we were emboldened to think that, nevertheless, there might be some parallelism in the very restricted type of case under discussion, particularly as the experiments showed that the *relative* rate was practically independent of concentration or temperature within a reasonable range of variation of conditions. The fact that the expectation based upon these assumptions is largely fulfilled is no proof of the validity of the assumptions, but it suggests further inquiries and we give it here in the belief that any indication may be valuable in a field in which so little is known definitely.

Summary

We have pointed out some seeming parallelisms between the melting temperature of a benzene derivative and the character of the radical, or radicals, present, particularly with respect to whether the directive influences assigned to these radicals are like or unlike. For example, when they are like, the *meta* isomer usually has the lower melting temperature; when unlike, the *ortho* melts lower.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 4]

STUDIES ON THE DIRECTIVE INFLUENCE OF SUBSTITUENTS IN THE BENZENE RING. VI

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In Part II[2] a method was described by which the relative rates of bromination of various aromatic amino and phenolic compounds were measured in aqueous solution. From the results attempts were made to estimate the directive influence of the substituents in these compounds. The present paper is a continuation of that investigation, applying the method to a much larger number of compounds and discussing the results more fully than was possible at that time.

In brief, the method consists in making competition experiments by adding to a mixture of two compounds an insufficient amount of a reagent which reacts with both, and by suitable analysis determining the extent of each reaction. When two organic compounds were competitors, the reagent was a standard bromide-bromate solution, which with acid generates bromine, and the analysis consisted usually in estimating gravimetrically the highest brominated product of one of the competitors. There was also a considerable number of competitions between organic compounds and inorganic reducing agents, which are oxidized by bromine. In these the reagent was free bromine water,[3] and the analysis was

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[2] Francis, Hill and Johnston, THIS JOURNAL, **47**, 2211 (1925).

[3] Francis, *ibid.*, **48**, 655 (1926).

a volumetric method for the unchanged reducing agent or its oxidation product.

The compounds used were all of the best grade obtainable, Eastman or Kahlbaum products, except for a few which were synthesized and purified for the purpose. The bromine titration was the principal criterion of purity.

In all, more than 1200 competition experiments were made. These were entirely similar to those already published,[4] and it seems impracticable to give them all in detail. By a combination of the results the relative velocity constants of bromination of all the compounds studied were estimated. These are presented in Table I, which is analogous to the one given previously,[5] but much longer, including 140 organic compounds. As before, slight adjustments in the observed ratios, averaging 15%, were necessary to make all the results consistent with one another. For convenience, the order is now alphabetical. K_1-aniline, which is of the order of 10^8, is taken as unity as a standard. K_1, K_2 and K_3 are the constants for the first, second and third substitutions (or in a few cases, additions or oxidations), respectively. The considerable changes in some of the values are not due to great inaccuracies in the previous work, since the changes in relative velocity of neighboring compounds are comparatively slight, but are due to better coördination of the several parts of the table, made possible by the inclusion of the additional compounds. For the most part, the change is merely a general compression of the upper part of the former table.

TABLE I

RELATIVE VELOCITY CONSTANTS OF BROMINATION

Referrred to K_1-aniline as unity

Compound	K_1	K_2	K_3
Acetanilide	0.13	..	..
Acetyl-*m*-aminophenol	16	?	?
Acetyl-*o*-toluidine	0.011	..	..
Acetyl-*p*-toluidine	.008	..	..
m-Amino-acetanilide	4	4[c]	4.5
p-Amino-acetophenone	11	21	..
m-Aminobenzoic acid	0.85	0.85	0.97
p-Aminobenzoic acid	6	11	.0002[b]
p-Aminobenzyl cyanide	0.3	0.6	..
m-Amino-dimethylaniline (3.5)[a]	.4	?	?
p-Amino-diphenylamine - *o* - sulfonic acid (2.6)[a]	89	?	..
m-Aminophenol	38	100	100
p-Aminophenylacetic acid	0.24	0.45	..
2-Aminotoluene-4-sulfonic acid	1.3	.3	..
2-Aminotoluene-5-sulfonic acid	2.7	.003[d]	..

[4] Ref. 2, pp. 2225–2227, and Ref. 3.

[5] Ref. 2, pp. 2228–2229.

