

DIRECTIVE INFLUENCE IN THE BENZENE RING

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An admirable review² by A. F. Holleman appeared two years ago upon the subject, "Some Factors Influencing Substitution in the Benzene Ring." The scope of the present paper is somewhat more limited. It is the intention to avoid unnecessary repetition and to discuss the subject from slightly different view points. The older theories, which are considered in all organic text books, will not be discussed except as related to more recent publications.

The term "directive influence" will be used to indicate the effect which a substituent already present in benzene exerts upon the position assumed by an entering group. The orienting effects of other factors such as temperature, solvent, catalysts, and the identity of the entering group are usually comparatively slight, except as steric influences are involved. They have been discussed adequately in Holleman's paper, and will not be considered here.

It is generally agreed that directive influence is a manifestation of the *relative* rates of substitution in the several available positions of a benzene nucleus. It is for this reason that conditions external to the molecule usually have little effect, since they are likely to influence the speed of each reaction to nearly the same extent. Indeed this idea has been extended to directive influence itself³ for certain types of substitution. But the relative rates themselves must be due to some strained condition in the molecule. I agree with Holleman that a study of the

¹ The author's own research in this field was conducted partly as a graduate student at Yale University, and partly as a National Research Fellow at the Massachusetts Institute of Technology.

² Holleman, *This Journal* **1**, 187-230 (1924).

³ Francis, *J. Am. Chem. Soc.* **47**, 2588 (1925).

rates of these reactions is the best method of attack; but disagree with him in his rejection⁴ of such ideas as the strength of Flürscheim's bonds⁵ on the basis that they are vague ideas incapable of measurement. The reaction velocities appear to be the most accurate means of determining the relative strength of these bonds.

FUNDAMENTAL CHARACTER OF DIRECTIVE INFLUENCE

It has been asserted that directive influence is a phenomenon which *merely* concerns rates of reaction. In support of this Lewis has stated, "There is no evidence at present that the compound produced (under the influence of an *ortho* orienting group) is any more stable than one which would be produced by the corresponding substitution in the *meta*."⁶ He is undoubtedly correct, since, using stability in a thermodynamic sense, the most stable isomer, that is, the one with the least free energy, cannot have been produced in *both* of the following two reactions: If nitrobenzene is chlorinated, the product is mainly *m*-nitrochlorobenzene; while the nitration of chlorobenzene gives chiefly the *para* isomer. Furthermore, in no case is there a true equilibrium between the isomers.

There is some evidence, however, that directive influence is not a phenomenon which is displayed only at the moment of reaction. It seems likely that in most cases the least reactive isomer is formed most rapidly, provided the question of reactivity be limited to the lability of the substituent which has just entered. This is evidently true in the chlorination of nitrobenzene, since *o*- and *p*-nitrochlorobenzenes are readily hydrolyzed to the corresponding nitrophenols, while the *meta* isomer resists hydrolysis. In the nitration of chlorobenzene the issue is the lability of the nitro group; and though there is no direct evidence, the data which follow make it probable that it would be displaced more readily from *m*-nitrochlorobenzene than from the *ortho* and *para* isomers.

⁴ Holleman, *J. prakt. Chem.* **74**, 157 (1906).

⁵ Flürscheim, *ibid.* **66**, 321 (1902); **71**, 497 (1905); *Ber.* **39**, 2015 (1906).

⁶ Lewis, Valence and the Structure of Atoms and Molecules. The Chemical Catalog Co. 1923. p. 146.

Fortunately there is an abundance of material upon the reactivity of $-\text{NO}_2$ or $-\text{Cl}$ in the higher derivatives of benzene, using sodium methylate as a reagent. *m*-Dichlorobenzene, for example, is hydrolyzed more readily than its isomers.⁷ The other results are summarized in table 1. The number of the substituent displaced by $-\text{OCH}_3$ is printed in bold type.

TABLE 1
Displacement of substituents with sodium methylate

Trichlorobenzenes ¹	1 2 3 ; 1 2 4; 1 3 5
Tetrachlorobenzenes ²	1 2 3 4 ; 1 2 3 5; 1 2 4 5
Pentachlorobenzene ²	1 2 3 4 5
Nitrodichlorobenzenes ³ ($-\text{NO}_2 = 1$).....	1 2 3 ; 1 2 4 ; 1 2 5; 1 2 6; 1 3 4; 1 3 5
Nitrotrichlorobenzenes ⁴ ($-\text{NO}_2 = 1$).....	1 2 3 4 ; 1 2 3 5; 1 2 3 6; 1 2 4 5; 1 2 4 6; 1 3 4 5
Chlorodinitrobenzenes ³ ($-\text{Cl} = 1$).....	1 2 3 ; 1 2 4; 1 2 5; 1 2 6; 1 3 4; 1 3 5
Chlorotrinitrobenzenes ⁵ ($-\text{Cl} = 1$).....	1 2 3 4 ; 1 2 3 5; 1 2 3 6 (unknown); 1 2 4 5; 1 2 4 6; 1 3 4 5
Dinitrodichlorobenzenes ⁶ (First two numbers = $-\text{NO}_2$).....	1 2 3 4 ; 1 2 3 5; 1 2 3 6; 1 2 4 5; 1 3 2 4; 1 3 2 5; 1 3 4 5; 1 3 4 6; 1 4 2 3; 1 4 2 5; 1 4 2 6
Dinitrotoluenes ⁷ ($-\text{Me} = 1$).....	1 2 3 ; 1 3 4 ; 1 2 5

¹ Holleman, *Rec. trav. chim.* **37**, 195 (1918).

² Holleman, *ibid.* **39**, 736 (1920).

³ Holleman, *ibid.* **35**, 1 (1916).

⁴ Holleman and Hoeften, *ibid.* **40**, 67 (1921).

⁵ van de Vliet, *ibid.* **43**, 606 (1924).

⁶ Holleman, *ibid.* **39**, 435 (1920).

⁷ Kerner and Parkin, *J. Chem. Soc.* **117**, 852 (1920).

In general that substituent is labile which is most out of position with respect to the directive influence of the other substituents, the influence of $-\text{NO}_2$ for this generalization being greater than that of $-\text{Cl}$. In fact Obermiller⁸ used this phenomenon as a test of directive influence, and so concluded that $-\text{NO}_2$ possesses greater power of orientation than $-\text{OH}$. This

⁷ Holleman, *Rec. trav. chim.* **35**, 1 (1916).

⁸ Obermiller, *J. prakt. Chem.* **89**, 70 (1914); *Z. angew. Chem.* **27**, 37 (1914).

cannot be true since in *m*-nitrophenol further substitution is always in the 2, 4, and 6 positions under the influence of $-OH$, and never in 5, where the nitro group would tend to place it. The above relation in the nitrochlorobenzenes holds also in a quantitative sense, rates of displacement of groups, as determined by Holleman⁹ depending upon the same factors. The relation was pointed out by Kerner and Parkin,¹⁰ and by Fraser and Humphries¹¹ who stated, "A group which causes *substitution* in the *meta* position will favor *replacement* in the *ortho-para* positions, and conversely." They also gave a mechanism for the displacement, which explains some of the exceptions.

Evidence for the fundamental character of directive influence is found also in a recent paper¹² in which there have been pointed out approximate relations of directive influence with melting temperatures and heats of fusion of isomeric derivatives of benzene. According to this, the *meta* isomer has the *lowest* entropy of fusion (heat of fusion divided by the absolute melting temperature) when the two groups are like in their directive influence, and the highest when they are unlike. Similarly in most of the commoner systems the *meta* isomer has the lowest melting temperature when the groups are like, and the *ortho* isomer has the lowest when they are unlike. These observations were made reasonable by the following considerations which, it is admitted, do not constitute a rigorous train of reasoning. When the two groups are like in their influence, there is coöperation between them in favoring further substitution in the *meta* isomer, and opposition in the *ortho* and *para* isomers. When they are unlike, the case is reversed, and the *ortho* isomer is the most reactive. It is thus not illogical to suppose that the most reactive isomer is the one most easily melted,¹³ that is, it is the one that has the lowest melting temperature and the lowest entropy of fusion. The implication is that in reactions suffi-

⁹ Holleman, *Rec. trav. chim.* **42**, 373-9 (1923).

