Ratio: As:N = 1:0.97; As:S = 1:1.11.

The author desires to express his sincere thanks to Professor C. Voegtlin for the suggestions and advice which rendered the work possible.

Summary

1.   New methods for the preparation of 2-aminophenylarsonic acid, 2,2'- and 4,4'-diamino-arsenobenzenes have been developed.

2.   3,3'-Diamino-arsenobenzene and the N,N'-dimethylenesulfonates of 2,2'-, 3,3'- and 4,4'-diamin-oarsenobenzenes have been prepared.

WASHINGTON, D. C.

STUDIES ON THE DIRECTIVE INFLUENCE OF SUBSTITUENTS IN THE BENZENE RING. II.   THE RELATIVE RATES OF BROMINATION OF CERTAIN ORTHO, META AND PARA ISOMERS[1,2]

BY A. W. FRANCIS, A. J. HILL AND JOHN JOHNSTON

In a previous paper[3] there was described an analytical method for the estimation of the *meta* isomer of various monosubstituted amines, phenols and nitro compounds in mixtures with the corresponding *ortho* and *para* compounds.   This method depends upon the fact that amines and phenols are brominated quantitatively in aqueous solution, the *meta* in each case yielding the tribromo compound whereas the *ortho* and *para* are only dibrominated.   This substitution offers also a convenient method of studying the directive influence of substituents, for it seemed probable that the rates of bromination of various compounds, and in the two or three available positions of a single compound, would vary considerably with change of the groups present, and that from these differences some estimate could be formed of the directive influences of the substituent groups.

The following pages recount the results of experiments upon the rate of bromination, in dilute aqueous solution, of a number of aromatic amino and phenolic compounds.   The work was undertaken as a means of ascertaining how the nature of the group already attached to the benzene nucleus affects the rate at which the bromine enters the ring in the several possible positions; and the results, it is believed, are of some significance in connection with the general problem of the factors which determine the

preferential formation of the *ortho, meta* or *para* isomers. For instance, the rate of bromination, in acidified aqueous solution, of the *meta* compound exceeds that of the *ortho* and *para* isomers when each group already present is one of those which have been characterized as *ortho-* or *para*-controlling, and conversely is least when one of the groups is *meta*-controlling.

When a second substituent group Y is brought into the monosubstituted benzene, C_6H_5X, it may enter in one of three positions; and the main product is usually either a mixture of *ortho* and *para* C_6H_4XY or the *meta* isomer. To enable one to predict which alternative will come to pass, several well-known rules have been formulated which in effect attribute to the group X already present a "directive influence" favoring one or another of these types of substitution; for instance, a halogen "directs" the entering group to the *ortho-para* positions, whereas if X is NO_2 or SO_3H the main product is the *meta* isomer. Now, Holleman has brought forward evidence[4] that these two types of substitution are not so sharply differentiated as they have been assumed to be; for example, nitration of toluene, benzyl chloride, benzal chloride, and benzotrichloride, yields in each case all three isomers, in proportions as follows.

| Compound nitrated | ─────Percentage formed of───── | | |
	Ortho	Para	Meta
$C_6H_5CH_3$	59	37	4
$C_6H_5CH_2Cl$	41	55	4
$C_6H_5CHCl_2$	23	43	34
$C_6H_5CCl_3$	7	29	64

From this it appears that the presence of chlorine in the side chain favors the *meta* position and hinders the reaction in the *ortho*. Now, since there is no evidence of a direct equilibrium as between the isomers, we must assume that the amount of each in the product depends upon its specific rate of formation under the particular conditions. Thus the results above imply that the presence of chlorine in the side chain increases the rate of formation of *meta* relative to that of *ortho* (and, to a smaller extent, of *para*) and, therefore, that the "directive influence" is an influence upon the rates of the possible reactions.

It appears, therefore, that if we are to be in a position to foretell the relative yields of the three isomers, or to ascertain conditions for the best yield of any one of them, we must try to learn more about the relative rate of reaction in this type of case and of the factors that influence it. This has been recognized before, notably by Holleman; but much remains to be done. The processes studied previously have been nitration, sulfonation and halogenation, the last two at elevated temperature. In every case, in order to save experimental complications, the *first* substitution

    [4] Holleman, Vermeulen and de Mooy, *Rec. trav. chim.*, **33**, 1 (1914). See Holleman, *Chem. Reviews*, 1, 187 (1924).

only was considered, and possible reactions were rejected when accompanied by additional substitution. For this reason, the rate of bromination in dilute aqueous solution has been largely neglected; but we took it up in the belief that we should in this way find it possible to secure significant results.

Attempts to measure directly the rate of bromination by free bromine water failed because of the enormous rapidity of the reaction; for instance, the bromination of a very dilute (0.00002 N) solution of aniline appeared to be complete in a few seconds. When the bromide-bromate solution was used, a rate was indeed observed; but this was found to be that of the liberation of bromine from the bromide-bromate, a rate which is smaller than that of the bromination of aromatic compounds with an amino or hydroxyl group. Since, however, we are more interested in knowing the *relative* rate of entrance of the first, second and third atom of bromine into these compounds than in the absolute rate of any of these reactions, we may attain to a satisfactory estimate of these relative rates by analysis of results obtained from series of experiments on partial bromination, in which advantage is taken of the comparative slowness of the bromide-bromate reaction itself. The method with aniline, for example, is as follows.

To a slightly acid solution of aniline, standard bromide-bromate solution[5] in quantity insufficient to convert all the aniline to tribromo-aniline is added rapidly and mixed thoroughly before the bromine begins to be liberated; the result is a mixture of aniline and its brominated derivatives, of which only the tribromo-aniline is precipitated, its solubility being negligible. After further acidification to complete the liberation of the bromine, and after a suitable interval, the precipitate is separated on a Gooch crucible, dried and weighed.

The results of a series of such experiments are given in Table I. Column 1 gives the amount of bromine (B moles) as derived from the volume of bromide-bromate solution added, but expressed as a fraction of the amount that would have been required for the complete conversion of the aniline taken (A moles) to tribromo-aniline. Column 2 gives the amount of tribromo-aniline actually formed (C moles), again expressed as a fraction of what would have been obtained if all the aniline taken had been completely tribrominated. For instance, when to 1 millimole of aniline is added 1 millimole of bromine, 0.128 millimole of tribromo-aniline will result, the amount of bromine added being one-third of that (3 millimoles) required