TABLE I (*Continued*)

	Compound	K_1	K_2	K_3
	4-Aminotoluene-2-sulfonic acid	0.09	.17	..
	Aniline	1.00	1.00	1.13
	Anisole (1.5)[a]	0.5	..	..
	Anthranilic acid	23	5	0.0002[b]
	Arsanilic acid	2.5	2	?[b]
	Benzanilide	0.01	..	..
	Benzene-azophenol	.22	?	?
	Benzyl-aniline	15	15	15
	Bromo-acetanilide	0.008	..	..
	3-Bromo-4-aminotoluene	.95	..	..
A[d]	*o*-Bromo-aniline	5	1.1	..
	m-Bromo-aniline	3	3	3.5
B	*p*-Bromo-aniline	0.55	1.05	..
	o-Bromophenol	.36	0.03	..
	p-Bromophenol	.19	.03	..
	Carbanilide (2.5)[a]	1.3	?	..
C	*o*-Chloro-aniline	5	1.1	..
D	*m*-Chloro-aniline	3	3	3.5
E	*p*-Chloro-aniline	0.52	1	..
	o-Chlorophenol	.34	0.03	..
	m-Chlorophenol	5.5	.2	0.05
	p-Chlorophenol	0.19	.03	..
	Cinnamic acid (addition)	.03	..	..
	Cinnamic aldehyde (addition)	.014	..	..
	Cinnamyl alcohol (addition)	42	..	..
F	*o*-Cresol	46	.1	..
G	*m*-Cresol	100	4	0.05
H	*p*-Cresol	14	0.06	..
	o-Cresotinic acid	0.6	.04[b]	..
	m-Cresotinic acid	2.1	.1	?[b]
	p-Cresotinic acid	0.3	.02[b]	..
	2,4-Diamino-chlorobenzene	12	12	..
	2,4-Diaminotoluene	3	3	..
	2,4-Dibromo-aniline	1.05	..	..
	2,6-Dibromo-aniline	25	..	..
	2,4-Dichloro-aniline	1	..	..
	2,5-Dichloro-aniline	20	4.5	..
	3,5-Dichlorosalicylic acid	0.01[b]	..	..
	Diethyl-*m*-aminophenol	4	?	?
	Diethylaniline (4.5)[a]	0.13	0.02	?
	2,4-Dihydroxybenzaldehyde	15	15	0.02[b]
	2,4-Dihydroxybenzoic acid	77	77	.45[b]
	Dimethylaniline (2.8)[a]	0.8	?	?
	2,4-Dinitrophenol	.013	..	..
	Diphenylamine (4.0)[a]	400	20	0.001
	Diphenylguanidine	0.005	?	..
	Diphenyl-*m*-phenylenediamine (7)[a]	3000	3000	?
	Ethyl *m*-aminobenzoate	0.8	0.8	0.9
	Ethyl *p*-aminobenzoate	6	11	..
	Ethylaniline	0.8	0.8	.8

TABLE I (*Continued*)

	Compound	K_1	K_2	K_3
	Ethyl anthranilate	17	3.5	..
	Ethylmetanilic acid (1.5)[a]	0.25	..	..
	Ethyl salicylate	.02	?	..
	Ethyl-*o*-toluidine	1.3	0.3	..
	Ethyl-*p*-toluidine	0.27	.5	..
	Formanilide (1.5)[a]	.06	..	..
	Hydrazobenzene (2.6)[a]	13	?	..
	Hydroquinone (oxidation)	15	..	..
	p-Hydroxybenzaldehyde	0.09	0.002	0.001[b]
	m-Hydroxybenzoic acid	.28	.03	.01
	p-Hydroxybenzoic acid	.3	.03	.005[b]
	p-Iodo-aniline	.24	.45	..
I	Metanilic acid	.52	.52	0.6
	Methylaniline	2	2	2
	Methyl anthranilate	16	3.5	..
	Methylanthranilic acid	19	4	..
	Methyl cinnamate (addition)	0.002	..	..
	Methyl salicylate	.05	0.0001	..
	2-Nitro-5-aminocresol-4-methyl ether	56	..	..
	3-Nitro-4-aminotoluene	7	..	..
	4-Nitro-2-aminotoluene	0.7	?	..
	5-Nitro-2-aminotoluene	11.5	..	..
J	*o*-Nitro-aniline	25	0.04	..
K	*m*-Nitro-aniline	0.46	.46	0.2
L	*p*-Nitro-aniline	8	.05	..
	3-Nitro-*p*-cresol	0.02	..	..
	m-Nitromethylaniline	.24	?	?
	p-Nitromethylaniline	1.6	?	..
M	*o*-Nitrophenol	0.03	0.01	..
	m-Nitrophenol	.02	.02	0.03
N	*p*-Nitrophenol	.03	.13	..
	5-Nitrosalicylic acid	.0005	?[b]	..
	p-Nitrosophenol	.006	.01	..
	Orcinol	1000	60	60
	Orcinol monomethyl ether	200	?	?
	Oxanilic acid	0.15	..	..
	Phenacetin (2.7)[a]	.01	?	..
	m-Phenetidine	12	12	14
	Phenetole (1.5)[a]	.5	..	..
P	Phenol	21	0.19	0.03
	Phenol-3,4-disulfonic acid	0.03	.004	..
Q	*p*-Phenolsulfonic acid	.17	.06	..
	Phenylacetanilide	.01	..	..
R	*m*-Phenylenediamine	5.5	5.5	5.5
	Phenylglycine	6	6	6
	Phenylhydrazine (oxidation)	100	100	..
	Phenyl salicylate	0.02	?	..
	Phenylurea	4	0.1	..
	Phloroglucinol	6000	500	500
S	Resorcinol	150	150	11