¹⁰ Kerner and Parkin, *J. Chem. Soc.* **117**, 852 (1920).

¹¹ Fraser and Humphries, *Chem. News* **126**, 258 (1923).

¹² Francis, Andrews, and Johnston, *J. Am. Chem. Soc.* **48**, 1624 (1926).

¹³ The original (p. 1630) must be consulted for an explanation of this statement.

ciently similar, there is some parallelism between the rate of reaction and the change of free energy. This is supported by the comparative constancy of directive influence (Holleman's "conservation of the substitution type"¹²) under wide variations of external conditions. Prins has stated,¹⁴ "We are convinced that at least for analogous reactions the velocity is determined by the atom energy."

The melting temperature relation was observed also by Pastak,¹⁵ but he discussed it in quite a different manner. He considered that the *meta* position was "normal" for like substituents and the *ortho* and *para* positions normal for unlike groups. This is logical for the products of nitration, but for halogenation the reverse would be expected. His "normal" isomers are the more reactive ones, and therefore, *less* stable rather than "more stable."

DISTINCTION BETWEEN ORTHO-PARA AND META ORIENTING GROUPS

The several rules which have been proposed for classifying the substituents according to directive influence, namely those of Hübner, Nölting, Körner, Armstrong, Brown and Gibson, and Vorländer, are well known, and have been discussed by Holleman. None of them holds for more than four-fifths of the known cases. But some recent contributions deserve attention.

Miss Hoffert¹⁶ observed that if the numbers of valence electrons of all the atoms of a substituent be added together, the sum is one less than a multiple of eight for *ortho-para* controlling groups, which are therefore negative, and one more than a multiple of eight for *meta* directing or positive groups. Thus the sum is 7 for the halogens, -OH, -NH₂, -CH₃, 15 for -CNS, -CNO, and 23 for -CH₂COOH, -NHCOCH₃; and it is 9 for -CN, 17 for -COOH, -NO₂, -COCH₃ and 25 for -SO₃H and CCl₃. In -CH=CHCOOH four electrons are shared in the double bond and should be subtracted, making the sum 23 in-

¹⁴ Prins, *Rec. trav. chim.* **44**, 169 (1925).

¹⁵ Pastak, *J. chim. phys.* **22**, 48, 264 (1925).

¹⁶ Hoffert, *J. Soc. Chem. Ind.* **42**, 348 (1923).

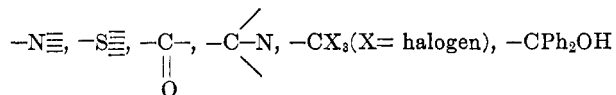
stead of 27, so that it is *ortho-para* directing. Other groups as $-\text{CHO}$ with 11, and $-\text{CH}_2\text{Cl}$, $-\text{CH}_2\text{OH}$, and $-\text{OCH}_3$ with 13 valence electrons each, have intermediate values and should give mixed derivatives.

Unfortunately there are exceptions to this ingenious rule. $-\text{OCH}_3$ is really a very strong *ortho-para* directing group; and according to the rule, $-\text{COOMe}$ should be an *ortho-para*, and butyl and $-\text{OPr}$ *meta* directing groups, whereas actually the reverse is true. Moreover, not four but two units should be subtracted for a double bond, because although two electrons are shared in a single bond, the rule does not call for a corresponding subtraction of two units. If a carbon-carbon double bond should receive exceptional treatment, so should other double bonds as in $-\text{NO}_2$ or $-\text{COOH}$.

Olivier¹⁷ has shown a parallelism between directive influence and ease of hydrolysis of benzyl chlorides. He stated that if the *para* isomer of $\text{XC}_6\text{H}_4\text{CH}_2\text{Cl}$ is most easily hydrolyzed, X is an *ortho-para* directing group; while if the *meta* isomer is most readily hydrolyzed, it is a *meta* directing group. This rule is most interesting from a theoretical standpoint as well as in ascertaining directive influence. It would be of great importance to know if any exceptions can be found. The work of Norris and his students upon derivatives of diphenylchloromethane¹⁸ is in substantial agreement with Olivier's results. Olivier's observations will be discussed later.

I have classified the groups empirically as follows:

Meta directing groups:



Ortho-Para directing groups:

Halogens, $-\text{N}=\text{}$, $-\text{O}-$, $-\text{S}-$, $-\text{C}\equiv$ (except those included in the *meta* category)

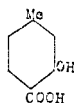
¹⁷ Olivier, *Rec. trav. chim.* **42**, 775 (1923).

¹⁸ Norris, Private communication.

in which the left hand valence is attached directly to a benzene ring, and the right hand valences to any atom or atoms. I know of no exceptions.

CUMULATIVE EFFECT OF TWO OR MORE SUBSTITUENTS

Holleman has given an extended discussion² of the combined effect of two or more groups upon further substitution. Indeed this has been involved in the bulk of his voluminous researches. It is generally agreed that each substituent continues to exercise its own peculiar influence, but just how the combined effect should be calculated is not so clear. Holleman has devised two methods, the *product rule* and the *sum rule*, both of which are useful, though somewhat empirical, and not altogether satisfactory. In my own research I have shown the cumulative effect of substituents in a different manner,¹⁹ by estimating the rate of bromination in aqueous solution of higher benzene derivatives, such as *m*-cresotinic acid.



This is a derivative of *m*-cresol, and also of salicylic acid. By multiplying together the velocity constants of bromination of these two, 100 and 0.4 (compared to aniline as unity), and dividing by that of phenol, 21 (so as not to count the effect of $-OH$ twice), the value 1.9 was obtained. The observed value was 2.1, which is within experimental error. Similarly 2,6-dibromo-aniline has a constant, 25, which is the square of that of *o*-bromoaniline, 5. It must be admitted that the agreement is not always so good.

ANALYTICAL METHODS

Any study of the positions assumed by substituents presupposes an accurate analytical method for the resulting mixtures of

¹⁹ Francis, *J. Am. Chem. Soc.* **48**, 1631 (1926).

isomers. Obviously no analysis for a single element would be of any use for this purpose. This does not mean, however, that there are no chemical methods which will avail. Selective displacement of groups²⁰ has been used in special cases to distinguish between isomers; and the analysis of mixtures of the xylenes is best accomplished by selective sulfonation.²¹ Dimroth has employed the fact that hydrazine hydrate reacts with *o*- and *p*-nitrobromobenzenes but not with the *meta* isomer.²² Presumably this differentiation would apply to the other nitrohalogenbenzenes.

The most general chemical method is that of aqueous bromination.²³ This applies to practically all phenols and amino and nitro compounds, which include a majority of the derivatives of practical importance. The method depends upon the fact that all positions *ortho* or *para* to an $-NH_2$ or $-OH$ group, and not already filled, are substituted by bromine. Thus a *meta* compound requires three equivalents of bromine, while an *ortho* or *para* isomer requires only two, one of the positions being already filled. Nitro compounds are first reduced quantitatively to the corresponding amino compounds with a definite amount of standard titanous chloride, and then titrated in the same solution with bromide-bromate reagent. The method does not distinguish between *ortho* and *para* isomers, but in studying directive influence this distinction is not usually so important as that of the *meta* from the *ortho* and *para* compounds; and if a complete ternary analysis is required, a combination of methods is most efficient, since the *para* isomer is usually the one most easily estimated by physical means. The bromination method does not require the extensive preliminary research upon each system of isomers which is involved in other analytical methods. A sample of 0.1 gram is sufficient for a determination, and the substance need not be free from foreign impurities. It is also

²⁰ Table I, Holleman, *Rec. trav. chim.* **23**, 253 (1904); **24**, 143 (1905); Wagner, *Ber.* **7**, 76 (1874).

²¹ Levinstein, *J. Soc. Chem. Ind.* **3**, 77 (1884).

²² Dimroth, *Ann.* **446**, 148 (1925).

