ORIENTATION AND RELATIVE REACTION RATE FACTORS IN AROMATIC SUBSTITUTION BY THE BENZENESULFONIMIDO RADICAL

by

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INTRODUCTION

This experimentation was undertaken to extend the present knowledge of homolytic aromatic substitution. Homolytic substitution in aromatic nuclei has recently been reviewed by Dermer and Edmison (42), and homolytic aromatic arylation has been reviewed by Augood and Williams (6). Both reviews have expressed a definite need for a more quantitative knowledge of homolytic substitution of the aromatic nucleus.

The original objective of this work was to determine the orientation of various meta-directing substitutents for benzenesulfonamidation, with radicals generated by the pyrolysis of benzenesulfonyl azide. This would have been an extension of the work by Curtius (30) and later the work of Dermer and Edmison (41). It was soon found, however, that most of the compounds considered to be meta-directing failed to produce the desired substitution products.

The final objective of this work was to determine the relative reaction rates, with respect to benzene, for benzenesulfonamidation of aromatic nuclei that were known to produce substitution products. The "competitive method" devised by Ingold (75) was used with benzene as the reference solvent.

In the course of this work, it became evident that quantitatively there was some discrepancy between the isomer ratios found by Dermer and Edmison (41) and those found in the competitive determinations. The substitution reactions again were accomplished and the products

then analyzed by what the author believes to be a more reliable method of analysis.

Recently, it has been found that an electronegative substituent in the para position of a phenyl radical gives the radical electrophilic character (6,28,65,67,87,106); it then is reasonable to assume that the proximity of the strongly electronegative sulfonyl group in the benzenesulfonimido radical also should render it electrophilic. The results of this experimentation are consistent with this hypothesis.

HISTORICAL

The historical section of this dissertation is intended only to be a summary of the previous work with organic azides and aromatic substitution and should not be considered as a comprehensive review. Organic azides have been reviewed recently by Boyer and Canter (21), and good discussions can be found in books by Sidgwick (107), and Degering (39). Ionic aromatic substitution has been reviewed by Ingold (75), and two excellent reviews have recently appeared on homolytic aromatic substitution (6,42).

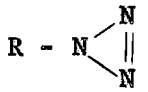
The author is indebted to the authors of these books and reviews for their opinions and correlations in preparing this summary.

ORGANIC AZIDES

Structure

The structure of the azides or tetrazenes, along with similar diazo derivatives, has been one of the most controversial problems of structural chemistry, and has been elucidated only since methods, such as X-ray and electron diffraction, have shown the actual positions of the atoms in the molecule.

A structure was proposed first by Emil Fischer (49) in 1878. This cyclic structure of three nitrogen atoms:



was postulated as the result of the preparation of phenyl azide by the reaction of nitrous acid on phenylhydrazine, which involves the loss of

water from the nitroso intermediate (50).

$$C_6H_5NHNH_2 + HNO_2 \longrightarrow C_6H_5N(NO)NH_2 + H_2O$$

$$C_6H_5N(NO)NH_2 \longrightarrow C_6H_5N_3 + H_2O$$

This structure also was supported by Curtius (34).

Hantzsch and Lifschitz (63) interpreted absorption spectra to support this structure as late as 1912, and as late as 1928 Lindemann and Thiele (84), using parachor measurements, suggested that the esters of hydrazoic acid may exist as cyclic structures.

An early competitor of the cyclic structure, and the forerunner for the presently accepted formula, was first proposed by Angeli (2) and later supported and advanced by Thiele (113). This structure was a linear structure containing a pentacovalent nitrogen atom;

$$R\text{——}N\text{═══}N\text{≡≡≡}N.$$

The actual structure of the azide ion was established by Hendricks and Pauling (66) by the complete X-ray analysis of sodium and potassium azides, and their results were confirmed by Langseth and Nielsen (78) using the Raman spectrum of the ion in solution. The ion has the three nitrogen atoms lying in a straight line and is arranged symmetrically with reference to the central atom;

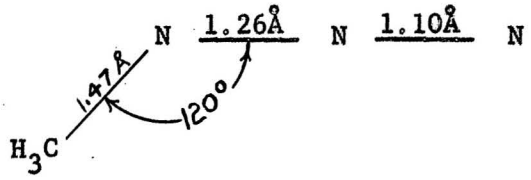
$$:\ddot{N}::N::\ddot{N}: .$$

Similarities of the azide group to the halogens made it seem unlikely that there was any great alteration, such as cyclization, when the azide ion became covalently bonded. However, no satisfactory classical linear formula could be written that would satisfy all chemical and physical properties. The formula of Angeli and Thiele possessed an unacceptable pentavalent nitrogen and related structures such as:

$$R:\ddot{N}::\overset{+}{N}::\overset{-}{\underset{\cdot\cdot}{N}}: \quad \text{and} \quad R:\overset{-}{\underset{\cdot\cdot}{\ddot{N}}}:\overset{+}{N}:::N:$$

would require that a compound like phenyl azide have a considerable dipole moment. Actually, phenyl azide has a moment of only 1.55D (108). For this reason a resonance hybrid, in which the two classical structures shown above are the main contributing isomers, has been postulated. This explains the low dipole moment since the two dipoles are nearly equal and in opposite directions.

Using the method of electron diffraction, Brockway and Pauling (24) determined the atomic distances in methyl azide and found the following configuration (107):



This is in close agreement with the nitrogen to nitrogen distances of 1.25 Å and 1.12 Å obtained from the calculation by the molecular orbital method and 1.22 Å and 1.10 Å obtained from dipole moment consideration (21). The angle of 120° is in agreement with absorption data (21). From the molecular orbital method of calculation an electronic charge distribution of -0.37, 0.52, and -0.15 for the nitrogen atoms in a covalent azide is predicted (20).

The overwhelming experimental evidence can leave little doubt that the azide is a linear rather than a cyclic group.

Preparation of Organic Azides

The preparation of organic azides is usually accomplished by direct displacement of another group by the azide ion, or by a stepwise introduction of the three azide nitrogen atoms. Other special methods (21) have been reported, such as addition of hydrazoic acid to olefins, rearrangements such as the Hofmann, basic cleavage of tetrazoles and

dihydrotetrazoles, and direct methylation of hydrazoic acid with diazomethane, but these methods are not of general preparative interest.

The direct replacement method is generally used for the preparation of aliphatic and acyl azides. It has been found that the azide group reacts similarly to the halogens in displacement reactions. For example, when an azide group is substituted for a halogen group on an asymmetric carbon atom, inversion is found to arise in the same manner as when one halogen is replacing another (80).

Curtius (31) was first to use this reaction to prepare benzyl azide from benzyl iodide and silver azide. This reaction has proved to be of very general usefulness since not only halogens, but sulfate, nitro, phenylazo, hydroxyl, nitrate, iodoxy and alkoxy groups also have been found to be displaced by the use of metallic or hydrogen azides (21). Methyl and ethyl azides are prepared by using this method (107).

$$(CH_3)_2SO_4 + 2NaN_3 \longrightarrow 2CH_3N_3 + Na_2SO_4$$

Direct replacement of a diazonium group by the azido group, first accomplished by Noelting and Michel (90), may be used in all cases in which the primary amine can be diazotized.

The reaction between an acid chloride and sodium azide can be carried out under anhydrous conditions according to procedures described by Schroeter (102), Forster (52), and Naegeli (88), or with aqueous sodium azide according to Lindemann (82,109).

The stepwise introduction method is usually not a practical method for the preparation of the aliphatic azides, but has often been used for the preparation of acyl and aromatic azides.

The first method of preparing aryl azides was discovered by Griess (58), the discoverer of phenyl azide. He prepared phenyl azide by the

action of the diazonium perhalide on ammonia;

$$C_6H_5N_2^+ Br_3^- + NH_3 \longrightarrow C_6H_5N_3 + 3HBr.$$

Variations on Griess's method have been reported using hydrazine, hydroxylamine, benzenesulfonamide or chloramine, with both aromatic and aliphatic diazonium groups to bring about the formation of azides (21,107).

The reaction of the arylhydrazines with nitrous acid, previously discussed, is also an important preparative reaction (50). The action of nitrous acid on the hydrazide of an acid produces an acyl azide (104), and hydrazines also have been reported to form aryl azides by gentle oxidation (49). It has been suggested that the symmetrical tetrazene first formed decomposes into the azide and an amine (107).

Sulfonyl azides have been prepared both by the displacement method, and by the nitrosation of a hydrazide (30).

Chemical Properties of the Azides

In general, azides are oily liquids or low-melting solids that decompose slowly if heated gradually, but explode violently on rapid heating. The reactions of the azide, or azido group, are conveniently arranged into three main classifications: displacement, decomposition, and addition reactions.

Displacement of the azide group in alkyl and aryl azides by other than hydroxyl and amino groups has not been reported. Curtius (31) observed that HN_3 was obtained by action of dilute H_2SO_4 upon aliphatic azides such as azidoacetic acid or benzyl azide (21). More recently, the isolation of trace amounts of acetanilide from a mixture of methyl azide, acetophenone and concentrated sulfuric acid, has indicated a transitory existence of hydrazoic acid from hydrolysis (21,110). The resistance to acid hydrolysis is a definite characteristic of the azide

group and the acid-catalyzed decomposition usually is favored under conditions where hydrolysis might take place. This decomposition generally is not base-catalyzed, and even when the azide group is subjected to such rigorous conditions as strong alkali and elevated temperatures, it fails to react (21). Activating groups in the organic molecule have been proved to promote hydrolysis. This is particularly true of the aromatic azides (21).

The acid azides are hydrolyzed by alkalis and acids to hydrazoic acid and the acid from which they are derived (107). However, in most cases this hydrolysis is accompanied by a certain amount of Curtius rearrangement.

The azides have been decomposed thermally and also by acid and by base catalysis. Generally, these decompositions take place with the formation of a multitude of products. Curtius (29,31,32,33), postulated that four different reactions occur simultaneously in the acid-catalyzed decomposition of alkyl azides (21).

A. $RCH_2N_3 \longrightarrow RCH{:}NH + H_2C{:}NR + N_2$

B. $RCH_2N_3 \xrightarrow{[H^+]} RCH_2NH_2 + N_2$

C. $RCH_2N_3 \longrightarrow RCH{:} + HN_3$

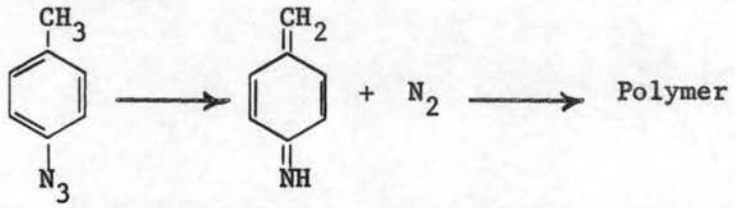
$RCH{:} + RCH_2N{:} \longrightarrow RCH{:}NCH_2R$

D. $RCH_2N_3 + H_2O \longrightarrow RCH_2OH + HN_3$

Later work by Sherk, Houpt, and Brown (105) established that reaction "A" predominates.

Acid-catalyzed decomposition of aryl azides was first observed by Griess (58,60). He found that phenyl azide, decomposed in the presence of halogen acids, produces the corresponding ortho- and para-haloanilines. With sulfuric acid, the para-aminophenol has been isolated (21).

Bamberger and his pupils (8,9,10) made a concentrated study of the decomposition of p-tolyl azide in aqueous sulfuric acid and found the reaction products to include amines, aminophenols and unidentified amorphous acids and bases. By carrying out this reaction at -20°C they were successful in isolating a low-molecular-weight polymer, which Bamberger considered to contain a repeating quinonoid structure. He postulated the following reaction:



Similar results were obtained with o-tolyl azide.

The close similarity of the reaction products from the acid decomposition of phenyl azide to the products obtained in the acid decomposition of N-phenylhydroxylamine suggested that perhaps the first step of the reaction was the formation of the hydroxylamine from the reaction of the azide with water;

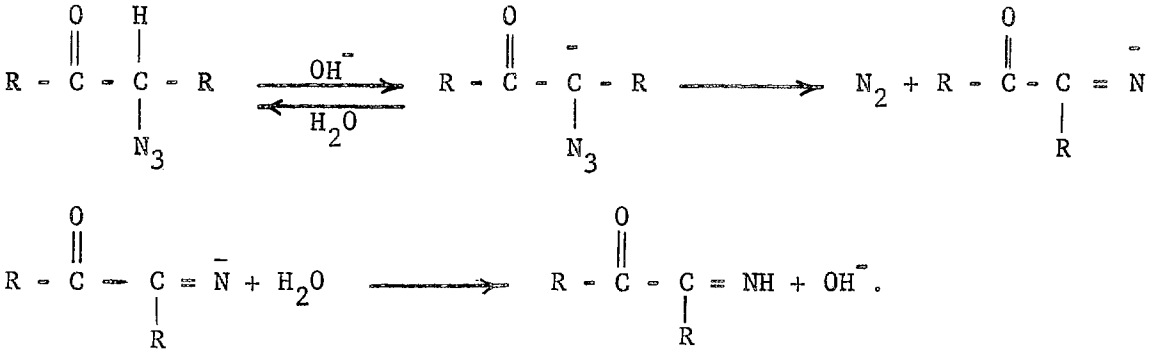
$$C_6H_5N_3 + H_2O \longrightarrow N_2 + C_6H_5NHOH.$$

No azoxy compound, the typical product of the hydroxylamine decomposition, has ever been isolated so this mechanism is doubtful. The similarity is no doubt due to the ability of both compounds to give a similar biradical intermediate (107);

$$C_6H_5NHOH \longrightarrow C_6H_5N: + H_2O$$

$$C_6H_5N_3 \longrightarrow C_6H_5N: + N_2.$$

Base-catalyzed decompositions are indeed rare and usually require an activating group, such as the α-azido carbonyl, and an α-hydrogen atom. A mechanism postulated for this decomposition (53) is;



Under reflux in sodium hydroxide, o-azidobenzaldehyde undergoes oxidation and reduction to anthranilic acid with the liberation of nitrogen (12). Anthranil was considered to be the intermediate (13).

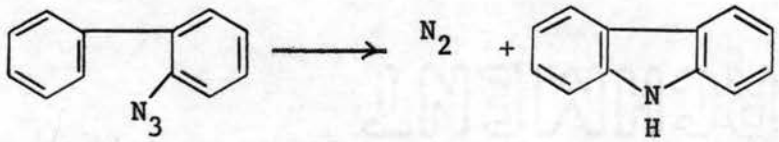
When decomposed thermally, alkyl azides can split at either the carbon-nitrogen or the nitrogen-nitrogen bond, and then the radicals which thus are formed can rearrange or couple. Curtius and co-workers (29,31,33,35) demonstrated this by decomposing benzyl azide and isolating N,N'-dibenzylbenzamidine, benzylidenimine and methyleneaniline. Methyl and ethyl azides (107) in the gas phase undergo a homogeneous unimolecular pyrolysis at a measurable rate to produce ethylene. Ethyl azide also shows nitrogen-nitrogen splitting and produces a mixture of amines as well as ethylene.

The aryl azides are usually more stable, although they decompose slowly between 150-200°C. Substitution in the ortho position usually decreases the azide stability. o-Nitrophenyl azide liberates nitrogen as low as 85°C. The aryl azides are apparently unable to rearrange, and most of their reactions seem to have a biradical;

$$C_6H_5N_3 \longrightarrow N_2 + C_6H_5N:$$

as an intermediate. This radical apparently is able to abstract hydrogen from the solvent to form an arylamine, or to dimerize to form an azobenzene derivative (107). An example of attack of aromatic nuclei by the radical has been reported, but polar attack seems at least as likely (42).

Attack of the aromatic nucleus is favored in those cases where ring closure results, particularly when the azido group is flanked by an electron-attracting group (111).



The acyl azides decompose thermally to give the Curtius rearrangement (109).

$$RCON_3 \longrightarrow RCON: \longrightarrow RNCO + N_2$$

The mechanism of this rearrangement has been the subject of a great deal of discussion and research. It is fairly well accepted that nitrogen is expelled with the formation of the biradical intermediate, but the details of the mechanism of the rearrangement are as yet undetermined. The radical evidently has a very short life; experiments with reactive groups readily available in an adjacent position have produced only the rearrangement products (83). An excellent review of the Curtius rearrangement was written by Peter A. S. Smith (109).

The rigid azides, such as the sulfonyl azides, the diazides of carbonic acid and the azides of sulfuric, carbamic and phenylcarbamic acids, fail to undergo rearrangement, but the biradical which is formed either couples or extracts hydrogen from an aromatic solvent (94,107).

Curtius and co-workers (30) and later Dermer and Edmison (41,46) have studied the products obtained in the decomposition of sulfonyl azides in the presence of aromatic solvents. The reaction can be conceived as follows (42):

A. $ArSO_2N_3 \longrightarrow ArSO_2N: + N_2$

B. $ArSO_2N: + Ar'H \longrightarrow ArSO_2NHAr'$

C. $ArSO_2N: + 2Ar'H \longrightarrow ArSO_2NH_2 + 2Ar'\cdot$.

The fate of the radical formed in reaction "C" as yet has not been determined.

Tables I and II, taken with some rearrangement from the Dermer and Edmison review (42), summarize both the results of Curtius, and those of Dermer and Edmison.

TABLE I

ISOMER RATIOS IN BENZENESULFONAMIDATION AT 105-115°C

Substrates	Average ratio of isomeric anilines*		
	ortho	meta	para
Toluene	60	12	28
Chlorobenzene	56	15	29
Bromobenzene	57	10	33
Anisole	49	21	30
Phenol	58	20	22

* Produced by hydrolysis of the sulfonanilides.

Arenesulfonyl azides with pyridine and quinoline form dipolar compounds, e.g., $C_5H_5\overset{+}{N}\text{-}\overset{-}{N}SO_2Ar$. This is analogous to the conversion of a tertiary amine to an amine oxide or to the reaction of tertiary phosphines with phenyl azide (22).

$$R_3N + [O] \longrightarrow R_3\overset{+}{N}\text{-}\overset{-}{O}$$

$$R_3P + C_6H_5N_3 \longrightarrow R_3\overset{+}{P}\text{-}\overset{-}{N}C_6H_5 + N_2$$

$$C_5H_5N + C_6H_5N_3 \longrightarrow C_5H_5\overset{+}{N}\text{-}\overset{-}{N}SO_2C_6H_5 + N_2$$

Decomposition in the presence of nitrobenzene and benzaldehyde, respectively, fails to give the substituted products, but nitric oxide was observed as a by-product in the attempted substitution of nitrobenzene (42).