TABLE I

PARTIAL CONVERSION OF ANILINE TO TRIBROMO-ANILINE BY VARIOUS PROPORTIONS OF BROMINE

Fractional amount of bromine taken $r = \dfrac{B}{3A}$	Fractional yield of tribromo-aniline $z = \dfrac{C}{A}$		
	Observed	Calcd. from (13)	Difference
0.050	0.001	0.003	−0.002
.100	.012	.012	.000
.167	.043	.034	+ .009
.250	.075	.072	+ .003
.333	.128	.126	+ .002
.400	.188	.179	+ .009
.500	.265	.270	− .005
.500	.270	.270	.000
.600	.369	.379	− .010
.667	.469	.463	+ .006
.750	.566	.577	− .011
.833	.693	.700	− .007
.900	.802	.811	− .009
1.000	1.003	1.000	+ .003
		Mean ±0.005	

for the complete bromination of 1 millimole of aniline. It will be noticed that the value of z (the fractional yield of tribromo-aniline) lags behind that of r (the fractional amount of bromine added, that for $z = 1$ being
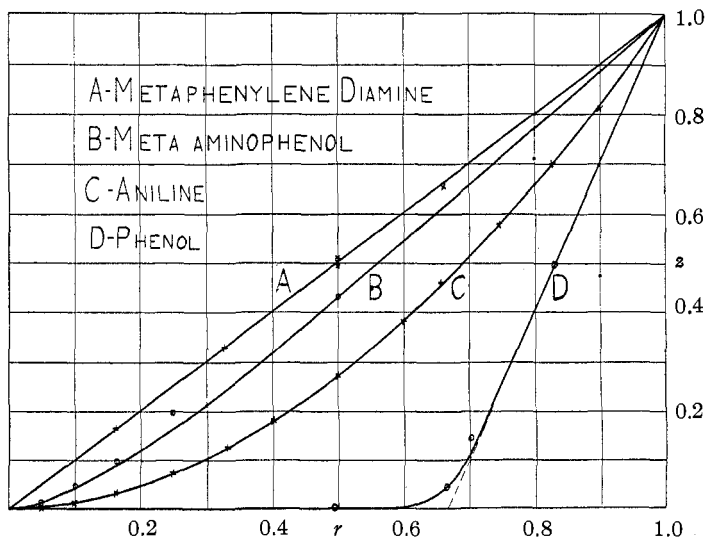

Fig. 1.—The relation between the fractional amount (r) of bromine added and the fractional yield (z) of tribromo compound.

considered unity); in other words, some of the bromine has formed mono- or dibromo-aniline. This becomes clearer when the corresponding values

of r and z are plotted against each other, which gives us a smooth, perfectly reproducible curve (C in Fig. 1).

The form of this curve depends obviously upon the relative magnitudes of the several velocity constants; for instance, if the second and third reactions were much faster than the first, the curve would be much higher than if they were relatively slower. Conversely, therefore, when we set up the theoretical expression, under appropriate assumptions, and compare these with the experimental curve of Fig. 1, it is possible to form an estimate of the *relative rate* of the several steps. The several reactions may be simultaneous or successive, so that we must consider both possibilities. It was found, however, that the expression derived on the basis that all three reactions are simultaneous, which is equivalent to saying that all three reactions are substitutions of 1, 2 or 3 atoms of bromine in aniline itself, is not of a form that corresponds (in this case) to the experimental curve. For this reason, and because simultaneous substitution is in effect a special case of successive substitutions, we do not discuss this alternative further, but proceed to develop the expression for successive reactions, and to show that this is in accordance with the observations.

Before doing this let us, however, discuss the simpler case of the rate of bromination of p-bromo-aniline, in which there are only two steps. Let us start with M moles of p-bromo-aniline, and B moles of bromine, in a total volume V; we shall find it convenient to write, in place of B, $2Mr$ where r is a fraction denoting the relative amount of bromine taken (B) compared with that which would be required ($2M$) for complete conversion of the mono- to tribromo-aniline. If at a time t there have been formed Mx moles of dibromo-[6] and from this in turn My moles of tribromo-aniline, the two differential equations are

$$\frac{d(Mx)}{dt} = K_1 \frac{M^2}{V} (1 - x)(2r - x - y) \tag{1}$$

$$\frac{d(My)}{dt} = K_2 \frac{M^2}{V} (x - y)(2r - x - y) \tag{2}$$

where K_1 and K_2 are the two velocity constants. Dividing (2) by (1) and letting $m = K_2/K_1$, we have

$$\frac{dy}{dx} = \frac{K_2}{K_1} \cdot \frac{x - y}{1 - x} = \frac{m(x - y)}{1 - x} \tag{3}$$

the solution of which is

$$y = C(1 - x)^m + \frac{1 - mx}{1 - m}. \tag{4}$$

When $x = 0$, $y = 0$; hence $C = 1/(m - 1)$, and

$$y = \frac{(1 - x)^m + mx - 1}{m - 1} \tag{5}$$

This gives us a relation between y and x, the relative amounts of second and

[6] That is, x is the fraction of the monobromo- which has been converted into dibromo-aniline, not the relative amount present at time t.

first substitution, respectively, in terms of the relative rate of the two reactions, which is valid throughout the course of the reaction. When all of the bromine has been used up, as is the case in the actual observations, we have the usual condition $x + y = 2r$; whence, by combination with (5),

$$(1 - 2r + y)^m + 2m(r - y) + y = 1 \qquad (6)$$

Equation 6 is the desired relation between r, the bromine taken, and y, the tribromo-aniline formed, in terms of m; wherefore it should be possible, by comparison with the experimental data, to find by trial a value of m such that the graph of (6) would coincide with the experimental curve. In this particular case the curves substantially coincide when $m = 1.9$, a result which at first sight is rather surprising, since it implies that dibromo-aniline is brominated more rapidly than p-monobromo-aniline. It will be shown, however, that this case is not unique.

If m is a small quantity (that is, if the second reaction is much slower than the first), it is clear that y will be inappreciable until x is almost unity; this is equivalent to the statement that bromine, added gradually to such a compound, will yield substantially no dibromo derivative until the process of conversion into the monobromo derivative is complete. On the other hand, if m is very large, x will never differ far from y; in this case, the practical result would be indistinguishable from that when the two bromine atoms react simultaneously. Consequently, one cannot safely argue from the seeming non-appearance of a possible intermediate product that this product does not in fact participate in the process.

The ratio m may have a wide range of values, and in general it cannot be foretold. In the special case of m being unity ($K_2 = K_1$), which is not unreasonable, Equation 5 is illusory. Putting $m = 1$ in (3) and integrating we find $y = x + (1-x)ln(1-x)$ and hence, for this particular case, the relation corresponding to (6) is

$$(1 - 2r + y)ln(1 - 2r + y) + 2(r - y) = 0 \qquad (7)$$

We may now revert to the more complex case of the bromination of aniline; there being now three possible successive reactions. Let us start with A moles of aniline and B moles of bromine, in a total volume V; again it is convenient to write, in place of B, $3Ar$ where r has the same significance as in Fig. 1. If at a time t there have been formed Ax moles of monobromo- and from this in turn Ay moles of dibromo- and Az moles of tribromo-aniline,[7] the three[8] differential equations are

[7] That is, x is the fraction of the aniline which has received at least one bromine atom; similarly, y is that which has received at least two, and z three.