²³ Francis and Hill, *J. Am. Chem. Soc.* **46**, 2498 (1924).

frequently applicable to the higher derivatives of benzene, which may require three, two, one, or no equivalents of bromine. An analysis can be completed in from ten to thirty minutes.

Mixtures of isomeric derivatives of benzene have usually been analyzed by physical means, of which the favorite is that employing freezing curves.²⁴ Isomers usually form ideal solutions with each other so that the freezing point of one isomer is depressed the same amount by equal percentages of either of the other two. This facilitates the construction of the ternary freezing diagram. After the isomer which crystallizes first from the melt has been identified, the crystallization temperature, corrected for supercooling, gives at once the percentage of that isomer. Another isomer is estimated by adding to the mixture a sufficient amount of that one to cause it to crystallize first. The operation is tedious and the effect of foreign impurities, even water, is difficult to estimate. These impurities cannot easily be removed without changing the relative amounts of the isomers. Moreover, the method is not as general as is commonly supposed, since the isomers of some systems, for example, the cresols, form compounds with each other. The technique has been improved recently by Johnston and his students.²⁵

Other physical methods which have been used are those depending upon differences in solubility,²⁶ critical solution temperature,²⁷ and density²⁸ of the isomers. A method employing absorption spectra²⁹ has been proposed for this differentiation.

METHODS OF STUDY

A complete understanding of the subject will be attained only by the proper interpretation of an enormous mass of experimental

²⁴ Holleman and others, *Rec. trav. chim.* **28**, 411 (1909); **30**, 55, 365 (1911); **31**, 244 (1912); **33**, 1 (1914); *Ber.* **44**, 704 (1911).

²⁵ Johnston, Kohman, and Andrews, *J. Phys. Chem.* **29**, 882, 914, 1041, 1048, 1317 (1925).

²⁶ Holleman and others, *Rec. trav. chim.* **18**, 267 (1899); **19**, 89, 367 (1900); *Z. physik. Chem.* **31**, 79 (1899).

²⁷ Hoeflake, *Rec. trav. chim.* **36**, 36 (1917).

²⁸ Lunge, *Chem. Ind.* **8**, 74 (1885). Compare Allen's "Commercial Organic Analysis." Blakiston, 1914, vol. VI, p. 70.

²⁹ Courtet and Dondelinger, *Bull. soc. chem.* **37**, 115 (1925).

data of which the present supply is entirely inadequate. Authorities are not even agreed as to the order in strength of directive influence of some of the commonest substituents, for example, methyl and the halogens,³⁰ the halogens among themselves,³¹ $-\text{NO}_2$ and $-\text{SO}_3\text{H}$.³² A partial explanation of this disagreement will be discussed later.

The obvious method of attack is to treat various compounds with a substituting agent, usually nitric acid, sulfuric acid, or a halogen, and to analyze the resulting mixture of isomers. Nitric acid has been preferred because of the low temperature of reaction, the ease with which substitution can be made to take place in steps, as desired, and the comparative ease of analysis. The directive strengths of two substituents are compared by choosing a disubstituted benzene, for example, *p*-chlorotoluene, in which the influences are opposed; that is the methyl group would tend to place a new substituent in the 2 position, and chlorine in the 3 position. But since chlorine directs mainly to the *para* position (which is blocked) and methyl preferably to the *ortho* position, the latter has an advantage in this case; and a true comparison can be obtained only by studying also the substitution of *o*- and *m*-chlorotoluene and mixtures of toluene and chlorobenzene, all of which has been done by Wibaut.³³

Another method is to compare the *rates* of substitution of several compounds in a similar way. This requires careful control of temperature, catalysts or impurities, and medium. It is not certain what conditions in various reactions are comparable, as Holleman himself has observed. He has initiated the bulk of the research upon both the methods mentioned.

In entering this field, I was led to investigate directive influence by studying the relative rates of bromination of various amino and phenolic compounds in aqueous solution. This method had

³⁰ Compare Holleman, ref. 2, p. 202 with Challenger and Collins, *J. Chem. Soc.* **125**, 1377 (1924).

³¹ Compare Holleman, ref. 2, p. 202, with Holleman, "Die direkte Einführung von Substituenten in den Benzolkern," Veit and Co., Leipzig, 1910, pp. 469-70.

³² Compare Holleman, ref. 2, p. 202, with Obermiller, ref. 8.

³³ Wibaut, *Rec. trav. chim.* **32**, 244 (1913); **34**, 241 (1915); *Chem. Zig.* **35**, 762 (1914).

been entirely neglected because of the evident obstacles that all the reactions are "instantaneous," and that they cannot usually be limited to a single equivalent of substitution. On the other hand, the reactions proceed quantitatively in the cold, and the products in most cases can be separated easily from the reaction mixture.

On the supposition that the rates are not identical, "competition" experiments were devised³⁴ in which two organic compounds in acidified aqueous solution were treated with an insufficient amount of bromine, in the form of potassium bromide and potassium bromate, which with acid generate bromine slowly. The two organic compounds thus compete for the bromine as it is generated, and the relative rates of the two bromination reactions can be estimated from the amount of either of the bromination products. The experiments can be so chosen that the analysis for this product is usually simple, generally filtering, washing, and drying a precipitate. The whole technique of these experiments thus becomes very simple, but the calculation of the results is complex. This is due to the fact that the substitution of two or three equivalents of bromine usually takes place in each competitor, and these several reactions are sometimes consecutive and sometimes simultaneous and sometimes partly both. In making the calculations "partial bromination curves"^{3,34} were used. These are derived from similar experiments upon a single compound with insufficient bromine, and show the relative yield of highest brominated product plotted against the relative amount of bromine added, compared in each case with the theoretical. Fortunately a comparatively small number of curves sufficed for all the compounds, since with a few exceptions, all *para* amino compounds follow one curve, all *ortho* amino compounds another, and all *meta* amino compounds a third, which is the same as that for aniline; and in most phenolic compounds the several substitutions were found to be successive and distinct. For details in choice of competitors, procedure, and calculations the reader is referred to the original publications.³⁵

³⁴ Francis, Hill, and Johnston, *J. Am. Chem. Soc.* **47**, 2211 (1925).

³⁵ Ref. 34, pp. 2222-4 and ref. 3, pp. 2589-90.

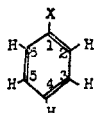
This method of experimentation was found to have certain advantages not entirely anticipated. One is that in the comparison of two reactions it is certain that the conditions are alike because they are identical. It is not necessary to control accurately the temperature or the concentration because it has been shown³⁶ that the *relative* rate of the two reactions is practically independent of these factors; and it is only the relative rate that is obtained, or is required. It is true that even the relative rate is affected considerably by the medium, for example the concentration of acid or alcohol (frequently necessary to maintain the substance in solution); but with suitable precautions no serious difficulty need arise. Another advantage in the method is the comparatively rapid progress that is possible because of the simplicity of experiments; and this is not negligible when it is considered that not by a few experiments, however accurate or refined, but only by thousands of them, can the problem of directive influence be solved. This does not mean that any care in manipulation was sacrificed to speed.

The conclusions of this work will be considered in connection with the corresponding ones of other investigators.

MECHANISM OF SUBSTITUTION IN THE BENZENE RING

The mechanism of substitution has been occasion of much controversy which still continues. This is due to the comparative lack of direct experimental evidence for any mechanism, and the consequent too free use of analogy. It is by no means certain that the same mechanism holds for all cases, although the constancy of directive influence suggests this. But if the fundamental character of directive influence, as discussed above, be accepted, a uniformity of mechanism is no longer required.

Holleman assumes the intermediate formation of an addition product. Using the Kekulé formula for the benzene ring,



³⁶ Francis, *ibid.* **48**, 655 (1926).

the substituent, X, is at one end of a conjugate double bond, 1-2-3-4 and either accelerates or retards the rate of addition to the conjugate system, according to Thiele's theory, and also to the simple bond, 1-2, but has little influence upon addition to the bond, 5-6. If the effect is acceleration, *ortho* and *para* substitution is favored; if it is retardation, *meta* substitution results. Van der Linden³⁷ has offered the objections that bromination of chlorobenzene ought to be more rapid than that of benzene itself; and that it should, on decomposition of the addition product, give some *p*-dibromobenzene as well as *p*-bromochlorobenzene. Both suppositions are contrary to fact. Moreover, Holleman has admitted³⁸ that no explanation is afforded as to why some groups accelerate and some retard the addition at the conjugate system, "the formation of intermediate addition products being even now hypothetical. Also the transition of these addition products into substitution products must be assumed as being performed with infinite velocity."