The reduction of the azide group to the amino group is extremely easy and proceeds in nearly quantitative yields. A variety of chemical

TABLE II

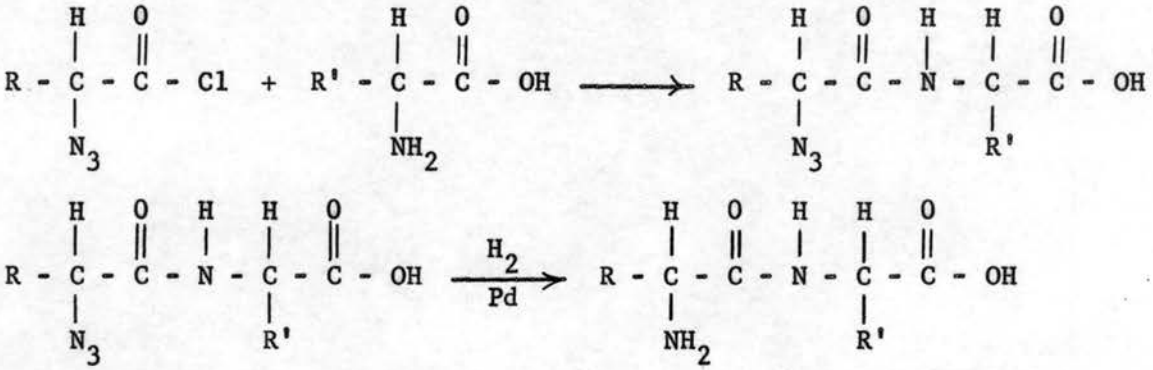
SUMMARY OF SULFONAMIDATION OF AROMATIC SUBSTRATES

Azides	Substrate							
	Benzene	Toluene	Aniline	Methyl-aniline	Dimethyl-aniline	Diphenyl-amine	para-Xylene	Naphthalene
$C_6H_5SO_2N_3$	Normal*	o m p 2.4:0:1		Normal	o m p 1:0:2	Normal*		
p-$CH_3C_6H_4SO_2N_3$	Normal*		ortho only	ortho only	ortho only		Normal*	1-isomer only
p-$ClC_6H_4SO_2N_3$							Normal*	
1,3-$C_6H_4(SO_2N_3)_2$					Fails		Normal*	
p-$CH_3CONHC_6H_4SO_2N_3$							Normal*	
1-$C_{10}H_7SO_2N_3$							Normal*	
2-$C_{10}H_7SO_2N_3$			ortho only	Normal*	Normal*		Normal*	1-isomer only
1,5-$C_{10}H_6(SO_2N_3)_2$							Normal*	
2-Anthraquinone-sulfonyl azide							Normal*	

* Normal substitution, but isomer ratios not reported or not possible.

and catalytic methods have been reported for this reduction. Both acid and basic media have been used chemically, the most common of which are zinc and hydrochloric acid and amalgamated aluminum in aqueous ammonia (21).

Palladium and platinum oxides have been reported as excellent catalysts for the reduction of azides (107). An application for this low-temperature reduction is found in the Bertho (18) synthesis of peptides.



Metallic and hydrogen cyanides, Grignard reagents, and tertiary phosphines add to the terminal nitrogen of the azide group;

$$C_6H_5N_3 + HCN \longrightarrow C_6H_5N{:}NNHCN$$

$$C_6H_5N_3 + RMgI \longrightarrow C_6H_5N{:}NN(MgI)R$$

$$C_6H_5N_3 + (C_6H_5)_3P \longrightarrow C_6H_5N{:}N\bar{N}\text{-}\overset{+}{P}(C_6H_5)_3 .$$

However, tautomerization has been reported in the case of the cyanide adduct and the hydrolysis product of the Grignard addition (21);

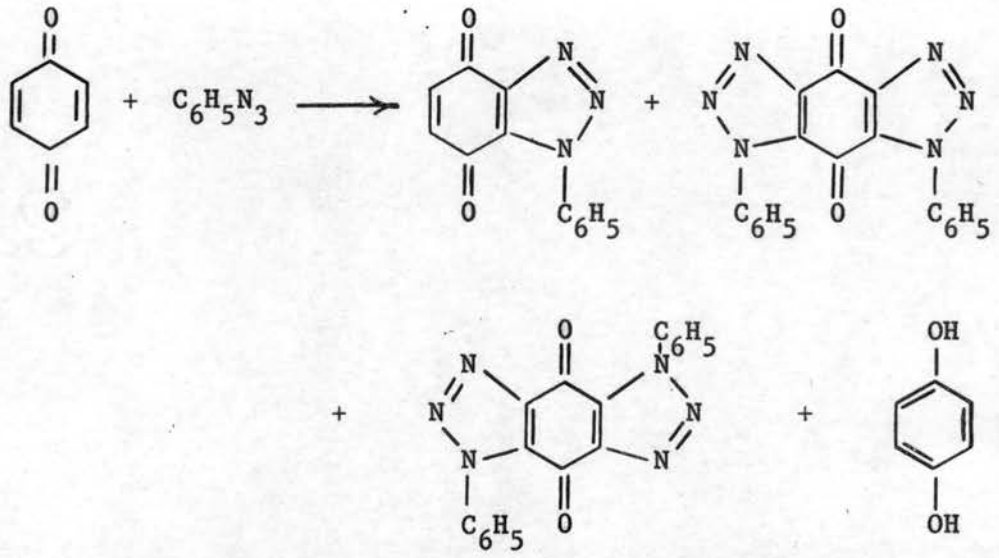
$$C_6H_5N{:}NNHCN \underset{}{\overset{10\%\ KOH}{\rightleftharpoons}} C_6H_5NHN{:}NCN$$

$$C_6H_5N{:}NNHR \rightleftharpoons C_6H_5NHN{:}NR .$$

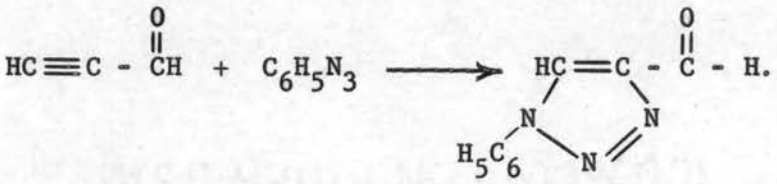
3-Methyl-1-phenyltriazene rivals diazomethane as a methylating agent.

Additions of azides into unsaturated bonds are in general more difficult than the additions of aliphatic diazo compounds. Conjugated olefins, such as styrene, are very unreactive, but if the double bond is in a strained ring, the additions occur readily (91). Wolff and Grau (118)

obtained a mono- and two bis-adducts from the reaction of phenyl azide with p-benzoquinone.



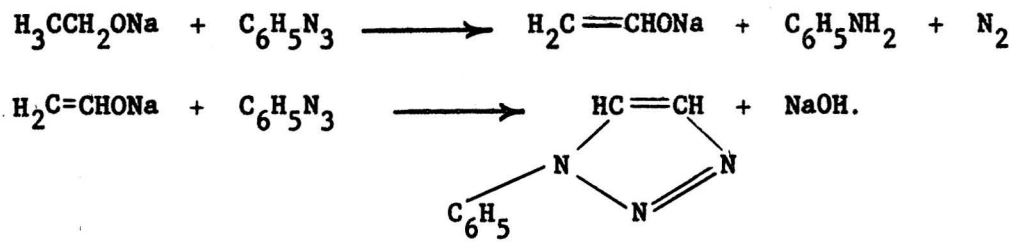
Acetylenes are somewhat more reactive towards the azide group than are olefins but still are less reactive than the aliphatic diazo compounds. The reaction is quite general, and phenyl azide usually adds to unsymmetrical alkynes so that the nitrogen attached to the phenyl group is also bound to the acetylenic carbon which bears the hydrogen substituent (21):



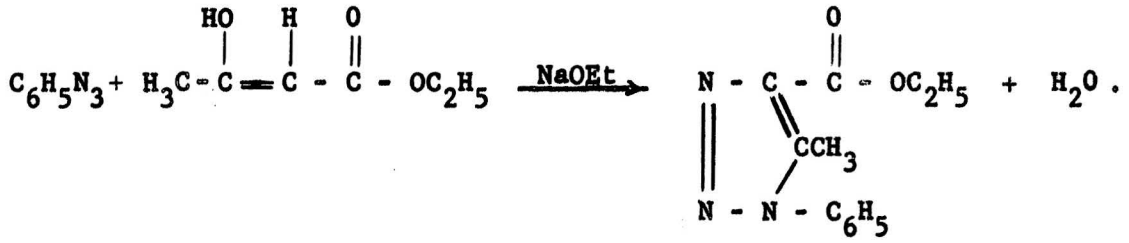
Azide groups, in general, do not add to nitriles.

The additions of azides in the presence of a base has been reported for a large number of compounds containing an active methylene group.

Phenyl azide and sodium ethoxide react when heated in ethyl alcohol to give phenyltriazole, aniline, nitrogen, and sodium hydroxide. The following mechanism has been postulated (17):



Phenyl azide reacts with acetoacetic ester in the presence of sodium ethoxide to form the ethyl ester of 4-carboxy-5-methyl-1-phenyltriazole:



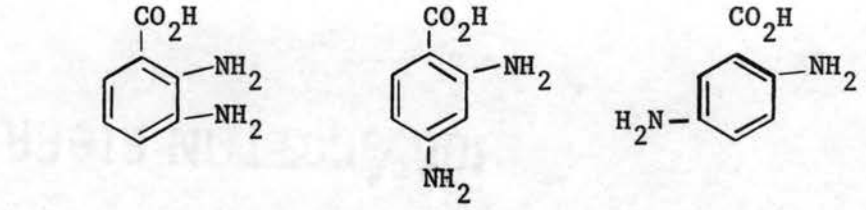
This reaction is apparently quite general; various other aryl azides will react with acetophenone, cyanoacetic ester, malonic ester, and other compounds containing enolizable methylene groups (16,21). Curtius (30) has demonstrated that the arenesulfonyl azides also add to active methylene groups in the presence of sodium ethoxide.

AROMATIC SUBSTITUTION

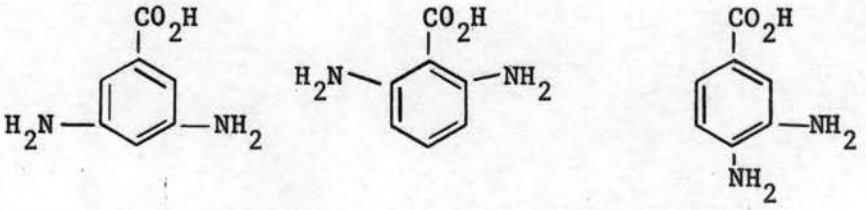
Early Concepts

Interest in orientation of various substituents commenced shortly after good procedures were developed for determining the exact position of a substituent on the aromatic nucleus. Such procedures were developed independently by Griess (59), Salkowsky (100), and Koerner (77), and demonstrated the relationship between di- and tri-substituted benzenes rather than between two disubstituted benzenes. The following will serve as an example (75):

The six known derivatives of diaminobenzoic acid



(A) (B) (C)



(D) (E) (F)

were decarboxylated and it was found that in two cases (A and F), one of the diaminobenzene derivatives (X) only was formed. In three cases (B, D, and E) another diaminobenzene derivative (Y) only was formed, and in the remaining case (C) still another diaminobenzene (Z) was produced. From this information, even though the exact configuration of the six diaminobenzoic acids had not been determined, one could prove that (X) is ortho, (Y) is meta, and (Z) is para diaminobenzene.

It was not long until a vast amount of experimental evidence established that there were two contrasting types of orientation, namely ortho-para and meta orientation, depending upon the group already present. Many rules were established during this time to explain or at least to correlate this data. Only the most highly accepted rules shall be discussed in this dissertation.

Koerner (77), Hubner (69) and Noelting (89) each established separate rules of orientation but all were actually based upon the postulate that

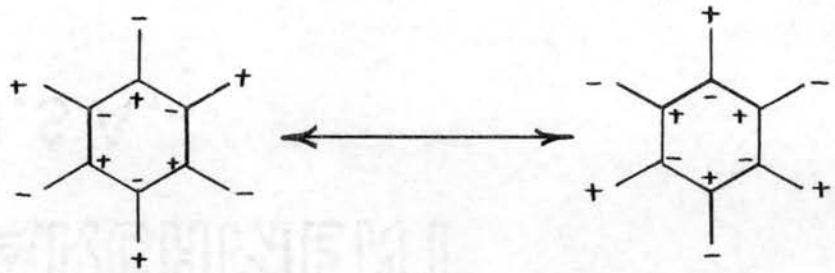
> negative groups, those that confer or enhance acid properties, will, provided that their electronegativity is strong enough, direct a new substituent to the meta position; and positive groups, those that confer or enhance basic properties, as well as neutral, and even weakly negative, groups, will direct new substituents into the ortho and para positions (75).

This rule was the forerunner of modern day "inductive effect" in aromatic substitution.

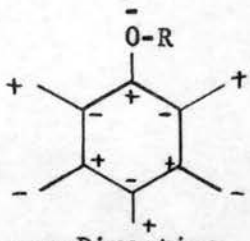
Armstrong (3) and later Vorlander (115) stated, in the form of rules, that if the atom attached to the benzene nucleus is involved in a multiple bond, the group directs to the meta position and all other groups direct to the ortho and para positions. Crum Brown and Gibson (25) formulated, at this time, their famous rule: "A substituent X would be meta directing if HX could be directly oxidized to HOX, ortho-para directing otherwise" (75). The rules of Armstrong, Vorlander and Brown and Gibson were forerunning rules of what later would become known as mesomeric or resonance effects in orientation of aromatic nuclei.

One of the first attempts to incorporate these rules into a theory was made by Flurscheim (51). This theory was based upon Werner's concept of chemical affinity which supposedly was initiated by the substituent and propagated around the ring giving to alternate carbon atoms small and large values of chemical affinity, respectively. Thus, groups were considered to be either groups of small affinity, those that directed entering groups to the meta position, or large affinity, those that directed to the ortho and para positions (75).

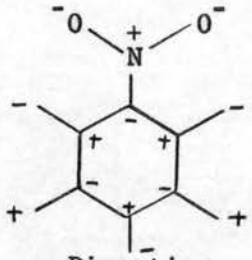
Another very closely related theory was the theory of alternate polarities (54,75). According to this theory, benzene resonates between the two forms



Thus, any group present on the ring could affect the ratio of these two forms and favor certain orientations. For example;



o-p-Directing



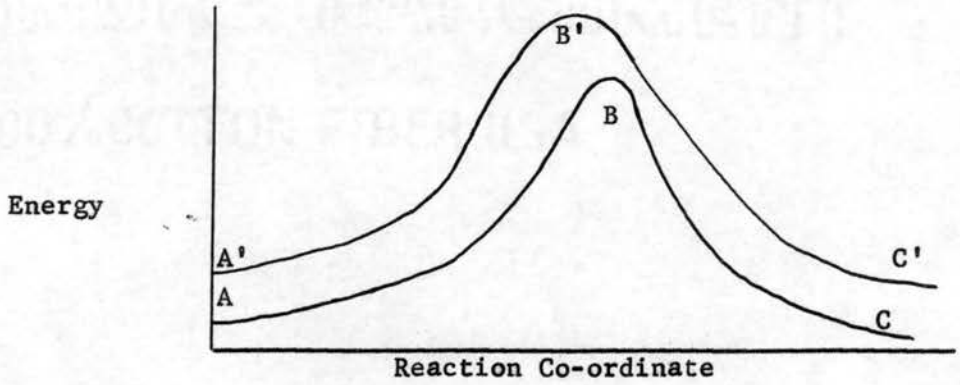
m-Directing

Holleman (72) pointed out, however, that any theory in which the meta carbon atom is postulated as being modified exactly in the same manner as the ortho and para carbon atoms must be incorrect because the rate of the reaction is increased by ortho- and para-directors and decreased by meta-directing groups. Thus, both the theory of chemical affinity and alternate polarities were discredited. Holleman postulated a direct addition of the entering group into the Kekule double bond with the group already present influencing the orientation by modification of the addition reaction. It is upon this concept that modern theories of aromatic substitution are based.

Modern Electronic Theories of Orientation

There are two approaches to the modern electronic theory of orientation. The first approach considers the "residual affinities" of a position for homolytic, and the permanent charge on the molecule for

heterolytic substitution. This approach is called the "isolated molecule" approach. The other method is the study of the energy of the intermediate in the reaction and is called the "transition state" approach. For example, consider the reaction paths ABC and A'B'C' of two reactions, such as the formation of an ortho and a meta isomer (6).



In the isolated molecule method, the sections of the two paths near A and A' are considered and from their relative positions the relative reaction rate between the two positions is predicted. The transition state method involves the relative energy differences between AB and A'B' and from this the relative reaction rate is derived.

The transition state method is quantitatively applicable to both homolytic and heterolytic substitution. The isolated molecule method is quantitative for homolytic substitution, but owing to time-variable perturbations which are set up by the approaching ion, is only qualitative in heterolytic substitution.

Augood and Williams (6) have an excellent discussion on the various methods used in determining the reactivity of a position by these two approaches.

The "English School" has developed an isolated molecule method that is descriptive rather than mathematical in nature. Though it is not useful quantitatively it has proved very valuable for qualitative

predictions. In general, there are four separate electronic effects possible for each group. The inductive ($\pm$I) effect is a permanent effect in the molecule caused by a pole, dipole, or an electronegative group; the mesomeric ($\pm$M) effect is a permanent resonance effect which either withdraws electrons (-) or forces electrons (+) into the reaction center; the inductomeric ($\pm I_d$) effect is a time-variable inductive effect set up by an induced dipole as the ion approaches; the electromeric ($\pm$E) effect is a time-variable resonance effect. Table III, from Ingold's book (75), illustrates these effects on some of the more common aromatic compounds.

TABLE III

CLASSIFICATION OF ORIENTING SUBSTITUENTS IN ELECTROPHILIC SUBSTITUTION (75)

Type	Electronic mechanism	Examples	Effect on Orientation	Effect on Reactivity
+I	Ph $\leftarrow$ R	Ph—CH_3	ortho-para	Activation
-I	Ph $\rightarrow$ R	Ph—CO_2Et	meta	Deactivation
		Ph—SMe_2	meta	Deactivation
-I+M	Ph $\rightarrow$ R	Ph—Cl	ortho-para	Deactivation
		Ph—OCH_3	ortho-para	Activation
+I+M	Ph $\leftarrow$ R	Ph—O^-	ortho-para	Activation

The inductomeric and electromeric effects are called into play only upon demand and, thus they always favor and never inhibit a given reaction. The electromeric effect when present is usually the strongest single effect and, thus usually determines the position of substitution.

Inductive effects usually influence the closer ortho position to a greater degree, while resonance effects have a greater influence on the para position.

Experimental Method

The competitive method first used by Ingold (76) is perhaps the best method for studying the rates of heterolytic and homolytic substitution, since it is independent of control. According to Ingold (75),

> One allows the compounds under comparison, say, benzene and toluene, in known proportions, to compete in the same homogeneous solution, for a small amount, in simplest principle an indefinitely small amount, of the common reagent, say, nitric acid; and then, without following what happens as a function of time, one determines the proportions of the products, in our example, nitrobenzene and total nitrotoluenes, after the conclusion of the reaction.

The relative specific reaction rates of the reactions can be calculated as follows (76): Let Y equal the amount of benzene, X the amount of the other aromatic substrate, and Z the amount of the compound which X and Y are competing for. Then the rate of disappearance of X and Y can be expressed by the two rate equations:

$$- dx/dt = k_x XZ \text{ and } - dy/dt = k_y YZ$$

or

$$- dx/dt = k_x X [X + Y - (X_o + Y_o) + Z_o]$$

and

$$- dy/dt = k_y Y [X + Y - (X_o + Y_o) + Z_o]$$

where X_o, Y_o, and Z_o represent the initial concentrations of X, Y, and Z respectively, and k_x and k_y are the respective specific reaction rate constants of X and Y reacting with Z. The above equations are simultaneously integrated:

$$k_x/k_y = (\log X_\infty - \log X_o)/(\log Y_\infty - \log Y_o)$$

where X_∞ and Y_∞ are the ultimate values of X and Y. Given the two equations of state:

$$X_\infty + Y_\infty = X_o + Y_o - Z_o \text{ and } R = (X_o - X_\infty)/(Y_o - Y_\infty)$$

where R is the ratio of the products, one then can find an expression for the relative reaction rate with respect to benzene (^X_HK), by calculation of the ratio of the specific reaction rate constants.

$$^X_HK = k_x/k_y = \frac{\log\left[1 - \frac{Z_o R}{X_o(1+R)}\right]}{\log\left[1 - \frac{Z_o}{Y_o(1+R)}\right]}$$

Thus it can be seen that if the initial concentrations and the ratio of the products are known the specific reaction rate constants can be easily calculated.