TABLE I (*Concluded*)

	Compound	K_1	K_2	K_3
	Resorcinol dimethyl ether (2.3)[a]	92	2	..
	Resorcinol mono-ethyl ether	63	?	?
T	Resorcinol monomethyl ether	60	?	?
	Rosaniline (5)[a]	2.2	?	?
	Salicyl alcohol	7	0.06	0.002[b]
U	Salicyl aldehyde	0.15	.01	.0006[b]
	Salicyl anilide	.09	.03	..
V	Salicylic acid	.4	.03	0.005[b]
W	Sulfanilic acid	2.6	5	.003[b]
	Sulfosalicylic acid	0.07	?[b]	..
	Thiocarbanilide (5)[a]	.12	?	?
	Thiophenol (2.5)[a]	.11	?	?
	Thymol	54	1	..
X	*o*-Toluidine	1.5	0.33	..
Y	*m*-Toluidine	1.4	1.4	1.5
Z	*p*-Toluidine	0.17	0.32	..
	Triphenylguanidine	.002	..	..
	Vanillic acid	.12	0.01[b]	..
	Vanillin	.05	.00003[b]	..
	Vanillyl alcohol	.02	..	..
	1,2-Xylenol-4	38	2.0	..
	1,3-Xylenol-2	35	..	..
	1,3-Xylenol-4	36	..	..
	1,4-Xylenol-2	52	3	..
	1,2-Xylidine-4	0.18	0.34	..
	1,4-Xylidine-2	2.7	1	..
	m-Xylorcinol	800	..	..

[a] The number of equivalents of bromine in titration when this is not indicated by the number of velocity constants.

[b] This constant is that for the displacement of a group by bromine.

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

[d] Capital letters are for reference from Table II.

It has been shown previously[3] that the observed ratios are practically independent of concentration, and of temperature, and probably of catalysts, but that they vary greatly with changes in the alcohol or acid concentration, the competitor which is brought nearer to saturation by the change in medium being favored in the competition for bromine. For this reason a comparison between the velocity constants of phenols and amino compounds is of little significance, since they are affected so differently by the acid medium, which was unavoidable. Certain compounds also, such as 2,6-dibromo-aniline and diphenylamine, seem to have abnormally high constants, probably because of their difficult solubility.[6] But fortunately, most of the desired comparisons are between similar compounds, and the velocity constants as given, were derived from experiments under practically identical conditions so that their ratios are significant.

[6] Ref. 3, p. 633.