[8] Unless it should be necessary to assume two separate rates for the first substitution (*ortho* or *para*, the *meta* being here negligible), three for the second and two for the third, or seven in all for aniline. This complex hypothesis, which would be very difficult to handle, proves to be unnecessary, as good concordance is obtained by the assumption of three velocity constants only; these may be looked upon as effective mean constants for the three main stages of the reaction.

$$\frac{d(Ax)}{dt} = K_1 \frac{A^2}{V} (1 - x)(3r - x - y - z) \tag{8}$$

$$\frac{d(Ay)}{dt} = K_2 \frac{A^2}{V} (x - y)(3r - x - y - z) \tag{9}$$

$$\frac{d(Az)}{dt} = K_3 \frac{A^2}{V} (y - z)(3r - x - y - z) \tag{10}$$

where K_1, K_2, K_3 are the three velocity constants.[9]   Dividing (9) by (8), and proceeding as with (1) and (2) we obtain Equation 5 again.   Similarly, dividing (10) by (8) and letting $n = K_3/K_1$ we have

$$\frac{dz}{dx} = \frac{K_3}{K_1} \frac{y - z}{1 - x} = \frac{n(y - z)}{1 - x} \tag{11}$$

whence, by integration and combination with (5) we have

$$z = 1 - \frac{mn(1 - x)}{(m - 1)(n - 1)} - \frac{n(1 - x)^m}{(m - 1)(m - n)} + \frac{m(1 - x)^n}{(n - 1)(m - n)} \tag{12}$$

From Equations 5 and 12, combined with the experimental condition $x + y + z = 3r$ (for, when the determination of z is made, all of the bromine added has reacted) we can, by a process of trial and error, derive values of m and n; this is a very tedious process, but in the present investigation it had to be carried out only once, for in each case either two of the constants proved to be equal, or all three were so different that the three stages did not in effect run concurrently.

Comparison with the observations on the bromination of aniline shows good agreement when $m = \infty$ and $n = 1.13$, that is, when $K_1 : K_2 : K_3 = 1 : \infty : 1.13$.   The infinite value does not seem to be accidental, since experimental errors would have tended to make the value too small rather than too large, and since neither o- nor p-bromo-aniline is brominated much faster than aniline.   This conclusion is equivalent to the supposition that the first two substitutions are simultaneous, but the third successive; and it suggests the intermediate formation of $C_6H_5NBr_2$.   On this basis the curve may be calculated more simply from Equation 5 (with y in place of x and z in place of y) combined with the condition $3r = 2y + z$; whence

$$\left(\frac{2 - 3r + z}{2}\right)^n + \frac{3n}{2}(r - z) + z = 1 \tag{13}$$

This equation fits the curve when $n = 1.13$, as may be seen from Table I in which the values so calculated are compared with those observed.   So we may write, for the bromination of aniline, $\overgroup{K_1 : K_2} : K_3 = \overgroup{1 : 1} : 1.13$, using the tie to indicate simultaneous substitution.   This relation indicates that in the bromination of aniline, no monobromo-aniline is formed, a deduction which is corroborated by experiments on a larger scale in which

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[9] Similar equations have been set up, and integrated in a few special cases, by A. C. Geitel [*J. prakt. Chem.*, **55**, 429 (1897)] in discussing the rate of decomposition of triglycerides by bases, dilute acids and water.

no monobromo-aniline could be isolated from the partial bromination products.

From Equation 13 we can calculate that the maximum yield $(y-z)$ of dibromo-aniline is not when $r = {}^2/_3$ as might be supposed, but when $r = 0.493$; the yield is then 34.4%, as compared with 30.6% when 2 moles of bromine for each mole of aniline has been added. This illustrates in a quantitative way why the best yield in certain reactions may result when the proportions are far from stoichiometric, depending as it does in such cases upon the relative rates of the several reactions involved. It appears, moreover, from the concordance of the results that these *relative* rates are not greatly affected by moderate changes of temperature, concentration or acidity, or by the presence of accidental catalysts; indeed, in the case of aniline all of these factors have been varied over a considerable range without affecting the *relative* rates.

When bromine in increasing amounts is added (as bromide-bromate) to a solution of phenol, the bromination proceeds in a manner quite different from that of aniline. No precipitate of tribromophenol appears until nearly two-thirds of the calculated amount of bromine has been added, although its solubility is only 1 part in 14,300;[10] then when r is greater than 0.67, the curve is a straight line (Curve D, Fig. 1). The corresponding values of r and z, as experimentally determined, follow.

| r | 0.500 | 0.667 | 0.700 | 0.833 | 1.000 |
| z | .005 | .045 | .143 | .491 | 0.970 |

From this behavior it is evident that the third substitution is much slower than the others. In this case the second substitution is also much slower than the first, as shown by the fact that after addition of the calculated amount of bromine for monosubstitution $(r = 0.33)$, the ether extract was nearly pure monobromophenol; and this is corroborated by the experiment on the "competition" of phenol with aniline for bromine, to be described presently. Similar results were obtained with most of the other phenolic compounds studied in this investigation.

The mode of bromination of a number of substances was investigated in a similar way, this being done primarily because the data are required for the interpretation of the "competition" experiments. In some cases the determination is complicated by incomplete precipitation of the final product of bromination or by partial precipitation of a less brominated product; in such cases appropriate corrections, based on special experiments, were made. For three substances the experimental data together with the derived values of m ($= K_2/K_1$) are presented in Table II, and some typical curves are given in Figs. 1 and 2. The general results, which were secured from some 120 experiments of this kind, are summarized in Table III

[10] Allen, "Commercial Organic Analysis," Blakiston, 1914, vol. III, p. 299. He had also observed the stepwise bromination of phenol.

which, however, gives only m and p ($= K_3/K_2$) as derived by mathematical analysis of the experimental bromination curves.
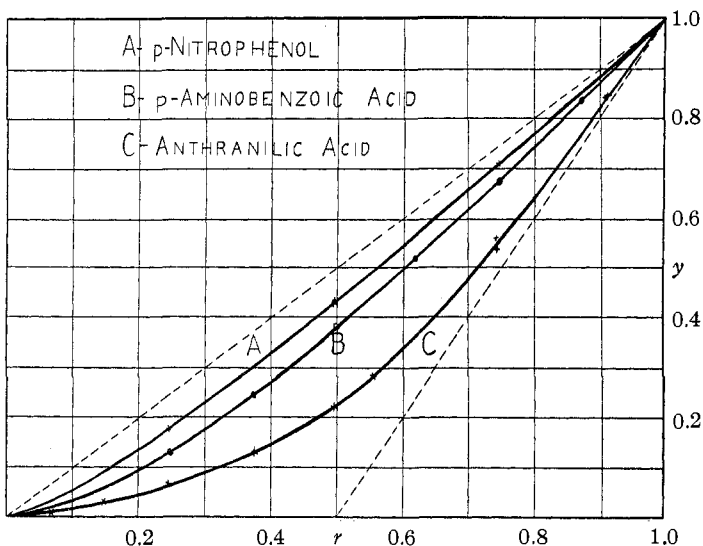

Fig. 2.—The relation between the fractional amount (r) of bromine added and the fractional yield (y) of dibromo compound.

In cases where the partial bromination curves could not be obtained directly because of too great solubility of the end product, the mode of bromination was obtained indirectly by competition experiments with a known competitor in various stages of the reaction; this is illustrated later in the case of m-aminobenzoic acid. This method is necessary also when there are too great differences between the several constants.

TABLE II

EXPERIMENTS ON PARTIAL[a] BROMINATION[b]

p-Bromo-aniline			p-Nitrophenol			p-Aminobenzoic acid		
r	y	m	r	y	m	r	y	m
0.167	0.067	1.8	0.10	0.03	2.4	0.250	0.130	1.87
.333	.203	1.9	.25	.18	4.4	.375	.243	1.83
.500	.377	1.9	.35	.27	4.2	.500	.375	1.86
.625	.518	1.9	.50	.44	4.5	.625	.520	1.90
.833	.764	1.6	.50	.45	4.7	.750	.676	1.99
1.000	.997	...	.60	.55	4.3	.875	.835	2.02
	—		.75	.71	3.6	1.00	.988	..
		1.9	1.00	1.00	...		—	
				—				1.9
				4.3				

[a] Compared with the calculated requirement of two moles.

