Francis–Flürscheim method of estimating nitro-compounds has not yet been described in a form to give results of high accuracy.

These processes (excepting the bromination) were synthesised into a complete method for the estimation of nitrobenzene and nitrobenzoic acids in mixtures containing also excesses of benzene and ethyl benzoate, and the method was used at this stage of development in order to obtain a rough estimate of the proportions in which the nitro-compounds would be formed in competitive nitration.

A first series of five nitrations (series A) was carried out as follows. Benzene (0·1 g.-mol.) and ethyl benzoate (0·1 g.-mol.) were together dissolved in acetic anhydride; and absolute nitric acid, freshly distilled with concentrated sulphuric acid, was separately dissolved in a small excess of acetic anhydride at 0°. The acetyl nitrate solution was added at a controlled rate to the mechanically stirred solution of the aromatic compounds at not much above the room temperature, the stirring was continued for a further 2 hours, and the mixture, after being kept for a further period, was poured on ice (400 g.), and left overnight to secure decomposition of the acetic anhydride. The solution, basified with sodium hydrogen carbonate, was extracted 12 times with 50 c.c. of pure ether, the extract was washed with water, and the washings were re-extracted with ether, the combined extracts being then dried with calcium chloride. The ether was evaporated slowly (20 drops a minute) through a long Dufton column, and the residue was hydrolysed with N-aqueous sodium hydroxide (250 c.c.) for 48 hours under reflux.

From the alkaline solution the benzene and nitrobenzene were extracted with the thoroughness employed in the previous ether extraction, and the dried extract was evaporated as before through a long Dufton column. The concentrate was transferred to a smaller still with a shorter column, most of the benzene was removed, and the nitrobenzene was estimated as already described. The alkaline aqueous solution was acidified with concentrated hydrochloric acid (50 c.c.), and the organic acids were extracted with 50 c.c. of pure ether 14 times. The extract was washed 4 times with a little water, and the washings re-extracted 9 times with 30 c.c. of ether. The ether was removed from the dried total extract by distillation through a tall column, and the crystalline residue was freed from the last traces of ether by a short exposure to the atmosphere. Nitrobenzoic acids were then estimated by reduction as already described. The results are in Table I. Expt. A, 3 shows that the acetyl nitrate is largely consumed in some process other than the nitration of the aromatic compounds.

TABLE I.

Competitive Nitrations (Series A).

(Benzene, 0·1 g.-mol. Ethyl benzoate, 0·1 g.-mol. Room temperature.)

No.	Time (hours).	HNO_3. (g.-mol.).	Ac_2O (total) (g.-mol.).	Products (g.-mols.). $Ph{\cdot}NO_2$.	$C_6H_4(NO_2){\cdot}CO_2Et$.	Ratio, $\frac{C_6H_4(NO_2){\cdot}CO_2Et}{Ph{\cdot}NO_2}$.
1	22	0·05	0·40	0·0144	0·000137	0·0095
2	46	,,	0·30	0·0243	0·000187	0·0077
3	840	,,	,,	0·0240	0·000447	0·018
4	42	0·10	0·20	0·0577	0·000408	0·0071
5	52	,,	,,	0·0588	0·000369	0·0063

On account of the results of Table I the analytical method was further tested with artificial mixtures of approximately the following composition: benzene, 0·05 mol.; ethyl benzoate, 0·10 mol.; nitrobenzene, 0·05 mol.; ethyl nitrobenzoates (mixtures of the three isomerides), 0·0003 mol. A series of 17 experiments showed that with mixtures of this type the nitrobenzene could be estimated to within 0·7% (errors negative), and the ethyl nitrobenzoates to within 3% (errors both positive and negative). In view of the very large differences in the concentrations of these materials, this degree of precision was considered satisfactory.

Two further experiments were carried out in order to extend the check on the method from the commencement of the analysis back to the conclusion of the nitration, the primary object being to test for any loss of ethyl nitrobenzoates by hydrolysis in the dilute acid solution in which the acetic anhydride is left to complete its decomposition. Artificial mixtures of the same type were prepared, and these, as well as the appropriate quantities of nitric acid and acetic anhydride, were added to ice; the whole mixture was then left, and subsequently worked up as in a competitive nitration. The results had the accuracy already stated.

Two additions to the analytical routine here outlined were made subsequently and are described in the next sub-section.

