

# HOMOLYTIC AROMATIC ARYLATION

D. R. AUGOOD<sup>1</sup>

*Atomic Energy Research Establishment, Harwell, England*

AND

GARETH H. WILLIAMS

*Chemistry Department, King's College, University of London, London, England*

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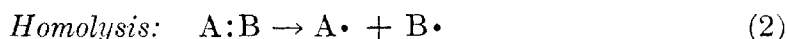
<sup>1</sup> Present address: E. I. du Pont de Nemours & Company, Sabine River Works, Orange, Texas.

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## I. INTRODUCTION

This article represents an attempt to assemble the relevant data, much of it recent, associated with homolytic aromatic substitution reactions and to assess the progress that has been made towards the complete understanding of this and other types of aromatic substitution. Certain assumptions are made, and undoubtedly the simplified picture presented will be modified by further experimental and theoretical work. Examination of the available data on the subject reveals a number of anomalies, and these have been included to serve as criticism of the outlined suggestions and as pointers to future lines of thought.

Ingold (195), in 1938, distinguished between two modes of bond fission:



where A and B are atoms or groups of atoms. The latter reaction is characterized by the production of neutral fragments, each possessing an odd unpaired electron. The term "free radical" is applied in this sense and so includes some inorganic substances, for example, nitric oxide.

Since more energy is required to separate the charged particles of equation 1 than the neutral fragments of equation 2, it would be thought that the latter reaction would be favored, and in the gas phase this is certainly true. However, for the majority of reactions in solution, particularly with solvents of high dielectric constant, fission by reaction 1 predominates because the solvation of the resulting ions results in an energetic advantage being given to this mode of fission. In solution, therefore, homolytic reaction is the exception rather than the rule.

The existence of organic radicals was experimentally demonstrated by Gomberg (132) in 1900, when working with the hexaarylethanes. The idea of an anomalous valency for carbon was not a popular one, but the accumulation of facts from many fields has resulted in the establishment of the concept. Organic free radicals have been divided into two classes: (1) those of long life, like the triarylmethyls, which are stabilized by resonance; (2) those of short life, like phenyl and methyl. It is with the reactions of radicals of the second type that this article is concerned.

The inference that short-lived radicals are unstable is erroneous; the contrary is the case. The reason why they cannot be prepared in large quantity is not that their molecules break down; indeed, a single radical completely isolated from all contact with other molecules would doubtless remain unchanged indefinitely.

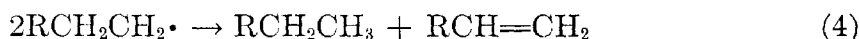
The reason is instead that these substances are so extraordinarily reactive that each entity undergoes some sort of chemical change, in an attempt to satisfy its normal valency requirements, before it has made a large number of collisions with other molecules. Strictly speaking, therefore, the term "short-lived," when applied in description of a free radical, means nothing unless the environmental conditions are also stated. It is very difficult to demonstrate physically the existence of these radicals in solution, as the techniques usually applied to the detection of radicals of the triarylalkyl type, e.g., color reactions and magnetic measurements, completely fail. The presence of radicals of short life is inferred from their reactions, on account of both the complex kinetics which they exhibit and the natures of the chemical products that are obtained.

Free radicals react in three main ways:

*By dimerization*, or combination of the radicals:



*By disproportionation*, involving mutual hydrogenation and dehydrogenation:



*By radical transfer*, which is expressed by the general equation:



In the last reaction the nature of the final products is also dependent on the radical  $R'\cdot$ . It may react as in equation 5 to give another radical  $R''\cdot$ , which may or may not be the same as  $R'\cdot$ . If it is the same, then a chain reaction has been set up and the process repeats itself until the chain is somehow interrupted. If the radical  $R'\cdot$ , or  $R''\cdot$ , is relatively unreactive, then the transference (reaction 5) has resulted effectively in the termination of the reaction.

In many instances these reactions may occur simultaneously, and the total reaction may appear very complex. In defined cases, however, certain of these reactions are favored relative to the others, and specific compounds preponderate in the product. This is illustrated by a comparison of the reaction medium of the gas phase with that of the liquid phase for, though the reactions may be initiated in the same way in both media, there are great differences in the types of reaction occurring. For example, in the photolysis of ketones and the pyrolysis of certain organometallic compounds, in the gas phase, where collisions between radicals can readily occur, reactions 3 and 4 predominate, whilst in solution, where the radicals are surrounded by solvent molecules, reactions between radicals are unlikely unless the life of a radical is for some reason prolonged. With labile radicals in solution the radical-solvent interaction (equation 5) is the most important reaction, and it is clear from this equation that the product is determined by both the radical and the solvent.

With aromatic solvents, alkyl radicals behave differently from aryl radicals. Thus alkyl radicals, in general, react with aromatic solvents by reactions other than that of direct substitution. They do, however, effect substitution in some cases, and this will be discussed at a later stage. Similar considerations are valid

in the comparison between the reactions of a given radical with either aliphatic or aromatic solvents, only the latter being susceptible to homolytic substitution.

During the last few years these homolytic aromatic substitution reactions have been studied in considerable detail, and the results have been periodically discussed. However, the data have not yet been assembled in a comprehensive review and the practical results have not been investigated as to their reliability and significance.

Dermer and Edmison (92), in their review article, have summarized the extensive practical work carried out over the whole subject field. The present review is concerned with a more limited field: namely, with the more recent quantitative work carried out with aromatic solvents and, unless specifically mentioned, aryl radicals, particularly phenyl. The article consists of two parts: firstly, a critical discussion of the appropriate practical work, leading to presentation of the relative rates for homolytic reaction and the corresponding partial rate factors; and secondly, an examination of the theoretical treatments for aromatic substitution. The application of the theoretical treatments to the case of homolytic reactions is considered, and the quantitative predictions suggested by calculations based on mathematical results already available from these methods are compared with the new experimental data.

## II. HETEROLYTIC AND HOMOLYTIC AROMATIC SUBSTITUTION

Although the reactions of organic compounds are reactions of nonionic substances when compared with those of inorganic compounds, it is accepted that the course of the majority of organic reactions is determined by the charge distribution within the molecule. Thus, owing to the fact that homolytic reaction is less frequently encountered, the so-called "normal laws" of aromatic substitution, developed as the result of experiment, are laws governing the *heterolytic* reactions in which the organic substances take part.

Heterolytic reagents are of two kinds: those which seek out the centers of high electron density, i.e., electrophilic reagents, and those which react at electron-deficient positions, i.e., nucleophilic reagents. Hence, in the majority of aromatic substitution reactions, such as nitration, halogenation, sulfonation, and diazocoupling, a proton is replaced by an electrophilic reagent capable of accommodating a pair of electrons, e.g., the nitronium ion,  $\text{NO}_2^+$ , which is responsible for most aromatic nitrations. Many nucleophilic reactions of aromatic substitution are also known, and these have been reviewed recently by Bunnett and Zahler (43).

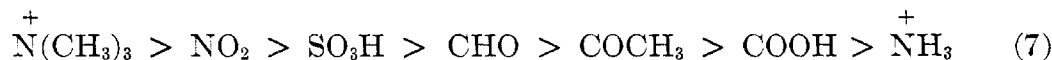
The history of the development of the theories of heterolytic aromatic substitution is long and outside the scope of this review (8, 246).

The more recent work of the so-called English School has resulted in the establishment of what may be called the "normal laws" of aromatic substitution. These are based mainly on studies of nitration (14, 15, 21, 185, 194, 197, 198, 247), i.e., a reaction of electrophilic substitution. On theoretical and experimental grounds a directing group (X), attached to the aromatic nucleus ( $\text{C}_6\text{H}_5$ ) in the compound  $\text{C}_6\text{H}_5\text{X}$ , may be placed in one of two main categories. Thus, for this

type of substitution [the rules are reversed for nucleophilic reactions (8, 19, 42, 43, 113, 246)], the following X substituents are ortho-para directing and activate the nucleus for reaction relative to benzene:



whereas the following groups are meta directing and deactivating:



The situation is a little more complex in that certain anomalies, which are accommodated by the general theory, occur. Thus, for example, the halogens are deactivating groups but are ortho-para directing.

The work of Ingold and coworkers in this field is well known (21, 194, 197, 198) and was important in providing quantitative data to describe the phenomena. The work resolved itself into two parts: (1) the determination of the quantities  $\overset{\text{X}}{\text{H}}K$ , i.e., the ratio of the total rate of nitration of the monosubstituted benzene derivative,  $\text{C}_6\text{H}_5\text{X}$ , relative to that of benzene,  $\text{C}_6\text{H}_6$ ; (2) the estimation of the proportions in which the three isomers  $r\text{-NO}_2\text{C}_6\text{H}_4\text{X}$  ( $r = o\text{-}, m\text{-}$  or  $p\text{-}$ ), were formed in the nitration of  $\text{C}_6\text{H}_5\text{X}$  alone.