[b] Symbols as in Equation 6; r and y are observed values, m is derived by Equation 6.

TABLE III

RELATIVE VELOCITY CONSTANTS (m AND p) FOR PARTIAL[a] BROMINATION (AS DERIVED FROM THE MEASUREMENTS OF THE FRACTIONAL CONVERSION TO THE HIGHEST BROMINATED PRODUCT)

Compounds	Ortho $m(=K_2/K_1)$	Para	Meta[b]	Meta $p(=K_3/K_2)$
Toluidines	0.32	2.7	1.0 (s)	1.13
Bromo-anilines	.25	1.9	1.0 (s)	1.13
Nitro-anilines	(.016)	(0.006)	1.0 (s)	0.12
Nitrophenols	.44	4.3	1.0	3.0
Aminobenzoic acids	.52	1.9	...	..
Phenylenediamine	..	..	1.0 (s)	1.0 (s)
Aminophenol	..	..	2.6	1.0 (s)
Cresol	..	..	...	(0.01)
Hydroxybenzoic acids	.06	0.09	...	..
Hydroxybenzaldehydes	.07	.04	...	..
Iodo-aniline	..	2.3	...	..
Phenylglycine	..	..	1	1

[a] Compared with the calculated requirement of two moles for *ortho* or *para* compounds, or three for *meta* compounds. (See Ref. 3.)

[b] S denotes simultaneous, as with aniline itself.

"Competition" Experiments

When two compounds, A (for example, 1 mole of aniline) and C (for example, 1 mole of phenol), are treated with an insufficient amount of a reagent B (for example, less than 6 moles of bromine) which reacts with both, they will compete for it in accordance with the relative rates of the reactions of B with A and with C, respectively. This is not a matter of equilibrium, for the reactions studied are quite irreversible, and the rates are therefore not affected by the precipitation or non-precipitation of the possible products. For this reason we have used the term "competition" in preference to "partition," as employed by Michael,[11] to convey more definitely· the idea of relative rates. It should be possible, therefore, to estimate, from the precipitate produced in such competitions, the relative rate of bromination of the two compounds; but the mathematical formulation will be deferred until an example has been given.

If to an acid solution of aniline and phenol in equivalent amounts we add bromide-bromate solution in increasing amounts, we obtain precipitates, the weights of which depend upon the amount of bromine added. In this case tribromo-aniline is precipitated completely before any tribromo-phenol appears; but to make certain, the precipitate before it was dried and weighed was washed with sodium hydroxide, which dissolves the latter but not the former. The results of a series of such experiments are given in Table IV, in which B denotes the number of moles of bromine added for 1 mole of A + 1 mole of C, and z_A is the weight of tribromo-aniline

[11] Michael, *Ber.*, **39**, 2138 (1906).

expressed again in moles (that is, as a fraction of what would be formed if all the aniline were converted to tribromo-aniline). On the basis, which is *a priori* probable and is justified by experience, that the mode of bromination of aniline in mixtures is the same as when aniline alone is present, we can deduce from Fig. 1 for each value of z_A the corresponding value of r_A, which is as before the fractional amount of bromine seized by A.
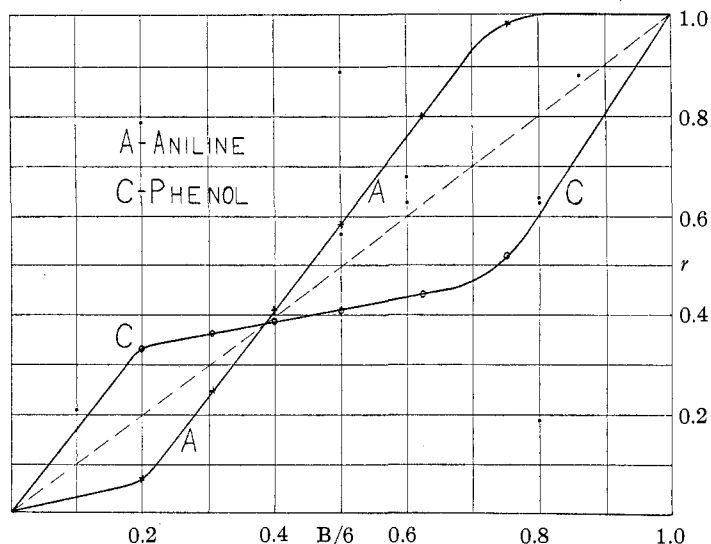

Fig. 3.—The competition of aniline (A) with phenol (C) for bromine; the relation between the fractional amount (B/6) of bromine added and the fractional amounts of bromination (r_A and r_C) of the two compounds.

The corresponding quantity taken by C is obtained by difference, $r_C = (B-3r_A)/3$. The values so derived are included in Table IV, and are plotted in Fig. 3.

TABLE IV

COMPETITION OF ANILINE (A) AND PHENOL (C) FOR BROMINE

Moles of bromine B		1.2	2.0	2.4	3.0	3.75	4.5
Moles of tribromo-aniline pptd.	z_A	0.006	0.100	0.188	0.372	0.654	0.964
Relative bromine taken by A	r_A	.067	.295	.411	.592	.805	.983
Relative bromine taken by C	r_C	.333	.371	.389	.408	.445	.517

From this it is evident that the bromine at first goes very largely to the phenol until the latter has acquired one atom of bromine ($r_C = 0.33$); its rate of further bromination now becomes much slower than that of aniline, which takes most of the bromine until it is tribrominated; finally, the bromination of the phenol is completed. This competition illustrates the striking differences in relative rate of the successive steps in the bromination of a pair of compounds competing for the bromine, and it points out how one

may readily err in drawing inferences as to relative reactivities. For instance, if the only experiment had been with $B = 3.0$, that is, with just enough bromine for one competitor (which would be the most likely experiment to try), one would conclude that aniline, since at that point it has taken 59% of the bromine, is brominated more rapidly than phenol. This particular competition, however, is not well suited to the estimation of the relative velocity constants, because K_{1C} is so much greater than K_{1A};[12] but from the relative slopes of the middle straight portions of the two curves (Fig. 3) one may estimate $K_{2C}/K_{1A} = 0.12$, approximately. One of the most favorable pairs of competitors is aniline and m-aminobenzoic acid, because the amino group is common to both, and the acidity of the latter allows quantitative separation of the products; but before taking this up we shall derive the mathematical formula for competition experiments.