Nitration.—All sources of serious error having been confined by exclusion to the nitration itself, a second series of competitive nitrations was carried through in order further to study this process. In the course of these 34 experiments (Series B) several possible sources of error were investigated. The proportion of ethyl benzoate nitrated is so minute that a very small proportion of a rapidly nitrating impurity (*e.g.*, a nuclear homologue) would seriously affect the results. We tried (*a*) purifying commercial ethyl benzoate by fractionation alone, (*b*) purifying it by partial freezing, and subsequent distillation of the less fusible portion and (*c*) preparing it ourselves from benzoic acid, which was prepared by oxidation of gum-benzoin. The conclusion was reached that the ethyl benzoate prepared by all these methods had the same properties with respect to the reaction studied. In a similar way we compared benzene samples derived from various sources and purified by various methods. We also compared different nitric acid samples, which were examined with special reference to possible effects due to oxides of nitrogen; also we examined different samples of acetic anhydride. As a result, our standard methods of obtaining materials for all the later experiments were as follows: Commercial ethyl benzoate was distilled five times through a Lapworth fractionating column, head and tail fractions being discarded, and the material being dried with sodium sulphate after each distillation. Kahlbaum's thiophen-free benzene was purified by partial freezing, dried with sodium, and fractionated. Kahlbaum's halogen-free nitric acid was freshly distilled with concentrated sulphuric acid. The acetic anhydride was Hopkin and Williams's " A.R." The nitrations were carried out in the dark, and allowed to proceed for 48 hours at room temperature. These conditions, except the time and in a minor degree the temperature, were maintained also in all later series of competitive nitrations.

These matters being largely routine, we do not quote the results of all the competitive nitrations of series B, but only a sufficient number to illustrate the discovery of another much more important source of error. This was detected when it was found that the apparent ratio of the ethyl nitrobenzoates to the nitrobenzene formed increased with the initial proportion of acetic anhydride. This means that acetic anhydride is being converted into a nitro-compound, which, after decomposition of the excess of acetic anhydride with water, is non-acidic and is therefore extracted with the aromatic nitration products. During the hydrolysis with alkali, however, this product becomes acidic, retains nitroxyl (power of reducing titanous chloride), and is thus estimated falsely as nitrobenzoic acids. The amount of this acidic nitro-compound (or rather, these compounds—for we shall show later that there are more than one) is of the order of 1/1000th of the acetic anhydride used, and thus is of the same order as quantities of nitrobenzoic acids requiring estimation.

TABLE II.

Competitive Nitration. Series B (abridged).

(Benzene, 0·1 g.-mol. Ethyl benzoate, 0·1 g.-mol. Nitric acid, 0·1 g.-mol. Time, 48 hours. Room temperature.)

No.	Ac_2O (g.-mol.).	Products (g.-mol.). $Ph{\cdot}NO_2$.	$C_6H_4(NO_2){\cdot}CO_2Et$.	Ratio, $C_6H_4(NO_2){\cdot}CO_2Et/Ph{\cdot}NO_2$.
4	0·2	0·05877	0·000516	0·0088
20	0·4	0·04027	0·001162	0·0286
27	0·6	0·02893	0·001163	0·0402
28	0·8	0·02369	0·001008	0·0426
25*	0·4	0·03400	0·000245	0·0072

* Nitration product extracted with sodium sulphite—see text.

Concurrently with this series of competitive nitrations, the formation and methods of removal of the unwanted by-products were investigated by experiments of several different types. The first consisted of a single " dummy nitration " (series A) in which the conditions of competitive nitration were copied with the exception that the benzene and ethyl benzoate were omitted from the nitration mixture, but added to the ethereal extract of the product in order to disturb the analytical routine as little as possible. The initial quantities were : nitric acid 0·075 g.-mol., acetic anhydride 0·475 g.-mol. The product which remained neutral after the alkaline hydrolysis contained no detectable nitroxyl, whereas the acid product contained 0·000263 g.-mol. of nitroxyl. This is of the order of the quantities of nitrobenzoic acids to be estimated in the competitive nitrations.

Secondly, the methods of removal of nitromethane were considered. Chattaway showed that tetranitromethane could be prepared from nitric acid and acetic anhydride (J., 1910, **97**, 2099), and hence tri- and di-nitromethane and nitromethane might be produced also from these initial materials. Tri- and di-nitromethane are sufficiently acidic to be eliminated when, after decomposition of the excess of acetic anhydride with water, the whole nitration product is extracted from an aqueous solution basified with sodium hydrogen carbonate. In order to eliminate nitromethane completely from an ethereal solution it was found necessary to extract it with 0·1N-aqueous sodium hydroxide. Further control experiments showed that this did not cause appreciable hydrolysis of ethyl nitrobenzoates under the conditions used. Therefore in all subsequent competitive nitrations the following addition was made to the analytical procedure. The ethereal extract of the whole nitration product was rapidly shaken three times with 30 c.c. of 0·1N-aqueous sodium hydroxide. The alkaline aqueous solution was extracted four times with 30 c.c. of ether, and these combined extracts were washed with a little water and added to the main extract.

A third, and somewhat lengthy, set of experiments was directed to the elimination of tetranitromethane. This has at least one property of the detected by-product since, being neutral, it would be extracted with the whole non-acidic nitration product, but, on alkaline hydrolysis, would be converted into the acidic substance, nitroform. It was hoped that the nitroform might be removed from the acid nitration product by distillation in steam, but in two nitrations, with the benzene and ethyl benzoate omitted at first but added before the separation (dummy nitrations, series B), it was found that only 41—42% of the acid product from the alkaline hydrolysis could be removed by distillation in steam. This indicates what is later confirmed, *viz.*, that there are at least two by-products to be dealt with.