The combined results of these experiments allowed the evaluation of the partial rate factors  $\overset{\text{X}}{\text{H}}k_r$ . Each of these factors expresses the change in the specific rate of substitution at any position  $r$  in the nucleus due to the presence of the group X, i.e., it is the *ratio* of the rate of reaction at the point  $r$  in the molecule  $\text{C}_6\text{H}_5\text{X}$  relative to that at any one position in benzene. It must be remembered that the quantities  $\overset{\text{X}}{\text{H}}K$  and  $\overset{\text{X}}{\text{H}}k_r$  are pure numbers; they have no dimension in time. Table 1 presents some of the values obtained.

For toluene the figures are greater than unity and show that the methyl group activates all the positions  $r$ , i.e., toluene is more readily nitrated than benzene. Moreover, the order of the  $\overset{\text{X}}{\text{H}}k_r$  values, i.e.,  $p > o > m$ , necessarily implies that this is the sequence of reactivities of the nuclear positions. The carboxy group,  $\text{COOC}_2\text{H}_5$ , shows general deactivation, with the meta position least affected, and the halogens show themselves to be exceptions to the rules, as mentioned above. Details concerning other groups, e.g., *tert*-butyl,

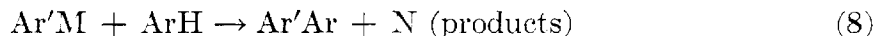
TABLE 1  
Partial rate factors for nitration (291°K.)

X	$\overset{\text{X}}{\text{H}}k_o$	$\overset{\text{X}}{\text{H}}k_m$	$\overset{\text{X}}{\text{H}}k_p$	$\overset{\text{X}}{\text{H}}K$	References
—CH <sub>3</sub>	40.0	3.0	51.0	23.0	(197)
—COOC <sub>2</sub> H <sub>5</sub>	0.0026	0.0079	0.001	0.0037	(198)
—F	—	—	—	0.15	(21)
—Cl	0.030	0.000	0.139	0.033	(21, 246, 247)
—Br	0.037	0.000	0.106	0.030	(21, 246, 247)
—I	—	—	—	0.18	(21)
—OH*	—	—	—	~10 <sup>4</sup>	
—NO <sub>2</sub> *	0.24 × 10 <sup>-6</sup>	2.75 × 10 <sup>-6</sup>	0.03 × 10 <sup>-6</sup>	~10 <sup>-6</sup>	(185, 246)

\* Approximate figures only.

are available (32, 60, 182). Data for halogenation (16, 17, 18, 28, 29, 61, 62, 90, 91, 223–228, 243) and sulfonation (107, 269, 278, 279) have been reported recently; e.g., for chlorination at ca. 25°C. the total relative rate values for all groups X fall into sequence (226) between the extreme figures of  ${}^{\text{N}(\text{CH}_3)_2}k_{\text{H}} \sim 10^{18}$  and  ${}^{\text{NO}_2}k \sim 10^{-6}$ ; and the partial rate factors for toluene (61, 62, 227) are  ${}^{\text{CH}_3}k_o = 600$ ,  ${}^{\text{CH}_3}k_m = 5$ , and  ${}^{\text{CH}_3}k_p = 870$ . The differences between these figures and those of table 1 show the electron demands of the reagents to be different (29, 228) and illustrate that any set of partial rate factors applies only to the reaction for which they were determined.

Although these laws were not so clearly defined at the time, it was the separation of the apparently anomalous substitution products arising from certain reactions that first indicated the possibility of another, i.e., nonionic, type of substitution. These reactions were those whereby the preparation of biaryls was accomplished, and it was suggested (141, 159, 174) by Hey and Waters, in 1934 and 1937, that in these reactions homolytic processes were occurring. In essence, the existence of short-lived free radicals of the type of phenyl was postulated, and these entities, being electrically neutral and therefore not subject to the same electrical effects as the heterolytic reagents, effected substitution in the aromatic molecule  $\text{C}_6\text{H}_5\text{X}$  without conforming to the normal laws of aromatic substitution. These reactions can be expressed by the general equation:



where the radical  $\text{Ar}'\cdot$ , produced from the compound  $\text{Ar}'\text{M}$ , in reaction with the aromatic solvent  $\text{ArH}$  forms the biaryl  $\text{ArAr}'$  and ejects a hydrogen atom which is incorporated in the product N. It was later found that in homolytic substitution in  $\text{ArX}$  the general tendency was for all groups X, whatever their directing effect in heterolytic substitution, to favor predominantly reaction at the para position. The meta position was thought to be least favored and the corresponding *m*-biaryl was rarely isolated. More recent work has, however, necessitated considerable revision of these ideas.

A number of different aspects of the problem therefore present themselves for review. The reactions of equation 8 must be defined and their homolytic character clearly established; the mechanism by which the substitution is effected has to be formulated; the reasons have to be ascertained for the erroneous conclusions, mentioned above, of almost invariable para homolytic reaction; the theoretical aspects of substitution have to be considered; and finally, the new concepts of free-radical reaction have to be related to theory and practice.

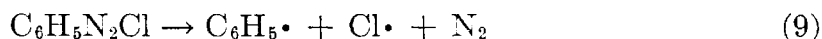
### III. HOMOLYTIC ARYLATION REACTIONS

Several main types of homolytic reaction, featuring interaction between aryl radicals and aromatic solvents and generally expressed by equation 8 above, may be considered. These and other reactions are reviewed by Dermer and Edmison (92). The reactions considered here are those which have been subjected to quantitative study. The biaryl  $\text{ArAr}'$  produced usually consists of a mixture of substituted biphenyls, and in the discussion which follows this mixture will be termed the "biphenyl fraction".

## A. DIAZO COMPOUNDS

1. *Diazonium chlorides etc., D reaction*

These reactions, designated by the letter D, are carried out by adding the solid diazonium chloride, or a similar compound, which is usually impure, to the organic solvent and heating the mixture. The primary reaction (241, 242, 282, 284) is the first-order decomposition of the wholly covalent molecule, producing  $\text{Cl}\cdot$  and  $\text{C}_6\text{H}_5\cdot$  radicals and liberating nitrogen:



The addition of some metals to the reaction mixture has been shown (284) to result in the formation of metallic chlorides or organometallic compounds, even in slightly alkaline media, and this demonstrates the existence of the highly reactive radicals. Clearly, the reactions of diazo compounds (267), 1-aryl-3,3-dialkyltriazenes (111), arylazotriarylmethanes (159, 181, 293-297), and stabilized diazonium compounds (181) are analogous.

2. *Diazonium hydroxides and acylarylnitrosamines*

## (a) Gomberg reaction, G reaction

The decomposition of diazohydroxides (7) in aqueous/aromatic systems was developed by Gomberg (133, 134) from the work of Bamberger (9, 10) and Kuhling (207-209). In aqueous solution at temperatures of 0-5°C. the diazotized amine is converted to a covalent diazohydroxide, and in the presence of a liquid aromatic compound the following reaction ensues:



The reaction is essentially heterogeneous, and success depends on the ability of the aromatic compound to extract the reactive covalent hydroxide from the aqueous phase as soon as it is formed by the hydrolysis (110, 142). This is neatly demonstrated (142) by the fact that benzoic and anthranilic acids do not take part in the Gomberg reaction unless first esterified, i.e., converted from easily ionized molecules, preferring aqueous solution, to typical organic esters.

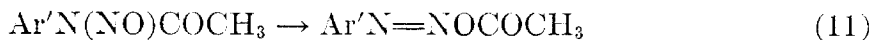
The reaction has been extended (142) to the employment of a solid aromatic compound  $\text{ArH}$  by using an organic solvent (chloroform, carbon tetrachloride) which is relatively inert towards the radicals involved and which in reaction forms compounds easily isolated from the desired substitution product  $\text{ArAr}'$ .

The products of reaction are usually very tarry and the yields of biaryl are low, ca. 10-20 per cent of the amine, with the formation of large quantities of intractable tar.

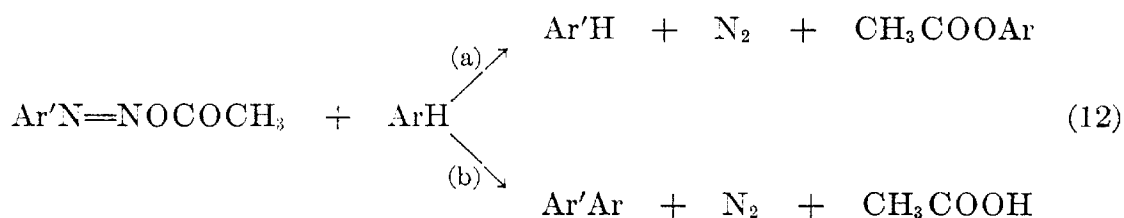
## (b) Hey reaction, H reaction

The decomposition of acylarylnitrosamines, a reaction largely developed by Hey (141), is closely related to the above Gomberg reaction. Not only does this reaction yield the same products in reactions with the same aromatic solvent as the Gomberg reaction, but it also appears to react by a similar mechanism. This

is not surprising in view of the fact that the acylarylnitrosamines rearrange, giving diazo-esters:



The reaction is accomplished by adding the (usually impure) nitroso compound to the aromatic solvent at moderate temperatures. It is, therefore, a homogeneous reaction, unlike the G reaction, and has lent itself to investigation of the reaction kinetics. Thus, it has been shown (47, 141, 171, 172, 187–191, 288) that the rate-determining step is the intramolecular rearrangement (equation 11). In a non-ionizing solvent homolysis then occurs rapidly and reaction (93, 153) with the solvent gives the products indicated by equations 12a and 12b:



This dual behavior, with the  $\text{Ar}'\cdot$  radical either abstracting a hydrogen atom or combining with the nucleus to form a biaryl, is now well established. It will be met again, and much controversy has centered around it (Section V,C).