With the exceptions noted by figures in parentheses after the names, all of the compounds on the list under suitable conditions can be titrated quantitatively with bromine, the number of equivalents consumed being indicated by the number of velocity constants. This furnishes a valuable method for estimation of some of the compounds, especially for analysis of mixtures of isomers which consume different amounts of bromine. The number of equivalents of bromine agrees in all cases with that predicted by the theory, that is, the number of positions *ortho* and *para* to an amino or hydroxyl group not already filled. But some groups, —COOH, —SO_3H, —CHO, —CH_2OH,[7] can be displaced by bromine. By controlling the conditions, compounds containing these groups in *ortho* or *para* positions can be titrated to either end-point, that is either with or without displacement of the group.[8]

A considerable number of other compounds were tried but found unsatisfactory either for titration or for competition experiments. These include most of those which have two hydroxyl or amino groups or derivatives of them *ortho* or *para* to each other, and so are oxidized to quinoid forms instead of being substituted in the ring. Hydroquinone is oxidized to quinone reversibly, provided bromine is not in too great excess, and shows no net consumption of bromine.[9] It seems to have a definite rate of oxidation, and accordingly is included in the table. It is, in fact, a very useful competitor, since the amount of quinone formed can be estimated very easily by adding potassium iodide, and titrating with thiosulfate the iodine produced by oxidation of the hydriodic acid. This gives consistent results with phenolic compounds, but not with amino compounds. The latter seem to have some interaction with the quinone. The following are oxidized irreversibly and not quantitatively.

Pyrocatechol	2,4,6-Triaminophenol	*o*- and *p*-Phenylenediamines
Pyrogallol	*p*-Phenetidine	2,5-Dihydroxybenzoic acid
Oxyhydroquinone	Aminothymol	2-Amino-4,6-dinitrophenol
o- and *p*-Aminophenols	5-Aminosalicylic acid	Methyl-*p*-amino-*m*-cresol
2,4-Diaminophenol	*p*-Amino-acetanilide	Diamino-oxydiphenyl
	Dimethyl-*p*-phenylenediamine	

The following show no consumption of bromine when titrated in the ordinary way.

o- and *p*-Nitro-acetanilides	Cyananilide	Oxanilide
Nitrophenacetin	*o*-Cresyl-*p*-toluenesulfonate	Oxal-*p*-toluidic acid
		Methyl-acetanilide

No compound without an amino or hydroxyl group, or a derivative of them, or a double bond could be titrated with bromine even when, as in *m*-xylene,

[7] In the case of salicyl alcohol it has been shown that the by-product is formaldehyde. Apparently bromomethanol, $BrCH_2OH$, is first formed, but decomposes spontaneously to formaldehyde and hydrobromic acid.

[8] Francis and Hill, THIS JOURNAL, **46**, 2498 (1924).

[9] Ref. 8, p. 2502.

m-chlorotoluene and *m*-dichlorobenzene, two directive groups are in co-operation.

The following give indefinite oxidation products, and so are unsatisfactory for rate comparisons.

1,3-Xylidine-4	α- and β-Naphthols	*p*-Nitroso-ethylaniline
Benzidine	α- and β-Naphthylamines	β-Phenylhydroxylamine
o-Tolidine	*p*-Amino-azobenzene	Acetylphenylhydrazine

p-Iodophenol, 2,4-dinitro-aniline, and 2,4-dinitromethylaniline are too difficultly soluble in aqueous solution for satisfactory experiments. Benzalaniline and acetylsalicylic acid are probably not brominated as such but, on hydrolysis the former in water and the latter in dilute alkali, the resulting aniline and salicylic acid are brominated as usual.

Discussion of Results

1. The conclusions of the former papers,[10] are confirmed except that in some systems containing two substituents alike in their directive influence, the *ortho* isomer exceeds the *meta* slightly in rate of bromination, namely, in the toluidines, the chloro-anilines and the bromo-anilines. This is contrary to expectation since the influence of the two groups should be co-operative in the *meta* isomer and opposing in the *ortho*. No reason is apparent, unless it be the fact that in the *meta* isomer substitution of two equivalents of bromine is simultaneous, and the directive influence is divided, while in the *ortho* isomer it is concentrated upon one position.

2. When one hydrogen atom of an amino group is substituted by an alkyl group, as in methyl and ethyl aniline and also in benzyl-aniline and phenylglycine, the titration is still quantitative, and there is little change in the rate of bromination. When both hydrogen atoms of an amino group, or the one in an hydroxyl group are substituted, as in diethylaniline, dimethylaniline, anisole, and phenetole, and also in resorcinol dimethyl ether, the titration is no longer quantitative (unless there be another strongly directive group, as in diethyl-*m*-aminophenol), and the rate is greatly decreased.