The following five reactions were investigated with respect to their possible use in removing tetranitromethane :

(1) $C(NO_2)_4 + 2NaOH \longrightarrow C(NO_2)_3Na + NaNO_3 + H_2O$

(2) $C(NO_2)_4 + 2NaHCO_3 \longrightarrow C(NO_2)_3Na + NaNO_3 + H_2O + 2CO_2$

(3) $C(NO_2)_4 + Na_2SO_3 + 2NaOH \longrightarrow C(NO_2)_3Na + Na_2SO_4 + NaNO_2 + H_2O$

(4) $C(NO_2)_4 + Na_2SO_3 + 2NaHCO_3 \longrightarrow C(NO_2)_3Na + Na_2SO_4 + NaNO_2 + H_2O + 2CO_2$

(5) $C(NO_2)_4 + 2K_4Fe(CN)_6 \longrightarrow C(NO_2)_3K + 2K_3Fe(CN)_6 + KNO_2$

The investigation of each reaction usually consisted of four parts :

(*a*) Tetranitromethane was prepared by Chattaway's method, and ethereal solutions of various concentrations were shaken for various times with an aqueous solution of the reagent under examination. The tetranitromethane remaining in the ether was estimated by reduction with titanous chloride.

(*b*) Dummy nitrations of the type already described were carried out (series C), and experiments similar to those under (*a*) were made with the ethereal solution of the non-acidic nitration product. The residual tetranitromethane was estimated either as such, or as nitroform after alkaline hydrolysis as in a competitive nitration.

(*c*) The tetranitromethane of expts. (*a*) was replaced by ethyl *m*-nitrobenzoate.

(*d*) Expt. (*c*) was repeated with nitrobenzene in place of ethyl *m*-nitrobenzoate.

Altogether 32 experiments were carried out, with results which may be summarised as follows :

(1) Sodium hydroxide appeared to reduce titranitromethane and hydrolyse ethyl *m*-nitrobenzoate at comparable speeds. Both reactions proceeded partially when ethereal solutions were shaken for several hours with N-aqueous sodium hydroxide.

(2) Sodium hydrogen carbonate reduces tetranitromethane much faster than it hydrolyses ethyl *m*-nitrobenzoate. But the former reaction is too slow for practical use, being incomplete after several days, whether the reagent is employed in the solid form or as a concentrated aqueous solution. The hydrolysis of ethyl *m*-nitrobenzoate under corresponding conditions was negligible.

(3) A solution of sodium sulphite and sodium hydroxide attacks tetranitromethane and ethyl *m*-nitrobenzoate at comparable rates.

(4) A solution of sodium sulphite and sodium hydrogen carbonate was found to be a satisfactory reagent. For instance, a solution of 0·001036 g.-mol. of tetranitromethane in ether (60 c.c.) was shaken for 6·5 hours with a solution of 0·01 g.-mol. of sodium sulphite and 0·003 g.-mol. of sodium hydrogen carbonate in water (25 c.c.) : 99·7% of the tetranitromethane was extracted. When ethyl *m*-nitrobenzoate was used only 1·2% of it was hydrolysed. Nitrobenzene was unaffected. When the products of dummy nitrations were similarly examined, only about 50—60% of the nitroxyl could be extracted. This confirms the previous conclusion that part of the by-product, which appears ultimately as an acidic nitro-compound, is not tetranitromethane, although another part has the properties of tetranitromethane.

(5) Potassium ferrocyanide gives results quite similar to those obtained with sodium sulphite and sodium hydrogen carbonate. The usual method was to shake an ethereal solution (about 50 c.c.) of the material to be examined with a solution of the ferrocyanide (4 g.) in water (20 c.c.) for about 7 hours.

We thus had two reactions, *viz.*, (4) and (5), by which to remove tetranitromethane from our nitration products. They worked equally well, and both were used in the later competitive nitrations of series B; the application of method (4) is illustrated in Table II (expts. 25 and 20). Both were used also in the benzene nitrations of series A, in the ethyl benzoate nitrations (series A), as well as, of course, in the dummy nitrations of series C. By the time we came to do the measurements to which all this work was preparatory, *viz.*, the competitive nitrations of series C and the benzene nitrations of series B, we had, for no particular reason, formed the habit of using method (4), and we therefore give the exact technique of this second modification in the original analytical procedure.