Investigation of the reaction in a wide variety of solvents has shown that the solvent has little effect upon the decomposition kinetics (141, 171, 172) and indicates that it is unlikely that the biaryl is produced by a chain reaction involving solvent radicals  $\text{Ar}\cdot$  and the diazoacetate (see Section III,B,2).

It was indicated in Section I that a free radical may react in any one of a number of different ways and that though a given mode may predominate, it does not do so exclusive of all others. It appears that the energy relationships are so balanced that many possible reactions have a definite and observable probability dependent upon the properties of the radical and the solvent. Huisgen (190) has shown that for equation 12, where  $\text{Ar}'\cdot = \text{C}_6\text{H}_5\cdot$  and  $\text{ArH} = \text{pyridine}$ , the ratio of reactions (a):(b)  $\sim 1:120$ , i.e., the aryl radical  $\text{Ar}'\cdot$ , from the diazo compound, prefers nuclear substitution of  $\text{ArH}$  to hydrogen abstraction. It is conceivable that this relationship could be changed by suitable choice of  $\text{ArH}$ , e.g., if the  $\text{Ar}'\cdot$  radical removed a hydrogen atom from the solvent to leave a radical  $\text{Ar}\cdot$  heavily stabilized by resonance. When an aliphatic solvent is used, reaction 12a is the predominant reaction (283).

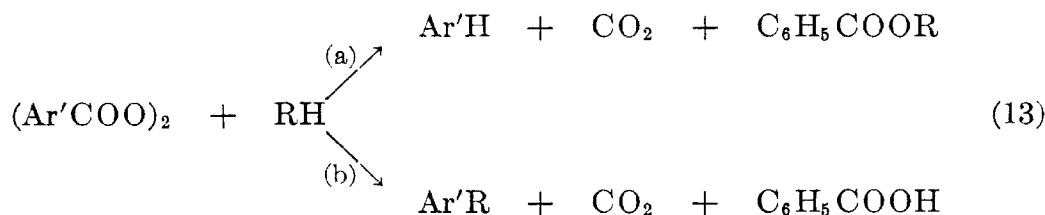
## B. DIACYL PEROXIDES, P REACTION

### 1. Use in preparation reactions

This is undoubtedly the "cleanest" of the reactions considered. The purified peroxide, often crystalline, is added to the aromatic solvent and the decomposition is effected by heating, usually to ca. 70–80°C. Smaller quantities of tars are obtained in the product and the reported yields are higher than with the D, G, and H reactions.



Gelissen and Hermans (23, 122–129) showed that the decomposition of diacyl peroxides in various solvents (RH) obeyed their "RH scheme" (*cf.* equation 12 above), though the mechanism was not clearly defined.



The accumulated evidence of this and later work (5, 23, 93, 296, 298) shows that the decomposition of any peroxide  $(\text{Ar'COO})_2$  in an aromatic solvent ArH gives rise only to the formation of compounds of the type  $\text{ArAr'}$ ; e.g., the decomposition in benzene of a symmetrical disubstituted peroxide yields only the mono-substituted biphenyl. Similarly, the decomposition of benzoyl peroxide in a solvent other than benzene yields a biaryl with substituents in only one nucleus. Two conclusions follow: (1) the radicals from the peroxides ( $\text{Ar'}$ •,  $\text{Ar'COO}$ •) do not recombine, and (2) the abstraction of hydrogen atoms from the solvent by either  $\text{Ar'}$ • or  $\text{Ar'COO}$ • is not the predominant reaction, since the radical  $\text{Ar}$ • so formed would yield the symmetrical biaryl  $\text{ArAr}$  by dimerization or solvent reaction (equations 12b and 13b). The main reaction with the aromatic solvent is therefore



## 2. Kinetics of the decomposition of diaroyl peroxides

Much recent work has been concerned with a study of the kinetics of the decomposition of benzoyl peroxide. Several mechanisms have been proposed for this reaction, but some of these have not taken due account of the nature of the products formed in the different cases and have tended towards overgeneralization.

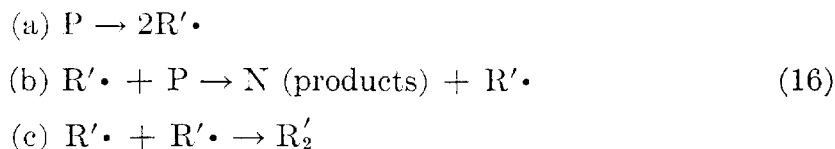
Brown (30), in 1940, showed by measurement of carbon dioxide evolution that the peroxide decomposition could be expressed by parallel first- and second-order reactions; i.e., if  $C$  represents the concentration of benzoyl peroxide,  $k'_{\text{I}}$  and  $k'_{\text{II}}$  are constants, and  $t$  is time:

$$\frac{-dC}{dt} = k'_{\text{I}}C + k'_{\text{II}}C^2 \quad (15)$$

The approximate first-order kinetics was confirmed by some workers (11, 78), but Nozaki and Bartlett (235, 236), in investigating a whole range of solvents, showed that in addition to unimolecular dissociation of the peroxide, now known (13, 94, 147, 148) to form two  $\text{C}_6\text{H}_5\text{COO}$ • radicals, there was also a chain decomposition induced by the radicals derived from either the peroxide P or the solvent SH. The chain termination was thought to be by the recombination of

two radicals:

*Scheme I*



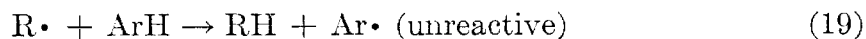
where  $R' \cdot$  = radical from either peroxide or solvent, i.e.,  $C_6H_5 \cdot$ ,  $C_6H_5COO \cdot$ , or  $S \cdot$ . Induced decomposition by  $S \cdot$  in stage (b) leads to the kinetic equation:

$$\frac{-dC}{dt} = k'_i C + k'_{ii} C^{3/2}
 \tag{17}$$

Nozaki and Bartlett indicated that the induced decomposition, contributing the term  $k'_{ii} C^{3/2}$  to the rate equation 17, was the main cause of variation in the observed rate of decomposition from one solvent to another, and that these rates were in the order:



Some workers (53) believed that the similarity of the  $S \cdot$  ( $Ar \cdot$ ) radicals, produced from a series of aromatic solvents, was the reason for the consistently small contribution that they made to the induced decomposition. Only in one instance (150) does it appear that the nature of the products from these aromatic systems has been considered and due reservation expressed concerning the solvent-radical mechanism. The significance of the solvent radicals (12, 22, 58, 210, 252) for the case of phenol is exceptional and is discussed at a later stage.<sup>3</sup> In an attempt to explain the kinetic behavior of the aromatic solvents, Nozaki and Bartlett (235, 236) intimated that if the disappearance of the chain carriers (equation 16,  $R' \cdot = R \cdot = C_6H_5 \cdot$  or  $C_6H_5COO \cdot$ ) was not due to the recombination of radicals (equation 16c) but resulted from reaction with the solvent to give an *unreactive* radical ( $S \cdot = Ar \cdot$ ):

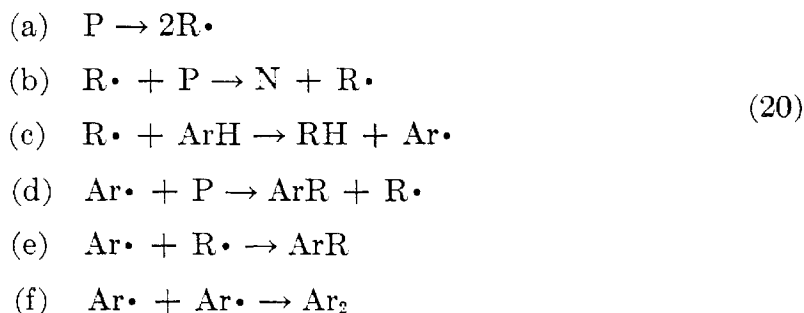


then the kinetics could be described by the equation obtained earlier by Brown (equation 15). In this event it is difficult to see how an unsymmetrical biaryl is formed at all (equation 16b precluded). In addition, the stability of  $Ar \cdot$  would not only tend to increase the probability of reactions of the type shown in equation 16c, but in so doing would result in the formation of the symmetrical biaryl  $ArAr$  (*cf.* Sections I and III,B,1, above).

A further scheme which has been postulated is that involving solvent radicals which are considered to yield biaryl by attacking the peroxide (equation 20b).

<sup>2</sup>Exclusive of phenols and amines; e.g., hydrocarbons, nitro compounds, and chloro compounds.

<sup>3</sup>See references 300 and 301.