Let us consider only the simplest case in which 1 mole of A and 1 mole of C compete for B (less than 2 moles), that is, in which only single-stage reactions are involved. Using symbols as previously defined, we have for this case

$$\frac{dr_A}{dt} = K_A \frac{1}{V}(1 - r_A)(B - r_A - r_C)$$

$$\frac{dr_C}{dt} = K_C \frac{1}{V}(1 - r_C)(B - r_A - r_C)$$

whence $$\frac{dr_C}{dr_A} = \frac{K_C(1 - r_C)}{K_A(1 - r_A)},$$

and by integration $$\frac{K_C}{K_A} = \frac{\log(1 - r_C)}{\log(1 - r_A)} \tag{14}$$

This equation applies to simultaneous, irreversible, one-stage reactions. It is not limited to the case in which A and C are initially present in equivalent amounts, though to have them so is usually convenient. It can be modified to suit other cases, but will serve our purpose as at any instant we may regard the competition as in large part between two single-stage reactions which do not necessarily represent the same step in bromination.

The results of the competition experiments between aniline (A) and m-aminobenzoic acid (C) are summarized in Table V. Cols. 1 and 2 are the direct experimental results; the values of r_A and r_C in the third and fourth were derived as in Table IV; and the fifth contains K_C/K_A as calculated from Equation 14. The procedure and method of calculation are illustrated in the following typical experiment (the seventh in Table V).

One millimole each of A and C was dissolved in 30 cc. of water acidified with 3 cc. of 50% sulfuric acid; to this was added 58 cc. of 0.125 N bromide-bromate solution (= 3.63 moles of bromine), and the solution was further acidified to complete the liberation of bromine. After a few minutes, the

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[12] The first subscript denotes that the K is the constant for the substitution of the first, second or third atom of bromine; the second refers to the competitor A or C.

TABLE V

COMPETITION OF ANILINE (A) WITH m-AMINOBENZOIC ACID (C) FOR BROMINE

B Moles of bromine	z_A Moles of tribromo- aniline pptd.	r_A Bromine taken by A	r_C Bromine taken by C	K_C/K_A
0.92	0.035	0.173	0.133	0.77
1.09	.054	.214	.150	.72
1.20	.056	.220	.180	.82
2.00	.127	.337	.329	.99
2.71	.240	.468	.436	.92
3.00	.284	.512	.488	.94
3.63	.433	.641	.569	.83
4.07	.526	.716	.642	.83
4.09	.566	.744	.622	.72
4.50	.585	.757	.743	.97
4.57	.635	.783	.721	.86
4.88	.703	.835	.791	.87
5.70	.944	.972	.928	.74
			Mean	0.84

colorless precipitate was separated on a Gooch crucible, washed with dil. alkali to dissolve tribromo-m-aminobenzoic acid, and finally with water; it was dried overnight at 60° and weighed. Its weight, 0.1428 g., divided by 0.3298 g. (the weight of 1 millimole of tribromo-aniline) gives 0.433 which is z_A; whence, from the curve for aniline in Fig. 1, r_A is 0.641, and consequently $r_C = B/3 - r_A = 0.569$. In applying Equation 14 to these values of r we make the tentative assumption that the mode of bromination of both compounds is similar and in effect equivalent to a pair of one-step reactions at any instant; and this assumption appears in this case to be justified by the lack of trend of the values of the ratio K_C/K_A calculated on this basis. Indeed, K_C/K_A is as constant as could be expected from the way in which it is derived; and it indicates that the presence of the carboxyl group slows the rate of bromination of aniline by about 16%. It would have been preferable to evaluate x_A and x_C, the proportions of the two primary substitutions, and thence from (14) have calculated K_{1C}/K_{1A}, the relative rate of the first step of bromination, but this could not in this case be done directly. For, though x_A could be calculated from the partial-bromination curve of aniline, x_C is not similarly available because the bromination curve of m-aminobenzoic acid cannot be obtained directly by reason of the solubility of the tribromo acid. Conversely, one may argue from the fair constancy of K_C/K_A in Table V that the bromination curve of m-aminobenzoic acid must be very similar to that of aniline, as given in Fig. 1.

The choice of pairs of competitors was made in accordance with the following desiderata: (1) the difference in rate should not be too large; (2) [a] the highest brominated product of one, preferably the faster, should be precipitated quantitatively, in order that the amount produced may

be evaluated by separating on a Gooch crucible, drying and weighing; [b] its lower brominated products should not be precipitated at all; [c] the products from the other competitor should either not be precipitated at all, or [d] should be soluble in alkali, and so admit of a separation.   These considerations,[13] though desirable, are not all necessary for a useful com-

Aniline	a,b	Phenol	a,(b),c,[a]d	m-Aminobenzene sulfonic acid
o- or p-Bromo-aniline	a,b	Resorcinol	b,c,[a]d	c
m-Bromo-aniline	a	Phloroglucinol	(a),b,d	o- or p-Aminobenzoic acid a,b
p-Iodo-aniline	a	Cresols	d	m-Aminobenzoic acid b,(c),d
Nitro-anilines	a	Thymol	d	o- or p-Hydroxybenzoic acid
o- or m-Toluidine	b	m-Aminophenol, (a),b,d		(a),d
p-Toluidine	(a)	m-Nitrophenol a,(b),d		m-Hydroxybenzoic acid c
m-Phenylenediamine	(a),b	o- or p-Nitro-		Phenylglycine b,d
Diphenylamine	a	phenol	(a),d	Vanillin d
		Sulfanilic acid	a,b,c[a]	o- or p-Hydroxybenzaldehyde a,d

[a] No precipitate until the two-thirds point is reached.

parison.   Thus: (a) incomplete precipitation may be compensated for by a correction for solubility; (b) if a lower brominated product is precipitated, its amount can be estimated by a bromine titration[14] of the filtrate, or of the weighed precipitate dissolved in alcohol; (c) the insolubility of the bromination product of the slower competitor will not be objectionable if its extent of bromination is kept within such a range that the precipitation is slight; (d) the product (or filtrate, or both) may be analyzed in some other way to distinguish between the products from the two competitors, for example, nitro compounds by titration with titanous chloride.[14,15] In several cases the premature precipitation of a partially brominated product, which would have invalidated the comparison, was prevented by addition of a sufficient amount of alcohol; this was evaporated at a low temperature by a current of air before filtration.

Altogether about 300 competition experiments for bromine, as between various pairs of substances, were carried out.   The method used was that already described and illustrated in the case of the pair aniline and m-aminobenzoic acid; in the interpretation of the results the data on partial bromination, summarized in Table III, were employed.   The main results are arranged briefly in Tables VI to XV, the meanings of the symbols being as follows.   B is the number of moles of bromine added for 1 mole of each competitor (the competitors being thus in equivalent quantities, except where noted otherwise); and z_A or y_A is the relative conversion (as determined by weighing) to the highest brominated product—tri or di, re-

[13] The following list indicates which of these conditions hold, a parenthesis about the letter denoting that the condition is almost fulfilled.

[14] As described in a previous paper, Ref. 3.

[15] Knecht and Hibbert, *Ber.*, **36**, 166, 1554 (1903); **40**, 3819 (1907).

spectively—from competitor A. These comprise the direct experimental data, from which the value of the ratio of the velocity constants K_C/K_A was derived; the numerical subscript 1, 2 or 3 denotes that the constant pertains to the substitution of the first, second or third bromine atom. The last column contains the value of this same ratio, as adjusted to secure consistency of all the results, taken from Table XVI. A number of experiments, made without adequate knowledge of the proper choice of competitors, could be regarded merely as preliminary, and so are not included.