Recently Barnett³⁹ and his collaborators have defended Holleman's theory with evidence by analogy in the anthracene series. They maintained that Holleman's intermediate quinoid formula,



involves a spatial configuration which permits the elimination of only one pair of constituents (those which are *cis*) and so gives no possibility of the formation, for example, of *p*-dibromobenzene from chlorobenzene and bromine. These conclusions have been attacked by Prins⁴⁰ on the basis that the analogy fails because the central ring of the anthracene molecule has lost its aromatic character in the addition products which had been isolated; and that if benzene should lose its aromatic charac-

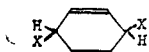
³⁷ Van der Linden, Verslagen Acad. Wetenschappen Amsterdam. Nov., 1911, p. 739.

³⁸ Ref. 2, p. 195.

³⁹ Barnett and Cook, *Rec. trav. chim.* **43**, 262 (1924); Barnett and Matthews, *ibid.* 530.

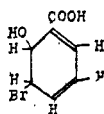
⁴⁰ Prins, *ibid.* 685.

ter in the same way, it would either polymerize, as do analogous terpenes, or add bromine to the double bonds. Furthermore, in the formation of the quinoid complex, there seems to be no reason why addition should be exclusively *trans*. This may be related to the theory of Terry and Eichelberger⁴¹ in regard to addition to double bonds. In their reply⁴² Barnett and Cook employed the Dewar formula for benzene, recently revived by Ingold and his collaborators.⁴³ They pointed out that compounds of the type,



are unknown when H and X have any considerable affinity for each other. But they admitted that their mechanism is not universal, and that in some cases there may be indirect substitution by way of a side chain.

The enhanced activity of halogens in aqueous solution has frequently been ascribed to the presence of hypohalous acids, which readily lend themselves to Holleman's mechanism by adding, supposedly, halogen and hydroxyl, and then eliminating the latter and a hydrogen atom in the form of water. If this mechanism were followed in the case of bromination of benzoic acid, for example, using Barnett's oriented addition, so as to place the hydroxyl group *cis* with respect to the hydrogen atom in the 5 position, the formula,



shows that the bromine atom would also be *cis* with respect to the hydrogen atom in the 6 position, and there certainly should be some elimination of HBr, leaving salicylic acid. In the medium employed, bromine water, this compound would be

⁴¹ Terry and Eichelberger, *J. Am. Chem. Soc.* **47**, 1067 (1925).

⁴² Barnett and Cook, *Rec. trav. chim.* **43**, 897 (1924).

⁴³ Ingold and others, *J. Chem. Soc.* **121**, 1153 (1922); **123**, 2066 (1923).

converted instantly to insoluble dibromosalicylic acid or tribromophenol, and could not fail of detection, even if present only in traces.

But even if, as Holleman maintains,⁴⁴ the failure of possible side reactions is no disproof of a mechanism, there is considerable evidence⁴⁵ that aqueous bromination is not due to hypobromous acid. A solution of the latter, if it is free from bromine, is much less reactive than bromine water, and shows mainly oxidizing rather than brominating properties. The suggestion was made that the high reactivity of bromine water is due to nascent bromine, that is, atomic bromine, either uncharged or charged positively; and this was supported by some results involving addition of halogens to double bonds. Br^+ (resulting from the partial ionization of Br_2 in aqueous solution) can be conceived as directly displacing a hydrogen atom of a benzene ring, and giving it its charge. The hydrogen ion thus formed would give hydrobromic acid with the Br^- ion, which had previously accompanied the Br^+ ion. This is a simpler but perhaps no more plausible mechanism for substitution. It does not account for nitration, unless indeed an NO_2^+ ion can be postulated.

There is thus involved the old controversy as to whether, with Michael⁴⁶ we believe that all reactions consist in the formation of complexes, followed by dissociation; or whether, according to Nef⁴⁷ dissociation into free radicals is prerequisite. Possibly neither theory is universal.

The best known rule for directive influence, that of Crum Brown and Gibson, was stated⁴⁸ in entirely empirical form, namely, that a substituent, X, controls the *meta* or the *ortho-para* positions according to whether or not the compound, HX, can be oxidized directly to HOX respectively. More recently

⁴⁴ Ref. 2, p. 194.

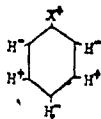
⁴⁵ Francis, *J. Am. Chem. Soc.* **47**, 2340 (1925).

⁴⁶ Johnson and Hahn's Henrich's "Theories of Organic Chemistry." John Wiley and Sons, New York, 1922. Chap. XXI.

⁴⁷ Nef, *J. Am. Chem. Soc.* **26**, 1549 (1904).

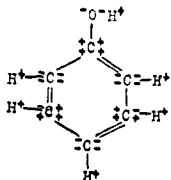
⁴⁸ Brown and Gibson, *J. Chem. Soc.* **61**, 367 (1892).

Fry⁴⁹ explained it as follows: X in HX is assumed to be negative, while in HOX it is positive because of the negative character of the hydroxyl group. If the oxidation proceeds readily, it may be assumed that the tendency of X to be positive is greater than that to be negative. X will tend, therefore, to be positive in the benzene ring also, forming $C_6H_5-X^+$ rather than the "electromer," $C_6H_5^+X^-$. Assuming that the hydrogen atoms and substituents in the benzene ring alternate in sign,



the positive hydrogens will be, in this case, those *meta* to the substituent, X. These only are the ones which can be substituted, since hydrogen is removed as an element of an inorganic compound, such as HOH or HBr, in which it is always positive. If HX is not readily oxidizable, the tendency of X is to be negative, and the reverse reasoning applies. The positive or replaceable hydrogen atoms are now those *ortho* or *para* to X. In intermediate cases, there may be mixtures of the above electromers, so that mixtures of products result.

This explanation was criticized by Stieglitz⁵⁰ because it involves negative hydrogen atoms which should be powerful reducing agents, especially in the presence of a substituting agent such as chlorine. He explained the Brown and Gibson rule in terms of polarized bonds, showing phenol thus,



A reagent, such as HOCl, is supposed to add to the strongly polarized double bond, 1-2, or the conjugate system, 1-4, the

⁴⁹ Fry, *J. Am. Chem. Soc.* **36**, 248 (1914).

⁵⁰ Stieglitz, *ibid.* **44**, 729 (1922).

negative $-OH$ going to the highly positive carbon atom, 1, and then regenerating the double bond by combining with the H^+ atom at 2 or 4. This is evidently an electronic picture of Holleman's mechanism, mentioned above, and has the same objections.

Stieglitz may have misinterpreted Fry's formulas, in that a negative hydrogen atom held by a non-ionizable bond may have very different properties from those of a hypothetical negative hydrogen ion. Certain it is that Fry's theories account beautifully for many displacement reactions in aromatic chemistry, for example, the lability of halogen *ortho* or *para* to a nitro group. The latter, according to Fry, is positive, making the halogen more negative, in which form it is more readily removed as an ion by hydrolytic agents. Holleman⁵¹ made an exhaustive criticism of Fry's views, the most important points being the following:⁵² (a) *m*-Dichlorobenzene is hydrolyzed more readily than its isomers to chlorophenol, whereas, according to Fry, the two chlorine atoms would have the same sign in the *meta* isomer, and opposite signs in the *ortho* and *para* isomers, so that the reverse should be expected. (b) Since Fry accounts for the hydrolysis of benzene sulfonic acid in acid solution to give benzene and in alkaline solution to give phenol, by postulating that the $-SO_3H$ group is positive and negative respectively in the two media, and since the two acid groups of benzene *p*-disulfonic acid presumably have opposite charges, the compound should be hydrolyzed to phenol in either medium, while actually it behaves like the mono acid, giving benzene or quinol.