The partial and the total rate factors with respect to benzene are obtained in the following manner:

$$k_x = 2\,^Xk_{\underline{o}} + 2\,^Xk_{\underline{m}} + {}^Xk_{\underline{p}}$$

where $^Xk_{\underline{o}}$, $^Xk_{\underline{m}}$, and $^Xk_{\underline{p}}$ are the partial rate constants for the <u>ortho</u>, <u>meta</u> and <u>para</u> positions, respectively, in substrate X, and allowance is made for the fact that there are two <u>ortho</u> and two <u>meta</u> positions and one <u>para</u> position. In benzene, where each position is equivalent,

$$k_H = 6\,^Hk,$$

and thus

$$6\,^X_HK = 6k_x/k_H = 2\,^X_Hk_{\underline{o}} + 2\,^X_Hk_{\underline{m}} + {}^X_Hk_{\underline{p}}$$

where $^X_Hk_{\underline{o}}$, $^X_Hk_{\underline{m}}$, and $^X_Hk_{\underline{p}}$ are the partial rate factors of substrate X with respect to benzene. The partial rate factors can be calculated from the total reaction rate with respect to benzene since the mole fraction (<u>o</u>) of the <u>ortho</u> isomer produced can be expressed by

$$(\underline{o}) = \frac{2{}^{X}_{H}k_{o}}{2{}^{X}_{H}k_{\underline{o}} + 2{}^{X}_{H}k_{\underline{m}} + {}^{X}_{H}k_{\underline{p}}}$$

or

$${}^{X}_{H}k_{\underline{o}} = 3{}^{X}_{H}K(\underline{o})$$

and, similarly, for the meta and para isomer

$${}^{X}_{H}k_{\underline{m}} = 3{}^{X}_{H}K(\underline{m}) \quad \text{and} \quad {}^{X}_{H}k_{\underline{p}} = 6{}^{X}_{H}K(\underline{p}).$$

There have been a number of assumptions made in this derivation which must therefore restrict this method (75,76).

(a) The relevant reaction stage must be of the same reaction order with respect to each of the two substances.

(b) There must not be a multiplicity of parallel relevant stages dependent on different active entities.

(c) There must be enough excess of the two competing components that the concentration of each component does not decrease appreciably during the course of the reaction.

Experimental Results

There has been a great deal of experimental work completed on the determination of isomer ratios. Since the ratios vary with such conditions as solvent and temperature, the discussion in this dissertation shall be limited to nitration, chlorination, bromination, sulfonation, phenylation, and substituted phenylation of the substrates which were used successfully in the experimental section of this thesis (73).

Electrophilic Substitution: Heterolytic substitutions show large deviations from the theoretically calculated orientations and reaction rates (6). The "English School" however, gives a fairly accurate qualitative approach. In many ways the "English School" approach might

actually be considered a series of orientation rules, which are based upon experimental evidence, rather than electronic theory. Many times the two variables, i.e., inductive and resonance effects, oppose one another, and an experiment must be made to see which effect is dominant. The value of this approach lies in the interpretation of vast amount of experimentation that has been accomplished. A comprehensive review of this work would certainly extend this dissertation unduly.

The "normal laws" of the so-called "English School," which have been based mainly upon nitration, place the various substituents into two main categories for electrophilic aromatic substitution (6).

(1) The ortho-para-directing substituents, which activate the aromatic nucleus in the following order;

$NH_2 > OH > OCH_3 > OCOCH_3 > CH_3 > Cl;Br > C_6H_5 > CH_2COOH$.

(2) The meta-directing substituents, which deactivate the aromatic nucleus in the following order;

$(CH_3)_3N+ > NO_2 > SO_3H > CHO > COCH_3 > COOH > NH_3^+$.

The ortho- and para-directing substituents activate not only the ortho and para positions, but also the meta position. The rate of nitration of the meta position of toluene, with respect to benzene ($\frac{X}{H}k_m$) is equal to 2.5 (75).

Halogens have been found to deactivate the ring even though they are ortho- and para-directing substituents. This is explained by the strong time-variable or electromeric effect controlling the orientation, and the strong inductive effect, induced by the electronegative halogen group, controlling the rate of reaction.

Temperature, medium, and catalyst also have been found to have an effect on the ratios of isomers (73). In contrast to its effect in

homolytic substitution, elevation of the temperature increases the amounts of ortho and meta isomers for ortho-para-orienting molecules, and the ortho and para isomers for the meta-orienting molecules. This can be explained as lack of importance of the greater stability of the 1,4-quinonoid structure at elevated temperatures. The changes in ratio with respect to medium and catalyst, though often quite large, are not general in nature.

Steric effects from both the ion and the substituent already present in the molecule have been recognized. Le Fevre (79) has stated that the higher percentage of para isomer as one nitrates the higher homologues of toluene is attributable to the steric effects of the substituent already present. Cohn, Hughes and Jones (75), using rate of nitration of these homologues compared to the rate for benzene, have verified this conclusion. Holleman (73) has shown that the size of the entering group has as much to do with the orientation as the size of the group already present. As can be seen in Table IV, if one increases the size of the approaching ion in the following order:

$$Cl^+ < NO_2^+ < Br^+ < HO_3S^+$$

the amount of ortho isomer decreases.

TABLE IV

RELATIVE ORIENTATION IN ELECTROPHILIC SUBSTITUTION REACTIONS (55,73,74,75,76)

Substrate		Entering Substituent			
		Cl	NO_2	Br	HO_3S
Toluene	o	57.7*	56.0	39.7	31.9
	m	0.5*	3.1	0.0	6.1
	p	41.8*	40.9	60.3	62.0
Chlorobenzene	o	39.0	30.1	11.2	0.0
	m	6.0	0.0	1.6	0.0
	p	55.0	69.9	87.2	100.0
Bromobenzene	o	45.1	37.6	13.1	0.0
	m	2.4	0.0	1.8	0.0
	p	52.5	62.4	85.1	100.0
Phenol	o	49.8	40.0	9.8	---
	m	0.0	0.0	0.0	---
	p	50.2	60.0	90.2	Mainly
Anisole	o		9.0	4.0	---
	m		0.0	0.0	---
	p		91.0	96.0	Mainly
Methyl benzoate	o		30.0		
	m		68.0		
	p		0.0		
Benzoyl chloride	o		8.0		
	m		90.0		
	p		2.0		

* Estimated from Condon's partial rate factors.

Tables IV and V show the ratios of the isomers and the relative rate with respect to benzene, respectively, for most of the substrates used in the experimental section of this dissertation.

TABLE V

RELATIVE RATES FOR ELECTROPHILIC SUBSTITUTION REACTIONS (75,98,112)

Substrate	Substitution Reaction		
	Nitration $^{x}_{H}K$	Halogenation $^{x}_{H}K$	Sulfonation $^{x}_{H}K$
Toluene	24.5	3.4×10^{2}	5.04
Chlorobenzene	0.033	0.11*	0.767
Bromobenzene	0.030	0.08*	0.813
Phenol	1.0×10^{4}	$1.1 \times 10^{11}_{9}$	
Anisole		$1.2 \times 10^{-4*}$	
Ethyl benzoate	0.0037	5.0×10	

* Chlorination; other values in this column are for bromination.

Nitration is perhaps the most characteristic of the ionic reactions, because it is relatively free from steric effects and also has little tendency to go through a free-radical mechanism. Sulfonation shows predominant <u>para</u> orientation because of steric effects. Halogenation shows unusual kinetic behavior because of parallel radical attack. For these reasons, most of the theory of ionic aromatic substitution is based upon nitration.

Nitration of phenol and anisole has been found to be very dependent upon conditions. Nitration with concentrated nitric acid that is free of nitrous acid (27), with nitrogen tetroxide in acetic acid (27), and with benzoyl or acetyl nitrate (61) gives an <u>ortho</u> to <u>para</u> ratio of 7/3, while dilute nitric acid, in the presence of nitrous acid,

gives an ortho to para ratio of about 1/7 (61). The latter has been considered to represent the actual ionic attack of the NO_2^+ ion and the former the attack of various oxides of nitrogen, probably either N_2O_4 or N_2O_5 (27). The oxides of nitrogen (114) or heavy metal nitrates such as those of iron and copper (7) in acetic acid, nitrate most of the compounds with ortho-para-directing groups already present on the ring with a predominance of ortho isomer. Those with meta-directing groups failed to react even under pressure or in the presence of aluminum chloride.

It is also interesting to note that the vapor phase chlorination of anisole in the presence of ultraviolet light produces an 80% yield of o-chloroanisole and some p-chloroanisole (4).

Radical Substitution: Homolytic substitution is in much better quantitative agreement with theoretical calculations than are the ionic substitutions, provided steric or polar effects are not present (6). Phenylation has proved to be the only substitution reaction studied in which these effects are not dominant, and even here some electrical effects may be present (99,117). Unfortunately, simple alkyl radicals, which are also neutral or nearly so, have not proved to be applicable to this type of aromatic substitution. Goldschmidt and Mensinger (56) found, however, that alkyl groups, generated by electrolysis and by pyrolysis of the acyl peroxides, substituted in the two and four positions of pyridine with a definite preference for the two position. Edwards and Mayo (48) found that for the attack on toluene and methyl benzoate by methyl radicals, which were generated from diacetyl peroxide, the relative rate with respect to benzene was 19.2 and 1.6, respectively. The high value for toluene is explained by the preference

of the methyl radical for abstracting hydrogen from the alkyl group, thus forming free benzyl radicals. Levy and Szwarc (81) have made a number of methylations of polynuclear hydrocarbons, and their results have shown a high degree of correlation with results from phenylation (6).

Phenyl radicals undoubtedly have been the most extensively studied radicals in homolytic substitutions. Generation of the phenyl radicals has been accomplished with diazotates, diazoacetates, diazo compounds, aroyl peroxides, metallo-organic compounds, and by the oxidation of phenylhydrazine with metallic oxides (42,64). The pyrolysis of aroyl peroxides has been used most extensively because it meets the requirements for the competitive reactions.

Hey and co-workers (6,67), using nitrobenzene and pyridine as reference solvents, and Dannley, Gregg, Phelps and Coleman (36,37), as well as Rondestvedt and Blanchard (99), using pyridine as the reference solvent, decomposed benzoyl peroxide in dilute solutions (0.01 - 0.06 mole fraction) in monosubstituted benzene derivatives and the respective reference solvent. Their results, along with those of Huisgen and Sorge (6,74), who also used pyridine as a reference solvent, but used an acylphenylnitrosamine to generate their phenyl radicals, appear in Table VI. The results of Hey and co-workers are in column (1), those of Dannley, Gregg, Phelps and Coleman and those of Rondestvedt and Blanchard are in column (2) and Huisgen and Sorge's results are in column (3).

TABLE VI

RELATIVE RATES OF PHENYLATION OF COMPOUNDS C_6H_5X (6)

X	(1) 80°C	(2) 70°C	(3) 20°C
NO_2	4.0		3.0
F	1.35		
Cl	1.44	1.35	1.5
Br	1.75	1.35	1.6
I	1.80	1.65	
CN		3.7	
CH_3	1.68		1.9
C_2H_5	1.24		
$\underline{i}$-C_3H_7	0.87		
$\underline{t}$-C_4H_9	0.87		
C_6H_5	4.0		3.0
CH_3O	2.5	1.2	2.0
SO_3CH_3		1.5	
CF_3		0.99	
$Si(CH_3)_3$		1.06	

Early studies of orientation in phenylation reactions showed a preponderance of the <u>para</u> isomer. However, this has been attributed to the ease of separation of this isomer compared to the others. With the use of new analytical techniques and new instruments, the results have become much more reliable and the <u>para</u> isomer is no longer believed to be predominate. A considerable number of investigators have been active in determining the orientation of various substituents in phenylation reactions (42). Table VII reviews the ratios obtained by using benzoyl peroxide to generate the phenyl radicals.

TABLE VII

RATIO OF ISOMERS FORMED BY THE PYROLYSIS OF BENZOYL PEROXIDE AT 70-80°C IN AROMATIC SUBSTRATES (6,42)

Aromatic Compound	Isomer Percentage		
	ortho	meta	para
$C_6H_5NO_2$	58	10	32
C_5H_5N	58	28	14
C_6H_5F	54.1	30.7	15.2
C_6H_5Cl	60.3	25.9	13.8
C_6H_5Br	49.3	33.3	17.4
C_6H_5I	51.7	31.6	16.7
C_6H_5CN	60.0	10	30
$C_6H_5CH_3$	66.5	19.3	14.2
$C_6H_5C_2H_5$	53	28	19
$C_6H_5C_3H_7$-i	31	42	27
$C_6H_5C_4H_9$	24	49	27
$C_6H_5C_6H_5$	48.5	23.0	28.5
$C_6H_5CF_3$	20	40	40
C_6H_5COOH	59	15	26
$C_6H_5OCH_3$	67	18	15
$C_6H_5CCl_3$	0	60	40
$C_6H_5SO_3CH_3$	53	33	14
$C_6H_5Si(CH_3)_3$	31	45	24

The isomer ratios for phenylation have been found to be independent of the source of the radical, provided that the reactions occur at the same temperature (6,68). The temperature on the other hand seems to have a fairly large effect on the final percentages of the isomers. The reaction at the ortho position, which has the smallest energy of activation, becomes less important on increasing the temperature (6). Solvent effects have been reported, but as yet the information is inconclusive (5,37).

The effect of a group in the para position of a phenyl radical was first observed by Dannley and Sternfeld (38), when they decomposed benzoyl peroxide, p-chlorobenzoyl peroxide and p-nitrobenzoyl peroxide individually in benzotrichloride and found the percentage of meta isomer to increase in the following order:

$$C_6H_4NO_2 > C_6H_4Cl > C_6H_5.$$

DeTar and Kazimi (43), decomposing 3- and 4-nitrobenzenediazonium chlorides in nitrobenzene, also observed an increase in meta isomer with respect to phenylation.

Hey and co-workers (6,28,65,67) have run competitive experiments, similar to those for phenylation, with para-substituted radicals, and have observed the results tabulated in Table VIII.

TABLE VIII

RELATIVE RATES OF ARYLATION WITH SUBSTITUTED PHENYL RADICALS AT 80°C (6)

Radical	$\frac{NO_2}{H}K$	$\frac{Cl}{H}K$	$\frac{CH_3}{H}K$
p-Nitrophenyl	0.94	1.17	2.61
p-Chlorophenyl	1.53	1.02	1.32
p-Methoxyphenyl	2.92	1.56	---
Phenyl	4.0	1.49	1.68
p-Tolyl	5.13	2.05	1.03

It can readily be seen that as the electronegativity of the para substitutent is increased,

$$H_3C- < H- < CH_3O- < Cl- < O_2N-$$

the rates of substitution of nitrobenzene and chlorobenzene are decreased and the rate of substitution of toluene is increased. This is exactly as one would expect for an electrophilic substitution.

Shih, Hey, and Williams (106) have recently measured the ratio of isomers formed in the arylation of nitrobenzene with p-chlorophenyl and p-bromophenyl radicals generated from the corresponding benzoyl peroxides. Morrison and Sweeney (87) measured the isomer ratio of isomers formed when p-nitrobenzoyl peroxide was decomposed in nitrobenzene and anisole. Table IX shows the results of Shih, Hey, and Williams, and the results of Morrison and Sweeney.

TABLE IX

ORIENTATION IN ELECTROPHILIC RADICAL SUBSTITUTION OF NITROBENZENE AND ANISOLE (87,106).

Radical	Substrate	Percentage of isomer		
		ortho	meta	para
Phenyl	nitrobenzene	62.5	9.8	27.7
p-Chlorophenyl	nitrobenzene	59.0	13.8	27.2
p-Bromophenyl	nitrobenzene	57.7	13.2	29.1
p-Nitrophenyl	nitrobenzene	58.0	13.0	29.0
p-Nitrophenyl	anisole	89.0	8.0	3.0

It is now obvious that one can speak of electrophilic and nucleophilic radicals, since the overall reaction is determined not only by the nature of individual positions of the substrate, but also by the charge distribution of the attacking radical. Electronic perturbations induced by this charge distribution render the quantitative calculations as invalid as the calculations for ionic substitutions.

EXPERIMENTAL

All reagents used in the experimentation for this dissertation were C.P.-grade with a few exceptions. In those cases where C.P.-grade materials were not available, purification was accomplished by fractional distillation of the liquids on a 30-plate Oldershaw column and by recrystallization of the solid chemicals.

SYNTHESIS OF THE ISOMERIC BENZENESULFONANILDIDES

Three methods were used in the synethesis of the benzenesulfonanilide derivatives. In all three procedures, the corresponding arylamine reacted with benzenesulfonyl chloride in the presence of a base. When possible, a ten percent sodium hydroxide solution was used as the reaction medium, but in a number of synthesis, the alkali caused undesirable hydrolysis or side reactions. In these latter syntheses, pyridine and toluene were used as reaction media.

Synthesis in Ten Percent Sodium Hydroxide Solution

Fifteen-hundredths mole of the appropriate arylamine was placed in a 500-cc Erlenmeyer flask. To this were added 250 cc of a 10% sodium hydroxide solution, and 20 cc of benzenesulfonyl chloride. The reaction flask was stoppered with a rubber stopper and shaken until the contents of the flask cooled to room temperature. This usually required about 30 minutes. The mixture then was placed on a steam bath and the temperature was maintained at approximately 85°C for one hour. During this time the flask was shaken occasionally. After this process, the reaction mixture was

treated with activated charcoal and filtered. To the filtrate was added enough concentrated hydrochloric acid to make the solution definitely acid and thus precipitate the derivative. The solution was cooled and filtered to remove the crude crystalline product, and this crude product was recrystallized five or six times from dilute ethanol. Dilute methanol was found to be a better recrystallization solvent for the isomeric benzenesulfontoluidides and xylene for the isomeric benzenesulfonamidobenzoic acids.

The yields of the purified products from this method varied but were usually around 30-50% of theoretical.

Since m-anisidine was not commercially available, it was prepared by the reduction of m-nitroanisole with tin and hydrochloric acid.