TABLE VI

THE COMPETITION FOR BROMINE (B) OF ANILINE (A) WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.
Anisole	1.5	0.15	0.74 }	0.67	o-Toluidine	1.0	0.05	1.6 }	1.4
	3.0	.61	.60 }			2.0	.17	1.7 }	
Cinnamic aldehyde	1.0	.09	.44	.44		3.0	.48	1.0 }	
					p-Toluidine	1.0	.11	0.15 }	0.15
p-Hydroxybenzaldehyde	1.5	.25	.08 }			2.0	.38	.14 }	
	3.0	.87	.08 }	.09	Phenylglycine	2.0	.14	2.0	3.0
	3.0	.88	.06 }		Salicylic acid	2.0	.24	0.55	0.5
m-Hydroxybenzoic acid	1.0	.08	.35 }		Salicyl-aldehyde	1.5	.23	.17 }	.15
	2.0	.28	.41 }	.33	Sulfanilic acid	3.0	.81	.13 }	
	2.0	.32	.26 }		Sulfanilic acid	2.0	.07	6.4 }	8.0
	3.0	.62	.31 }			2.0	.05	7.8 }	
p-Hydroxybenzoic acid	2.0	.31	.46 }	0.4	Vanillin	2.0	.41	0.11	0.16
	3.0	.65	.41 }					K_{2C}/K_{1A}	
m-Aminobenzenesulfonic acid	2.0	.18	.59 }	.54	o-Cresol	4.0	.86	0.07	0.07
	3.5	.52	.54 }		p-Cresol	4.0	.91	.036	.036
m-Nitro-aniline	1.0	.06	.41 }	.5	Thymol	2.0	.06	1.24	1.2
	2.0	.23	.44 }					K_{3C}/K_{1A}	
	2.0	.21	.53 }		m-Cresol	4.0	.43	0.06 }	0.055
						5.0	.90	.05 }	

TABLE VII

THE COMPETITION FOR BROMINE OF m-PHENYLENEDIAMINE (A) WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.
p-Aminobenzoic acid	2.5	0.54	1.07	1.0	Sulfanilic acid	2.5	0.67	0.54	0.50
m-Aminophenol	2.0	.17	5.5	6.2	m-Toluidine	3.0	.84	.13	.2
Anthranilic acid	2.0	.29	5.7	4.2					
m-Bromo-aniline	2.0	.47	0.43	0.43				K_{2C}/K_{1A}	
p-Hydroxybenzoic acid	1.0	.32	.06	.04	m-Cresol	1.2	0.05	0.9 }	0.7
o-Nitro-aniline	1.5	.26	4.4	4.5		2.0	.28	.52 }	
p-Nitro-aniline	2.0	.50	1.06	1.2		3.0	.55	.54 }	
o-Cresol	2.0	.39	3.6	4.4				K_{3C}/K_{1A}	
p-Cresol	2.0	.41	2.7	1.8	Resorcinol	2.4	0.09	1.59 }	1.6
Phenol	2.5	.48	1.2	2.1		3.0	.23	1.42 }	

TABLE VIII

THE COMPETITION FOR BROMINE OF m-AMINOPHENOL (A) WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.
Anthranilic acid	1.5	0.30	0.43	0.66
Cinnamyl alcohol	2.0	.45	1.0	1.0

TABLE VIII (Concluded)

Competitor (C)	B	z_A	K_{1C}/K_{1A} Calcd.	Adj.
m-Cresol	2.0	.30	2.1 }	2.2
	2.0	.28	2.6 }	
o-Cresol	1.5	.30	0.53	0.7
p-Cresol	2.0	.51	.29	.28
o-Nitro-aniline	2.0	.45	.55 }	
	2.5	.61	.53 }	.74
	2.5	.58	.66 }	
Phenol	2.5	.60	.53	.34
Potassium iodide	2.0	.35	2.05	2.0
Resorcinol	2.0	.04	9.3	8.0

TABLE IX

THE COMPETITION FOR BROMINE OF PHENOL (A) WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	z_A	K_{1C}/K_{3A} Calcd.	Adj.
Cinnamic acid	3.0	0.64	0.44	0.44
Diethylaniline	3.0	.28	2.0	2.0
p-Nitrophenol	3.0	.33	1.25	1.3
Titanous chloride	3.0	.48	1.08	1.2

			K_{2C}/K_{3A}	
m-Hydroxybenzoic acid	4.0	.50	1.0	1.2

			K_{3C}/K_{3A}	
m-Nitro-aniline	5.0	.20	7.4	7.4

TABLE X

THE COMPETITION FOR BROMINE OF SULFANILIC ACID (A)[a] WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	z_A	K_{3C}/K_{3A} Calcd.	Adj.	Competitor (C)	B	z_A	K_{3C}/K_{3A} Calcd.	Adj.
p-Aminobenzoic acid	5.0	0.13	0.06	0.07	p-Hydroxybenzaldehyde	5.0	0.73	0.24	0.24
Anthranilic acid	5.0	.14	.07	.07	m-Hydroxybenzoic acid*	5.0	.16	10.8 }	7
Cinnamic acid*	3.0	.35	2.5	2.5		5.3	.35	6.8 }	
Salicylic acid	5.0	.41	1.7	1.7	p-Hydroxybenzoic acid	5.0	.18	9 }	11
Salicyl-aldehyde	5.0	.76	0.2	0.2		5.0	.14	13 }	

[a] In this table the group is displaced from both competitors except where noted thus *. (See Ref. 3.)

TABLE XI

THE COMPETITION FOR BROMINE OF p-AMINOBENZOIC ACID (A) WITH VARIOUS COMPOUNDS (C)

Competitor (C)	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor (C)	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.
3 Aniline—1/2(A)	1.5	0.43	0.07	0.06	Phenol—2(A)	2.0	0.20	1.85	2.1
m-Bromo-aniline	2.0	.46	.48	.44	m-Phenylenediamine	2.0	.23	0.8	1.0
p-Nitro-aniline	2.0	.49	1.3 }	1.2	Phenylglycine	2.0	.65	.34	0.2
	2.0	.48	1.4 }		m-Toluidine	2.0	.66	.16	.2
p-Cresol	2.0	.41	2.7	1.8	Sulfanilic acid	2.0	.60	.49 }	.5
						2.0	.61	.48 }	

TABLES XII—XIV

THE COMPETITION FOR BROMINE OF A WITH VARIOUS COMPOUNDS (C)

XII: A = Anthranilic acid

Competitor (C)	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor (C)	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.
3 Aniline + 1/2 A	1.5	0.36	0.025	0.015	2 Phenol	2.0	0.20	0.57	0.5
o-Nitro-aniline	1.0	.07	1.4	1.1	p-Cresol	1.0	.13	.36 ⎫	.42
p-Nitro-aniline	1.0	.14	0.25	0.28		1.0	.14	.33 ⎭	
m-Phenylenediamine	2.0	.28	.19	.3				K_{2C}/K_{1A}	
Sulfanilic acid	2.0	.54	.17	.12	m-Cresol	2.0	.15	0.20 ⎫	.28
m-Toluidine	1.0	.17	.06	.04		3.0	.42	.36 ⎭	