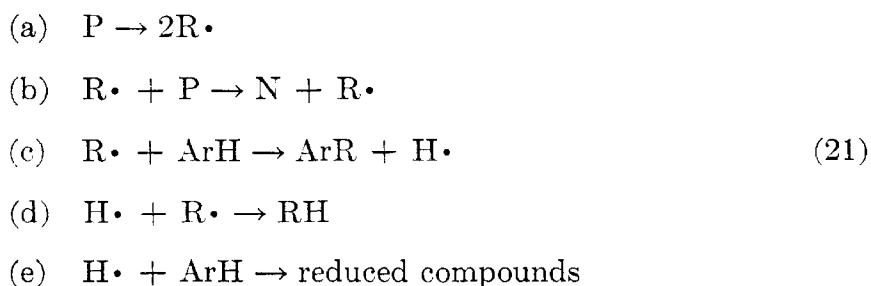
*Scheme II*

where  $\text{R}\cdot = \text{C}_6\text{H}_5\cdot, \text{C}_6\text{H}_5\text{COO}\cdot$ .

This mechanism was also suggested independently (96) in an attempt to explain the products of the reaction even after the kinetic work had been reported. Scheme II, however, cannot explain, either singly or together, why these solvents show no induced rate, although this is necessitated by equation 20, for  $\text{Ar}\cdot$  will be similar to  $\text{R}\cdot$  and must react in a similar fashion (equation 20b), and also why no dimerization products like  $\text{ArAr}$  (equation 20f) are found.

It is now possible to clarify the situation, at least for the typically aromatic solvents, for a different explanation consistent with both the kinetics and the type of product obtained may be offered. The relevant experimental data are summarized in the following conclusions: (1) The dimerization reaction (equation 16c) has been shown absent (see III,B,1, above), and so chain termination must involve the solvent in a reaction of the type shown in equation 19. (2) In order to explain the low induced rate observed for these solvents an inactive radical  $\text{Ar}\cdot$  was postulated in equation 19. This is difficult to reconcile with the facts that (a)  $\text{Ar}\cdot$  must be similar to  $\text{R}\cdot$  ( $= \text{C}_6\text{H}_5\cdot, \text{C}_6\text{H}_5\text{COO}\cdot$ ) and so must take part in the reaction, and (b) the symmetrical biaryl  $\text{ArAr}$  is not formed. (3) Evidence summarized in the preceding section (III,A,2; III,B,1), showing that hydrogen-atom abstraction was the minor reaction, must be considered.

Thus the chain-termination step, that is, the interaction between the radical  $\text{R}\cdot$  and the solvent  $\text{ArH}$ , produces not an inactive solvent radical but the very highly reactive hydrogen atom. This hydrogen atom reacts immediately either with another radical  $\text{R}\cdot$  or with the solvent and becomes effectively lost, i.e.:

*Scheme III*

where  $\text{R}\cdot =$  radical from peroxide, i.e.,  $\text{C}_6\text{H}_5\cdot$  or  $\text{C}_6\text{H}_5\text{COO}\cdot$ . Hydrogen-atom

removal by reaction 21d leads to:

$$\frac{-dC}{dt} = k_i C + k_{ii} C^{3/2} \quad (22)$$

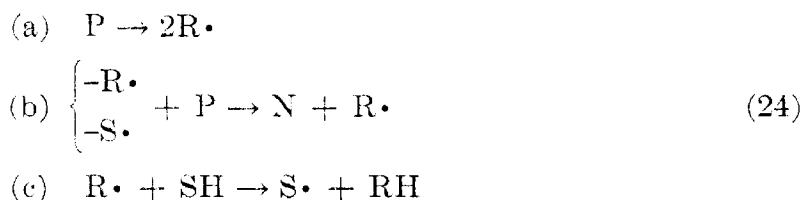
and hydrogen-atom removal by reaction 21e leads to:

$$\frac{-dC}{dt} = k_i C + k_{ii} C^2 \quad (23)$$

The most important feature of scheme III is that solvent radicals play no part in the chain decomposition, and it is a necessary corollary of such a scheme that these radicals are formed only in negligible amount. It is seen that the hydrogen atom may be removed by one of the two processes, either by  $R\cdot$  or by the solvent, and that for each separate case the overall kinetic equation is different. Qualitative reasoning indicates that the former is more probable (192, 288) for in the solvent cage, containing  $(2C_6H_5COO\cdot, ArH)$ , when substitution is effected by a  $C_6H_5\cdot$  radical, formed by decarboxylation of one  $C_6H_5COO\cdot$  radical, the hydrogen atom liberated is able to unite with the remaining  $C_6H_5COO\cdot$  radical to form benzoic acid. Experimentally, in the majority of peroxide reactions, the quantity of benzoic acid produced does account for about half of the peroxide. Such pseudo-termolecular collisions are quite feasible in the liquid-phase system under discussion. This suggestion accounts for the difficulty of isolating reduced material from these reactions (192). If, however, an acceptor radical,  $R\cdot = C_6H_5COO\cdot$ , is not available to absorb the hydrogen atom, then this may be accommodated by a solvent molecule (5). The kinetics will tend towards equation 23 and reduced compounds will appear in the reaction product.

When phenols<sup>4</sup> (12, 235, 236) and possibly amines (120, 121, 183, 238) (*cf.* equation 18) are used as solvents, hydrogen abstraction from the OH and NH<sub>2</sub> groups can take place and the high rate of induced decomposition, brought about by the important solvent radicals, leads to scheme IV, which is essentially that of equation 16:

*Scheme IV*



where  $R\cdot =$  radical from peroxide, i.e.,  $C_6H_5\cdot$  or  $C_6H_5COO\cdot$ .

Strong chain decomposition occurs (reactions 24b and 24c), and if this is sufficiently important all the peroxide P is consumed in the form of  $R\cdot = C_6H_5COO\cdot$ , the benzoyloxy radicals being unable to lose carbon dioxide because of the high rate of their reaction with the solvent. This leads to the kinetic equation:

<sup>4</sup> See references 300 and 301.

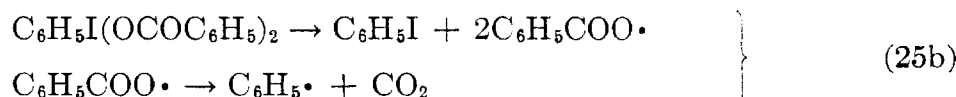
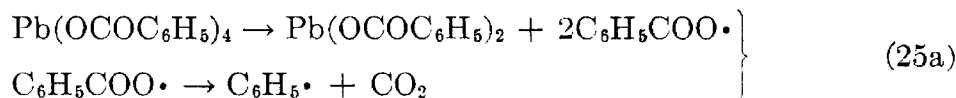
$$\frac{-dC}{dt} = k_i''C + k_{ii}''C^{3/2} \quad (25)$$

This observation is relevant to later discussion.

The foregoing argument demonstrates the dangers of overgeneralization and the importance of considering both the kinetics and the products together in presenting a reaction mechanism. The importance of both solvent and radical is emphasized (see Section I). Here, for a given radical, the change in solvent from a nonphenolic aromatic compound to phenol has produced a change in the nature of the decomposition.

#### C. LEAD TETRABENZOATE AND PHENYL IODOSOBENZOATE

Recent work (169, 170) has shown that these compounds decompose in a manner analogous to benzoyl peroxide, yielding benzoyloxy and phenyl radicals (equations 25a and 25b).



The phenyl radicals are capable of effecting the phenylation of the aromatic compound in whose solution the decomposition is carried out, and the phenylation reaction has been subjected to quantitative study.

#### D. HOMOLYTIC NATURE OF THE REACTIONS

The inclusion of free-radical intermediates in some of the above reactions has been questioned by Hodgson (180), who proposed that they were not present in reactions in aqueous media, i.e., the G reaction, and that the substitutions effected by them could be explained on an ionic basis. Some of these criticisms have been answered by Hey and Waters (175). It is now certainly true that, dependent on conditions, both ionic and radical mechanisms can take place in some cases (95, 96, 154, 155, 160, 161, 163, 165, 255), e.g., the Pschorr reaction, but the following considerations show that all the reactions discussed above are essentially homolytic in character.

- (i) In Section III,A,2 it was shown that, in the G reaction, benzoic acid does not undergo substitution unless it is first esterified, i.e., the reaction takes place in the nonaqueous phase, where covalent molecules may be expected to decompose to yield free radicals.
- (ii) Similar chemical products are derived from all the above cases, i.e., G, H, and P reactions. The H and P reactions are known to be homolytic, as indicated by their kinetics, the insensitivity of the reaction rate to the polarity of the solvent (33), the absence of any correspondence between decomposition rate and acid dissociation constant,

etc. In this context it may be noted that the phrase "similar products" does not bear close scrutiny if applied to work done before 1951 (table 3). The more recent work, however, justifies its use.

- (iii) Arising from the more recent investigations, mentioned under paragraph (ii) above, it has been shown (5, 97, 161, 164, 170) that a given aromatic compound, ArX, gives identical proportions of the three isomers, *r*-C<sub>6</sub>H<sub>5</sub>C<sub>6</sub>H<sub>4</sub>X, when it reacts with radicals derived from any of the four main sources. Thus, since the H and P reactions are homolytic, the G reactions must also be so. These isomer percentages are given in table 2.

The values (table 2) indicate that for all these reactions it is the aryl radical itself, usually C<sub>6</sub>H<sub>5</sub>, and no other entity, such as ArN<sub>2</sub>• or Ar'COO• for the G and P reactions, respectively, which effects the substitution, for this is the only intermediate which is common to all the reactions employed.