The ethereal extract of the whole nitration product was concentrated as before by slow distillation through a Dufton column, but from a ground-jointed bottle instead of a flask; and then, instead of proceeding immediately with the hydrolysis, the distillation of ether was stopped before it was quite finished and the column was washed with ether back into the bottle. A solution of crystallised sodium sulphite (2·5 g.) and sodium hydrogen carbonate (0·3 g.) in water (25 c.c.) was then added, and the bottle was stoppered and shaken for 7·5 hours at room temperature. The faintly yellow ethereal layer was washed twice with 25 c.c. of water, once with 30 c.c. of 0·05N-aqueous sodium hydroxide, and again twice with 25 c.c. of water. The orange-red sulphite solution was extracted 6 times with 25 c.c. of ether, and the ether was washed once with 25 c.c. of water, once with the 30 c.c. of the aqueous sodium hydroxide used previously, and twice with water. The combined water washings were extracted 6 times with 30 c.c. of ether, and the extract was washed with the same sodium hydroxide solution and then with water. The last wash-water was combined with the sodium hydroxide solution and extracted 4 times with 25 c.c. of ether, the extract being washed with a little water. The ether was removed from the combined and dried ethereal extracts by slow distillation through a Dufton column, and the residue was hydrolysed as before. This procedure ensures the removal of any trace of nitromethane that might be formed from tetranitromethane during the distillation or sulphite treatment; and of any nitrophenols that might have arisen by the action of sulphite on dinitrobenzenes.

A fourth set of experiments was carried out in order to discover how to deal with the second by-product arising from the nitration of the acetic anhydride. We still do not know what this is. It is non-acidic, and not reduced by sodium sulphite or potassium ferrocyanide; but it is converted by sodium hydroxide into an acidic, nitroxyl-containing substance, which is not volatile in steam (this is more definitely proved later). This last property suggested that the second by-product might be a rather complex substance, and might be formed, therefore, at a late stage of a long sequence of reactions. If so, it should be possible to minimise or eliminate the formation of the substance by cutting down the time of reaction; for by reducing the time we favour the products of earlier as against those of later stages of a series of consecutive reactions. Thi idea was worked out in a series of 8 benzene nitrations run for different times (series A). The conditions were substantially those of the competitive nitrations, except that the ethyl benzoate was left out of the nitration mixture, but added to the ethereal extract of the product before the separation in order to keep standard the conditions of analysis. The benzene was put in, and the nitrobenzene formed was measured, in order to show the time-variation of an initial process typical of the two rates we want to compare. The ethyl benzoate was left out of the nitration since the object was to discover conditions in which no nitro-acids were produced which would be estimated incorrectly as nitrobenzoic acids. The nature of the time effect is shown in Table III, in which we have included only experiments run for the longest and shortest times investigated; the other experiments gave consistent intermediate values. It will be observed that when the time is reduced from 48 to 9 hours the amount of nitrobenzene drops very little. The tetranitromethane, which must be the product of several consecutive reactions, is reduced much more, though not nearly enough to allow us to abandon the process already worked out for removing it. In contrast, the second by-product is reduced to almost a negligible quantity.

TABLE III.

Benzene Nitrations. Series A (abridged).

(Benzene, 0·1 g.-mol. Nitric acid, 0·1 g.-mol. Acetic anhydride, 0·4 g.-mol. Room temperature. In some experiments sulphite–bicarbonate was used to extract tetranitromethane, and in others ferrocyanide, the two reagents being equally effective.)

	Time	Products (g.-mol. × 10^{-5}).		
No.	(hours).	Nitrobenzene.	Tetranitromethane.	2nd By-product.
3	48	5511	66·9	44·8
8	9	5079	23·2	4·2

The fifth group of experiments consisted in a short series (A) of ethyl benzoate nitrations, with benzene omitted from the nitration but added before the separation of products. The results, not quoted in detail, show that, in nitration for 9 hours at room temperature the amount of ethyl nitrobenzoates formed from 0·1 g.-mol. of ethyl benzoate, the quantities of nitric acid and acetic anhydride being as stated in Table IV, is about 40 × 10^{-5} g.-mol., *i.e.*, approximately ten times the quantity of the second by-product. This means that, in a competitive nitration under corresponding conditions, the error in the estimation of ethyl nitrobenzoates, due to the second by-product, would be of the order of 10%. However, this error can obviously be reduced by shortening the time still further, or, alternatively by reducing the temperature.

To complete our preparations for the measurements of relative nitration rates, we examined the possibility of the formation of a by-product from benzene, *viz.*, *o*-dinitrobenzene, which up to the present might not have been distinguished from the second by-product from acetic anhydride. *o*-Dinitrobenzene will be produced in appreciable quantity if there is any significant amount of dinitration of benzene. Being non-acidic it would accompany the neutral nitration product; it might not be reduced by sulphite or ferrocyanide, but it might be hydrolysed by alkali to *o*-nitrophenol, which, as a nitroxyl-containing acid, would be estimated with the nitrobenzoic acids. A direct comparison was therefore made between the volatility in steam of *o*-nitrophenol and of the second by-product (free from nitroform) derived from one of the benzene nitrations, distillates and residues being tested for nitroxyl as usual by reduction with titanous chloride. It was found that, under conditions in which *o*-nitrophenol is practically completely distilled, the second by-product remains almost wholly in the undistilled material. The second by-product cannot therefore contain any appreciable quantity of *o*-nitrophenol.