In his reply⁵³ Fry postulated that in both the cases cited the two groups have like signs, and that in (b) there is an unsymmetrical distribution of charges. In (a) the negative tendency of chlorine is reinforced by the coöperation of the two substituents, and the greater ease of hydrolysis may be due to this.

Reference has been made to the theory of indirect substitution by way of a side chain. Holleman and Euwes⁵⁴ showed the

⁵¹ Holleman, *ibid.* **36**, 2495 (1914).

⁵² Van der Vliet also emphasized these points, *Rec. trav. chim.* **43**, 606 (1924).

⁵³ Fry, *J. Am. Chem. Soc.* **37**, 883 (1915).

⁵⁴ Holleman and Euwes, *Rec. trav. chim.* **27**, 443 (1908).

improbability of this in the case of toluene since benzyl bromide does not rearrange to give *o*- or *p*-bromotoluene under conditions favorable to their formation. On the other hand, Holleman himself has found⁵⁵ that *o*-nitrobenzotrichloride upon hydrolysis, gives not *o*-nitrobenzoic acid, but *o*-chlorobenzoic acid, the nitro group being displaced by chlorine.

In the sulfonation of aniline Bamberger⁵⁶ has shown that aniline sulfate, phenyl sulfamic acid, and *o*-aminobenzenesulfonic acid are probably intermediate to the production of sulfanilic acid. Phenol is likewise supposed to be substituted in the *ortho* position by $-\text{COOH}$ ⁵⁷ or $-\text{SO}_3\text{H}$ ⁵⁸ only after the intermediate formation of the esters, $\text{C}_6\text{H}_5\text{OCOOH}$ and $\text{C}_6\text{H}_5\text{OSO}_3\text{H}$, respectively. Skraup and Poller⁵⁹ investigated the conversion of acetyl *m*-cresol to 2-methyl 6-hydroxyacetophenone, and considered that the migration of the acetyl group was due to *resubstitution* and not to indirect substitution, because in presence of *m*-chlorobenzoyl chloride, acetyl chloride was split out and a derivative of benzophenone resulted. They seem to have overlooked the possibility that the *m*-chlorobenzoyl group was first substituted for the acetyl group in $-\text{OH}$, and that it then rearranged, perhaps more easily than the acetyl group.

Chattaway and Orton⁶⁰ have shown that *N*-chloro-acetanilide, $\text{C}_6\text{H}_5\text{NClCOCH}_3$, rearranges to give *p*-chloro-acetanilide, and that three chlorine atoms can thus be introduced into the 2, 4, and 6 positions by way of the $-\text{NH}$ group of acetanilide. They did not prove, as has been asserted,⁶¹ that halogenation takes place in the same manner in the case of free bases, although this is a natural inference.

More definite evidence for this mechanism, involving the

⁵⁵ Holleman, Vermeulen, and de Mooy, *ibid.* **33**, 1 (1914).

⁵⁶ Bamberger, *Ber.* **23**, 461 (1895); **30**, 654, 1281, 2279 (1897).

⁵⁷ Schmidt, *J. prakt. Chem.* **31**, 407 (1885).

⁵⁸ Baumann, *Ber.* **9**, 55, 1715 (1876); **11**, 1907 (1878).

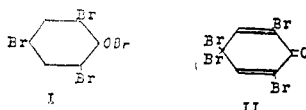
⁵⁹ Skraup and Poller, *Ber.* **57B**, 2033 (1924).

⁶⁰ Chattaway and Orton, *Ber.* **32**, 3573, 3635 (1899); *J. Chem. Soc.* **75**, 1046 (1899); **77**, 134, 789, 797 (1900).

⁶¹ Bernsthen—Sudborough's "Organic Chemistry." D. van Nostrand, New York. (1922). p. 395.

intermediate formation of -NHBr , -NBr_2 , and -OBr compounds in the bromination of amines and phenols is presented in my papers.^{19, 23, 34} It is shown, for example, that in aniline and in thirteen *m*-amino compounds and also in four derivatives of resorcinol, two of the three bromine substitutions are simultaneous, thus corresponding with the number of hydrogen atoms in the side chains. In no case is this number exceeded by the number of simultaneous substitutions. The mechanism is supported also by the peculiar dependence of the manner of bromination upon this number of hydrogen atoms.

Of important bearing upon this theory is the structure of tribromophenol bromide, to which Benedict⁶² assigned formula I, but which Thiele and Eichwede⁶³ claimed to be II, because



on long heating with lead acetate in acetic acid, it gave 2,6-dibromoquinone. This would seem to give opportunity for drastic rearrangements, however, while the rapid reaction with potassium iodide in cold aqueous solution, regenerating tribromophenol, decidedly favors Benedict's formula. Thiele failed to form from the compound a semicarbazone, the semicarbazide being oxidized and completely destroyed.

Kastle and his co-workers⁶⁴ made a careful study of the structure and decided in favor of Thiele's formula. They overlooked some of their own evidence, however. On heating to 125° , tribromophenol bromide loses one atomic equivalent of bromine forming $\text{C}_{12}\text{H}_4\text{O}_2\text{Br}_6$, which Benedict considered to be III, and Kastle IV.



⁶² Benedict, *Ann.* **199**, 127 (1879).

⁶³ Thiele and Eichwede, *Ber.* **33**, 673 (1900).

⁶⁴ Kastle, *Am. Chem. J.* **27**, 31 (1902).

Kastle's co-workers considered the following facts to be proofs of the incorrectness of Benedict's formula: (a) the failure of tribromophenol bromide to form a benzene sulfonic ester with sodium benzene sulfinate; (b) its failure to form an ethyl ether with zinc ethyl; (c) its rearrangement in concentrated sulfuric acid to tetrabromophenol. (a) The observed reaction in the first case giving $C_{12}H_4O_2Br_6$ and $C_6H_5SO_2Br$ is no better explained by Thiele's formula. The powerful oxidizing action of tribromophenol bromide and the reducing tendency of sodium benzene sulfinate make it comprehensible with either formula. (b) In the second case the formation of ethyl bromide and zinc tribromophenolate is just what should be expected, and is more consistent with Benedict's formula than with Thiele's. (c) Kastle's mechanism for the rearrangement to tetrabromophenol is complicated, and subject to the objection that by it the sulfonic group might be expected to be left in the ring to some extent. Consideration of the well known fact that nitration of aniline in concentrated sulfuric acid gives largely the *meta* derivative, makes it reasonable to suppose that in the same medium the bromine attached to oxygen isomerizes into a *meta* position, especially when all ortho and para positions are filled, possibly because of the formation of an oxonium salt. It is not even necessary to assume Benedict's bimolecular mutual bromination, to which Kastle objects.

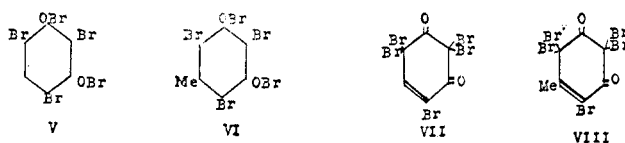
The formation of 2,6-dibromoquinone by boiling tribromophenol bromide with silver nitrate or lead acetate is merely analogous to the formation of quinone itself by oxidation of aniline or its *para* derivatives, since tribromophenol bromide is itself an oxidizing agent. Kastle's failure to cause the same reaction by means of silver oxide or calcium carbonate, nullifies this evidence for Thiele's formula. Kastle's other observations are explained equally well by either formula. A serious objection to that of Thiele is the failure of additional bromine to add to the double bonds of the quinoid ring, as it does to those of quinone itself.

The structure seems now to be settled satisfactorily as the "bromoxyl" formula by Lauer,⁶⁵ who showed that chlorination

⁶⁵ Lauer, *J. Am. Chem. Soc.* **48**, 442 (1926).

of tribromophenol gives a different product from that obtained by bromination of 2,6-dibromo-4-chlorophenol, in contrast to the requirement of Thiele's formula.