XIII: A = p-Bromo-aniline

Competitor	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.
m-Aminobenzoic acid	2.0	0.24	0.98	1.16	Salicylic acid	2.0	0.54	0.74	0.7
m-Amino benzenesulfonic acid	1.0	.11	.79 ⎫	0.76	o-Toluidine	1.5	.16	2.3 ⎫	2.0
	3.0	.57	.64 ⎭			2.0	.34	1.7 ⎭	
m-Nitro-aniline	1.0	.16	.45	.7	p-Toluidine	1.0	.26	0.23	0.2

XIV: A = p-Toluidine

Competitor	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.	Competitor	B	y_A	K_{2C}/K_{1A} Calcd.	Adj.
p-Hydroxybenzaldehyde	1.0	0.20	0.9	0.6					
m-Hydroxybenzoic acid	1.5	.26	2.0	2.2	o-Nitro-aniline	2.0	.30	0.26 ⎫	0.2
o-Nitrophenol	2.0	.83	0.12	0.08		2.0	.33	.17 ⎭	
Salicyl-aldehyde	1.0	.19	1.07	1.0	p-Nitro-aniline	2.0	.29	.30	.29
Vanillin	1.0	.16	1.5	1.1					

TABLE XV

VARIOUS COMPETITION EXPERIMENTS

Competitor (A)	Competitor (C)	B	y_A	K_{1C}/K_{1A} Calcd.	Adj.
o-Bromo-aniline	m-Nitro-aniline	1.5	0.32	0.08	0.11
	Salicylic acid	2.0	.62	.10	.11
	o-Toluidine	1.0	.09	.24	.3
p-Iodo-aniline	m-Aminobenzene sulfonic acid	1.0	.14	1.28	1.3
	p-Hydroxybenzaldehyde	1.0	.25	0.4	0.3
p-Nitrophenol	m-Hydroxybenzoic acid	2.0	.16	24	30
		3.0	.37	28	
Phloroglucinol	Resorcinol	2.0	.86	13	10
		3.0	.99	8	

It will be observed that the tables include results on three unsaturated compounds, cinnamic acid and aldehyde, and cinnamyl alcohol, which show quantitative addition, instead of substitution as in the other compounds listed, and that these rates of addition of bromine are of the same order of magnitude as the rates of substitution by bromine.[16] On the other hand, maleic and fumaric acids react with bromine very slowly under our conditions.

In addition, two inorganic reactions, namely, $Br_2 + 2KI \longrightarrow 2KBr + I_2$

[16] Sudborough and Thomas [J. Chem. Soc., **97**, 719 (1910)] measured the rate of bromination of cinnamic acid in carbon tetrachloride, but not of any other compound on our list; comparison is, therefore, not possible.

and $Br_2 + 2TiCl_3 + 2HCl \longrightarrow 2TiCl_4 + 2HBr$, were included.   In the former, the iodine liberated was titrated with thiosulfate; in the latter, the excess of titanous chloride was titrated hot with ferric alum, as in the determination of the nitro group.[3]   The results show that the organic substitutions under investigation are comparable in speed with inorganic metatheses, and suggest that in this respect there is little difference in kind between what many regard as ionic and non-ionic reactions.

In order to form an approximate estimate of the absolute velocities of these brominations, an attempt was made to measure directly the velocities of some of the slowest substitutions; in these trials free bromine water was used because the rate of reaction of the bromide-bromate mixture to produce bromine is too low for this purpose.   When bromine water was mixed with a solution of p-hydroxybenzaldehyde, which then was at a concentration of only 0.00025 N, the substitution of the third atom of bromine (which involves the displacement of the aldehyde group) was in 20 seconds about 80% complete; on this basis K_3 is of the order of 5×10^4. By successive comparison of this constant with K_3-sulfanilic acid, K-cinnamic acid, K_3-phenol, K_2-phenol, and K_1-aniline, the last appears to be of the order of 10^8.   Since, however, only the *relative* values of the velocity constants are of importance to the present purpose, and since K_1-aniline is most easily compared directly with a number of others, it is taken as standard.

The final results, arranged in order of decreasing K_1, are presented in Table XVI, K_1 for aniline being taken as unity.   In order to make the results consistent, some slight adjustment of individual ratios of constants was necessary; in these adjustments, which averaged about 15%, greater weight was given to the experiments between those pairs of competitors which appeared to yield the most trustworthy results.   Of course, the values tabulated can be regarded as little more than preliminary estimates, for it was thought better to cover a wide range of compounds than to try for a high degree of accuracy, but we venture to believe that the relative magnitudes are substantially of the right order.

TABLE XVI

RELATIVE VELOCITY CONSTANTS OF SUBSTITUTION OF THE FIRST, SECOND AND THIRD ATOM OF BROMINE, REFERRED TO K_1 — ANILINE AS UNITY[a]

Compound	K_1	K_2	K_3
Phloroglucinol	>8000	>8000	>8000
Resorcinol	800————800		26
m-Cresol	220	11	0.055
Potassium iodide	200	..	....
Thymol	160	1.2	....
Cinnamyl alcohol	100	....	....
m-Aminophenol	100	260————260..	
o-Nitro-aniline	73	0.03	....
o-Cresol	70	0.07	....

TABLE XVI   (*Concluded*)

Compound	K_1	K_2	K_3
Anthranilic acid	67	35	0.0001
Phenol	34	0.12	.0083
p-Cresol	28	0.036	....
p-Nitro-aniline	19	0.04	....
m-Phenylenediamine	16———————16———————16		
p-Aminobenzoic acid	16	30	0.0001
Sulfanilic acid	8	2.7	.0015
m-Bromo-aniline	5————————5		6
o-Bromo-aniline	4.5	1.13	....
m-Toluidine	3.2————————3.2		3.6
Phenylglycine	3	3	3
o-Toluidine	.1.4	0.45	....
Aniline	1.00————————1.00		1.13
m-Aminobenzoic acid	0.83————————0.83		0.93
p-Bromo-aniline	.71	1.13	....
Anisole	.67	....	....
m-Aminobenzene sulfonic acid	.54————————0.54		.6
m-Nitro-aniline	.5———————— .5		.06
Salicylic acid	.5	.034	.0025
Cinnamic aldehyde	.44	.....	....
p-Iodo-aniline	.4	.9	....
p-Hydroxybenzoic acid	.4	.03	.016
m-Hydroxybenzoic acid	.33	.01	.01
Vanillin	.16	.000015	....
p-Toluidine	.15	.4	....
Salicyl-aldehyde	.15	.01	.0003
p-Hydroxybenzaldehyde	.09	.005	.0003
Diethylaniline	.016	.008	....
o-Nitrophenol	.012	.005	....
p-Nitrophenol	.011	.047	....
Titanous chloride	.01	....	....
m-Nitrophenol	.006	.006	.02
Cinnamic acid	.0036	....	....

[a] A tie line indicates that the substitutions so tied appear to be simultaneous.

Discussion of Results

Table XVI presents relative values of the velocity constants of substitution of the first, second and third atom of bromine in a series of compounds, as estimated from our experimental work on bromination in acidified aqueous solution. In these rates of bromination certain regularities appear, which pertain to this series of cases but are not necessarily of universal applicability.