In the final series of competitive nitrations the reaction time was diminished to 6 hours, and the temperature was also reduced. The previous nitrations had been done at, or slightly above, 20°; but now the standard temperature was taken as 18°, the upper limit during admixture of the reagents being 18·5°. By these means we expected to make the error due to the second by-product of the same order as the error of analysis.

Results.—The reagents used in the competitive nitrations were taken in the following quantities: benzene 0·1 g.-mol., ethyl benzoate 0·1 g.-mol., nitric acid 0·1 g.-mol., and acetic anhydride 0·4 g.-mol. The nitric acid was mixed at 0° with 0·1 g.-mol. of acetic anhydride, and the aromatic compounds were mixed at 18° with the remaining 0·3 g.-mol. of the acetic anhydride. The addition of the nitrating solution to the other materials occupied about 20 minutes. Mechanical stirring was employed. The mixture was kept at 18° for 6 hours, counting from the mean time of addition of the nitrating solution, and then poured on ice. The nitration products were separated and estimated as already described.

The quantities of nitrobenzene and of ethyl nitrobenzoates produced are given in Table IV. The estimates of ethyl nitrobenzoates are rendered a little too high owing to incomplete elimination of the " second by-product." The order of magnitude of this error is elucidated later. The indicated uncertainty in the mean of the uncorrected ratios R is the probable error calculated by the usual formula.

TABLE IV.

Competitive Nitrations (Series C).

No.	Products (g.-mols. × 10^{-5}). Nitrobenzene.	Ethyl nitrobenzoates.	Ratio, R = $C_6H_4(NO_2)\cdot CO_2Et/Ph\cdot NO_2$.
1	3219	14·4	0·00447
2	3040	16·0	0·00526
3	3195	14·4	0·00451
4	3037	13·7	0·00451
5	3434	13·8	0·00402
6	3412	16·8	0·00492
7	2948	13·1	0·00444
8	2798	12·4	0·00442

Mean R (uncorrected) = 0·00457 ± 0·00009.

In order to provide a " blank " for the difficult part of these analysis, *viz.*, the estimation of ethyl nitrobenzoates, a short series of benzene nitrations was subsequently carried out (Series B). The experimental conditions were the same as for the mixed nitrations, except that the ethyl benzoate was left out of the nitration mixture but was added to the nitration product before separation in order not to disturb the analytical routine. The results are in Table V. The second by-product is the material which would have been estimated as ethyl nitrobenzoates in a competitive nitration.

TABLE V.

Benzene Nitrations (Series B).

No.	Products (g.-mols. × 10^{-5}). Nitrobenzene.	Tetranitromethane.	2nd By-product.	
1	3929	12·1	1·5	Mean = 1·2 × 10^{-5} g.-mol.
2	4301	12·8	0·9	
3	4195	11·5	1·4	
4	4007	12·0	1·1	

Since the figures in the fourth column of this table are above the magnitude of the analytical error (± 0·4 × 10^{-5} g.-mol.), it is clear that finite amounts of the second by-product must be formed in these nitrations, and therefore in the competitive nitrations, but it is not easy to compute the correction to be applied to the estimates of ethyl nitrobenzoates in Table IV. An upper limit to the magnitude of the correction can be given, because we have shown (section in small type) that when, as by a reduction in the time, the reaction is confined to a more initial period, the quantity of second by-product is reduced in greater proportion than is the quantity of nitrobenzene. Taking average figures from Tables IV and V we find that the dilution effect of the (chemically rather unreactive) ethyl benzoate additionally present in the competitive nitrations reduces the amount of nitrobenzene formed from 4108 to 3135 × 10^{-5} g.-mol., *i.e.*, by the factor 0·76. Therefore the quantity of second by-product must have been reduced from 1·2 × 10^{-5} to something less than 0·9 × 10^{-5} g.-mol. The negative correction to be applied to the estimates of ethyl nitrobenzoate lies therefore between 0·9 × 10^{-5} g.-mol. and zero, and arbitrarily we take the mean, 0·5 × 10^{-5} g.-mol. Recalculating the values of the ratio R from these corrected estimates we find 0·00441 ± 0·00015. Here the indicated error covers the whole range of uncertainty in the correction. Assuming that all corrections within this range have equal probability, we can calculate an over-all probable error and thus obtain :

$$\text{Mean } R \text{ (corrected)} = 0{\cdot}00441 \pm 0{\cdot}00010.$$

We have still to calculate k_y/k_x, which is appreciably different from R, owing to the fact that the benzene underwent as much as 31% of the possible amount of nitration, so that the original equivalence of the benzene and ethyl benzoate concentrations was not maintained throughout the reaction. We find :

$$k_y/k_x = 0{\cdot}00367 \pm 0{\cdot}00008.$$

In other words, the specific rate of nitration of ethyl benzoate is 272 ± 6 times smaller than that of benzene under the conditions used.

(2) *Proportions of Isomerides Formed in the Nitration of Ethyl Benzoate with Acetyl Nitrate in Acetic Anhydride at* 18°.