Let us consider now pentabromoresorcinol and pentabromo-orcinoI, to which Benedict assigned formulas V and VI. No evidence has been advanced against these structures except the analogy with tribromophenol bromide. The compounds are more stable than the latter, but are readily reduced to tribromo-resorcinol and tribromo-orcinoI respectively, two of the bromine atoms being much more reactive than the other three. This lability is not shown as well by the more commonly used formulas, VII



and VIII. These structures have also the serious objection that they show one double bond in the ring, although there is no additional consumption of bromine even on long standing. On titration of resorcinol or orcinoI with bromine in aqueous solution, a fairly good end point for *pentabromination* may be obtained, using as an indicator the odor of bromine or the color change of a moistened KI-starch paper suspended in the neck of the flask. The liquid reacts with potassium iodide after three molecular equivalents have reacted. Similarly, phloroglucinol reacts with six or three equivalents under corresponding conditions, but the excess over six equivalents is less permanent, since there is gradual oxidation with rupture of the ring.⁶⁶ The correspondence of the capacity for labile bromine with the number of hydroxyl groups, in phenol, resorcinol, orcinoI, and phloroglucinol is striking support for Benedict's views.

GENERAL INFLUENCE OF SUBSTITUENTS

Studies in this field have been complicated greatly by the fact, not yet fully recognized, that some effect other than direc-

⁶⁶ Benedict, *Ann.* **189**, 165 (1877); *Monats.* **6**, 702 (1885); Zincke and Kegel, *Ber.* **23**, 1729 (1890).

tive influence, as defined above, is exerted by substituents in the benzene ring upon the rate of further substitution. Thus it is well known that nitrobenzene is nitrated less readily than benzene, while phenol is much more reactive, and toluene slightly more so, than benzene. Holleman⁶¹ has described this by stating that the rate of *ortho* and *para* substitution is much greater than that of *meta* substitution. But chlorobenzene also is less readily substituted than benzene, although halogens are *ortho-para* controlling. That is, halogens in this respect are in the class with the nitro group and other "acid" groups, and not with $-\text{OH}$, $-\text{NH}_2$, and $-\text{CH}_3$.

This classification is parallel with that of the effect of groups upon the acidity of phenols, and the degree of dissociation of acids, and is commonly called the "negative nature of atomic groups." These influences are shown also in the researches of Norris⁶⁵ and his students upon the reactivity of atoms not connected directly with the benzene ring.

It seems, therefore, that two or more influences of the groups are superimposed. These influences may be transmitted around the ring in both directions either with undiminished or with gradually decreasing intensity.⁶⁷ The capacity of the benzene ring for transmitting two or more influences may be due to the sharing by adjacent carbon atoms of the ring of *three* electrons^{67,68} instead of two, so that the induced shifts may be irregular; that is, the three electrons may not all shift together. This is analogous to the simultaneous transmission of two messages over the same wire at different frequencies. This will be discussed later.

This other influence, which is a property of various substituents, seems to result in an acceleration or retardation of substitution which is independent of the position of the group. For this reason I have called it "General Influence," and made an attempt to dissociate it from directive influence. The influences of some groups in amino and phenolic compounds are estimated¹⁹ as shown in table 2.

⁶⁷ Compare Højendahl, *J. Chem. Soc.* **125**, 1381 (1924).

⁶⁸ Kermack and Robinson, *ibid.* **121**, 437 (1922).

In phenolic compounds, as in benzene itself the general effect is a retardation for acidic groups and an acceleration for methyl (and, of course, for $-\text{NH}_2$ and $-\text{OH}$ if the experimental method had permitted their calculation). In amino compounds the general effect is always an acceleration, and is in nearly reverse order to that upon phenolic compounds. The general influence was estimated in amino compounds by comparing the mean of the first velocity constants of bromination of the *ortho* and *meta* isomers of a system with that of aniline. The directive influence was found by dividing this same mean by that of the *ortho* isomer. The former calculation thus eliminates the effect of position of the group, and the latter evaluates it.

TABLE 2
Influences of substituents in the benzene ring
(Effect upon first velocity constant of bromination)

SUBSTITUENT	AMINO COMPOUNDS		PHENOLIC COMPOUNDS	
	General	Directive	General	Directive
NO_2	3.4	0.14	0.0012	0.8
COOC_2H_5	3.7	0.22	0.001	
CHO			0.005	0.73
COOH	4.4	0.19	0.016	0.84
SO_3H	2.2	0.24		
Br	3.8	0.78		
Cl	3.8	0.78	0.065	4.0
CH_3	1.45	0.97	3.2	1.5

Other examples of this general effect can be found in the literature. Thus Wibaut⁶⁹ showed that toluene is nitrated in preference to chlorobenzene when mixed, although the directive influence of chlorine is greater than that of methyl when substituted in the same benzene ring. Holleman recognizes general influence in his factor, "X."⁶⁹

Olivier has made a thorough study of the rates of hydrolysis of various substituted benzyl chlorides.⁷⁰ His results can be

⁶⁹ Ref. 2, p. 206.

⁷⁰ Olivier, *Rec. trav. chim.* **41**, 646 (1922); **42**, 516, 775 (1923).

summarized in table 3, which gives the relative velocity constants at 83° compared with that of benzyl chloride itself as unity.

The order is evidently $p > o > m$ for *ortho-para* directing groups and the reverse for *meta* directing groups, showing the importance of position, and the close relation to directive influence of which p/m is a good index. The striking observation is, however, the fact that the halogen derivatives, like the *meta* controlling groups, all have constants below that of benzyl chloride instead of above, like methyl. In other words they have a *general* retarding effect like the other "acid" groups, but a special or directive influence like that of methyl. The results are analogous to my own, mentioned above.

I believe that disregard of the distinction between these two influences has been the cause of much confusion and some controversy regarding directive influence.

TABLE 3
Relative velocity constants of hydrolysis of benzyl chlorides

SUBSTITUENT	PARA	ORTHO	META	p/m
CH ₃	10.6	4.84	1.39	7.6
Cl.....	0.62	0.355	0.237	2.61
Br.....	0.50	0.286	0.215	2.34
I.....	0.477	0.287	0.201	2.38
COOH.....	0.165		0.245	0.68
NO ₂	0.074	0.084	0.090	0.82

STRUCTURE OF BENZENE

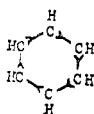
Obviously the chief difficulty about the structure of benzene is the distribution of the three extra bonds, or in modern terms, of the six spare electrons. I prefer to consider them as shared between carbon atoms, making three instead of two for each nuclear bond, and thus providing the mechanism for complex shifts, as already described. The actual positions of the three cannot be defined as yet. An attractive picture of the arrangement, because of its high symmetry, is that of Orelkin⁷¹ who placed the six spare electrons at the corners of an octahedron;

⁷¹ Orelkin, *J. Russ. Phys. Chem. Soc.* **54**, 493 (1923). *C. A.* **18**, 2501.

and at the same time at the mid-points of the lines connecting *meta* carbon atoms, the ring being "puckered," that is, the carbon atoms being in two different planes. In this arrangement two of these electrons form a perfect square with the two shared by two adjacent carbon atoms, simulating a double bond, except that the four electrons are not the exclusive property of the two carbon atoms involved. Morse⁷² placed the carbon atoms at the corners of an octahedron. This seems to be a mere speculation already disproved by chemical evidence.

Lely⁷³ has proposed a rather fantastical triangular formula, which must have some merit since it aroused, the criticism of no less than eight other chemists.⁷⁴ He attacked the Kekulé formula by claiming that the molecular refraction of benzene proves the absence of double bonds. This was denied vigorously by van Laar,⁷⁵ who showed that three double bonds are indicated by the value of the constant "a" in van der Waal's equation of state. Schoorl⁷⁶ stated that the molecular refraction of benzene corresponds with theory for three double bonds, but not if their conjugation is considered.

Dominikiewicz⁷⁷ has revived Stark's theory,⁷⁸ which involves the idea that two valences of one carbon atom satisfy one of the next.



This ought to be discredited because it implies the existence of isomeric *ortho* derivatives if the two substituents are different.

Huggins⁷⁹ and Beckenkamp⁸⁰ drew an analogy between the

⁷² Morse, *Phys. Rev.* **19**, 243 (1922).