Table X contains the names and melting points of the isomeric derivatives that were prepared by this procedure:

TABLE X

MELTING POINTS OF THE BENZENESULFONANILIDE DERIVATIVES PREPARED IN 10% NaOH

	Melting point, °C		
	Found	Literature	Ref.
o-Benzenesulfonanisidide	88-89	89	45
m-Benzenesulfonanisidide	80.0-80.5	82.5-83.5	96
p-Benzenesulfonanisidide	92.0-93.0	95	23
o-Benzenesulfonamidobenzoic acid	213-214	214-215	92
m-Benzenesulfonamidobenzoic acid	197-200	-	-
p-Benzenesulfonamidobenzoic acid	211-212	212	101
o-Benzenesulfonamidobromobenzene	128-130	130-131	96
m-Benzenesulfonamidobromobenzene	117.5-118.5	117.5-118.5	96
p-Benzenesulfonamidobromobenzene	134	134	96
o-Benzenesulfonamidochlorobenzene	129-130	129	97
m-Benzenesulfonamidochlorobenzene	119-120	121	97
p-Benzenesulfonamidochlorobenzene	120-121	121	97
o-Benzenesulfontoluidide	121-123	124	70
m-Benzenesulfontoluidide	90.5-92.5	95	71
p-Benzenesulfontoluidide	120-120.5	120-121	116
Benzenesulfonanilide	106-107	108.5-109	55

Synthesis in Pyridine

One-tenth mole of the arylamine, 12.6 cc of benzenesulfonyl chloride, and 150 cc of pyridine were placed in a 500-cc roundbottom flask. The flask was then equipped with a reflux condenser, and the reaction mixture was heated to reflux temperature. After 2½ hours of refluxing, the pyridine mixture was cooled in an ice bath, and poured into a beaker containing ice and concentrated hydrochloric acid. Additional hydrochloric acid was added when necessary to make the solution definitely acid. The contents of the beaker were cooled and filtered to remove the crude product. The product was recrystallized three times from dilute ethanol. The yield of purified product, using this method, was about 50% of theoretical. In Table XI are listed the names and melting points of the isomeric derivatives that were prepared by this procedure:

TABLE XI

MELTING POINTS OF BENZENESULFONANILIDE DERIVATIVES PREPARED IN PYRIDINE

Compound	Melting point, °C		
	Found	Literature	Ref
o-Methyl benzenesulfonamidobenzoate	104	107	103
m-Methyl benzenesulfonamidobenzoate	158-160	---	---
p-Methyl benzenesulfonamidobenzoate	153-155	---	---
p-Benzenesulfonamidobenzonitrile	172-175	175-176	19
o-Benzenesulfonamidonitrobenzene	100-101	104	86
m-Benzenesulfonamidonitrobenzene	130-132	133-135	86
p-Benzenesulfonamidonitrobenzene	138-139	139	86

Basic hydrolysis of the methyl benzoate and benzonitrile derivatives produced the corresponding benzenesulfonamidobenzoic acid.

Synthesis in Toluene (93)

This synthesis was used only to prepare the isomeric benzenesulfonamidophenols, to prevent substitution on the hydroxyl group rather than the amino group.

Six and four-tenths grams of benzenesulfonyl chloride, 10.9 grams of the corresponding aminophenol, and 100 cc of toluene were placed in a standard reflux apparatus, and refluxed for one hour. The toluene solution then was treated with charcoal, filtered and cooled. The white crystalline product that formed was filtered and recrystallized from toluene. Table XII gives the isomeric benzenesulfonamidophenols and their melting points.

TABLE XII

MELTING POINTS OF ISOMERIC BENZENESULFONAMIDOPHENOLS

Compound	Melting point, °C		
	Found	Literature	Ref.
o-Benzenesulfonamidophenol	139-140	141	93
m-Benzenesulfonamidophenol	131.0-131.5	---	--
p-Benzenesulfonamidophenol	155-156	156	1

Preparation of the Isomeric Benzenesulfonamidoanilines (86)

Fourteen grams of the corresponding benzenesulfonamidonitrobenzene were added to 100 cc of hot water in a 500-cc roundbottom flask. To this mixture were added 2 grams of acetic acid and 10 grams of iron powder. A reflux condenser then was placed on the flask, and the mixture was refluxed for 1½ hours. Additional hot water was added as the reduction progressed.

After this time, the solution was made basic with sodium bicarbonate, heated and filtered rapidly while hot. The filtrate was cooled, and in the case of the meta derivative, a white crystalline product developed. The other two derivatives were obtained by extraction of the precipitate with hot ethyl alcohol, and precipitation of the product from the alcohol solution by adding water. The para derivative was recrystallized from

ethanol, the ortho derivative from dilute ethanol, and the meta derivative from water. Table XIII lists the derivatives and their melting points.

TABLE XIII

MELTING POINTS OF THE ISOMERIC BENZENESULFONAMIDOANILINES

Compound	Melting point, °C		
	Found	Literature	Ref.
o-Benzenesulfonamidoaniline	168-169	165-167	86
m-Benzenesulfonamidoaniline	97.5-98	98	86
p-Benzenesulfonamidoaniline	173-174	173	86

PROCEDURE FOR THE PREPARATION OF BENZENESULFONYL AZIDE

To 44 grams of sodium azide dissolved in 100 cc of warm water were added 180 cc of 95% ethanol and the mixture was cooled to room temperature. Ninety grams of benzenesulfonyl chloride, diluted with twice their volume of 95% ethanol, were slowly added by means of a separatory funnel, while the contents were stirred by a mechanical stirrer. The benzenesulfonyl chloride solution was added over a period of two hours, and the reaction was allowed to continue for an additional hour.

The mixture was transferred to a one-liter separatory funnel and 200 cc of H_2O were added. Upon standing, a clear colorless oil separated at the bottom of the funnel, and the oil was separated from the water layer. The water layer was extracted with two, 100-cc portions of diethyl ether and the extract was added to the oil. The ether solution then was washed four or five times with one-hundred-milliliter portions of water, and then was dried over anhydrous sodium sulfate. Removal of the ether from the benzenesulfonyl azide was accomplished by reduced pressure

distillation while heating on a water bath. Yields usually were approximately 78 grams (84%), based upon the benzenesulfonyl chloride. The benzenesulfonyl azide was stored under refrigeration until used.

ANALYTICAL PROCEDURE

The reaction product from each experiment was analyzed for the o-, m-, and p- derivatives, and also for benzenesulfonamide and benzenesulfonanilide. The analyses were accomplished by using a Model 12-C Perkin Elmer Spectrometer, with a 0.1 mm fixed-thickness sodium-chloride cell. Dioxane was employed as a solvent. The procedure is adapted from one which Phillips Petroleum Company uses to determine the composition of petroleum chemicals.

Five-tenths gram of each component to be analyzed was dissolved in 5 cc of dioxane. This solution was placed in the fixed-thickness cell, and the spectrum of the solution was scanned between 9.5 and 14.5 microns, using an instrument gain of 14.5. Figures 1, 2, 3, 4, 5, 6, 7 and 8 show the spectra.

A wave length, at which it had a higher absorbance than the other components, was selected for each component. Table XIV shows the wave length selected for each component in each analysis.

The absorptions at these wave lengths were checked for deviations from Beer's law, by plotting concentration versus a function of absorbance (see Figure 9). In every case, the selected wave length had negligible deviation from Beer's law with the exception of the 11.05 micron peak used in the analysis of the p-benzenesulfonamidobenzoic acid (see Figure 10). In this case, a correction was applied.