The proportions in which *o*-, *m*-, and *p*-nitro-derivatives are formed when ethyl benzoate is nitrated with nitric acid at – 40°, at 0°, and at 30° have been determined by Holleman (*Z. physikal. Chem.*, 1899, 31, 79). We have carried out the same determination for nitration with acetyl nitrate in acetic anhydride at 18°, the reagent and temperature employed in the competitive nitrations. We had to use, however, a more concentrated solution of acetyl nitrate in acetic anhydride, and also a larger proportion of acetyl nitrate relatively to ethyl benzoate, than in the competition experiments, in order to obtain sufficient nitro-esters for the estimation of the separate isomerides. The mixed nitro-esters were hydrolysed to nitro-acids, in which the *o*-, *m*, and *p*-isomerides were estimated by a modification of Holleman's leaching-out method.

Analysis.—In the leaching-out method, an acid is estimated in admixtures with other acids by the increase in acidity which it brings about in a solution previously saturated with respect to all the other acids. Thus *o*-nitrobenzoic acid is leached out from a mixture of the three isomerides by means of a solution saturated with the *m*- and the *p*-acid. In this process any non-isomeric, acid impurities would also be leached out and estimated as *o*-nitrobenzoic acid; wherefore the original method is extended by separately leaching out, and estimating, the non-isomeric acids by the use of a solution saturated with the *o*-, *m*-, and *p*-nitro-acids (Baker and Ingold, J., 1927, 569).

It was arranged to use sufficient water to leach out the whole of each of the acids to be estimated in one step (Holleman conducted successive leachings). The leachings were carried out at 25·0°, and each leaching solution was made with 150 c.c. of water and the stated quantities (more than enough to secure saturation) of two, or of all three, of the nitro-acids : ortho- 2 g., meta- 1 g., para- 0·1 g. The quantities of mixed acids used for the determinations of the *o*-, *m*-, and *p*-nitro-acids, and of the non-isomeric acids, were respectively about 1 g., 0·5 g., 0·8 g., and 0·5 g.

Each determination required two flasks, each fitted with a mercury-sealed stirrer and immersed to the neck in the thermostat. Each flask was charged with 150 c.c. of water, and with the nitro-acids with which the leaching solution was to be saturated; and to one flask was added a weighed quantity of the mixed acids requiring analysis. The flasks were stirred for not less than 20 hours, and a sample was withdrawn from each by means of a pipette fitted with a detachable filter tube, which was allowed to come into adsorption equilibrium with the solution before passage of the sample. The samples were titrated with 0·05N-barium hydroxide, phenolphthalein being the indicator; the difference of titre measured the increase of acidity due to the leached out acid. After further periods of stirring, further samples were similarly withdrawn and titrated in order to check the completeness of the leaching.

The increase of acidity due to the addition of a nitrobenzoic acid to a saturated solution of its two isomerides is in general not exactly equivalent to the added acid, because the dissolution of this acid causes a change in the solubility of the isomerides with which the solution remains saturated. It is therefore necessary empirically to determine the correction which will convert observed increases of acidity into weights of leached out acid. For the sparingly soluble *p*-nitro-acid, over the required range, the correction is negligible. For the more soluble *o*- and *m*-acids, it is not: it appears that the addition of *o*-acid to a solution saturated with respect to the *m*- and *p*-acids throws the *m*-acid out of solution, whilst the addition of *m*-acid to a saturated solution of the *o*- and *p*-acids causes more *o*-acid to dissolve. The following data were determined, and used to construct correction curves:

o-Nitrobenzoic acid (added to 150 c.c. of water containing dissolved and suspended *m*- and *p*-nitrobenzoic acids, at 25°; weights in mg.):

Added	126·4	143·1	197·9	200·8	220·8	237·6	244·4	300·5
Found	101·4	118·3	166·2	169·9	191·3	209·5	215·1	268·8
Corr.	+25·0	24·8	31·7	30·9	28·5	28·1	29·3	31·7

m-Nitrobenzoic acid (added to 150 c.c. of water containing dissolved and suspended *o*- and *p*-nitrobenzoic acids, at 25°; weights in mg.):

Added	246·8	287·9	322·8	326·3	347·4	369·0	398·8
Found	267·8	315·3	350·9	357·8	376·1	411·7	450·9
Corr.	−20·8	27·4	28·1	31·5	28·7	42·7	52·1

Nitration.—Materials were obtained and purified as for the final series of competitive nitrations.

Ethyl benzoate (0·15 g. mol.) was mixed with acetic anhydride (0·1 g.-mol.). Nitric acid (0·75 g.-mol.) was mixed with acetic anhydride (0·75 g.-mol.) at 0°, and this solution was added with mechanical stirring to the ester solution at 18·0—18·5°. The mixture was kept at 18° for 8 hours, and poured on ice. After the acetic anhydride had decomposed, the solution was basified with sodium hydrogen carbonate and extracted with ether. The extract was washed with sodium hydroxide and water, dried, and evaporated. The tetranitromethane and a good deal of ethyl benzoate were removed by distillation from a boiling water-bath, at pressures reduced finally to 1 mm. By using a glycerol-bath, the ethyl nitrobenzoates were collected at 1 mm. pressure and at bath-temperatures between 100° and 170°; they distilled mainly at 128°/1 mm.