For the restricted field of discussion (aryl radicals with aromatic solvents) the evidence is in favor of homolytic reaction in all the D, G, H, and P reactions. The substitution is effected by the aryl radical with expulsion of a hydrogen atom (equation 14).

Returning to the historical development of free-radical substitution, it was stated above (Section II) that Hey and Waters (140, 159, 174) in 1934-37 had indicated that the apparently anomalous products isolated from these reactions could be explained by the existence of free radicals of the type of free phenyl. Before 1951, many reactions of this kind were carried out and it was believed that the general tendency was for the group X, whatever its directing effect in heterolytic substitution, to direct a homolytic reagent primarily to the para position. The meta position was least favored and the corresponding product rarely observed. These conclusions were based on a considerable volume of experimental evidence, which is summarized in table 3. They are, however, now known to be largely incorrect. This situation has arisen (286) as a result of several factors:

- (i) It should be appreciated that many free-radical processes go to make up the overall homolytic reaction (Sections I and II). Since each inde-

TABLE 2\*  
*Ratios of isomers for arylation with various radical sources (cf. table 15)*

Solvent ArX	Radical Source	Reaction	Isomer Percentages			References
			Ortho	Meta	Para	
C <sub>6</sub> H <sub>5</sub> Cl	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> , (C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub>	G, P†	62.2 ± 2	24.0 ± 2	13.8 ± 2	(5, 161)
C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> , (C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub>	G, P†	58 ± 4	10 ± 2	32 ± 4	(161, 164)
	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> , (C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub>	G, H, P†	60-70	0-10	30-40	(97)
	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> , ( <i>p</i> -BrC <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub>	D, G, H, P		12.1		(164)
	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> , ( <i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub>	D, G, H, P		8.6		(164)

\* See Section VI,B for relevant discussion.

† Spectroscopic values.

TABLE 3  
Isomers obtained in preparative arylation reactions

Reagent (Ar'• Producer)	Solvent ArX	Substitution	Reaction	References
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i>	G	(133)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i>	D	(181)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> > <i>o</i>	G, H	(141)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> , <i>o</i>	D	(111)
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> , <i>o</i>	G	(140)
<i>r</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i>	G	(181)
3-BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i>	G	(52)
4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> < <i>o</i>	H	(116)
β-Naphthylamine.....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> > <i>o</i> and <i>p</i> < <i>o</i>	G, H	(110, 162)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	<i>p</i> > <i>o</i>	P	(159)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> Cl	Mixture	G, H	(141)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> Br	<i>p</i> , <i>o</i>	G	(133)
Methyl 4-aminophthalate.....	C <sub>6</sub> H <sub>5</sub> Cl	<i>p</i> , <i>o</i>	G	(46)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> Cl	<i>p</i>	P	(159)
4-CH <sub>3</sub> OOCCH <sub>2</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> Cl, C <sub>6</sub> H <sub>5</sub> Br	<i>p</i> , <i>o</i>	G	(157)
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> Cl, C <sub>6</sub> H <sub>5</sub> Br	<i>p</i> , <i>o</i>	G	(116, 134)
Methyl anthranilate.....	C <sub>6</sub> H <sub>5</sub> Cl, C <sub>6</sub> H <sub>5</sub> Br	<i>p</i> , <i>o</i>	G	(157)
4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> Cl, C <sub>6</sub> H <sub>5</sub> Br	<i>p</i> > <i>o</i> > <i>m</i>	H	(116)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> , <i>p</i>	D	(233)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> , <i>p</i>	D	(296)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G, H	(9, 10, 133, 140)
4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G, H, D	(9, 10, 117, 202, 207-209)
4-ClC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(157)
2-BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(116)
4-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(134)
4-BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(134)
4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>o</i> > <i>p</i> > <i>m</i>	H	(117)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	<i>p</i>	P	(108, 212)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	<i>m</i> -C <sub>6</sub> H <sub>4</sub> (CH <sub>3</sub> ) <sub>2</sub>	( <i>o</i> , <i>p</i> )*	G, H	(141)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	<i>s</i> -C <sub>6</sub> H <sub>3</sub> (CH <sub>3</sub> ) <sub>3</sub>		G, H	(141, 158)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(108)
4-BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> > <i>p</i>	G	(149)
4-IC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> , <i>p</i>	G	(149)
3-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> > <i>p</i>	G, H, D	(108)
Methyl 4-aminophthalate.....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> , <i>p</i>	G	(46)
4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> OCH <sub>3</sub>	<i>o</i> , <i>p</i>	H	(117)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> COOCH <sub>3</sub>	<i>p</i>	G	(133)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> COOC <sub>2</sub> H <sub>5</sub>	<i>p</i> , <i>o</i> , <i>m</i>	G	(141, 159)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> COOC <sub>2</sub> H <sub>5</sub>	<i>p</i> , <i>m</i>	P	(159)
(3-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> COOH	<i>p</i> , <i>m</i>	P	(173)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CHO	<i>p</i>	H	(141)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> CN	<i>p</i>	G	(133)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	2-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	<i>p</i> to NO <sub>2</sub>	G, H	(141)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	D	(233)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α > β > γ	G, H	(111, 151, 152)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	D	(293-297)
<i>r</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α > β > γ	G, D	(111, 178)
4-ClC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	G	(45)
{ 4-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	G	(156)
{ 3-NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> C <sub>6</sub> H <sub>5</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	G	(156)
β-Naphthylamine.....	C <sub>6</sub> H <sub>5</sub> N	α, β, γ	D	(111)
4-Aminophthalimide.....	C <sub>6</sub> H <sub>5</sub> N	α, β, γ	D	(111)
4-C <sub>2</sub> H <sub>5</sub> OC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	G	(45)
4-HOOCCH <sub>2</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	G	(45)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	P	(114)
(C <sub>6</sub> H <sub>5</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α > β, γ	P	(173, 237)
( <i>r</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	No reaction	P	(173; cf. 63)
(4-ClC <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	P	(173)
(4-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	α, γ	P	(173)

TABLE 3—*Concluded*

Reagent (Ar'• Producer)	Solvent ArX	Substitution	Reaction	Reference
(2-C <sub>10</sub> H <sub>7</sub> COO) <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> N	$\alpha, \beta, \gamma$	P	(173)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OH	$p > o$	G	(64, 178)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> OH	$p$	G	(56, 57)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	2-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> OH	$p$ to OH	G	(56, 57)
Anthranilic acid.....	C <sub>6</sub> H <sub>5</sub> OH	$o > p$	G	(135)
{ 4-Chloroanthranilic acid.....	C <sub>6</sub> H <sub>5</sub> OH	$o$	D	(193)
{ 6-.....				
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub>	$p, o$	G	(179)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>10</sub> H <sub>8</sub>	1 > 2	H	(192)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>10</sub> H <sub>8</sub>	1 > 2	G	(232, 284)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	2-CH <sub>2</sub> C <sub>10</sub> H <sub>7</sub>	1	H	(192)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	2,6-(CH <sub>3</sub> ) <sub>2</sub> C <sub>10</sub> H <sub>8</sub>	1	H	(192)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	2-C <sub>2</sub> H <sub>5</sub> OC <sub>10</sub> H <sub>7</sub>	1 > 3 > 6	H	(192)
Methyl anthranilate.....	2-CH <sub>3</sub> OC <sub>10</sub> H <sub>7</sub>	1	D	(111)
Methyl anthranilate.....	C <sub>10</sub> H <sub>8</sub>	1	G	(142)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub>	$p$	D	(232)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub>	$p$	G	(142)
4-O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub> .....	C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub>	$p$	G	(142)
4-Anisidine.....	C <sub>6</sub> H <sub>5</sub> COC <sub>6</sub> H <sub>5</sub>	$p$	G	(142)

\* Letters  $o, p$  in parentheses indicate substitution ortho to one group in the solvent and para to the other.

pendent reaction has some probability of occurrence, the final product is often complex and intractable. Highly substituted compounds such as quaterphenyl (1, 5, 122, 125, 174) are sometimes present and tars are usually formed. Since these tars and resins have often been ignored, the isolated yield, represented by the biphenyl fraction, has been low and subject to uncertainty (*cf.* Dermer and Edmison (92, table 2)).

- (ii) In the prepared biphenyl fraction, the para isomer, being the most symmetrical, is usually the least soluble and most easily crystallized and is, therefore, the isomer most readily identified. This gave rise to the concept of para reaction, noted above. As pointed out by Hey (160) in 1948, the predominance of the ortho isomer in reactions with anisole is significant, and it may be seen from table 3 that this is also true of toluene (299).
- (iii) The reactions have most often been used (7) solely as a means of preparing the  $p$ -arylated compounds ArAr', and residues have been discarded without identification.

In table 3 the columns give, in order, the reactants, i.e., the producers of Ar'• radicals (in this column  $r$ -NO<sub>2</sub>C<sub>6</sub>H<sub>4</sub>NH<sub>2</sub>, for example, indicates that all three nitroanilines were used with similar results); the solvents ArH (usually C<sub>6</sub>H<sub>5</sub>X, where X is the directing group); the position of substitution relative to the directing group; the type or types of reaction; and the appropriate literature references. In designating the reaction the scheme above is used.