When the amino group is acylated, it is so weakened that usually only one equivalent of bromine is consumed when titrated in the ordinary way. Thus acetanilide can be titrated quantitatively, the product being *p*-bromo-acetanilide. This is not necessarily inconsistent with the trichlorination of acetanilide by Chattaway and Orton,[11] since they allowed much more time for the second and third substitutions. The presence of another acidic group in the molecule, bromine or nitro group, prevents even this substitution, as in *o*- and *p*-nitro-acetanilides. The effect is not simply a blocking of the *para* position, since acetyl-*p*-toluidine consumes one equivalent of bromine. Acetyl *o*-toluidine, bromo-acetanilide, phenylacetanilide,

[10] (a) Ref. 2 and (b) Francis, THIS JOURNAL, **47**, 2588 (1925).

[11] Chattaway and Orton, *Ber.*, **32**, 3573 (1899).

benzanilide and oxanilic acid also fall in this class. Formanilide takes a little more than one equivalent of bromine. In phenylurea the effect of the —$CONH_2$ group is intermediate between that of an alphyl and an acyl group, two equivalents being consumed, the second much more slowly than the first.

When the second amino hydrogen is lacking, as in methylacetanilide, there is no bromination. This is true also of phenols in which the hydroxyl hydrogen is substituted by an acid group, as in acetyl-salicylic acid and *o*-cresyl-*p*-toluenesulfonate. Holleman has made a similar observation regarding the great decrease in directive influence of the phenolic hydroxyl group on esterification.[12]

All the observations of this section support the idea previously advanced,[13] that bromination in aqueous solution involves the intermediate substitution in the directive group. This is further favored by the fact that resorcinol, orcinol, 2,4-dihydroxybenzoic acid, and 2,4-dihydroxybenzaldehyde, which have two hydroxyl groups *meta* to each other, seem to have two simultaneous substitutions. This is true also of aniline and all (13) of the *m*-amino compounds.[10b] That is, the number of simultaneous substitutions is frequently equal to, but never exceeds the number of hydrogen atoms in the directive groups.

3. The directive influences of several substituents in the same ring are usually cumulative.[14] This is indicated by the fact that 5-nitro-2-aminotoluene, for example, has a constant of 11.5, which is nearly the product of those of *p*-nitro-aniline, 8, and *o*-toluidine, 1.5, from which it is derived. In other words an *ortho*-methyl group increases the constant of *p*-nitro-aniline nearly 50%, just as it does that of aniline itself. Similarly, the constant of *m*-cresotinic acid can be calculated by multiplying together those of *m*-cresol and salicylic acid, and dividing by that of phenol. All of the examples (32) where such calculations should be possible are given in Table II. All but nine of these agree as well as could be expected from such experiments. The discrepancies in the other cases are due to some effects as yet unexplained. These observations are closely related to those of a former paper,[10b] namely, that the several velocity constants of a system of isomeric amino compounds have ratios which are independent of the other substituents, and depend only upon the type of compound, *ortho*, *meta*, or *para*.

4. Chlorine and bromine seem to have identical directive influences[15] as shown by the agreement of velocity constants of the bromo-anilines, 2,4-dibromo-aniline, and *o*- and *p*-bromophenols with those of the corre-

[12] Holleman, *Chem. Rev.*, **1**, 211 (1924).

[13] Ref. 2, p. 2230; Ref. 8, p. 2502.

[14] Compare Ref. 12, pp. 206–207.

[15] Compare Holleman, *Rec. trav. chim.*, **34**, 204 (1915).