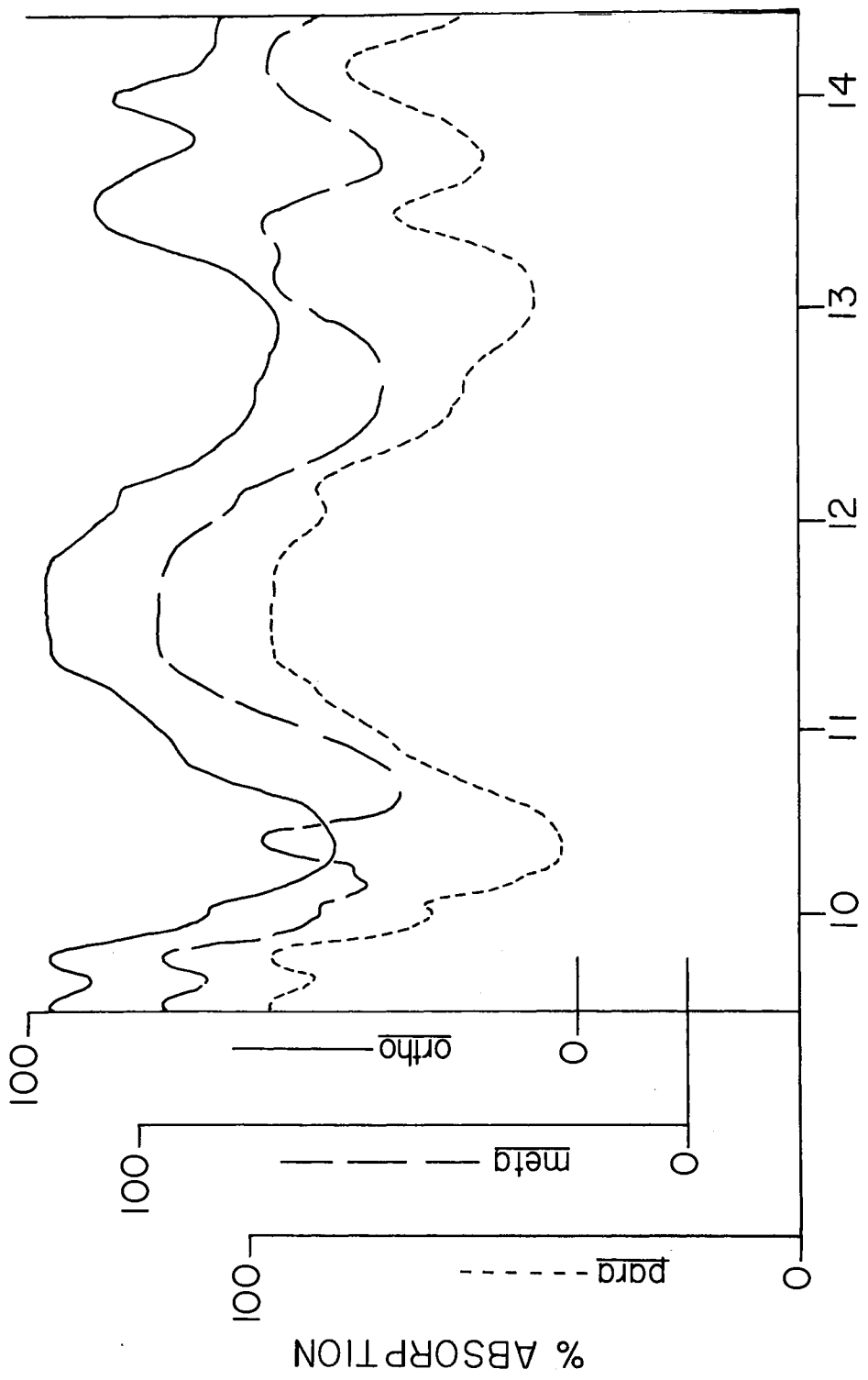


FIGURE 1. Absorption Curves of the Benzenesulfonamidoanilines

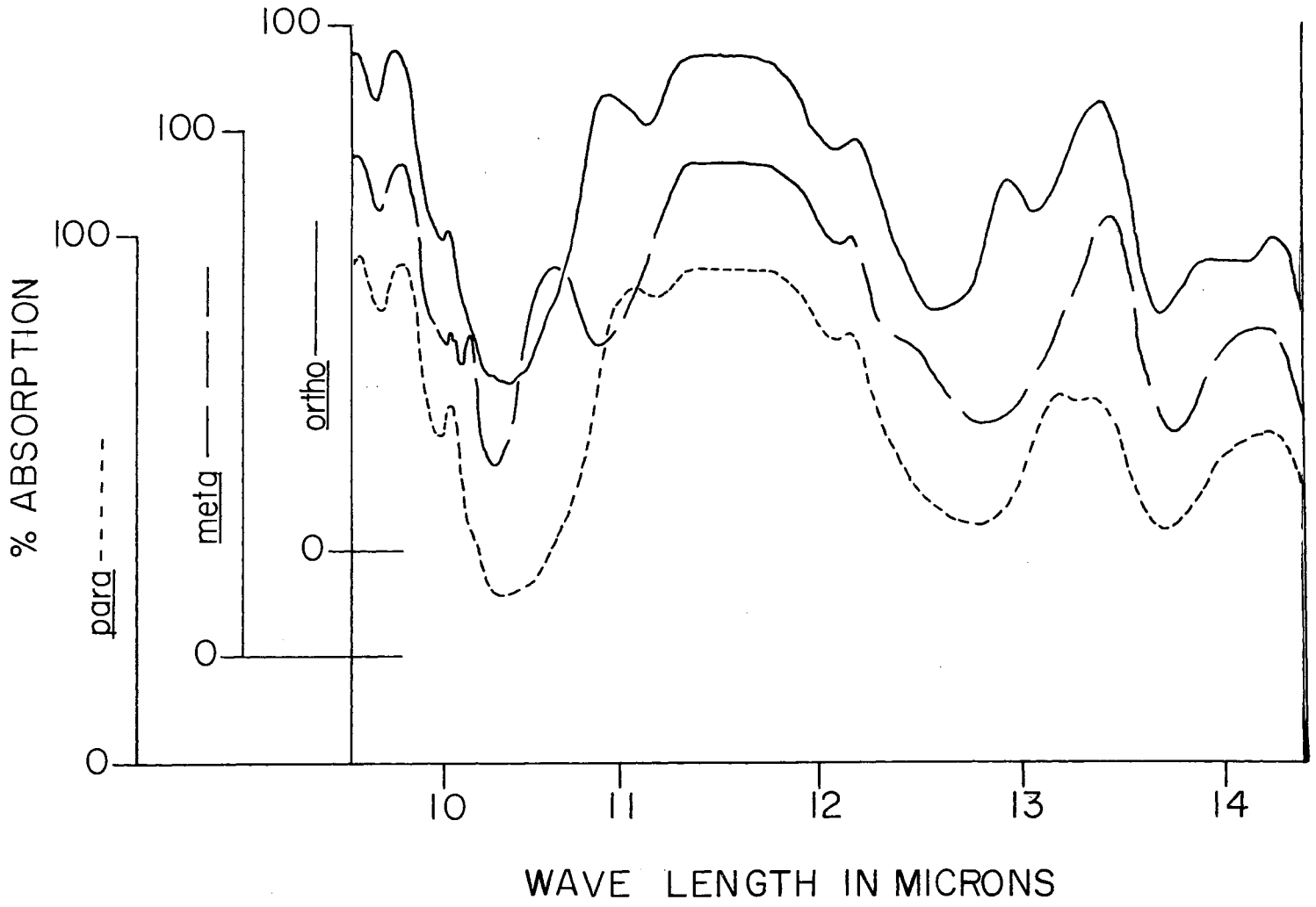


FIGURE 2. Absorption Curves of the Benzenesulfonamidobenzoic Acids

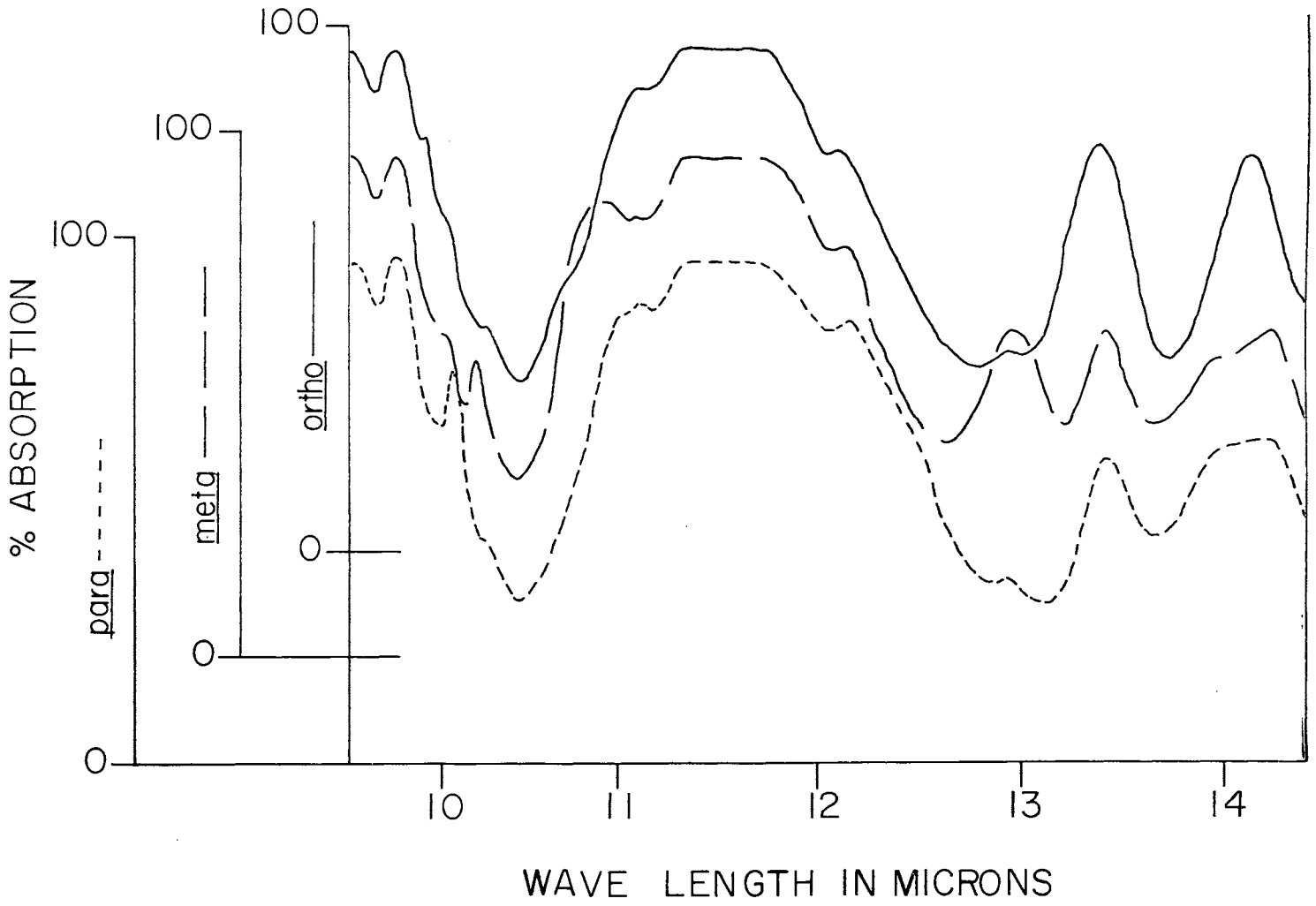


FIGURE 3. Absorption Curves of the Benzenesulfonamidobromobenzenes

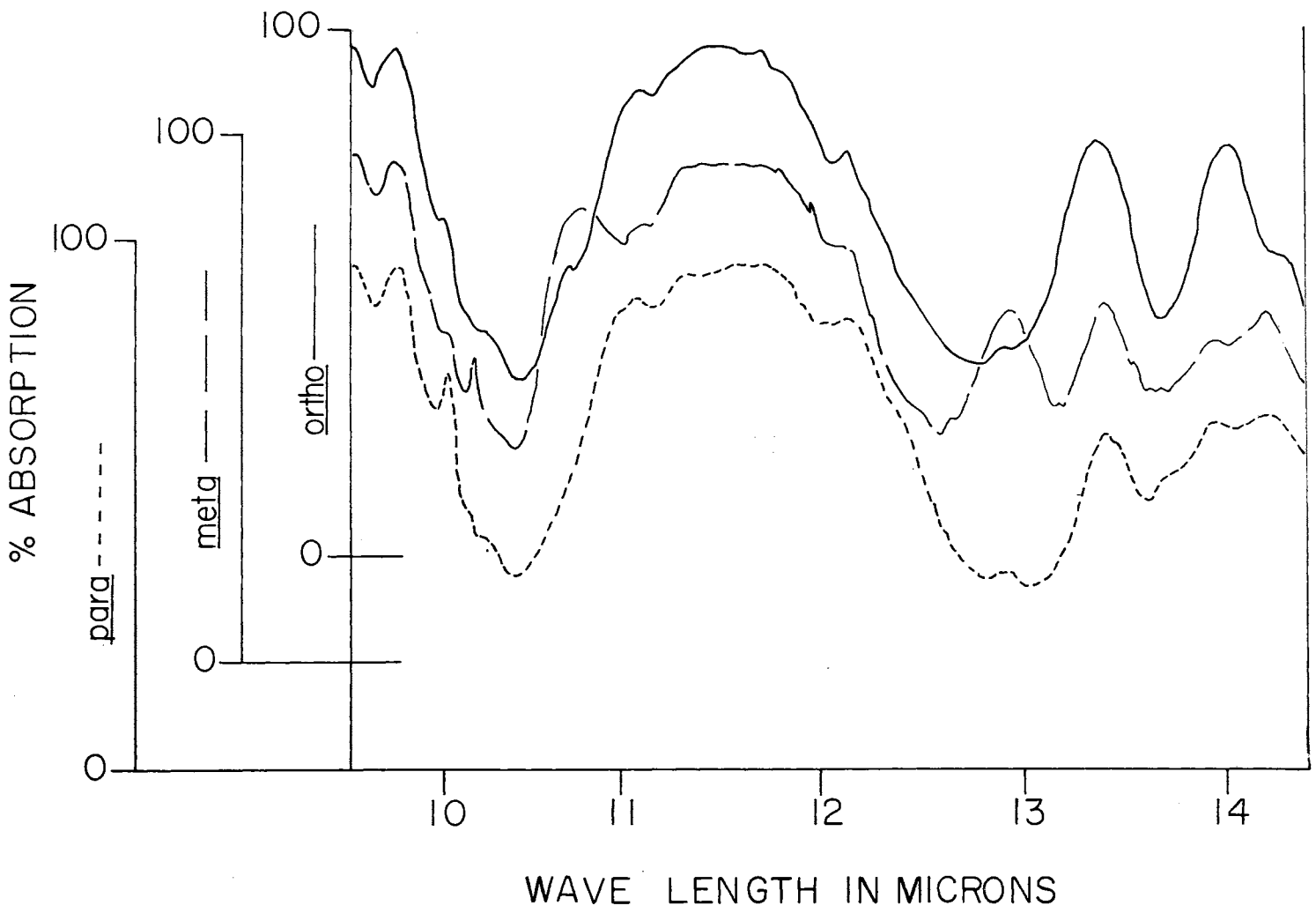


FIGURE 4. Absorption Curves of the Benzenesulfonamidochlorobenzenes

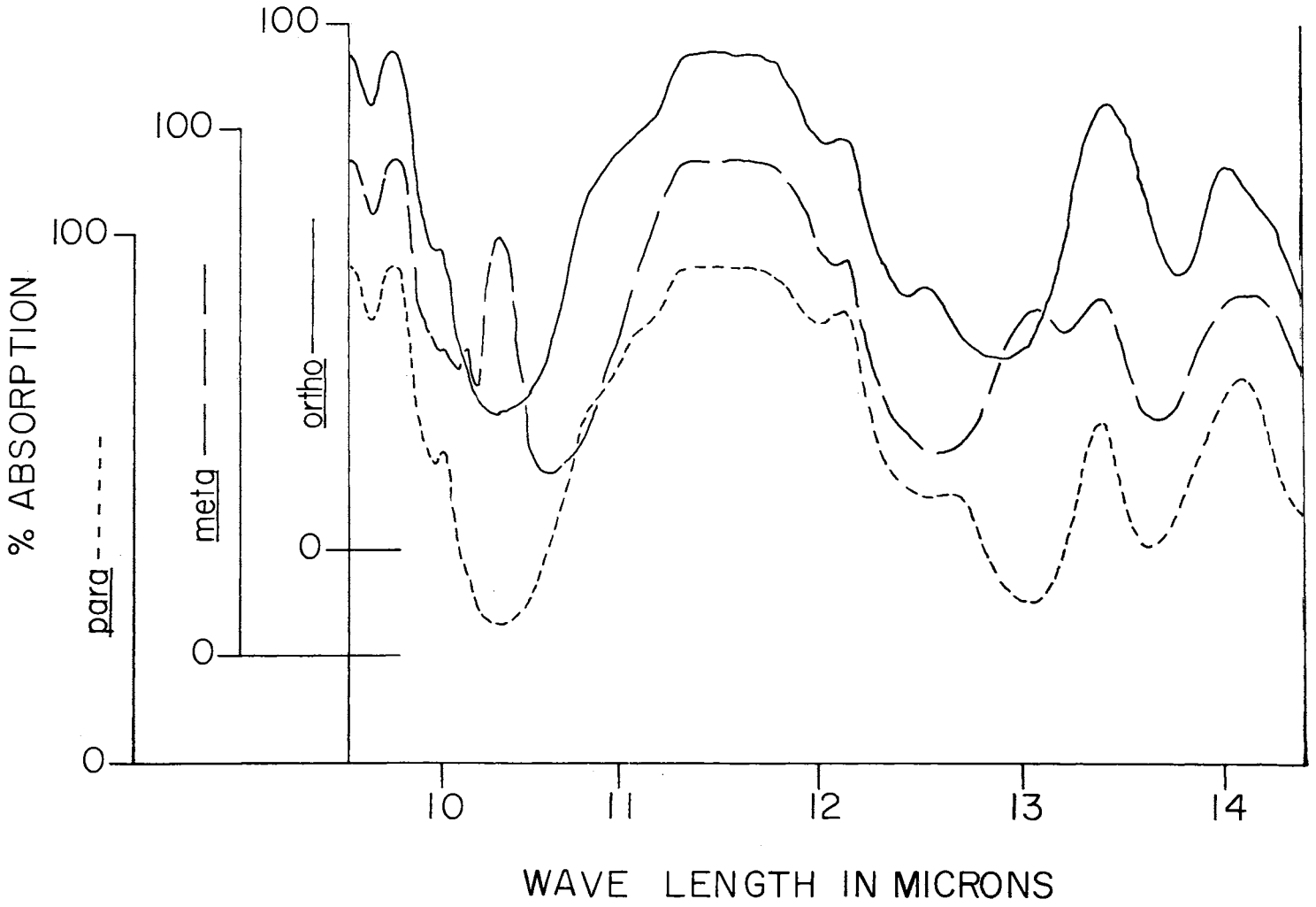


FIGURE 5. Absorption Curves of the Benzenesulfonamidophenols

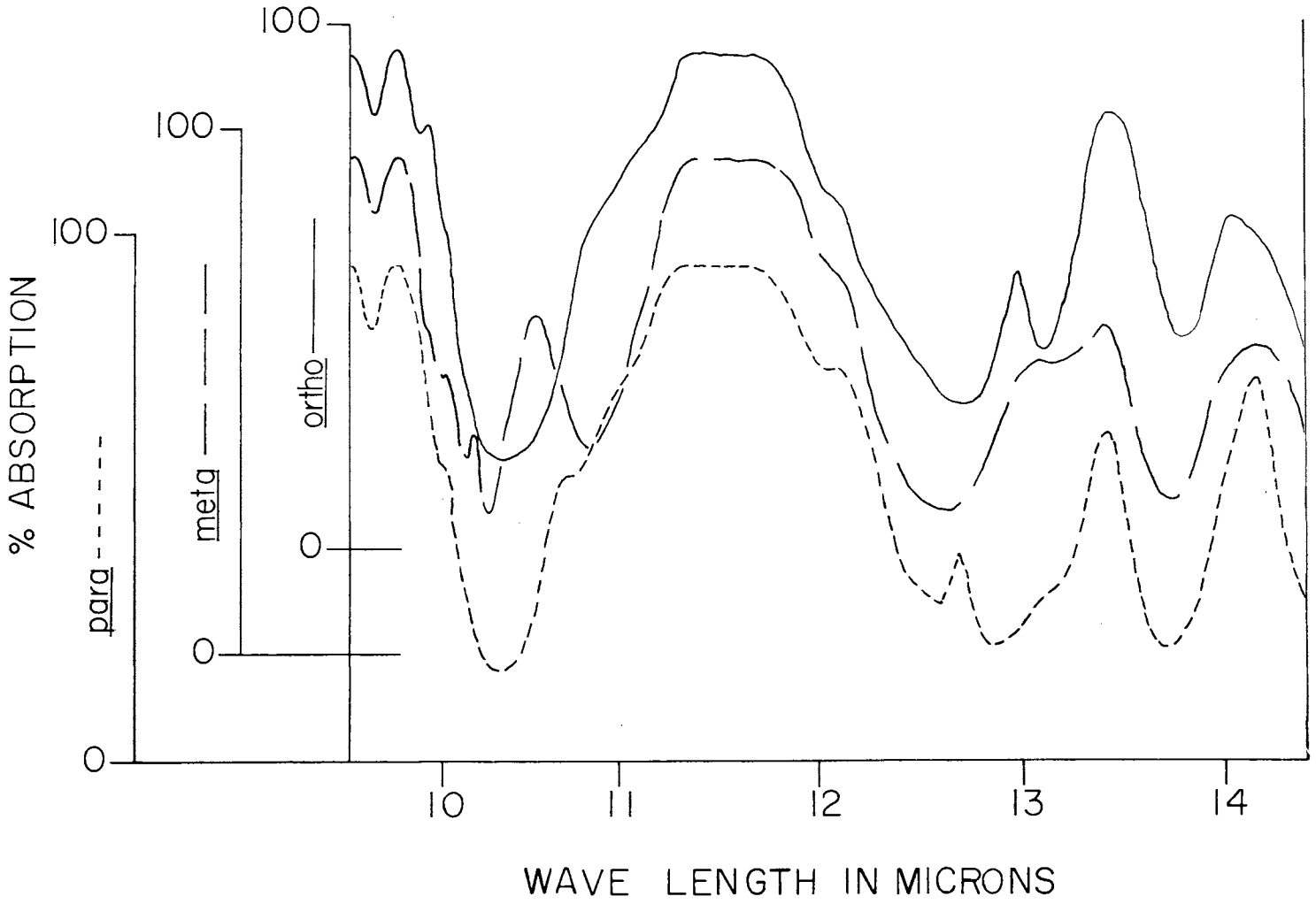


FIGURE 6. Absorption Curves of the Benzenesulfonanisidides

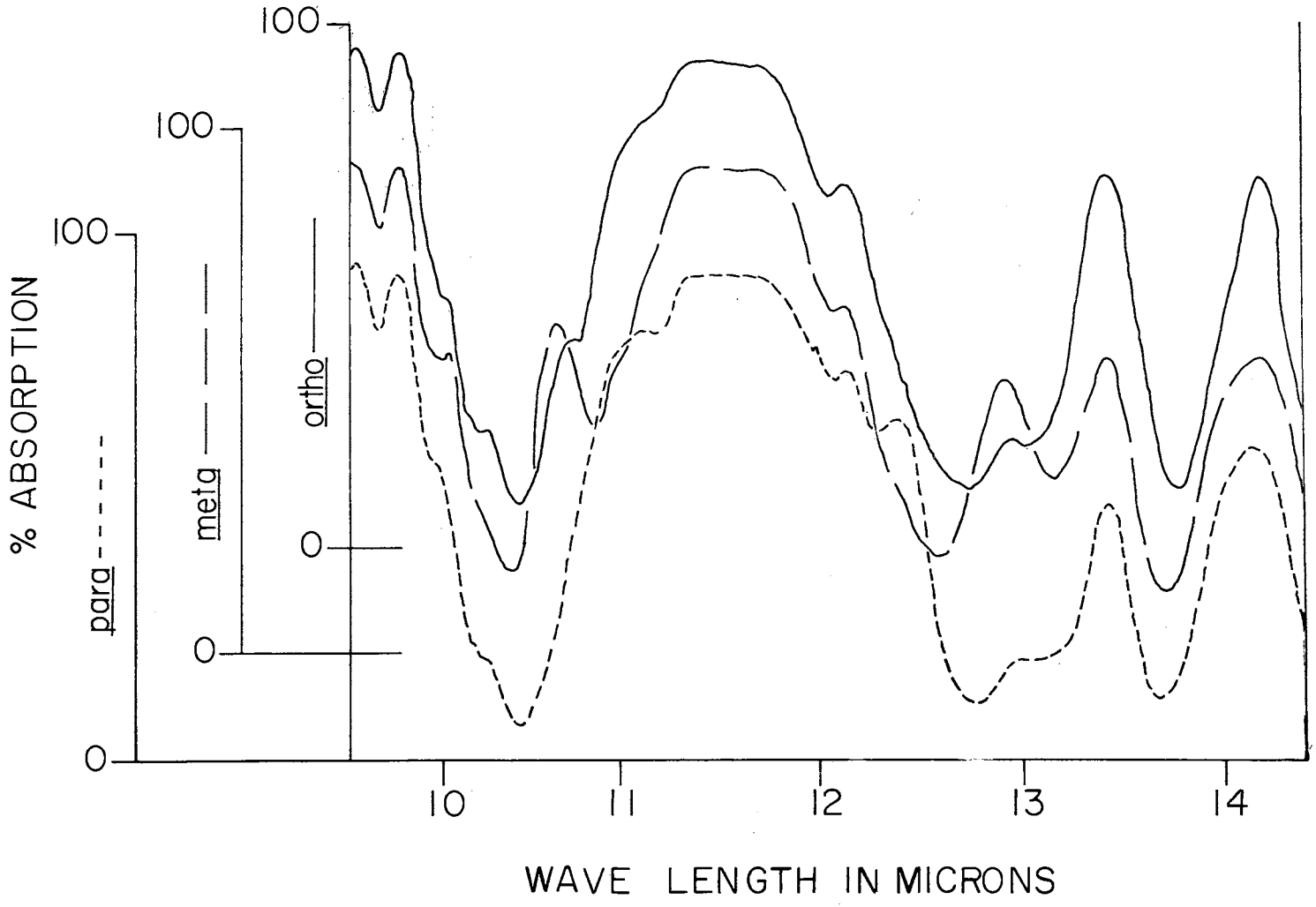


FIGURE 7. Absorption Curves of the Benzenesulfontoluidides

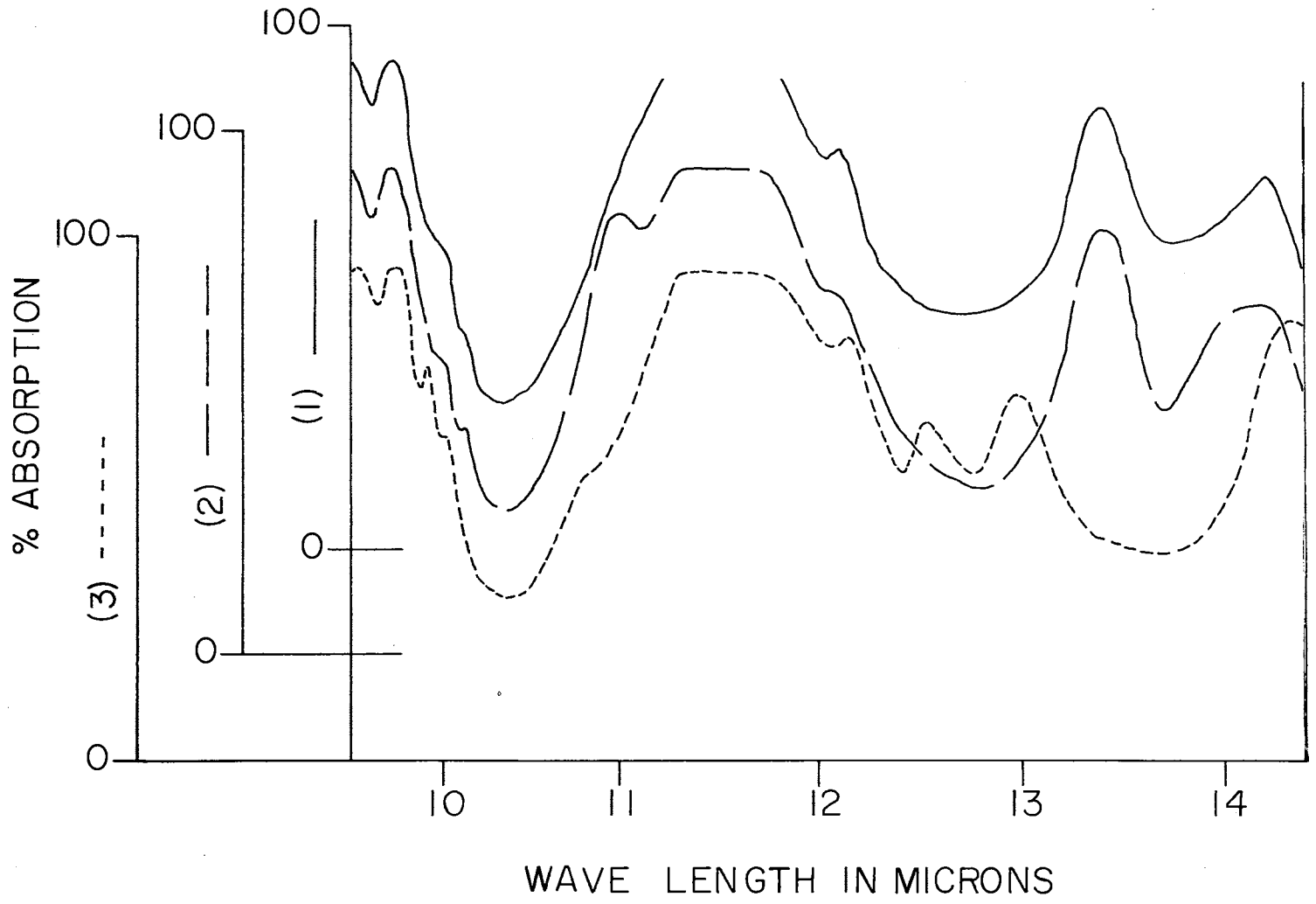


FIGURE 8. Absorption Curves of Benzenesulfonamide (1), Benzenesulfonanilide (2), and Benzoic Acid (3).

TABLE XIV

WAVE LENGTHS SELECTED FOR DETERMINATION OF THE PRODUCTS FROM THE BENZENESULFONAMIDATION OF VARIOUS SUBSTRATES

Substrate	Wave length, microns					
	Isomeric substitution products			Other products		
	o-	m-	p-	BSA	BA	Bz
Aniline	14.00	10.35	14.15	14.30	11.00	-----
Anisole	14.00	10.45	14.15	14.30	11.00	-----
Benzene	-----	-----	-----	12.80	11.00	-----
Bromobenzene	14.15	12.90	10.05	13.70	11.00	-----
Chlorobenzene	14.00	10.75	10.00	13.75	10.90	-----
Phenol	14.00	10.30	12.70	13.80	10.95	-----
Toluene	14.20	10.60	12.35	13.75	10.95	-----
Benzoic acid	12.90	10.60	11.05	14.30	14.10	12.55

BSA = Benzenesulfonamide
BA = Benzenesulfonanilide
Bz = Benzoic acid

Another 0.5 gram of each component, and also 0.5 gram of the unknown to be analyzed were each dissolved in separate 5 cc samples of dioxane. The slit width was adjusted at each wave length so that pure dioxane gave a recorder deflection of approximately 20.0 cm. The transmittance of each solution was measured as a function of the recorder deflection at each of five selected wave lengths. On a typical benzenesulfonamidochlorobenzene determination, the following deflections were obtained at 14.00, 10.75, 10.00, 13.75 and 10.90 microns (see Table XV).