Where possible the isomer formed in greatest yield is indicated. This information should, however, be treated with caution for the reasons stated above.

Table 3 is not fully comprehensive. It does not include the work carried out



on furan, thiophene (133), or quinoline (173), which is small in quantity and not directly relevant. The results receive confirmation from other work: e.g., (1) the electrolysis of benzoic acid in pyridine (114) gives  $\alpha$ - and  $\gamma$ -phenylpyridines, and (2) the decomposition of diphenyliodonium hydroxide in pyridine (253) yields all three isomers. (See references 131, 164, 253, and 299; also Section VI,A.)

Consideration of table 3 confirms a mode of substitution different from the normal ionic one and suggests invariable ortho-para-directing effects for the group X. It is necessary to turn to the years since 1951 to see how these ideas have become modified.

#### IV. THEORETICAL ASPECTS OF AROMATIC SUBSTITUTION

##### A. INTRODUCTION

In order to orientate the theoretical aspects of free-radical substitution with those for ionic substitution it is necessary to present the development of the various treatments and the relationships between them.

Any reaction involving a given molecule can be described (41, 70, 130) by a reaction path ABC (figure 1), wherein an energy barrier, the height of which is equal to the energy of activation, has to be surmounted in the process of movement along the reaction coordinate towards the reaction product C. In order to predict the relative rates of reaction at two sites, it is necessary to possess a means of evaluating both the reaction paths ABC and A'B'C'. Owing to inherent difficulties of calculation, it is usually impossible to carry out these estimations

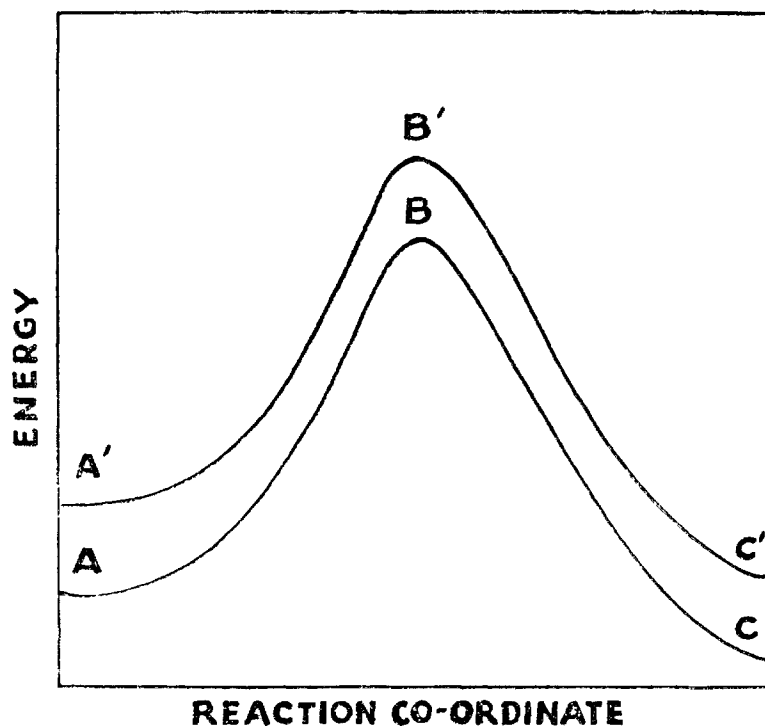


FIG. 1. Reaction paths for a given molecule

rigorously, and certain assumptions have to be made in order that some result may be obtained. In heterolytic reactions the electrically charged entities taking part in the reaction engage in strong long-range Coulombic interaction and here, therefore, the electrical charge distribution in the initial molecule (A, figure 1) plays the dominant role and decides the products of the reaction. It will be remembered that the early experimental data were concerned only with heterolytic substitutions (Section II), and thus the earlier theoretical treatments describe this form of reaction alone, i.e., they are concerned with a description of the charged ground state of the molecule. Unfortunately, the perturbations caused by approach of the electrically charged reagent to the molecule produce difficulties in mathematical description of the reaction and these early treatments were not able to progress far towards a truly quantitative understanding of aromatic substitution as it was then known.

In homolytic reactions, on the other hand, where the electrical perturbations are small, the order of reactivity of a number of given positions might be described by a sequence of "residual affinities." Any atom in a lower order of bonding would then, because of its "residual affinity," be more amenable to reaction than any other atom. This implies that the differences in energies between the initial molecules and certain ideal states determine the reaction products and that the order of relative rates is independent of the attacking reagent.

From the above it follows that a broad classification of the topic may be made and three groups of theories are distinguished:

- (i) Methods involving consideration of the electrical charge configurations of the isolated molecules A, referring qualitatively to heterolytic reactions.
- (ii) Methods based on the evaluation of the aforementioned "residual affinities" which are applicable, not only qualitatively but probably quantitatively, to homolytic reactions.
- (iii) Methods based on the possibility of calculating, for each type and position of reaction, the energy of activation or the height of the energy barrier (AB, figure 1) involving the corresponding activated complex. These results are applicable, in a quantitative sense, to both homolytic and heterolytic substitution.

It is customary to consider (i) and (ii) together, as the "isolated molecule" (I.M.) method of approach, and (iii) separately as the transition state (T.S.) method (41, 54, 70, 73, 74, 76, 100-105, 136, 137). Thus, the first treatment considers the reaction path in the neighborhood of A (figure 1) and involves the assumptions that the outcome of the reaction is decided by the molecule itself and that the relative positions of A and A' decide the relative rate of reaction between the two positions considered. The second method, on the other hand, is concerned with the relative heights AB, A'B' of the corresponding reaction paths.

## B. GENERAL ASSUMPTIONS OF THE ISOLATED MOLECULE (I.M.) AND TRANSITION STATE (T.S.) METHODS

The general methods, assumptions, and equations used in the I.M. and T.S. treatments and in the interpretation of experimental results must now be considered.

1. Since the mobile  $p$ - $\pi$  electrons in aromatic systems are more easily polarized, and are also delocalized over a much larger area than the  $\sigma$ -bond electrons, the contribution of the latter to the variable part of the activation energy may be ignored. Thus, each theory operates on the  $p$ - $\pi$  electrons alone and the  $\sigma$ -bond effects are assumed negligible.

2. At the present stage, the complicating effects of steric hindrance are assumed absent. These effects can only be explained qualitatively in systems of this complexity and must be left untreated in any current mathematical appreciation. Likewise, experimental data which are free of the uncertainty arising from steric effects must be used in testing the theoretical work.

3. For any reaction, the theory of absolute reaction rates (130), in considering the reaction path of figure 1, indicates that the rate of reaction is

$$k \propto e^{\Delta S^\ddagger/R} \cdot e^{-\Delta H^\ddagger/RT} \quad (26)$$

If the entropy of reaction  $\Delta S^\ddagger$  is incorporated into the frequency factor  $P$ , and if  $\Delta H^\ddagger$ , the heat of activation, is replaced by the energy of activation  $\Delta U$  (AB, figure 1), the equation degenerates (70) to that of Arrhenius:

$$k = P e^{-\Delta U/RT} \quad (27)$$

The reasonable assumption is now made that in a series of similar reactions, employing similar molecules in reaction with a stated reagent, the entropy term  $\Delta S^\ddagger$  and/or the frequency factor  $P$  remains constant. This has been observed to be true in many instances (27, 34-40, 200, 201, 246). Thus, the application of equation 27, with the replacement of the term  $\Delta U$  by an energy difference evaluated by any of the theories, should allow the corresponding value of  $k$  to be obtained.

4. If  ${}^H k$  and  ${}^X k_r$  represent actual rates of reaction for any position in benzene and the position  $r$  in  $C_6H_5X$ , respectively, then two equations similar to equation 27 give the partial relative rate factor  $\frac{{}^X k_r}{{}^H k}$  as

$$\frac{{}^X k_r}{{}^H k} = \frac{{}^X k_r / P}{{}^H k / P} = \exp\left(\frac{\Delta^H U - \Delta^X U_r}{RT}\right) \quad (28)$$

where the terms  $\Delta^H U$  and  $\Delta^X U_r$  are the energy differences calculated for the reaction using  $C_6H_6$  and the  $r^{\text{th}}$  position of  $C_6H_5X$ , respectively.

5. Consider predictions made by the I.M. and T.S. methods for heterolytic substitution. The former treatment assumes that the course of the relative reaction for two different sites or compounds may be predicted from a knowledge of the distribution of the ground state charges alone. The T.S. method, which

involves evaluation of the corresponding energies of activation (figure 1), might predict a reverse order of reactivity if the reaction paths for the different sites or compounds crossed. A review which includes a discussion on the effects of such crossing has recently been published (41). The following generalizations may be made:

- (i) The possibility of crossing is greatest for the ionic reactions where time-variable perturbation effects, dependent on the Coulombic interaction between the reagents, are present. Qualitative considerations are introduced into the theories to allow for this (Section IV,C,1).
- (ii) Reliance may be placed on the prediction for heterolytic substitution if the results of both I.M. and T.S. methods agree.
- (iii) Homolytic substitution is decided by energy-difference relationships (Section IV,A), and therefore the predictions of the I.M. and T.S. methods might be expected to be in agreement and to have more significance than those for heterolytic reactions. Such an agreement will become apparent at a later stage (Section IV,C,5; Section IV,D,2).