TABLE II

CUMULATIVE EFFECT OF DIRECTIVE INFLUENCE OF SUBSTITUENTS

Compound	Calcd. from[a]	K_1 Calcd.	K_1 Obs.
2-Aminotoluene-4-sulfonic acid	IX	0.78	1.3
2-Aminotoluene-5-sulfonic acid	WX	3.9	2.8
4-Aminotoluene-2-sulfonic acid	IZ	0.09	0.09
3-Bromo-4-aminotoluene	AZ	.85	.95
o-Cresotinic acid	FV/P	.87	.6
m-Cresotinic acid	GV/P	1.9	2.1
p-Cresotinic acid	HV/P	0.27	0.3
2,4-Diamino-chlorobenzene	$R\sqrt{CE}$	8.9	12
2,4-Diaminotoluene	$R\sqrt{XZ}$	2.8	3
2,6-Dibromo-aniline	A^2	25	25
2,5-Dichloro-aniline	CD	15	20
5-Nitro-2-aminotoluene	LX	12	11.5
3-Nitro-4-aminotoluene	JZ	4.25	7
4-Nitro-2-aminotoluene	KX	0.7	0.7
3-Nitro-*p*-cresol	HM/P	.02	.02
5-Nitrosalicylic acid	NV/P	.0006	.0005
Orcinol	GS/P	700	1000
Orcinol monomethyl ether	GT/P	286	200
1,2-Xylenol-4	GH/P	67	38
1,3-Xylenol-4	FH/P	31	36
1,2-Xylidine-4	YZ	0.24	0.17
1,4-Xylidine-2	XY	2.1	2.7
m-Xylorcinol	SF^2/P^2	700	800
2,4-Dibromo-aniline	AB	2.75	1.05
2,4-Dichloro-aniline	CE	2.6	1.0
2,4-Dihydroxybenzaldehyde	SU/P	1	15
2,4-Dihydroxybenzoic acid	SV/P	3	160
2,4-Dinitrophenol	MN/P	0.00004	0.013
Phloroglucinol	S^3/P	1070	6000
Sulfosalicylic acid	QV/P	0.0032	0.07
1,3-Xylenol-2	F^2/P	101	35
1,4-Xylenol-2	FG/P	220	52

[a] Letters show the method of calculation from the first velocity constants of the indicated compounds in Table I.

sponding chlorine derivatives. Iodine is apparently different in influence judging from the only derivative available, *p*-iodo-aniline, which has a much lower constant than *p*-bromo-aniline.

5. In considering the *ortho* and *meta* isomers of the system, $C_6H_4(X)$-OH, bromination should be accelerated in one case as compared with phenol, and retarded in the other, depending upon the directive influence of X. If the relative acceleration in one case were equal to the relative retardation in the other, as might be expected, the geometric mean of the first constants of the two isomers should be equal to the first constant of phenol. Similarly, K_1-aniline should be the geometric mean of the first

constants of the *ortho* and *meta* isomers of any system of amino compounds. This is not the case, the cresols being all very high and the nitrophenols and hydroxybenzoic acids very low in velocity of bromination. These discrepancies seem to be coördinated best by assigning to each substituent a *general* influence, affecting all the isomers of a system in the same direction, and a *special* influence corresponding to "directive influence," distinguishing the isomers. The general influence is defined as the ratio of the geometric mean of the first constants of the *ortho* and *meta* compounds to that of phenol (or aniline). The special influence is defined as the ratio of this mean to the first constant of the *ortho* compound. That of the *para* compound is not included in these calculations because it might give undue weight to the *ortho-para* combination as opposed to the *meta*. These influences are summarized in Table III.

TABLE III

DIRECTIVE INFLUENCE OF SUBSTITUENTS IN THE BENZENE RING

(Effect upon first velocity constant of bromination)

Substituent	Amino compounds		Phenolic compounds	
	General	Special	General	Special
NO_2	3.4	0.14	0.0012	0.8
$COOC_2H_5$	3.7	0.22	.001	..
CHO	...	..	.005[a]	.73[a]
COOH	4.4	.19	.016	.84
SO_3H	2.2[a]	.24[a]	..	..
Br	3.9	.78	..	..
Cl	3.9	.78	.065	4.0
CH_3	1.45	.97	3.2	1.5

[a] For purposes of comparison, the first constants of *o*-aminobenzenesulfonic acid and *m*-hydroxybenzaldehyde, which were not available, were estimated from their isomers and by analogy with other systems, as 9 and 0.08, respectively.

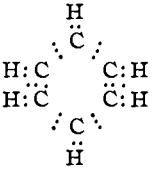
The distinction between *meta* and *ortho-para* orienting groups appears in the great difference in value for the special influence. The method is somewhat arbitrary, but at least it gives *numerical* values corresponding roughly with directive influence which, so far as the author is aware, has not been done before in so comprehensive a manner. As shown previously,[16] the influences are in substantial accord with those given qualitatively by previous authors.

In phenolic compounds the general effect is a retardation for acidic[17] groups, and an acceleration for methyl. In amino compounds it is always an acceleration, and is in nearly the reverse order to that upon phenolic compounds. With regard to the influence of bromine, this effect appears also in the occasionally greater values of K_2 than K_1, or K_3 than K_2, since the special or directive influence of bromine would always oppose further substitution.