⁷³ Lely, *Chem. Weekblad.* **19**, 593 (1922); **20**, 90 (1923); **21**, 114 (1924); **22**, 371 (1925).

⁷⁴ *Ibid.* **20**, 27, 28, 29, 143, 144, 145, 279, 297 (1923); **21**, 174 (1924).

⁷⁵ van Laar, *ibid.* **22**, 286 (1925).

⁷⁶ Schoorl, *ibid.* **22**, 343 (1925).

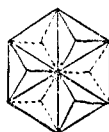
⁷⁷ Dominikiewicz, *Roczniki Chemje* **3**, 326 (1923); *C. A.* **19**, 2190.

⁷⁸ Ref. 46, pp. 209-225.

⁷⁹ Huggins, *J. Am. Chem. Soc.* **44**, 1607 (1922); **45**, 264 (1923).

⁸⁰ Beckenkamp, *Z. anorg. allgem. Chem.* **137**, 249 (1924).

structure of benzene and that of graphite, based upon crystallographic data. From the structure assigned to graphite at that time, from X-ray spectra, Huggins assumed benzene to have a puckered hexagon formula, corresponding to Körner's centroid model.



Huggins defended this structure against objections that have been raised to it, (a) that di- and trisubstituted derivatives with different groups should show optical isomerism; (b) that substituents in *meta* positions should form closed rings, such as anhydrides, more readily than *ortho* substituents; (c) that 1,5 rather than 1,8 rings should be formed with naphthalene derivatives. He argued as follows: (a) The degree of optical rotation may be so small that experiments in the attempt to find it may have been insufficiently accurate or exhaustive. (b) Repulsion between *meta* substituents distorts the structure so that they are not really very close. (c) The only criterion for the numbering, 5,6,7,8 in naphthalene has been the 1,8 closed rings, so that, very probably, compounds such as acenaphthene and naphthalic anhydride are really 1,5 and not 1,8 derivatives.

It ought to be possible to test this last point by carrying out Fittig and Erdmann's synthesis⁸¹ of α -naphthol from γ -isocrotonic acid, using instead a compound with some substituent in the phenyl group, and comparing the resulting compound with known derivatives of α -naphthol. Huggins says, "Recent evidence from crystal structure proves this benzene structure to be the correct one." It has now been shown⁸² that graphite has a plane structure instead of a puckered one, so that a similar one for benzene is probable.

In contrast to Huggin's central accumulation of electrons, Crocker⁸³ considered that they are repelled to the outside, which

⁸¹ Fittig and Erdmann, *Ber.* **16**, 43 (1883).

⁸² Hassel and Mark, *Z. Physik.* **25**, 317 (1924); Bernal *Proc. Roy. Soc.* **106A**, 749 (1924).

⁸³ Crocker, *J. Am. Chem. Soc.* **44**, 1618 (1922).

is logical considering their electrical properties. The carbon atoms are thus placed in a single plane.

Pauling⁸⁴ has proposed a formula for benzene which is an electronic picture of the Claus formula since it involves "μ-electrons" which are shared between *para* carbon atoms. It is open to the objection that it assumes each carbon atom to be combined with *three* others, although in no case of rupture of the benzene ring is this condition realized.

PRINS' THEORY

The most recent comprehensive theory of substitution in the benzene ring is that of H. J. Prins,¹⁴ although it has had a gradual development⁸⁵ and is still stated somewhat cautiously. It is practically the same as that of Flürscheim,⁵ but stated in modern terms and freed from its principal objections. The paper should be widely read; it is in the English language.

The theory is stated in two ways which are equivalent; but the first involves "atom energy" and "bond energy," which are somewhat vague terms, and may not be generally acceptable, so that I prefer the other as being more readily explicable.

He considers that under the influence of a strongly electrophilic substituent (one with a pronounced affinity for additional electrons) such as chlorine, a carbon atom has less attraction for the electrons which it shares with the *ortho* carbon atoms. These electrons, therefore, are forced towards the latter atoms forming an octet, which includes also the other electrons around those atoms. The *meta* atoms coming thus under the influence of negative *ortho* atoms, repel their electrons toward the *para* atom forming an octet there. The general action of a negatively charged atom must be distinguished from the distribution of energy over the nucleus. Thus chlorine causes a general decrease of atom energy. This effect is strongest in the *ortho* atoms, and thus nearly neutralizes the distribution effect, so that the directive influence is almost exclusively *para*. An

⁸⁴ Pauling, *ibid.* **48**, 1132 (1926).

⁸⁵ Prins, *Chem. Weekblad.* **14**, 83 (1917); **15**, 93, 571 (1918); *Rec. trav. chim.* **43**, 685 (1924).

electrophilic atom indirectly bound to the nucleus as in $-\text{CCl}_3$, causes *meta* substitution; but this is not true for the tertiary butyl group, $-\text{CMe}_3$, because of the weakly electrophilic character of methyl. Prins does not make clear the disposition of the six extra electrons. There are no figures in his paper.

A THEORY OF SUBSTITUTION IN THE BENZENE RING

Substantially the same idea is contained in the following theory as elaborated by me. Indeed it can be considered as largely anticipated also by the theories of Flürscheim,⁵ Vorländer,⁸⁶ Fry,⁴⁹ Stieglitz,⁵⁰ and others^{67, 68, 87} if properly interpreted, but it seems to overcome some of the objections that have been offered to them. The following postulates are made:

1. Each nuclear bond of benzene consists of three shared electrons. The aromatic character is due to this. Each other single bond involves only two shared electrons. A shared electron presumably revolves around both atomic nuclei, but in the figures it is represented by a dot between the atoms. This may be considered the electric center of its orbit, but hereafter will be denoted merely by the term "electron."

2. Any substituent in benzene shifts the electrons of all the bonds. The three electrons of the nuclear bonds may not all shift together; but because of their pronounced tendency to pair, two of them may shift together, and the third be free to move in response to electrostatic influences, and even shift in a direction opposite to that of the pair. In most cases, for lack of data to decide the exact nature of the shifts, the three are represented together in the drawings. The direction and amount⁸⁸ of the shift depend upon the sign and degree of the polarity tendency of the substituent. The test for this is usually the relative stability of the hydrogen and hydroxyl compounds of the substituent (essentially the Brown and Gibson rule); but a safer criterion for groups, such as $-\text{CCl}_3$ or $-\text{CN}$, is to

⁸⁶ Vorländer, *Ber.* **52**, 263, (1919).

⁸⁷ W. A. Noyes, *Ber.* **57**, 1233 (1924).

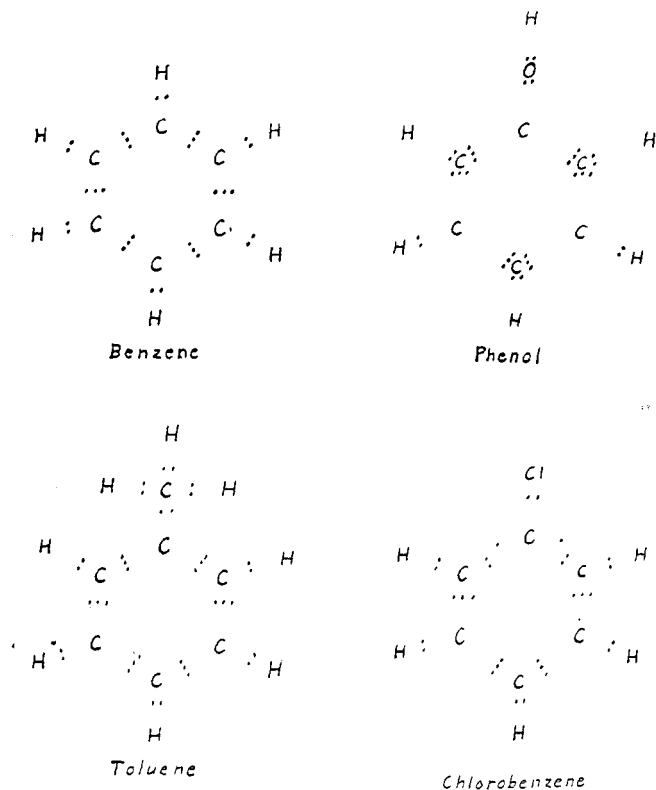
⁸⁸ The idea of gradual shift of shared electrons from those of a completely non-polar bond to those of an ionizable bond, and the method of representation of the bonds are due to G. N. Lewis, ref. 6, p. 83.

consider the polarity tendencies of the extreme atoms. This will be explained later.