1. In aniline and in all the *m*-amino compounds investigated, two of the substitutions of bromine (but never three, except in *m*-phenylene-diamine) are simultaneous, but in no case (except resorcinol, which has two hydroxyl groups) does a phenolic compound behave in this way. This suggests that in the former cases the two bromine atoms are sub-

stituted first in the amino group, and thence by interchange go into the ring, whereas phenolic compounds can substitute only one bromine atom at a time in the directing group. In harmony with this is the relatively slow rate of *successive* bromination of diethylaniline, and also anisole, in which the bromine atoms would be less likely to enter the side chain. Neither of these is brominated quantitatively. They take about 4.5 and 1.5 molecular equivalents, respectively. The suggested mechanism is consistent with the observations of Chattaway and Orton on halogenation in aqueous solution of acyl-amino compounds,[17] although they showed no evidence in regard to free amino or phenolic compounds. It is also consistent with the mechanism given for nitration and sulfonation of aniline[18] and phenol.[19]

2. The rate of substitution of the first atom of bromine in the *ortho* isomer is always greater than in the *para* isomer. In the latter the bromine enters an *ortho* position; in the former, probably a *para* position. On the other hand, the rate for the second atom may be greater than that for the first, for a *para*, but in no case for an *ortho* compound. This statement is consistent with the previous one, since the second atom of bromine entering an *ortho* compound goes probably into an *ortho* position, and this is apparently an inherently slower process.

3. When each of the two groups attached to the ring tends to direct the entering group to the *ortho* or *para* position with respect to itself, the *meta* isomer has the highest first velocity constant; but when one of these groups is of those generally recognized as *meta*-controlling, the first constant for the *meta* isomer is lower than that for the *ortho* or *para*. This is to be expected, since for *meta* compounds in the former case the effects of the two groups are coöperative, whereas in the latter case they are opposed; and conversely with respect to substitution in the *ortho* or *para* isomers.

When both of the groups are amino or hydroxyl, the effect is still more marked; when they are *meta* to each other, the rate is very much enhanced, but when they are in the *para* position, the rate appears to be very slow, since both *p*-aminophenol and hydroquinone, under our conditions, are oxidized to quinoid form rather than brominated. The coöperative effect of hydroxyl groups in the *meta* position is shown also in the high velocity constants for phloroglucinol.

4. It is desirable to arrange the various substituents in the order of their directive influence. According to Holleman[20] and also Obermiller,[21]

[17] Chattaway and Orton, *Ber.*, **32**, 3573, 3635 (1899); *J. Chem. Soc.*, **75**, 1046 (1899); **77**, 134, 789, 797 (1900).

[18] Bamberger, *Ber.*, **28**, 401 (1895); **30**, 654, 1281, 2274 (1897).

[19] Baumann, *Ber.*, 9, 55, 1715 (1876); 11, 1907 (1878).

[20] Holleman, "Die direkte Einführung von Substituenten in den Benzolkern," Veit and Co., Leipzig, 1910, pp. 469–470.

[21] Obermiller, "Die Orientierenden Einflüsse und der Benzolkern," J. A. Borth, Leipzig, 1909, p. 58.

the arrangement is $OH > NH_2 > Cl > CH_3$ for o-p groups: but they are not in accord with regard to the order of the *meta*-controlling groups. Holleman considered it to be $COOH > SO_3H > NO_2$, and Obermiller $NO_2 > SO_3H$.

An analysis of Table XVI gives results in agreement with the above o-p list except that methyl and the halogens are not strictly comparable. For instance, the higher K_1 for m-bromo-aniline than for m-toluidine seems to indicate that bromine exceeds methyl because of the greater coöperative effect; but the lower value for p-toluidine than for p-bromo-aniline seems to show that methyl is the stronger because of its greater retarding effect. Closely related to this is the observation of Wibaut[22] that toluene is nitrated in preference to chlorobenzene in a mixture, though when methyl and chlorine are substituted in the same ring, the influence of the latter is greater.

For the *meta*-controlling groups an analysis of the K_1's gives the order $NO_2 > CHO > COOH > SO_3H$, agreeing with Obermiller rather than Holleman; but it is not unreasonable to assign some weight to the K_2's in order to compare aqueous bromination with other types of substitution, since the latter are brought much less readily to the di- or trisubstituted stage, and mononitration might be regarded as roughly equivalent to di-bromination.   If this be done, the nitro group becomes last, in agreement with Holleman.

The analysis of these rates brings out a number of questions which can be answered only when the appropriate compounds have been investigated, and extension of this work is now in progress.   For this reason, largely, further attempts to discuss our findings in relation to the views held by the various authors upon this complex subject will be postponed.

Summary

1.   A method is described by means of which the relative rate of the several successive steps in the bromination of certain aromatic amino and phenolic compounds in acid aqueous solution may be estimated by determining the weight of the highest brominated product precipitated by various proportions of bromine.

2.   A method is described of carrying out somewhat similar experiments, in which two compounds compete for insufficient amounts of bromine. From the results of such competitions, combined with the results of the partial bromination of each compound singly, the relative velocity of each step of bromination of the series of compounds may be estimated.

3.   In this way about 100 velocity constants of bromination were evaluated.   The relative accelerative (or retarding) effect of the presence of certain groups, as derived from these constants, is in general accord with

[22] Wibaut, *Rec. trav. chim.*, **34**, 241 (1915).

that given by previous authors, based upon other kinds of experimental work; and the data indicate that the so-called directive influence is less easy to specify than has by many been supposed. For instance, in an equimolal solution of aniline and phenol to which bromine in increasing quantities is added, the bromine goes almost wholly to the phenol until the latter has been converted to monobromophenol, then almost wholly to the aniline until the substance has been converted completely into tri-bromo-aniline, and finally to change the mono- into tribromophenol.

4. The rate of successive stages of bromination of amino and phenolic compounds is in harmony with the idea that in such cases there is inter-mediate substitution of bromine in the side chain.

NEW HAVEN, CONNECTICUT

SPECTROPHOTOMETRIC DETERMINATION OF HYDROGEN-ION CONCENTRATIONS AND OF THE APPARENT DISSOCIATION CONSTANTS OF INDICATORS IV. 1-NAPHTHOL-2-SODIUM SULFONATE INDOPHENOL[1]

BY WALTER C. HOLMES[2] AND EDWARD F. SNYDER[3]

The first paper of this series[4] included several representative absorption curves of 1-naphthol-2-sodium sulfonate indophenol in aqueous solutions of various Sörensen (P_H) values. Although this dye was primarily designed by Clark and Cohen[5] to serve as an oxidation-reduction indicator rather than as an acid-base indicator it is exceptionally suitable, in some respects, for the latter application in connection with spectrophotometric methods. The bands of both color forms occur in spectral regions in which the eye is relatively sensitive to variations in intensity. Any point of transition in the color change, accordingly, can be expressed by means of a ratio R_2 which defines the relative intensities of the two bands. A ratio of this type is sensitive to minimum variation in Sörensen value; furthermore, it is not affected by variation in indicator concentration, owing to its character and to the complete conformity to Beer's law shown by the indicator over a wide range in concentration in aqueous solutions.

Aqueous solutions of the dye are decidedly unstable. The rate of forma-

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[4] Holmes, THIS JOURNAL, 46, 627 (1924).

[5] Clark and Cohen, Pub. Health Repts., 38, 933–58 (1923).