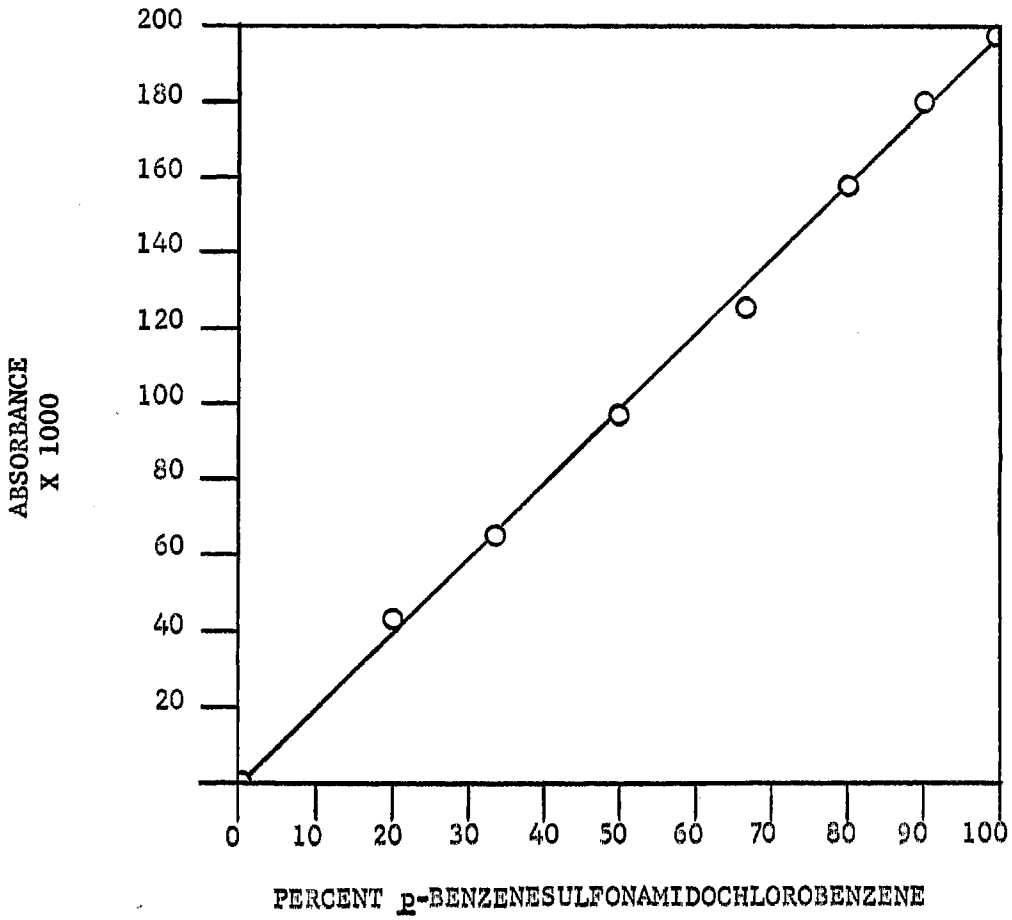


Figure 9. Absorbance-Concentration Curves for p-Benzenesulfonamidochlorobenzene Determinations at 10 Microns.

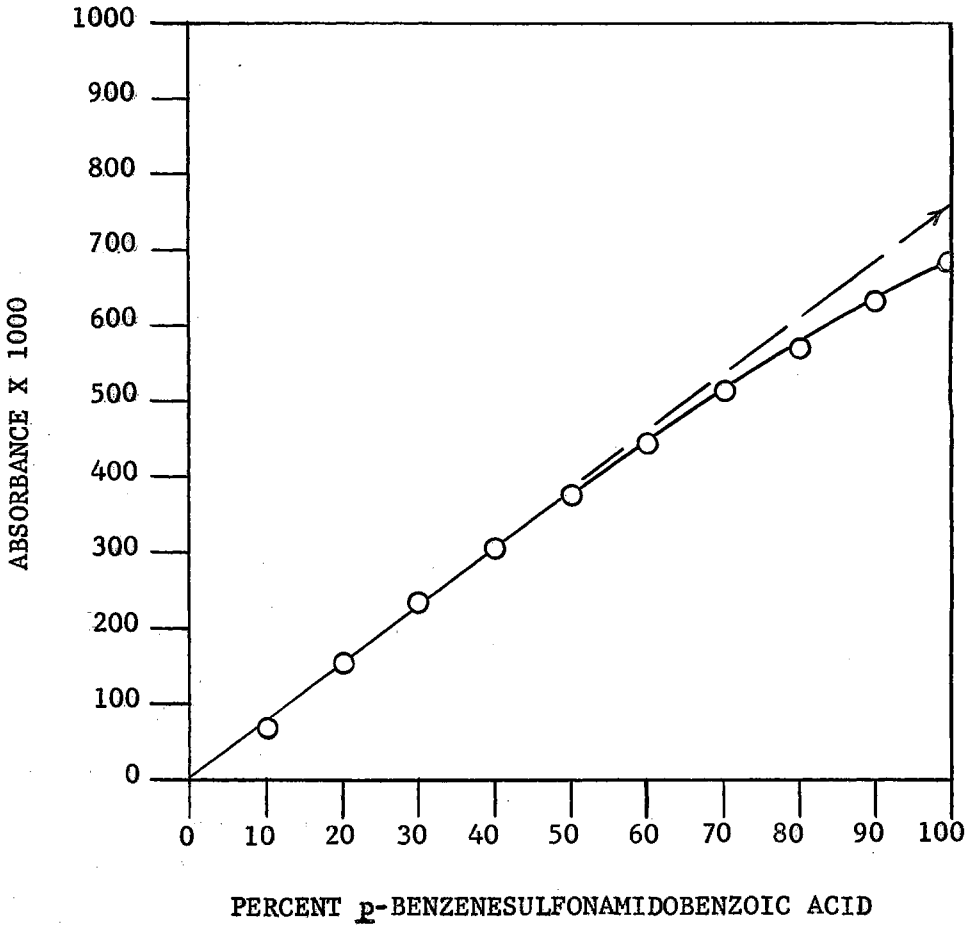


Figure 10. Absorbance-Concentration Curves for p-Benzenesulfonamidobenzoic Acid Determinations at 11.05 Microns.

TABLE XV

RECORDER DEFLECTIONS IN DETERMINATION OF PRODUCTS FROM A CHLOROBENZENE EXPERIMENT

Wave length	14.00	10.75	10.00	13.75	10.90
Solvent	20.73	21.70	21.40	21.40	21.30
o-	3.50	16.90	19.50	12.70	11.30
m-	8.60	4.65	19.10	11.38	8.50
p-	7.45	14.88	13.05	10.40	8.10
BSA	6.44	17.70	18.55	8.01	13.70
BA	6.50	14.60	18.70	11.35	5.85
U	5.65	15.10	17.60	11.20	7.60

BSA = Benzenesulfonamide
BA = Benzensulfonaniline
U = Unknown

From these deflections then were obtained values of 1000 log ($I_{s/I}$) where I_s is the recorder deflection produced by the solvent, and (I) is the recorder deflection for the solution being measured, in centimeters. Log ($I_{s/I}$) is the absorbance of the solute, and it is multiplied by 1000 to avoid using decimals. Table XVI contains calibration data for the chlorobenzene runs, and includes 1000 log ($I_{s/I}$) values of each solution at each wave length.

TABLE XVI

1000 LOG ($I_{s/I}$) VALUES FOR CHLOROBENZENE RUNS (CALIBRATION)

Wave length	14.00	10.75	10.00	13.75	10.90
o-	773	109	040	227	275
m-	382	669	045	274	399
p-	445	164	215	313	420
BSA	508	088	062	427	192
BA	504	172	058	275	561
U	564	157	085	281	448

BSA, BA, U--See Table XV

The calculation of the composition of the unknown was then accomplished by the use of a successive approximation method to solve the following simultaneous equations:

$$A_{(14.00)} = A_{\underline{o}(14.00)}X_{\underline{o}} + A_{\underline{m}(14.00)}X_{\underline{m}} + A_{\underline{p}(14.00)}X_{\underline{p}} + A_{BSA(14.00)}X_{BSA} + A_{BA(14.00)}X_{BA}$$

$$A_{(10.75)} = A_{\underline{o}(10.75)}X_{\underline{o}} + A_{\underline{m}(10.75)}X_{\underline{m}} + A_{\underline{p}(10.75)}X_{\underline{p}} + A_{BSA(10.75)}X_{BSA} + A_{BA(10.75)}X_{BA}$$

$$A_{(10.00)} = A_{\underline{o}(10.00)}X_{\underline{o}} + A_{\underline{m}(10.00)}X_{\underline{m}} + A_{\underline{p}(10.00)}X_{\underline{p}} + A_{BSA(10.00)}X_{BSA} + A_{BA(10.00)}X_{BA}$$

$$A_{(13.75)} = A_{\underline{o}(13.75)}X_{\underline{o}} + A_{\underline{m}(13.75)}X_{\underline{m}} + A_{\underline{p}(13.75)}X_{\underline{p}} + A_{BSA(13.75)}X_{BSA} + A_{BA(13.75)}X_{BA}$$

$$A_{(10.90)} = A_{\underline{o}(10.90)}X_{\underline{o}} + A_{\underline{m}(10.90)}X_{\underline{m}} + A_{\underline{p}(10.90)}X_{\underline{p}} + A_{BSA(10.90)}X_{BSA} + A_{BA(10.90)}X_{BA}$$

Where

$A_{(\text{wave length})}$ = Function of the absorbance of unknown solution at a particular wave length,

$A_{\underline{o}(\text{wave length})}$ = Function of the absorbance of solution of ortho derivative in dioxane at a certain wave length,

X_o = Weight fraction of ortho derivative in unknown,

and similar quantities are included for the meta and para isomers.

These equations are only absolutely correct when there is no chemical interaction between the various components. Knowns were used in each case to prove that the interactions were not so great as to give erroneous results. The solving of the simultaneous equations was facilitated by the use of a calculation sheet as shown in Table XVII.

TABLE XVII

CALCULATION SHEET FOR CHLOROBENZENE EXPERIMENT

Component Wave length	o- 14.00	m- 10.75	p- 10.00	BSA 13.75	BA 10.90
Unknown	564(1)	157	085	281	448
ortho	---	027	010	057	069
meta	003(2)	---	000	002	004
para	089	033	---	063	084
BSA	025	004	003	---	009
BA	254	087	029	138	---
Total	371(3)	151	042	260	166
Difference	193(4)	006	043	021	282
Last approximation	25.0(5)	0.9	20.0	4.9	50.3
Normalization	24.7	0.9	19.8	4.8	49.8

(1) $A_{(14.00)}$

(2) $A_{m(14.00)}X_m$

(3) $A_{m(14.00)}X_m + A_{p(14.00)}X_p + A_{BSA(14.00)}X_{BSA} + A_{BA(14.00)}X_{BA}$

(4) $A_{(14.00)} - (3) = A_{o(14.00)}X_o$

(5) $X_o \times 100 = A_{o(650)}X_o \quad A_{o(650)} \times 100$

SUBSTITUTION OF AROMATIC NUCLEI THROUGH THERMAL DECOMPOSITION OF BENZENESULFONYL AZIDE

This portion of the experimental work is divided into two parts. Part One is a further investigation, using an improved method of analysis, of the orientation in aromatic substitution by the benzenesulfonimido radical which was started by Curtius and co-workers (30) and later studied by Dermer and Edmison (41,46). Part Two is a competitive study, similar to the studies by Ingold (76) of ionic substitution and later the study by Hey (67) of substitution by phenylation, using benzene as a reference solvent.

All substrates used in this investigation were fractionally distilled twice. A 30-plate Oldershaw column was used, and only the middle fraction was saved. This fraction was stored over anhydrous sodium sulfate until used.

For comparative purposes, the decompositions were always carried out in a five mole percent solution, and the temperature was maintained between 105 and 120°C. Different concentrations (0.05-0.15 mole fraction), different temperatures (105-170°C), and dropwise additions were investigated, but no effect on the yield, by-product or isomer ratio was observed.

Preparation of the Substitution Products

In general, the same procedure was used for both the determinations of orientation and the studies of competitive reactions. The main difference between the two was that in order to raise the temperature of the reaction mixture to 105-120°C for the competitive experiments which involved benzene, it was necessary to apply a small increase in pressure. This was accomplished by means of a column of mercury. See Figure 11.

A standard reflux apparatus equipped with a calcium chloride drying tube was used for the orientation experiments.

To the reaction flask were added 13.7 grams (0.075 mole) of benzenesulfonyl azide and 1.5 moles of substrate. In the competitive runs, 0.75 mole of benzene and 0.75 mole of the monofunctional derivative of benzene were added. This solution was heated to 105-120°C for a period of 48 hours.

At the end of the 48-hour period, the mixture, which was now a black solution with some black solid particles suspended in it, was distilled under reduced pressure to remove the excess substrate, and

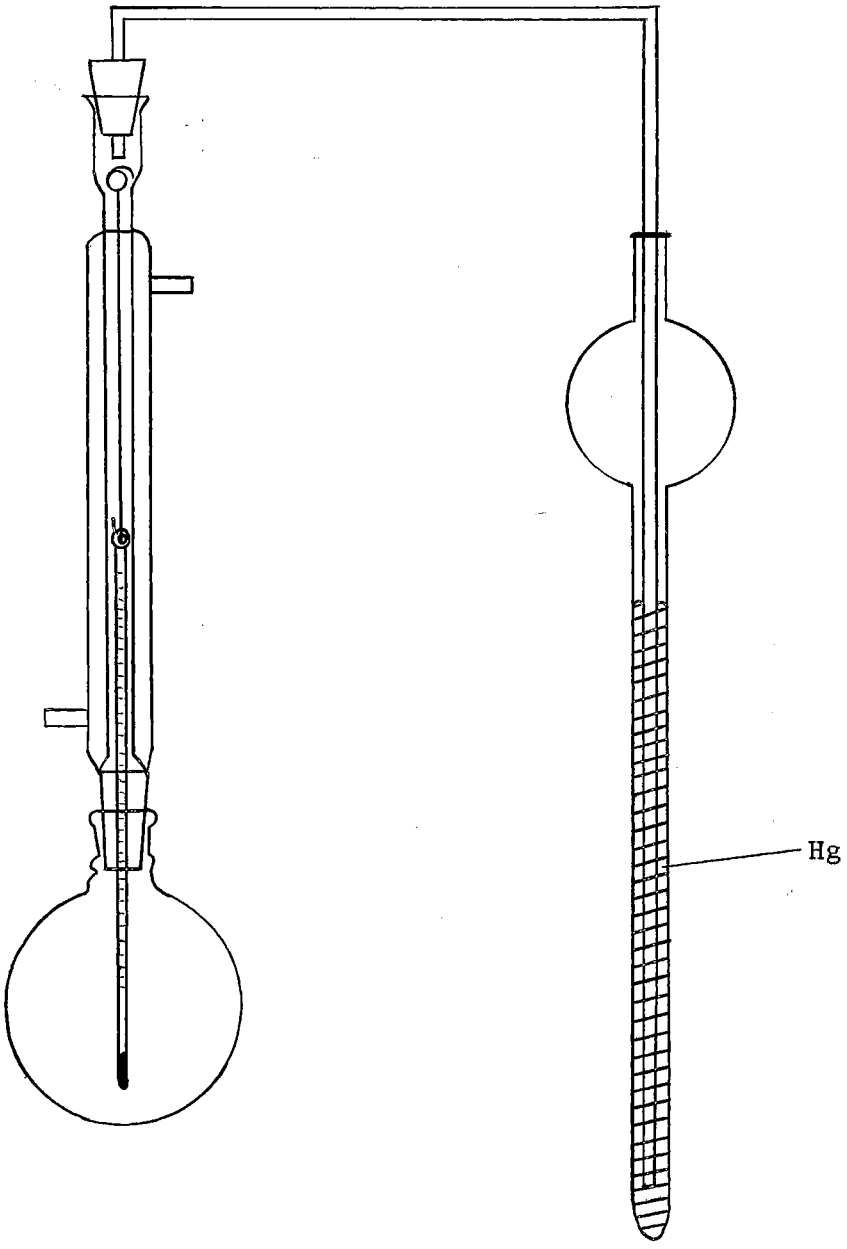


Figure 11. Apparatus for Competitive Reactions

finally steam-distilled to remove the last traces of substrate. The steam distillation was continued until the distillate was no longer cloudy, and then an additional one liter of distillate was collected.

The kettle containing the residue then was cooled, the water content was estimated and enough sodium hydroxide was added to make a 5% solution. All of the residue appeared to go into solution.

In the runs with methyl benzoate, benzonitrile, benzoyl chloride and other derivatives capable of being hydrolyzed to the benzoic acid derivative, this basic solution was refluxed for 12 hours. The other runs did not require this hydrolysis and were used directly.

The basic solution then was extracted with three 200-cc portions of ether to remove any ether-soluble impurities. It was treated with charcoal and filtered, and the filtrate was made definitely acidic by the addition of concentrated hydrochloric acid. This solution, when aniline was used as the substrate, was neutralized with sodium bicarbonate before subsequent ether extraction.

The acid solution was cooled in an ice bath and a precipitate formed. The solution was placed in a one-liter separatory funnel and extracted with copious quantities of ether. Most of the precipitate was soluble in the ether, but some remained at the interface between the water and the ether. This precipitate was removed by filtration. The water layer was extracted with ether until evaporation of the ether layer left no residue. The extraction usually required a liter and a half of ether.

The ether extract was treated with charcoal, filtered, placed in an evaporating dish, and the ether was allowed to evaporate at room temperature. A white crystalline residue, which was composed of the substitution products and benzenesulfonamide, remained.

In some cases, such as the non-competitive runs with methyl benzoate, the products were recrystallized from appropriate solvents, but usually the products were pure enough, after evaporation of the ether, to be analyzed. Excessive recrystallization might change the isomer ratio.

The procedure related above was checked with known compositions of the components, and in each case the extraction was accomplished without appreciable change in composition. However, it was found that, unless large quantities of ether were used in the extraction, some benzenesulfonamide was not recovered.

In the case of the benzoic acid derivatives, prepared by hydrolysis, the products were analyzed for benzoic acid also. Usually the acid was found to be absent, but occasionally it was necessary to correct for this impurity.

RESULTS

Successful experiments and determinations, both competitive and non-competitive, were accomplished with anisole, bromobenzene, chlorobenzene, methyl benzoate, and toluene.

Although the majority of the experiments with phenol produced an oily tar, one of the competitive runs produced a crystalline product, which was used to determine both the isomer ratio and the competitive constants. The results from this one run appear to correspond with results from other substrates, but it must be remembered that three non-competitive and five competitive runs were unsuccessful. The success of only the one experiment cannot be explained; apparently the conditions were the same in all cases.

Tables XVIII-XXIII show the percentage yields (based upon benzenesulfonyl azide), isomer ratios, ratio of substituted benzenesulfonanilides to benzenesulfonanilide (R), the total relative reaction rate ($_{H}^{X}K$), and the partial relative reaction rate ($_{H}^{X}k_{o}$), with respect to benzene.

The total relative-reaction-rate factor was calculated, for each competitive reaction, by use of the following equation:

$$_{H}^{X}K = k_x/k_y = \frac{\log\left[1 - \frac{Z_o R}{X_o(1 + R)}\right]}{\log\left[1 - \frac{Z_o}{Y_o(1 + R)}\right]}$$

where Z_o is the moles of benzenesulfonyl azide (0.075), X_o the moles of

aromatic substrate (0.75), and Y_o the moles of benzene (0.75). This equation is derived on page 22 of the historical section of this dissertation.