The nitro-esters were saponified for 24 hours at 100° with twice the theoretical amount of N-aqueous sodium hydroxide; and, after acidification with hydrochloric acid, the nitro-acids were isolated by extraction with ether.

The nitro-acids contained a good deal of benzoic acid, most of which was removed by distillation in steam, though with some loss of nitro-acids. The distillations were controlled by titration of successive portions of the distillate first with barium hydroxide, and secondly with titanous chloride. Under the conditions used, the removal of most of the benzoic acid involved a loss of about 4% of nitro-acids. The distribution of this loss amongst the three isomerides was computed on the basis of measurements of the rates at which the three nitro-benzoic acids distil in steam when introduced into the still in the quantities in which they would be present in the purification of a nitration product. Thus a 4·0% loss was found to be distributed as follows: ortho- 0·9; meta- 2·1; para- 1·0%.

The nitro-acids recovered by ether extraction from the residue of the distillation in steam contained non-volatile impurities, which were largely removed by sublimation. The specimen was placed in a boiling tube, into which a somewhat shorter and narrower water-cooled tube was fitted. The outer tube was immersed in a bath at 130°, whilst the pressure in the annular space was reduced to 0·04 mm. In this apparatus an artificial mixture of mononitrobenzoic acids distilled completely to form a firm cake on the inner tube, from which it could readily be detached. When applying this method to the mixed nitro-acids recovered from the steam-distillation, the heating bath was carried up to 160°. A little tar remained in the outer tube. The distilled acids, which had a very pale cream colour, were detached from the inner tube, and ground for analysis. They still contained acidic impurities, which were dealt with in the estimation process as already described.

Results.—We first record the detailed results of a typical analysis (nitration IV, analysis 2):

Non-nitrobenzoic acids. Mixed acids taken for analysis, 0·5187 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*-, *m*- and *p*-nitro-acids. Samples of 25 or 50 c.c. were withdrawn, but titres are given below as for 50 c.c. samples. Barium hydroxide solution, N/19·95.

Time stirred (hours)	21	25	40	48
Analysis titre (c.c.)	69·56	69·48	69·52	69·67
Control titre (c.c.)	68·15	68·07	68·09	68·43
Difference (c.c.)	1·41	1·41	1·43	1·24

Mean difference, 1·38 c.c. Barium hydroxide equivalent to non-nitrobenzoic acids per g. of sample, 7·93 c.c. (Calculated as benzoic acid this is equivalent to 4·9% by weight. All other nitration products had smaller proportions of non-nitro-benzoic acids, the smallest being 2·8%, calculated as benzoic acid.)

o-*Nitrobenzoic acid.* Mixed acids taken, 1·0048 g. Leaching solution, 150 c.c. of water with dissolved and suspended *m*- and *p*-nitro-acids. Titres given as for 50 c.c. samples. Barium hydroxide, N/19·95.

Time stirred (hours)	21	25	39
Analysis titre (c.c.)	32·64	32·67	32·61
Control titre (c.c.)	22·07	22·21	22·26
Difference (c.c.)	10·57	10·46	10·35

Mean difference, 10·46 c.c. Excess acidity due to the whole analysis sample, 31·38 c.c. Excess acidity due to *o*-nitrobenzoic acid, 23·41 c.c. Corresponding weight of nitrobenzoic acid, 0·1960 g. Correction for changes of solubility, + 0·0285 g. Weight of *o*-nitrobenzoic acid, 0·2245 g. = 22·3% of sample.

m-*Nitrobenzoic acid.* Mixed acids taken, 0·5040 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*- and *p*-nitro-acids. Titres as for 50 c.c. samples. Barium hydroxide, N/19·95.

Time stirred (hours)	20	26	28
Analysis titre (c.c.)	60·85	60·58	60·77
Control titre (c.c.)	44·54	44·45	44·48
Difference (c.c.)	16·31	16·13	16·29

Mean difference, 16·24 c.c. Excess acidity due to whole analysis sample, 48·72 c.c. Excess acidity due to *m*-nitrobenzoic acid, 44·72 c.c. Corresponding weight of nitrobenzoic acid, 0·3743 g. Correction for changes of solubility, — 0·0289 g. Weight of *m*-nitro-acids, 0·3454 g. = 68·5% of sample.

p-*Nitrobenzoic acid.* Mixed acids taken, 0·6072 g. Leaching solution, 150 c.c. of water with dissolved and suspended *o*- and *m*-nitro-acids. Titres as for 50 c.c. samples. Barium hydroxide, N/19·95.