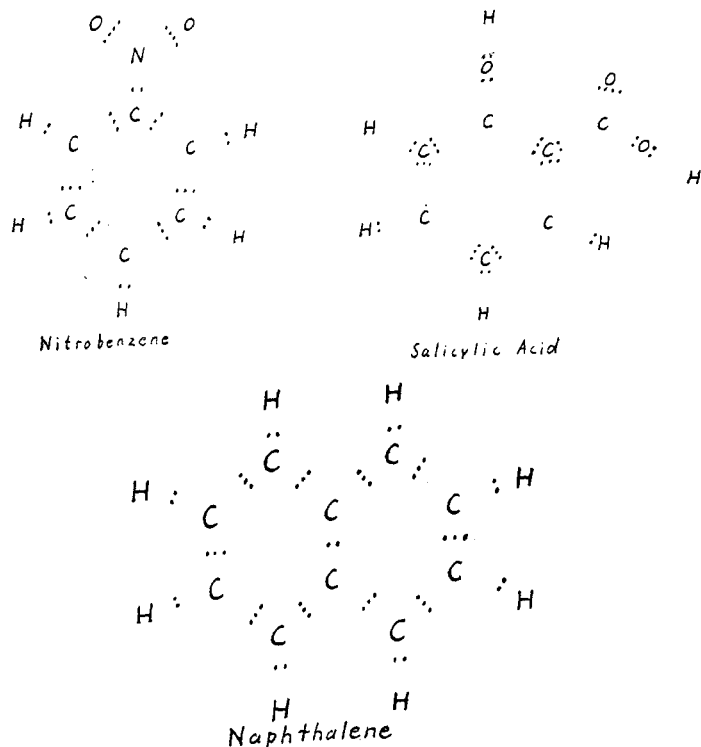
3. A carbon atom towards which electrons have been shifted tends to attract its other electrons forming a compact octet. A carbon atom away from which electrons have been shifted tends to repel its other electrons forming an open octet. This is based upon considerations of symmetry.⁸⁹

4. A bond is the more easily broken if the shift of its electrons is in such a direction as to accentuate the normal polarity of the atom or group to be displaced. Thus, hydrogen is easily displaced if electrons are shifted away from it, while a halogen atom is labile if electrons are shifted toward it.

The following figures illustrate the theory:



⁸⁹ This is contrary to the assumption of Lewis (ref. 6, p. 85) that all the valence electrons of a molecule are shifted in the same direction, but is suggested by him as a possibility (p. 150) in certain cases. His first assumption is inapplicable to substitution in the benzene ring. Cf. also Lapworth, *Mem. Manchester Phil. Soc.* 64 (iii) 1 (1920); *J. Chem. Soc.* 121, 416 (1922); *C. A.* 16, 2047-8.



Hydroxyl tends to be negative, and in order to acquire that polarity, attracts the electrons which it shares with carbon. The latter then repels its other six electrons, forming an open octet. The two *ortho* carbon atoms then have compact octets, the two *meta* carbon atoms open ones, and the *para* atom a compact one. The more positive hydrogen atoms are the *ortho* and *para* ones, and these are the ones substituted. In aqueous solution they have practically the reactivity of ions.³⁶ In toluene the arrangement of electrons is analogous with that of phenol, but the shifts are much less extensive because of the weaker polarity tendency of methyl. In chlorobenzene the shifts of the electron pairs are similar to those in toluene, but the third electrons in the 1-2 and 1-6 bonds are attracted directly by the chlorine atom, and so shift in the opposite direction to that of the

pair. This distortion of the octets of the *ortho* carbon atoms greatly decreases the lability of the *ortho* hydrogen atoms, so that there is a general decrease in reactivity, and substitution is preferably in the *para* position.

In nitrobenzene the nitro group tends, as in nitric acid, to be positive, and the shifts are opposite to those in toluene. The *meta* hydrogen atoms are more labile. In nitrochlorobenzenes, however, chlorine atoms in the *ortho* and *para* positions would be the ones displaced because they are more negative. Similarly the *meta* isomer of the dichlorobenzenes is most readily hydrolyzed because the two chlorine atoms reinforce and accentuate each other's negative character, whereas in the *ortho* and *para* isomers they oppose each other, and so are nearly neutral.

The carboxyl group of salicylic acid is easily displaced because it is forced by the hydroxyl group to be strongly positive, and thus more readily combines with an hydroxyl ion forming carbonic acid. Similar reasoning applies to the $-\text{COOH}$, $-\text{CHO}$, $-\text{CH}_2\text{OH}$, and SO_3H groups when *ortho* or *para* to an amino or hydroxyl group. $-\text{CH}_2\text{OH}$ is somewhat anomalous, since it is an *ortho-para* directing group, and so in benzyl alcohol must be slightly negative. It may be that it is labile in salicyl alcohol only in a strongly oxidizing medium such as bromine water. The by-product in this case is formaldehyde, formed presumably from the unstable bromomethanol. Thus, when the weakly negative tendency of the group has been overcome by hydroxyl, and become positive, it is attracted away from the nucleus by negative bromine, being replaced by positive bromine.

Analogous reasoning accounts for the fact that benzene sulfonic acid, which in acid solution can be hydrolyzed to benzene and sulfuric acid because of the normal positive character of $-\text{SO}_3\text{H}$, is hydrolyzed by alkali to phenol and sodium sulfite, since the strongly positive sodium ion overcomes that slightly positive character, and combines with the group. The same idea applies to benzene *p*-disulfonic acid, thus meeting the criticism of Fry's theory by Holleman and van der Vliet. There is no probability that one $-\text{SO}_3\text{H}$ group is positive and the other

negative. A perfectly symmetrical structure for naphthalene is given, without the elimination of the 9-10 bond,⁸⁴ for which there is no justification; and the slight preference for substitution in the α -position is indicated. Other cases of orientation in naphthalene are analogous to those in benzene.

In considering Olivier's results on the hydrolysis of benzyl chlorides, we have two pictures of the $-\text{CH}_2\text{Cl}$ group,



If the group is in such a position with respect to other substituents that hydrogen would be reactive (positive), the group also would be positive as in (a). The carbon atom has an open octet and the negative character of chlorine is accentuated, so that it is labile. If the group is in a different position, *meta* to an *ortho-para* directing group, for example, the carbon atom has a compact octet, (b), and the chlorine atom is more positive and less readily hydrolyzed. This corresponds precisely with Olivier's observations.⁷⁰

Reference has been made to the $-\text{CCl}_3$ and $-\text{CN}$ groups which are obvious exceptions to the Brown and Gibson rule, since they are *meta* directing, although their hydrogen compounds cannot be oxidized to their hydroxyl compounds. If we write their electronic formulas however,



we see that the combined action of the chlorine atoms in the former case, and the negative tendency of trivalent nitrogen in the latter, impose an open octet upon the carbon atom, which is thus positive and *meta* directing. The tertiary butyl group, $-\text{CMe}_3$, would be expected to be analogous to $-\text{CCl}_3$; yet it is *ortho-para* directing. Prins' explanation of this case has already been mentioned, namely, that the weakly electrophilic character of methyl is not transmitted through the carbon atom. A some-

what similar reasoning applies to other substituents involving aliphatic chains (for example, the cinnamic acid group), all of which are *ortho-para* directing. It would seem that in some cases a carbon chain has considerable damping effect upon the transmission of induced alternating polarity.

The theory explains all the phenomena cited by Fry in the same way that he does, but avoids some objections to his theory. One is that he does not make it clear why one positive hydrogen should be attacked more rapidly than another; why, for example, phenol should be so much more reactive than chlorobenzene. This is readily explained by assuming that by gradual shift of the electrons many gradations of positivity or negativity are realized. There are no strongly negative hydrogen atoms, but only more or less positive, or slightly negative ones.