Using the average total relative reaction rate, along with the average of the mole fractions of each isomer obtained from the noncompetitive determinations, the partial relative reaction rates were determined by use of the following equations:

$$ {}^{X}_{H}k_{\underline{o}} = 3{}^{X}_{H}K(\underline{o}), \quad {}^{X}_{H}k_{\underline{m}} = 3{}^{X}_{H}K(\underline{m}), \quad \text{and} \quad {}^{X}_{H}k_{\underline{p}} = 6{}^{X}_{H}K(\underline{p}) $$

where (o), (m), and (p) are the mole fractions of the ortho, meta, and para isomers respectively in the reaction product.

Analysis of the noncompetitive experiments with aniline as the substrate revealed that the favored reaction route apparently was not through the radical intermediate but through an ionic mechanism whereby hydrazoic acid was split out to form benzenesulfonanilide. This is similar to the reaction of benzenesulfonyl chloride and aniline. Ammonia gas was observed as a by-product from these reactions. Table XXIV lists the percentage yields based on benzenesulfonyl azide, the mole percentage composition of the products, and the isomer ratios of the substitution products. Noncompetitive experiments were not attempted because of the competing ionic process.

TABLE XVIII

RESULTS WITH ANISOLE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA[3]	BA[4]
1	O[1]	8.1	41.3	72.3	0.5	27.2	0.0	---
2	O	6.0	30.7	70.7	3.2	26.1	0.0	---
3	C[2]	8.0	42.7	26.6	0.0	17.9	0.0	55.5
4	C	8.0	42.7	36.0	0.0	15.0	0.0	49.0
5	C	5.6	30.7	28.3	0.0	17.5	2.7	51.5
6	C	7.1	38.7	29.4	0.0	15.3	7.8	47.5

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio ortho	meta	para	R	X_{H^K}
1	72.3	0.5	27.2		
2	70.7	3.2	26.1		
Ave.	71.5	1.8	26.7		
3	59.8	0.0	40.2	0.802	0.793
4	70.6	0.0	29.4	1.041	1.041
5	61.8	0.0	38.2	0.889	0.886
6	65.8	0.0	34.2	0.941	0.922
Ave.	64.5	0.0	35.5		0.910

(C)

Partial Rate Factors

	$X_{H^k_o}$	$X_{H^k_m}$	$X_{H^k_p}$
Average for anisole	1.95	0.05	1.46

(1) Orientation run
(2) Competitive run
(3) Benzensulfonamide
(4) Benzenesulfonanilide

TABLE XIX

RESULTS WITH BROMOBENZENE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA[3]	BA[4]
1	O[1]	4.6	21.3	45.1	4.7	39.8	10.4	---
2	O	5.0	21.3	48.2	5.5	42.3	4.0	---
3	O	4.4	18.7	49.2	3.7	46.1	1.0	---
4	O	6.0	26.7	45.9	4.5	40.6	9.0	---
5	C[2]	5.0	26.7	13.3	3.0	18.3	15.5	49.9
6	C	7.0	38.7	13.0	2.0	13.5	16.2	55.3
7	C	5.0	25.3	18.6	3.6	19.4	12.7	45.7
8	C	5.0	26.7	12.7	3.5	18.7	17.7	47.4

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio ortho	meta	para	R	$\frac{X}{H}K$
1	50.3	5.2	44.4		
2	50.2	5.7	44.1		
3	49.7	3.7	46.6		
4	50.4	4.9	44.6		
Ave.	50.2	4.9	44.9		
5	38.4	8.7	52.9	0.693	0.689
6	45.6	7.0	47.4	0.515	0.507
7	44.7	8.7	46.6	0.910	0.922
8	36.4	10.0	53.6	0.736	0.737
Ave.	41.3	8.6	50.1		0.714

(C)

Partial Rate Factors

	$\frac{X}{H}k_o$	$\frac{X}{H}k_m$	$\frac{X}{H}k_p$
Average for bromobenzene	1.08	0.10	1.92

(1), (2), (3), (4)--See Table XVIII

TABLE XX

RESULTS WITH CHLOROBENZENE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA(3)	BA(4)
1	O(1)	6.0	29.3	41.7	0.6	57.7	0.0	---
2	O	7.5	37.3	48.3	0.0	51.7	0.0	---
3	O	9.0	48.0	40.8	3.8	39.8	15.6	---
4	C(2)	5.0	26.7	17.4	0.0	21.9	0.3	60.4
5	C	4.6	24.0	18.5	4.5	23.1	0.8	53.1
6	C	6.5	34.7	18.4	2.9	15.7	2.9	60.1
7	C	6.5	36.0	22.4	0.7	18.0	7.3	51.6
8	C	6.7	37.3	17.2	0.0	19.4	6.6	56.8
9	C	6.5	36.0	20.1	0.5	21.1	4.7	53.6

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio ortho	meta	para	R	X_K / H
1	41.7	0.6	57.7		
2	48.3	0.0	51.7		
3	48.3	4.5	47.2		
Ave.	46.1	1.6	52.3		
4	44.3	0.0	55.7	0.651	0.634
5	40.1	9.8	50.1	0.868	0.867
6	49.7	7.8	42.4	0.616	0.604
7	54.5	1.7	43.8	0.797	0.800
8	47.0	0.0	53.0	0.644	0.634
9	48.2	1.2	50.6	0.778	0.780
Ave.	47.3	3.4	49.3		0.720

(C)

Partial Rate Factors

	$X_H k_o$	$X_H k_m$	$X_H k_p$
Average for chlorobenzene	1.00	0.03	2.26

(1), (2), (3), (4)--See Table XVIII

TABLE XXI

RESULTS WITH METHYL BENZOATE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA[3]	BA[4]
1	O[1]	6.9	37.3	31.7	36.7	2.9	28.7	---
2	O	7.4	40.0	31.5	36.2	4.4	27.9	---
3	O	5.2	28.0	37.1	36.3	1.5	25.1	---
4	O	3.2	18.7	27.4	36.9	0.2	35.5	---
5	O	6.6	32.0	35.6	51.0	0.0	13.4	---
6	C[2]	11.4	66.7	10.5	13.0	1.4	23.1	52.0
7	C	11.1	62.7	11.2	15.9	1.9	13.1	57.9
8	C	10.8	58.7	9.5	16.1	2.2	5.6	66.6
9	C	9.6	52.0	10.8	15.4	0.7	1.7	71.4

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio ortho	meta	para	R	X_K / H
1	44.5	51.5	4.0		
2	43.7	50.2	6.1		
3	49.5	48.5	2.0		
4	42.5	57.2	0.3		
5	41.1	58.9	0.0		
Ave.	44.3	53.2	2.5		
6	42.2	52.2	5.6	0.479	0.461
7	38.6	54.8	6.6	0.501	0.485
8	34.2	57.9	7.9	0.417	0.413
9	40.2	57.2	2.6	0.377	0.374
Ave.	38.8	55.5	5.7		0.433

(C)

Partial Rate Factors

	X_k / H_o	X_k / H_m	X_k / H_p
Average for methyl benzoate	0.58	0.69	0.06

(1), (2), (3), (4)--See Table XVIII

TABLE XXII

RESULTS WITH PHENOL

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole %				
				ortho	meta	para	BSA(3)	BA(4)
1	C(2)	5.7	33.3	18.6	0.5	17.9	14.9	48.1

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio			R	X_K H
	ortho	meta	para		
1	50.3	1.4	48.3	0.769	0.765

(C)

Partial Rate Factors

	$X_{H}^{K}{}_{o}$	$X_{H}^{k}{}_{m}$	$X_{H}^{k}{}_{p}$
Phenol	1.15	0.03	2.22

(2), (3), (4)--See Table XVIII

TABLE XXIII

RESULTS WITH TOLUENE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA(3)	BA(4)
1	O(1)	11.0	61.3	52.5	1.2	35.7	10.6	---
2	O	8.8	49.3	54.8	1.4	31.4	12.4	---
3	C(2)	6.5	36.0	30.9	0.0	17.5	3.6	48.0
4	C	3.0	16.0	29.0	0.0	19.6	0.0	51.4
5	C	4.6	25.3	29.2	0.7	18.7	3.3	48.1

(B)

Isomer Ratios and Total Rate Factors

Exp. No.	Isomer ratio ortho	meta	para	R	X_K/H
1	58.8	1.3	39.9		
2	62.6	1.6	35.8		
Ave.	60.7	1.5	37.8		
3	63.8	0.0	36.2	1.008	1.000
4	59.1	0.0	40.3	0.946	0.960
5	60.1	1.4	38.5	1.010	1.000
Ave.	61.2	0.5	38.3		0.987

(C)

Partial Rate Factors

	X_k/H_o	X_k/H_m	X_k/H_p
Average for toluene	1.80	0.04	2.24

(1), (2), (3), (4)--See Table XVIII

TABLE XXIV

RESULTS WITH ANILINE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole %				
				ortho	meta	para	BSA(3)	BA(4)
1	0(1)	9.5	56.0	8.4	1.4	13.2	15.4	61.6
2	0	11.5	68.0	11.2	1.8	13.5	18.0	55.5
Ave.				9.8	1.6	13.4	16.7	58.5

(B)

Isomer Ratios

Exp. No.	Isomer Ratio		
	ortho	meta	para
1	39.6	6.2	54.2
2	42.5	6.5	51.0
Ave.	41.0	6.4	52.6

(1), (3), (4)--See Table XVIII

Experiments for the study of orientation were attempted with benzoyl chloride and benzonitrile, but the yields were so small that no competitive reactions were attempted.

Both substrates produced large amounts of tars and unidentified black amorphous acids. The radical which was produced apparently favored the abstraction of hydrogen to form benzenesulfonamide, rather than the aromatic substitution. The small percentage yields of the isomeric derivatives from the benzonitrile experiments were within the experimental error of the analysis, but the percentage of meta isomer in the benzoyl chloride runs is definitely significant. Table XXV and Table

TABLE XXV

RESULTS WITH BENZONITRILE

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA(3)	BA(4)
1	0(1)	0.7	5.3	0.0	0.0	0.0	100.0	---
2	0	1.0	8.0	0.0	1.4	0.0	98.6	---
3	0	1.0	8.0	0.0	1.3	2.5	96.2	---
4	0	2.0	16.0	0.0	2.7	2.3	95.0	---
Ave.				0.0	1.4	1.2	97.4	---

(1), (3), (4)--See Table XVIII

TABLE XXVI

RESULTS WITH BENZOYL CHLORIDE

(A)

Yields and Composition of Products

Exp. No.	Type	Wt., g.	Yield, %	Composition, mole % ortho	meta	para	BSA(3)	BA(4)
1	0(1)	1.0	7.3	0.0	16.5	1.2	82.3	---
2	0	0.6	4.0	0.5	13.7	0.0	85.8	---
3	0	1.3	9.3	0.0	7.4	0.0	92.6	---
4	0	0.8	6.7	0.0	3.4	0.5	96.1	---
Ave.				0.1	10.3	0.4	89.2	---

(B)

Isomer Ratios

Exp. No.	Isomer ratio ortho	meta	para
1	0.0	93.2	6.8
2	3.5	96.5	0.0
3	0.0	100.0	0.0
4	0.0	87.2	12.8
Ave.	0.9	94.2	4.9

(1), (3), (4)--See Table XVIII

XXVI list the percentage yields and composition of the products from reaction with benzonitrile and benzoyl chloride, respectively.

Attempts to cause reaction of benzenesulfonyl azide with benzoic anhydride, benzotrichloride, benzamide, and benzoic acid were unsuccessful. In each case a very small quantity of benzenesulfonamide was produced and identified by use of the infrared spectrum. The main product was a black amorphous acid. Attempts to identify this product have been unsuccessful. Attempted hydrolysis with concentrated hydrochloric acid or concentrated sodium hydroxide solution at reflux temperature failed to change the appearance or properties of the material.

The material is soluble in any base such as sodium hydroxide or pyridine, but is insoluble in water, acid, or the usual organic solvents. The melting point is very high; the substance fails to melt when placed directly upon a hot plate. If held above a direct flame it seems to char, but does not melt or burn. Elemental analysis shows the presence of both sulfur and nitrogen.

Benzenesulfonyl azide reacted with benzene to produce benzenesulfonamide and benzenesulfonanilide. The ratio of these two products, along with yield information, appears in Table XXVII.

TABLE XXVII

RESULTS WITH BENZENE

Exp. No.	Wt., g.	Yield, %	Composition, mole %	
			BSA(3)	BA(4)
1	5.0	30.7	17.5	82.5
2	5.0	30.7	16.1	83.9
3	4.8	29.3	19.3	80.7
Ave.			17.6	82.4

(3), (4)--See Table XVIII

DISCUSSION OF RESULTS

Isomer Ratios

Tables IV, VII, and XXVIII clearly show that various groups on an aromatic nucleus cause orientation in benzenesulfonamidation more like that which occurs in ionic substitution rather than that which takes place in homolytic phenylation.

TABLE XXVIII

SUMMARY OF RESULTS

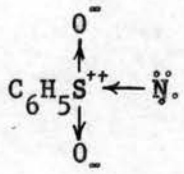
Average Isomer Ratio, Total Relative Rate ($^{X}_{H}K$), and Partial Relative Rate ($^{X}_{H}k_{o}$, $^{X}_{H}k_{m}$, $^{X}_{H}k_{p}$) Factors for the Benzenesulfonamidation of Various Aromatic Substrates

Substrate	Isomer ratio			Rate factors			
	o-	m-	p-	$^{X}_{H}K$	$^{X}_{H}K_{o}$	$^{X}_{H}k_{m}$	$^{X}_{H}k_{p}$
Benzene	----	----	----	1.000	1.00	1.00	1.00
Toluene	60.7	1.5	37.8	0.987	1.80	0.04	2.24
Anisole	71.5	1.8	26.7	0.910	1.95	0.05	1.46
Phenol	50.3	1.4	48.3	0.765	1.15	0.03	2.22
Chlorobenzene	46.1	1.6	52.3	0.720	1.00	0.03	2.26
Bromobenzene	50.2	4.9	44.9	0.714	1.08	0.10	1.92
Methyl benzoate	44.3	53.2	2.5	0.433	0.58	0.69	0.06
Aniline	41.0	6.4	52.6	-----	----	----	----
Benzoyl chloride	0.9	94.2	4.9	-----	----	----	----

The relative amount of ortho isomer, however, in each case is greater than would be expected for subsititution by even the smallest positive ion. It is reasonable to assume that even though the nitrogen atom

itself is small, the benzenesulfonimido group would be subjected to more steric effects than, for example, the smaller positive chloride ion. However, the experimental results do not support this assumption. This high percentage of ortho isomer is a characteristic of radical attack (Table VII), and suggests a radical mechanism for the reaction under study.

Hey and co-workers (28,65,67,106), as well as Dannley and Sternfeld (38), and DeTar and Kazimi (43), have demonstrated that an electronegative group in the para position of a phenyl radical results in ionic character of the radical. This electronic effect is evidently an inductive rather than a resonance effect, because methoxy, as well as nitro, chloro, and bromo groups, has been found to impart this ionic character. The benzenesulfonimido radical has a sulfonyl group, one of the strongest electronegative groups, adjacent to the reaction site:



and therefore it would be reasonable to assume that it would show even greater ionic character than p-bromophenyl, p-nitrophenyl, p-chlorophenyl, or p-methoxyphenyl radicals.

As in the case of other electrophilic and nucleophilic radicals, a quantitative calculation is not available, and when a radical has as strong an electronegative group as the sulfonyl group in proximity to the reaction site, a direct comparison with phenylation as a criterion for a radical mechanism is unreasonable. Therefore, the author believes that the reaction proceeds by attack of an extremely electrophilic radical, rather than by an ionic mechanism.

Rates of Reaction

The relative reaction rates of benzenesulfonamidation of aromatic nuclei, tabulated in Table XXVIII, are not in close agreement with the relative reaction rates of either ionic substitution or of homolytic phenylation of aromatic nuclei, which are tabulated in Tables V and VI, respectively.

Substituents on the aromatic nucleus of the substrate apparently deactivate the nucleus slightly for benzenesulfonamidation, though the magnitude of the deactivation is very small and perhaps even within experimental error. All substituents have been found to facilitate phenylation, and in ionic substitutions, the substituents almost invariably have a much larger effect on the rate. The large effects of substituents upon the rate of substitution by other electrophilic radicals, as found by Hey and co-workers (27,65,67), (Table VIII), are definitely not present in substitution by the benzenesulfonimido radical.

The main significance of the values which were determined for the relative reaction rates in benzenesulfonamidation is that a substituent already present on the nucleus has very little effect on the reaction rate. This indicates that the attacking radical has a very short life and is not selective in its choice of molecules. The short life of the radical is reasonable to assume, if the conclusions based on the experimentation of Lindemann and Schultheis (83) are correct, because a close relationship should exist between the benzenesulfonimido radical and the radical formed as an intermediate in the Curtius rearrangement.

The relationship between the relative reaction rates and the dipole moments of the various substrates (Figure 12) is interesting, because it indicates that the rate of benzenesulfonamidation may be a function of the permanent electronic effects in the substrate.

The order of the relative rates of reaction with respect to benzene,

$$CH_3;\ OCH_3 \ > \ Br;\ Cl \ > \ CO_2CH_3,$$

also is interesting, because it indicates that although the magnitude of the difference is small, the order is the same as that of ionic aromatic substitution. This order is also apparent in substitutions with p-nitrophenyl, the most electrophilic radical listed in Table VIII, but not with the other electrophilic radicals listed therein.

Reactions with Aniline

The halogen-like character of the azide group is demonstrated in the reaction of benzenesulfonyl azide with aniline to produce benzenesulfonanilide. In the basic medium, the benzenesulfonyl azide and aniline evidently react to split out hydrazoic acid in a manner analogous to the splitting out of hydrogen chloride by benzenesulfonyl chloride and aniline. Ammonia gas was observed as a by-product. This probably arises from the pyrolysis of the HN_3:

$$3HN_3 \longrightarrow 4N_2 + NH_3 .$$

The isomer ratios from the experiments with aniline are consistent with those for the other substrates. However, the small fraction of the substitution products in the total reaction products makes the analytical procedure less reliable.