Time stirred (hours)	21	39	40
Analysis titre (c.c.)	69·36	70·15	69·36
Control titre (c.c.)	66·88	67·65	66·95
Difference (c.c.)	2·48	2·50	2·41

Mean difference 2·46 c.c. Excess acidity due to whole analysis sample, 7·38 c.c. Excess acidity due to *p*-nitrobenzoic acid, 2·57 c.c. Weight of *p*-nitrobenzoic acid, 0·0212 g. = 3·5% of sample.

Correction of percentages. Corrections to the given percentages by weight of the sample are necessary on account of impurities in, and losses from, the sample. The observed percentages by weight of *o*-, *m*-, and *p*-nitrobenzoic acids in the sample total 94·3%, and the remaining 5·7% is attributed to non-nitrobenzoic acids present as impurities. The percentages by weight of *o*-, *m*-, and *p*-nitrobenzoic acids, not in the sample itself, but in the total nitrobenzoic acids in the sample, are therefore: ortho- 23·5, meta- 72·8, para- 3·7%. The purification losses of the three nitrobenzoic acids, determined as described in the section in small type, are: ortho- 0·9, meta- 2·2, para- 1·0% by weight of the nitrobenzoic acids in the purified sample. Therefore the percentages of the isomerides, calculated in the total mononitro-compounds formed in the nitration, are : ortho- 23·4, meta- 72·1, para- 4·5%.

In all, five nitrations were carried out; but the first two were done before the technique of purification and analysis was fully elaborated, and the results were therefore unreliable. The last three nitrations gave material for five independent analyses, the results of which are in Table VI. The meaning of the three sets of percentages will be clear from the preceding paragraph.

TABLE VI.

Nitrations of Ethyl Benzoate.

Percentages of *o*-, *m*-, and *p*-isomerides.

Expt. No.	In sample.				In isomerides in sample.			In isomerides formed.		
	Non-.	Ortho-.	Meta-.	Para-.	Ortho-.	Meta-.	Para-.	Ortho-.	Meta-.	Para-
III	5·8	22·7	68·2	3·3	24·1	72·4	3·5	24·0	71·7	4·3
IV 1	3·2	23·8	69·9	3·1	24·6	72·2	3·2	24·5	71·5	4·0
IV 2	5·7	22·3	68·5	3·5	23·5	72·8	3·7	23·4	72·1	4·5
V 1	3·4	23·4	70·7	2·5	24·2	73·2	2·6	24·1	72·4	3·5
V 2	3·1	23·8	70·6	2·5	24·5	72·9	2·6	24·4	72·1	3·5

The final mean values for, and formal probable errors in, the percentages in which the three mononitro-isomerides are formed in the nitration of ethyl benzoate with acetyl nitrate in acetic anhydride at 18° are therefore as follows :

ortho-, 24·1 ± 0·1%; meta-, 72·0 ± 0·1%; para-, 4·0 ± 0·1%.

(3) *Partial Rate Factors for the Nitration of Ethyl Benzoate by Means of Acetyl Nitrate at* 18°.

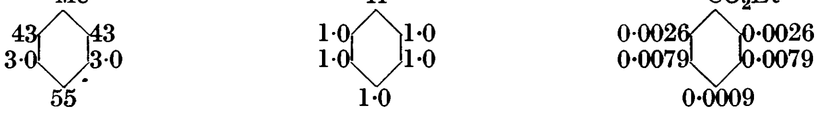
By combining the results of the sections (1) and (2) we can calculate the partial rate factors for the nitration of ethyl benzoate under the conditions used. A partial rate factor is defined as the factor by which the replacement of a hydrogen atom in benzene by an orienting substituent, in our case carbethoxyl, alters the probability of substitution at an individual nuclear carbon atom (if there are several equivalent atoms we suppose them labelled).

The probability of substitution at a particular carbon atom in benzene is taken as equal to unity. The probability for the whole benzene molecule is thus 6. The probability for the whole ethyl benzoate molecule is therefore 6 × 0·00367 = 0·0220, from the rate data. From the orientation data it follows that this probability is distributed amongst the five available positions, taken in order round the ring, in proportion to the factors 24·1/2, 72·0/2, 4·0, 72·0/2 and 24·1/2%.

Thus the partial rate factors for ethyl benzoate are as shown in the third of the following formulæ. The partial rate factors for toluene, for the same nitrating agent and interpolated to the same temperature from the results of Part II, are given for comparison.

Effect of Me *and* CO_2Et *on Probability of Substitution.*

(Nitration with Acetyl Nitrate in Acetic Anhydride at 18°.)



Class 1. Standard. Class 2.

Just as the methyl substituent (Class 1) activates all positions, but the *o*- and *p*-positions more than the *m*-, so the carbethoxyl group (Class 2) deactivates all positions, the *o*- and *p*- more than the *m*-.

THE SIR WILLIAM RAMSAY AND RALPH FORSTER LABORATORIES,
UNIVERSITY COLLEGE, LONDON.

[*Received, March* 9*th*, 1938.]