6. Partial and total rate factors relative to benzene are obtained as follows (21): If the absolute reaction rates are considered, then for substitution of  $C_6H_5X$ , where there are two ortho positions, two meta positions, and one para position available for reaction, the total absolute rate is given by:

$${}^xK = 2{}^xk_o + 2{}^xk_m + {}^xk_p \quad (29)$$

For benzene, with six equivalent positions, the corresponding rate is

$${}^H K = 6{}^H k \quad (30)$$

By measuring relative total rate ratios, an arbitrary value may be assigned to one compound so that numerical significance may be given to the other terms. Benzene is taken as the reference molecule and the total rate of substitution in benzene (equation 30) is taken to be equal to six, whereby  ${}^H k$  is unity. From equations 29 and 30 we then have:

$$6{}^x_H K = 2{}^x_H k_o + 2{}^x_H k_m + {}^x_H k_p \quad (31)$$

The value of  ${}^x_H K$  can be measured experimentally by the competitive method, using mixtures of  $C_6H_5X$  and  $C_6H_6$ .

The partial relative rate factors  ${}^x_H k_r$  are obtained if the proportions in which the isomers are formed are measured; thus, if the ortho isomer forms the fraction ( $o$ ) of the product mixture, then:

$$\text{i.e.,} \quad \left. \begin{aligned} (o) &= \frac{2{}^x_H k_o}{2{}^x_H k_o + 2{}^x_H k_m + {}^x_H k_p} \\ {}^x_H k_o &= 3{}^x_H K(o) \end{aligned} \right\} \quad (32)$$

Similar equations can clearly be derived for the meta and para cases, due allowance being made for the statistical number of these positions available for re-

action. The process is likewise extended to the treatment of molecules like biphenyl, naphthalene, etc.

Several very important points arise from these considerations:

- (i) The rate ratio  $\frac{X}{H}K$  may be obtained (1) indirectly by experiments using a third substance, e.g.,  $C_6H_5Y$ , since

$$\frac{X}{H}K = \frac{Y}{H}K \cdot \frac{X}{Y}K \quad (33)$$

Thus, once the value of  $\frac{Y}{H}K$  is established, the molecule  $C_6H_5Y$  can be used as the experimental reference compound and competitive work may be carried out by using mixtures of  $C_6H_5X$  and  $C_6H_5Y$  rather than mixtures of  $C_6H_6$  and  $C_6H_5X$ . This may be desirable on account of a possible simplification of the experimental procedure. Moreover, by comparing the directly determined value of  $\frac{X}{H}K$  with that obtained by the use of equation 33, a check on the experimental accuracy may be obtained.

- (ii) If, from calculations based on any theory, the total reaction rate is desired, then equation 31 must be employed, i.e., the individual partial rate factors  $\frac{X}{H}k_r$  are obtained, perhaps by equation 28, and are summed by the use of equation 31. This follows from the Arrhenius equation (equation 27), which shows that addition of energy terms, appearing as indices in the exponential, leads to multiplication rather than addition of the rate constants. Thus, for example, it is not allowable (176) to employ the summation of the free valence numbers for the various positions in a molecule in order to assess the total reactivity of the molecule [see Sections IV,C,5,(iii) and V,B,6]. This comment applies rigorously to all cases, even those where one or two positions have very largely enhanced reactivities, e.g., in the polynuclear hydrocarbons (205, 206).

7. If *p*-diX-substituted, or *s*-triX-substituted benzene is considered (5), then, for both instances, all the nuclear positions available for substitution are equivalent, e.g., for *p*-diX-substituted benzene, any position is ortho to one X and meta to the other X group; hence,

$$6 \frac{p-X_2}{H}K = 4 \frac{p-X_2}{H}k_{o,m} \quad (34)$$

where the subscript *o,m* indicates that the relative rate for this individual position has some dependence on the positions of the two directing X groups.

It has been shown for heterolytic substitution and for some homolytic reactions (21, 27, 200, 201, 246) that the effect of the substituent is concerned mainly with the energy of activation for reaction at any position in the nucleus, i.e., it may be assumed that the frequency factor, *P* in equation 27, will remain sensibly constant in the competitive reaction involving either  $C_6H_5X$  or *p*-diX-benzene. This was seen to be a requirement for the validity of the competitive method (see Sections IV,B,3 and IV,B,4).

The experimental evidence shows that the energy of activation at an available

position is formed by addition of the corresponding energies of activation contributed by all the directing groups. If this is true of homolytic substitution reactions, then noting from (ii) above that addition of activation energies implies multiplication of rate constants, the partial rate factor  $\overset{\text{X}}{\text{H}}k_{o,m}$  from equation 34 is given by the product of  $\overset{\text{X}}{\text{H}}k_o$  and  $\overset{\text{X}}{\text{H}}k_m$ , where each of these latter factors corresponds to the effect produced at the attacked position  $r$  by one of the X groups, either ortho or meta to  $r$ . Hence,

$$\overset{\text{X}}{\text{H}}k_{o,m} = \overset{\text{X}}{\text{H}}k_o \cdot \overset{\text{X}}{\text{H}}k_m \quad (35)$$

and

$$6^{p-\text{X}_2}K = 4\overset{\text{X}}{\text{H}}k_o \cdot \overset{\text{X}}{\text{H}}k_m \quad (36)$$

Similar considerations are valid for  $s$ -triX-benzene, where each nuclear position is ortho to two X groups and para to the third, i.e.,

$$6^{s-\text{X}_3}K = 3(\overset{\text{X}}{\text{H}}k_o)^2 \overset{\text{X}}{\text{H}}k_p \quad (37)$$

From the experimental values of  $\overset{\text{X}}{\text{H}}K$ ,  ${}^{p-\text{X}_2}K$ ,  ${}^{s-\text{X}_3}K$ , the three unknowns  $\overset{\text{X}}{\text{H}}k_o$ ,  $\overset{\text{X}}{\text{H}}k_m$ , and  $\overset{\text{X}}{\text{H}}k_p$  may be obtained by solution of a cubic equation derived from equations 31, 36, and 37. If these values agree with those obtained using the data of the isomer proportions and  $\overset{\text{X}}{\text{H}}K$  (equation 32), then the postulate of the additivity of activation energies will be verified. It is to be noted that this method assumes the absence of steric hindrance (see Section IV,B,2).

8. The effect of temperature upon the relative rates and isomer proportions may be evaluated by consideration of equations 27, 28, 31, and 32. It is clear that the effect can be observed directly only via the partial rate factors  $\overset{\text{X}}{\text{H}}k_r$ , and not through the total rate values  $\overset{\text{X}}{\text{H}}K$ . The effect on the latter can be found, however, by finding the changes in the  $\overset{\text{X}}{\text{H}}k_r$  values and employing equation 31. Using the Arrhenius equation, equations 27 and 28, and the temperatures  $T_1$  and  $T_2$ , we have:

$$(\overset{\text{X}}{\text{H}}k_{r,T_2}) = (\overset{\text{X}}{\text{H}}k_{r,T_1})^{T_1/T_2} \quad (38)$$

Further, by inclusion of equation 32 and putting  $T_1/T_2 = \eta$ , the relationships between the isomer proportions are given by equations of the form:

$$(o)_{T_2} = \left[ \frac{2\left(\frac{o}{2}\right)^\eta}{2\left(\frac{o}{2}\right)^\eta + 2\left(\frac{m}{2}\right)^\eta + (p)^\eta} \right]_{T_1} \quad (39)$$

By these and similar relationships, the partial rate factors, isomer proportions, and total rate factors may be obtained at any temperature. The inherent assumption that has been made is that the  $P$ -factor remains constant (see Section IV,B,3).

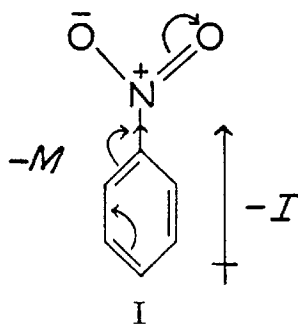
### C. ISOLATED MOLECULE (I.M.) APPROACH

Each of the following theories represents an attempt to describe substitution phenomena. In each case, the possibility of application to homolytic substitution

is discussed. It will be seen that the first three methods described are applicable mainly to heterolytic substitution, while the last two have been developed specifically for the free-radical reactions.