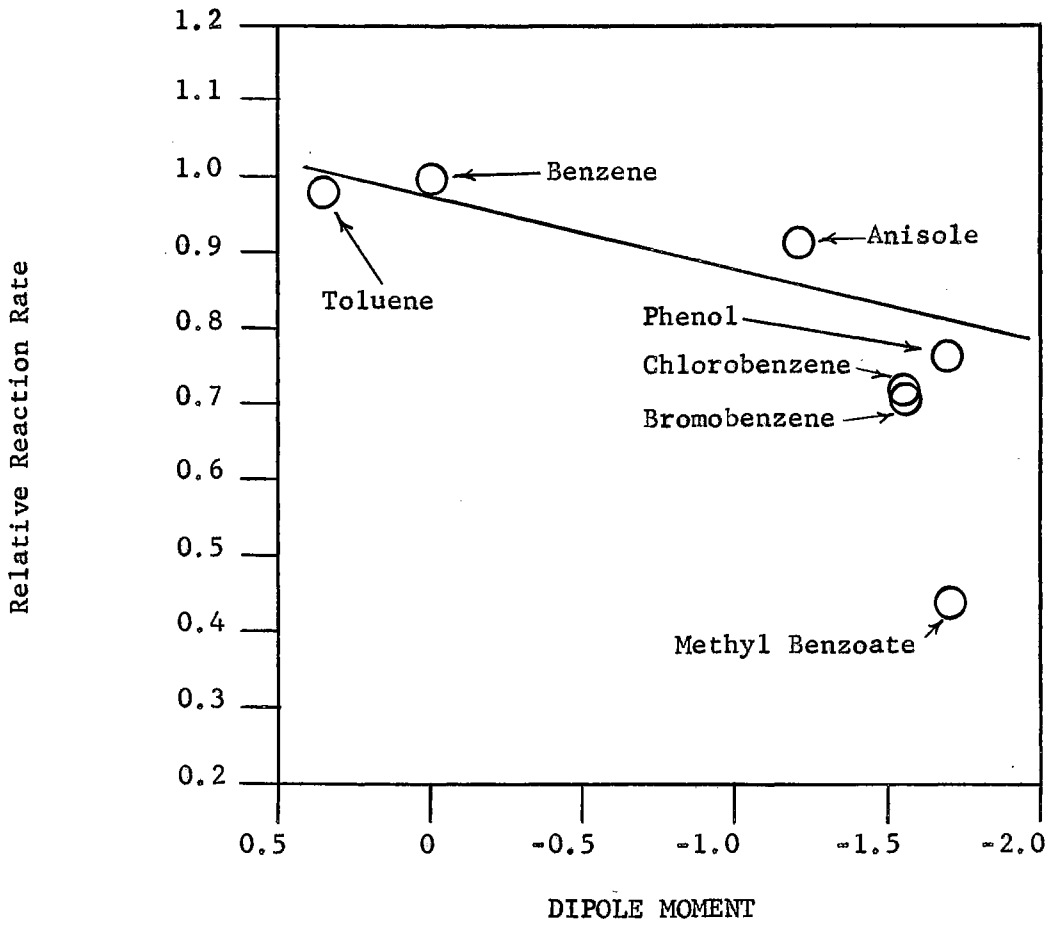


Figure 12. Dipole Moment-Relative Reaction Rate Curve

Reaction with Phenol

The unexpected results from the reactions with phenol are not understood, particularly since one reaction did produce the expected products. The author believes that the substituted products are present in the oily residue, but that impurities prevent recovery. All of the common organic solvents, as well as water, were used in attempts to purify the product by recrystallization, but in each case an oil, rather than the crystalline product developed.

Results Using the meta-Directing Substrates

The meta-directing compounds usually gave little or no substitution products, but produced large quantities of black amorphous acids. In most cases, a small amount of benzenesulfonamide was isolated. Therefore, the radical apparently had a preference for extracting hydrogen rather than for aromatic substitution.

The author believes that these amorphous acids are the result of a reaction of the radical with the meta-directing group to produce a product which perhaps then polymerizes. The mechanism of the reaction whereby nitrobenzene and benzenesulfonyl azide liberate nitric oxide (41), and the failure of benzenesulfonyl azide to react normally with benzaldehyde (35) could also be explained by this type of an attack. The comparatively low relative reaction rate of methyl benzoate might also be attributed to a preference of attack on the substituent group, rather than an actual deactivation of the aromatic nucleus.

The possibility that the radical attacks a molecule of benzenesulfonyl azide, or rearranges in some manner, cannot be overlooked since the amorphous product is not completely absent in reactions with the ortho-para-directing substrates. The low concentration of azide in

the solution, particularly if the radical has a short life as previously discussed, makes the former seem unlikely. Edmison and Davis (47) have demonstrated on a similar amorphous product, from the decomposition of p-benzenedisulfonyl azide, that treatment with PCl_5 produces the p-benzenedisulfonyl chloride. This would eliminate the possibility of a rearrangement, provided the two products are analogous.

Ratio of Benzenesulfonamide to Benzenesulfonanilides

Unfortunately, the results of this experimentation are inconclusive, quantitatively, as to the ratio of benzenesulfonamide to benzenesulfonanilides. The poor precision in determination of the amounts of benzenesulfonamide is probably due to the difficulty of extraction of this product from the reaction mixture. Qualitatively, it appears that the less reactive aromatic nuclei tend to promote a higher benzenesulfonamide to benzenesulfonanilides ratio.

Analyses of the products from the reactions with benzene resulted in good precision in the amounts of benzenesulfonamide. Statistically, the benzenesulfonamide to benzenesulfonanilide ratio from a reaction with benzene should be 1/3; the experimental results show a ratio of 17.6/82.4 which indicates that aromatic substitution is favored over the extraction of hydrogen in reactions with benzene.

Comparison with Previous Results

The isomer ratios which were previously obtained by Dermer and Edmison (41,46), Table I, and the isomer ratios found in this experimental work are not in quantitative agreement, even though there exists a qualitative relationship.

The author believes that the results of this experimental work are more reliable, because the analysis was performed directly on the substituted benzenesulfonanilides rather than on the hydrolysis products, and the method of analysis used in this experimentation probably was superior, considering the nature of the reaction products.

The main difference between these experimental results and those of Dermer and Edmison is in the amount of meta isomer reported. The complete infrared spectrum of the substitution products, which also were isolated in the previous work, revealed only enough meta isomer to account for the quantity reported in this experimental work.

The analysis using the Beckman, Model DU, Ultraviolet Spectrometer, such as used by Dermer and Edmison, would be very sensitive; on pure components a high degree of accuracy and precision would be obtained, but a slight amount of impurity would produce a fairly large error. The analysis using the Perkin Elmer, Model 12-C, Infrared Spectrometer, such as used in this work, would be less sensitive; the precision on pure components would not be as great, but unless the impurities were present in a greater percentage than 3%, they would have little effect upon the final results.

CONCLUSIONS

The question naturally arises as to whether the substitution is accomplished through a radical or an ionic mechanism.

Just as in the Curtius rearrangement, the first and probably the rate-determining step is undoubtedly the decomposition of the azide to form molecular nitrogen and a biradical.

$$C_6H_5SO_2N_3 \longrightarrow C_6H_5SO_2N: + N_2$$

This is supported theoretically since the remaining nitrogen atom would contain six electrons and four atomic orbitals, one 2s, and three 2p orbitals. This is based upon Hundt's rule which states that, "the order of filling of equivalent orbitals, in normal atoms, is that each such orbital tends to accept one electron before any acquires a second." The theoretically most stable configuration then would be the biradical with two unpaired electrons.

Dermer (46) has demonstrated that the decomposition of benzenesulfonyl azide produces radicals by decomposing small amounts in freshly distilled vinyl monomers. The benzenesulfonyl azide was found to have a definite catalytic effect in initiating polymerization, and this action could be inhibited by such inhibitors as hydroquinone or p-benzoquinone.

The Mechanism of the Substitution

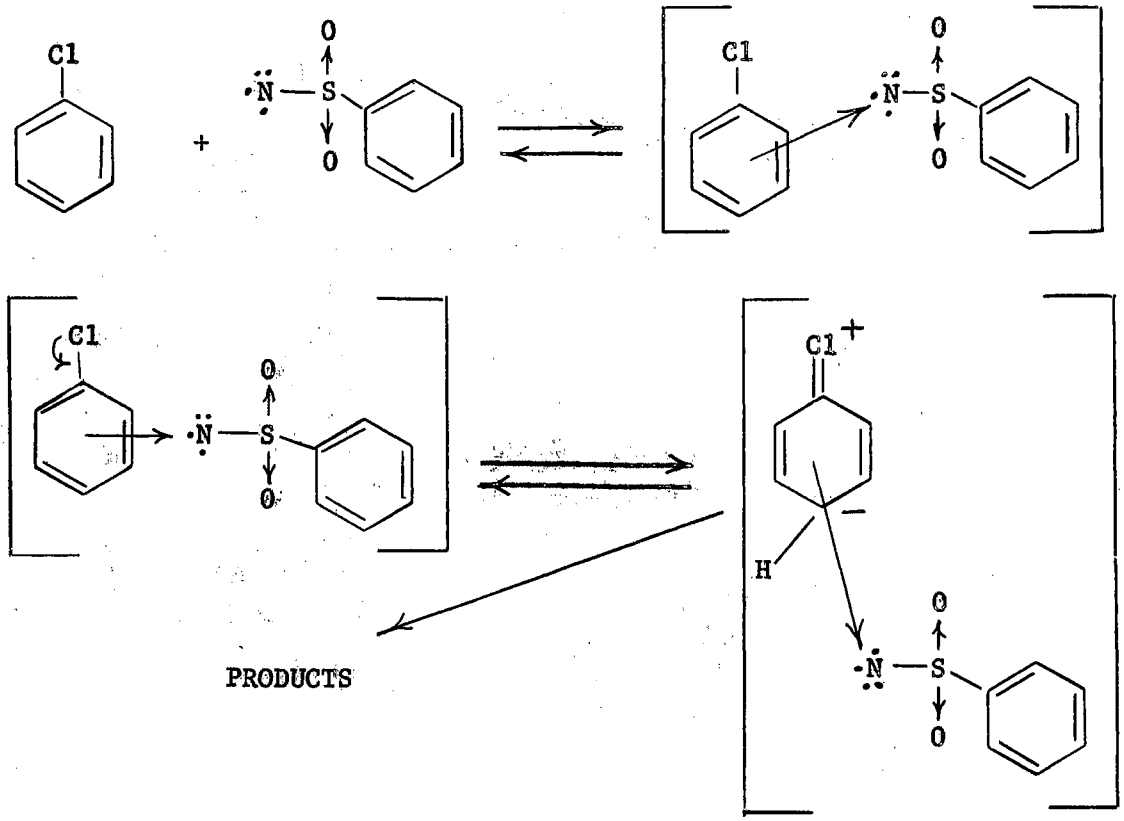
The results of this experimental work at first might seem ambiguous, because the substitution is oriented in a manner similar to an ionic substitution, but the relative reaction rate is similar to

that of a free radical substitution. These results appear more reasonable, however, in the light of previously discussed experiments of Hey and co-workers (28,65,67,106), with electrophilic radicals.

What is the nature of the attacking group, and by what method does the substitution occur, in the benzenesulfonamidation of an aromatic nucleus? The limited scope of this experimentation would certainly not allow one to prove, but only to suggest a possible mechanism.

The relative-rate-of-reaction factors show that substituents have very little effect on the rate of substitution. This means that the benzenesulfonimido radical has a very short life and reacts with the first molecule with which it comes into contact. Therefore, the orientation of the benzenesulfonamidation must occur in the transition state of the substitution reaction.

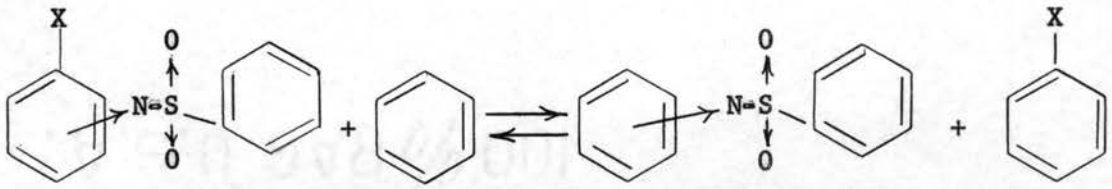
This transition state might be visualized as a π-complex similar to the π-complexes postulated by Dewar (44), for the extremely reactive electron-deficient cations in aromatic substitution. Hammond and co-workers (62) have presented experimental evidence which indicates that certain radicals can also form π-complexes with aromatic compounds. Price and Convery (95) as well as Milyutinskaya, Bagdasar' yan and Izrailevich (85), using isotope-effect techniques, have demonstrated that the formation of an addition intermediate is actually the rate-determing step for phenylation of 2,4-dinitrobenzene and of benzene. The π-complex must have an existence long enough that the electronic effects of the substrate, under the influence of the strong inductive effect of the sulfonyl group at close range, can direct the benzenesulfonimido group to a position favored by high electron density.



The remainder of the reaction proceeds as a regular radical substitution.

The failure of the meta-directing compounds to produce the expected substitution products could be attributed to complexing of the radical with the electron-rich group, rather than with the electron-poor aromatic nucleus.

If this proposed mechanism is correct, one can explain the difference between the benzenesulfonimido radical and other electrophilic radicals. If the life of the π-complex is sufficiently long, the relative reaction rate will be a function of the difference between the thermodynamic stability of the π-complex of the aromatic substance being studied, and the π-complex of the reference solvent, as shown by the following equilibrium:



If the π-complex has a very short existence before being converted to the substitution products, this equilibrium is never attained, and there will be little difference between the relative reaction rates of the two aromatic substrates. In the extreme case, if the formation of the products from each π-complex were instantaneous, the relative reaction rates for any two aromatic compounds would be equal. The benzenesulfonimido radical, being very reactive, forms π-complexes with very short lives, and substitutes in various aromatic nuclei at nearly the same rates.

The greater the electrophilic character of the radical the more the orientation in substitution by it should approach that of ionic electrophilic substitution. Orientation in substitution by the benzenesulfonimido radical, which is very electrophilic in character, is similar to that in ionic substitution.

Although the π-complex used in the postulated mechanism was independently conceived, Benkeser and Schroeder (15) postulated a similar π-complex to explain their results with aromatic substitution by the triphenylmethyl radical. Their paper was published while this dissertation was in its final stages of preparation.

The results of Benkeser and Schroeder (15) are interesting, because the order of relative reactivity is

$$C_6H_5OCH_3 > C_6H_5Cl > C_6H_6 > C_6H_5CO_2CH_3 > C_6H_5CF_3$$

and nitrobenzene fails to react. The variation of the relative reactivities which they found is much larger than that found in this

experimental work, but this can be explained by the relatively sluggish nature of the triphenylmethyl radical as compared with the benzenesulfonimido radical. They also postulated that the surprising lack of susceptibility to steric hindrance of the triphenylmethyl group in attacking the ortho position is due to complexing of the radical fairly close to the negative substituent. The same argument could be applied to explain the similar results found with the benzenesulfonimido radical.

Comparison with Aromatic Nitration

Comparison of benzenesulfonamidation with nitration of aromatic nuclei with oxides of nitrogen, benzoyl nitrate, and metal nitrates in acetic acid reveals a great deal of similarity. In both substitutions the ortho position is favored, and substitution on the nucleus usually fails to occur with meta-directing aromatic compounds. Radical mechanisms have been observed in other reactions of the oxides (57); perhaps the mechanism of their attack on aromatic nuclei is similar to that of benzenesulfonamidation.

SUGGESTIONS FOR FUTURE WORK

A careful investigation of the reaction products should be made in order to account for the portion of the benzenesulfonyl azide which is not converted either into substitution products or benzenesulfonamide. One would expect to find such products as substituted biphenyls formed from combinations of aryl radicals which are formed by the extraction of hydrogen from the aromatic molecules. N,N-diarylbenzenesulfonamides might also be present as the result of combination of these radicals with benzenesulfonimido radicals from the azide.

$$C_6H_5SO_2N: + 2C_6H_5R' \longrightarrow C_6H_5SO_2NH_2 + 2R'C_6H_4\cdot$$

$$2R'C_6H_4\cdot \longrightarrow R'C_6H_4C_6H_4R'$$

$$C_6H_5SO_2N: + 2R'C_6H_4\cdot \longrightarrow C_6H_5SO_2N(C_6H_4R')_2$$

The black amorphous acid obtained in the reaction of benzenesulfonyl azide with the meta-directing substrates certainly represents a difficult identification problem. Not only identification of the solids, but also a careful analysis of the liquids and gaseous by-products should be undertaken.

Effects of temperature, pressure and catalyst on the composition of the products should be thoroughly studied. The isomer ratios from phenylation are apparently very dependent upon temperature (6), but preliminary experimentation in this research indicates very little or no effect of a difference of reaction temperature, over a range of 105-170°C, provided the temperature is above the decomposition

temperature of the azide. Preliminary experiments also indicated that small quantities of powdered copper lowered the decomposition temperature of benzenesulfonyl azide about 5°C.

An obvious extension of this work would be to generate the benzenesulfonimido radical from a different source, and see if the orientation and relative reaction rate are independent of the source of the radical, as was found with phenylation. Benzenesulfonylhydroxylamine and a N-halobenzenesulfonamide under conditions similar to the Lossen and Hoffman rearrangements, respectively, or perhaps decomposition of chloramine T or benzenesulfonhydrazide might be considered as possible methods to generate the radical. Edmison (46) used chloramine T in an attempt to benzenesulfonamidate nitrobenzene, and though no substitution products were obtained, the results apparently were similar to those obtained with benzenesulfonyl azide decomposition.

The substitution of other arene- and alkanesulfonimido radicals, generated from the corresponding azides, could be studied to see if the relative reaction rates and orientation induced by various substituents on the aromatic substrate are comparable to those found for benzenesulfonamidation. Other rigid azides might also be tried, such as the diazide of carbonic acid and the azides of carbamic acid and phenylcarbamic acid.

The study of the influences of different substituents could also be accomplished by benzenesulfonamidation of various <u>para</u>-disubstituted benzenes, such as <u>p</u>-chlorotoluene, and determining of the composition of the substitution products. This would have the advantage of yielding only two substitution products and would, therefore, simplify the analytical procedure.

Other analytical techniques should be investigated, such as the isotope dilution method, to see if their results agree with those obtained in this experimental work using infrared absorption techniques.

Finally, an interesting study could be made of the competing ionic and radical mechanisms in the reaction of benzenesulfonyl azide and aniline. Effects of temperature, pressure, and catalyst could be studied to see what would favor the ionic and what the radical mechanism. By substituting different groups in various positions in both the amine and the radical, and comparing the ratio of products obtained, one could determine the influence which the various substituents had upon the course of the reaction.

SUMMARY

The orientation and the relative reaction rates of homolytic aromatic substitution by the benzenesulfonimido radical were studied.

The benzenesulfonimido radicals were generated by decomposing benzenesulfonyl azide thermally at 105-120°C in an excess of the aromatic substrate or substrates. The total and partial relative-reaction-rate factors were determined by using a competitive method with benzene as a reference solvent.

Determinations of the composition of the products of the reaction were accomplished by use of a Perkin Elmer Model 12-C Infrared Spectrometer. Table XXVIII in the discussion of this dissertation summarizes the results; this table is repeated here for convenient reference.

SUMMARY OF RESULTS

Average Isomer Ratio, Total Relative Rate ($^{X}_{H}K$), and Partial Relative Rate ($^{X}_{H}k_{o}$, $^{X}_{H}k_{m}$, $^{X}_{H}k_{p}$) Factors for the Benzenesulfonamidation of Aromatic Substrates

Substrate	Isomer ratio			Rate factors			
	o-	m-	p-	$^{X}_{H}K$	$^{X}_{H}k_{o}$	$^{X}_{H}k_{m}$	$^{X}_{H}k_{p}$
Benzene	----	----	----	1.000	1.00	1.00	1.00
Toluene	60.7	1.5	37.8	0.987	1.80	0.04	2.24
Anisole	71.5	1.8	26.7	0.910	1.95	0.05	1.46
Phenol	50.3	1.4	48.3	0.765	1.15	0.03	2.22
Chlorobenzene	46.1	1.6	52.3	0.720	1.00	0.03	2.26
Bromobenzene	50.2	4.9	44.9	0.714	1.08	0.10	1.92
Methyl benzoate	44.3	53.2	2.5	0.433	0.58	0.69	0.06
Aniline	41.0	6.4	52.6	-----	----	----	----
Benzoyl chloride	0.9	94.2	4.9	-----	----	----	----

The nature of the attack of the benzenesulfonimido radical is related to that which was recently postulated for homolytic attack by other electrophilic radicals. Based upon the findings of this experimentation, a mechanism is postulated for the reaction. Briefly, this mechanism is that immediately upon forming, the radical forms a π-complex with the aromatic substrate. This π-complex has an existence of long enough duration that the electronic effects of the substrate, under the influence of the strong inductive effect of the sulfonyl group at close range, can direct the benzenesulfonimido radical to a position favored by high electron density. The remainder of the reaction proceeds as do other radical substitutions of the aromatic nucleus.

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