[16] Ref. 2, p. 2231.

[17] That is, substituents which increase the acidity of phenols, regardless of directive influence.

The observations of this series of papers seem in general consistent with Flürscheim's formulas;[18] but his "strong" and "weak" bonds can be represented better by a simple assumption of G. N. Lewis[19] that completely non-polar bonds are due to the sharing of a pair of electrons, and that as a bond becomes more polar, the pair of electrons shifts toward the less positive constituent. Thus in benzene derivatives a substituent can be assumed to displace the pair of electrons, which it shares with a carbon atom of the ring, in a manner characteristic of itself. This shift produces an effect upon the carbon atom which causes another shift in the electrons shared by it with its adjacent carbon atoms. Since each bond of the ring consists probably of *three* electrons instead of two, these shifts may be very complex, that is, the three electrons may not all shift together, and two or more types of influence may be superimposed upon each other. Thus,



the influences may be transmitted around the ring, in both directions, either undiminished or with gradually decreasing intensity, to nuclear hydrogen atoms, or through a nitrogen or oxygen atom to the hydrogen atoms of the controlling group. Two or more substituents probably would have a cumulative effect. The data are inadequate to permit a decision as to just what these shifts are, but the mechanism seems to have unlimited possibilities for accounting for the numerous observations of physical and chemical properties of aromatic compounds.

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Summary

1. By means of competition experiments 264 velocity constants of bromination for 140 aromatic organic compounds in aqueous solution have been estimated. Most of these compounds can be titrated quantitatively with a standard bromide-bromate solution. About 45 similar compounds were tested and found unsatisfactory either for titration or for competition experiments.

[18] Flürscheim, *J. prakt. Chem.*, **66**, 321 (1902); **71**, 497 (1905); *Ber.*, **39**, 2015 (1906).

[19] Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Co., New York, **1923**, p. 83.

[20] Francis, THIS JOURNAL, **47**, 2340 (1925).

2. The relative rate of successive stages of bromination of amino and phenolic compounds is in harmony with the idea that in such cases there is intermediate substitution of bromine in the side chain.

3. The directive influences of several substituents in the same ring are usually cumulative.

4. Chlorine and bromine seem to have exactly the same directive influence.

5. A method has been devised for estimating numerical values for directive influences. Another effect, called "general influence," has been found, by which a substituent may accelerate or retard the rate of substitution regardless of its position. This seems to be related to its effect upon the acidity of compounds, or the so-called "negative nature of atomic groups," and is not parallel with directive influence.

6. By application of the electron conception of valence, a structure has been devised for the benzene ring, sufficiently complex to account for the phenomena of substitution.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

THE BASE STRENGTH OF ALPHA-ALKOXYL AMINES. THE EFFECT OF OXYGEN ON THE BASICITY OF AMINES

BY T. D. STEWART AND J. G. ASTON

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A number of amino ethers of the type $(R_2N—CH_2)OR'$ have been prepared by McLeod and Robinson[1] using the reaction $H_2CO + R_2NH + R'OH \longrightarrow R_2N—CH_2—OR' + H_2O$. These compounds are simply tertiary amines containing no unsaturated (ethylenic or carbonyl) groups, and are unusual only in having an oxygen and a nitrogen atom attached to the same carbon atom. Compounds of a similar nature are found among the heterocyclic ring compounds. The aldehyde ammonias, if not polymerized, would have a similar structure. Robinson and Robinson[2] term the compounds pseudo bases and represent them by the structure $R_2N{=}CH_2...OR$, where the dotted line "symbolizes a partial intramolecular electrovalency connecting the nitrogen and oxygen atoms." This is done to account for the rapid reaction toward the Grignard reagent in which the alkoxyl group (OR) is replaced by an alkyl group (R), and the rapid hydrolysis in acid which results in formaldehyde and a diethylamine salt. They discard the possibility that any appreciable amount of the base can exist in the quaternary form $[R_2N{=}CH_2]^+ OR^-$ because it may be distilled without decomposition. Such a compound would be analogous to an alkyl pyridinium base and, therefore, a very strong base.

[1] McLeod and Robinson, *J. Chem. Soc.*, **119**, 1470 (1921).

[2] Robinson and Robinson, *ibid.*, **123**, 523 (1923).