### 1. Ideas of the English School

The electronic interpretation by the English School (8, 21, 194, 196–198, 246) of the “normal laws” of substitution (see Section II) is as follows: In general, according to the classification of group X, the group is assigned a  $\pm I$  (inductive) and a  $\pm M$  (mesomeric) effect. Thus, the  $\text{NO}_2$  group is said to exert the effects  $-I$ , i.e., withdrawal of electrons from the ring by a mechanism analogous to electrostatic induction, and  $-M$ , i.e., withdrawal of electrons by the tautomeric mechanism. Both mechanisms affect the ortho and para positions to a greater extent than the meta position and, in this sense, the tautomeric mechanism is considerably the more selective. The result, in nitrobenzene (I), for example,



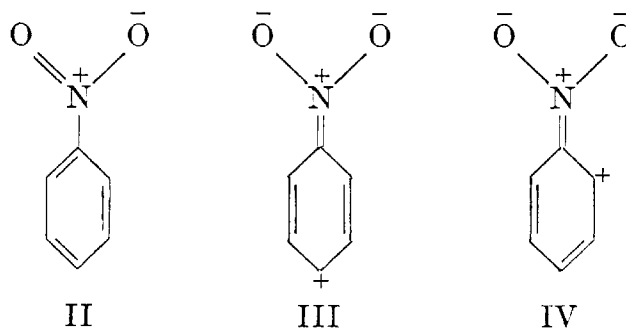
is such that an electrophilic reagent (e.g.,  $\text{NO}_2^+$ ) finds difficulty in attacking the ortho and para sites, and so the  $\text{NO}_2$  group is said to be deactivating and meta directing.

In some cases the approach of the reagent causes electrical perturbation of the molecule with consequent modification of the expected results. Time-variable effects—namely, the  $\pm I_d$  (inductomeric or dynamic inductive) and  $\pm E$  (electromeric) effects—were therefore postulated to allow for this. These effects are called into play only on the demand of the approaching reagent, and thus they can only aid reaction and never inhibit it.

These descriptions are essentially qualitative and unable to explain free-radical substitution effects (Section II).

### 2. Resonance theory

Directing effects observed in ionic substitution are explained by the charge distribution existing in a hybrid molecule constructed by the summation of contributions from a number of separate canonical forms, which can be represented by classical valence-bond formulae (239, 291). Thus, for example, for nitrobenzene the following structures (II, III, and IV) are among those which contribute to the hybrid structure.



The structures indicate that electrophilic substitution (for example, by  $\text{NO}_2^+$ ) will be rendered more difficult compared with benzene, and the substituent will be directed to the meta position.

The theory is capable of mathematical treatment (48, 54, 88) by the valence-bond method but has served mainly as a means of semiquantitative description of heterolytic reactions. In the form presented, the method is inapplicable to free-radical substitution, but with certain modifications (Sections IV,C,4 and IV,D,1) can attempt such description.

### 3. Molecular orbital (M.O.): the polarized state

This treatment, which was developed in an attempt to explain the facts of heterolytic substitution, departs somewhat from the strict I.M. procedure, since points slightly displaced from A (figure 1) are considered (41, 70, 73, 74, 130, 292). If an ion, e.g.,  $\text{NO}_2^+$ , approaches a molecule at position  $r$ , electrons will tend to congregate at this site. This results in a decrease in the electronegativity of  $r$  and a change in the Coulomb integral of the carbon atom occupying position  $r$  from  $\alpha_r$  to  $(\alpha_r + \delta\alpha_r)$ , where  $\delta\alpha_r$  is negative. The resulting change,  $\delta U$ , in the energy of the system is given by a Taylor series of the form:

$$\left. \begin{aligned} \delta U &= \frac{(\partial U)}{(\partial \alpha_r)} \cdot \delta \alpha_r + \frac{1}{2} \frac{(\partial^2 U)}{(\partial \alpha_r^2)} \cdot \delta \alpha_r^2 + \\ &= q_r \cdot \delta \alpha_r + \frac{1}{2} \pi_{r,r} (\delta \alpha_r)^2 + \end{aligned} \right\} \quad (40)$$

where the quantity  $q_r$  is termed the  $\pi$ -electron charge density and  $\pi_{r,r}$  the self-polarizability of the  $r^{\text{th}}$  carbon atom. It is to be noted that this assumes that long-range Coulombic forces are dominant and exchange forces are not present. If these latter forces were engaged, then equation 40 should contain terms like  $\partial U / \partial \beta_{r,s}$  to allow for effects brought about by changes in the bonding of the  $r^{\text{th}}$  carbon atom.

The first term in equation 40 is the most important and, since  $\delta\alpha_r$  is negative, the most reactive position for heterolytic substitution is that where  $q_r$  is largest, i.e., that of the greatest electronic charge. This is in accord with the above treatments, in all of which the charge distribution in the ground state determines the products.

If all the  $q_r$ 's are identical (e.g., in unsubstituted hydrocarbons like naphthalene), the difference in reactivity is given by the second term involving  $(\delta\alpha_r)^2$ .

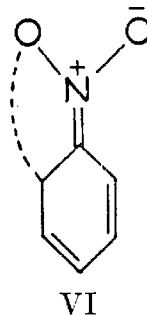
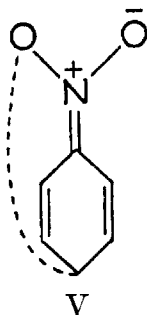


In this instance, the substitution depends only on the magnitude and not on the sign of  $\delta\alpha_r$ . Hence, both electrophilic and nucleophilic substitution will take place preferentially at the same site.

If all the quantities of equation 40 were known, including bonding terms, then some attempt might be made to obtain the corresponding partial rate factors by means of equation 28. The difficulties involved in carrying out such calculations are, however, prohibitive. The method is important in treating the electron configuration as a whole by mathematical argument, and the inherent inclusion of the polarizability effects is significant. The experimental facts can be explained in a qualitative sense but quantitative prediction cannot be made.

#### 4. Valence libre

This concept, which was developed by French theorists (48, 54, 85-88, 244, 245) from an idea of Svartholm (270), was an attempt to adapt the resonance theory (Section IV,C,2) to the treatment of homolytic substitution. Since canonical forms containing electrical charges in the nucleus are of no apparent importance in free-radical reactions, these structures, which occur in the normal resonance theory (formulas II, III, and IV), are replaced by structures bearing formal bonds (formulas V and VI). The "valence libre" of a given atom is then defined as the weighted sum of all structures in which the chosen atom is not joined by a double bond to one of its neighbors. Some possible structures for nitrobenzene are shown in formulas V and VI, wherein the ortho and para po-



sitions are the only ones for which formal-bond structures of this type can be written. Structures containing more than one such bond, when suitably weighted, are included in the treatment. The total weight of these structures for a given atom is then a measure of the residual affinity of the atom concerned. The weighting is carried out by using suitable experimental data referring to bond lengths (48, 245). The structures (V and VI) for nitrobenzene show that preferential ortho-para reaction should take place in homolytic substitution.

The treatment has been applied (245) to linear and condensed polynuclear hydrocarbons and appears satisfactory in explaining the reactivities of selected positions and the corresponding carcinogenic activity of such compounds. No calculations for the case of a monosubstituted benzene ( $C_6H_5X$ ) have been published except for an attempt to treat toluene (245). It is doubtful whether the method should be applied to heteromolecules (99). The treatment suffers from its rather pictorial approach (99, 232).

An interesting point, which does not appear to have been expressed, is that whatever the nature of the group X, provided there is some conjugation or hyperconjugation with the benzene ring, the ortho and para positions will always appear more reactive than the meta position in homolytic substitution, owing to the inclusion of structures of the type illustrated in formulas V and VI. Moreover, since these structures are additional to any containing formal bonds within the benzene ring itself (e.g., the Dewar structures), the treatment suggests that homolytic attack should be facilitated, relative to benzene, by the presence of the group X in the molecule  $C_6H_5X$ . If conjugation is small as, for example, in *tert*-butylbenzene, this activating effect should be of minor importance (see Section VII,A,4,(v)).

### 5. Free valence

The idea of free valence was introduced by Coulson (68, 69). Using the molecular orbital (M.O.) theory, the mobile bond order  $p_{rs}$  between the nuclear carbon atoms  $r$  and  $s$  is defined by

$$p_{rs} = \sum c_{rj}c_{sj} \quad (41)$$

where  $c_{rj}$  and  $c_{sj}$  are the coefficients of the molecular orbitals of the electrons in the bonds  $r-j$  and  $s-j$ . The total bonding  $N_r$  exhibited by the atom  $r$  is then

$$N_r = \sum p_{rs} + C_r \quad (42)$$

where  $C_r$  is the contribution from the  $\sigma$ -electrons. The free valence,  $F_r$ , of  $r$  is then given by

$$F_r = (N_{\max} - N_r) \quad (43)$$

where  $N_{\max}$  is the maximum bonding that a carbon atom of the type  $r$  can attain (76, 136, 137). The value of  $(N_{\max} - N_r)$  is a measure of the amount of additional bonding which this atom  $r$  could show and provides an index for homolytic reactivity.

Each reactivity is associated with the difference between a fixed bonding value, calculated for the initial molecule (A, figure 1), and that idealized maximum of which the carbon atom concerned is capable. This change  $F_r$  in bonding must be associated with a corresponding energy difference,  $({}^x E'_r - {}^x E')$ , where  ${}^x E'$  and  ${}^x E'_r$  are the  $\pi$ -electron energies of the corresponding initial and  $r$ -substituted molecules. This difference may be taken as determining  $\Delta^x U_r$  in equation 28. (It is the evaluation of this energy difference which suggests a parallelism with the method of Wheland (see Section IV,D), where the energy difference between the ground state and the transition complex is calculated.)

A qualitative relationship between  ${}^x F_r$  and  $\Delta^x U_r$  has been demonstrated by Burkitt, Coulson, and Longuet-Higgins (44: *cf.* 143). The contribution of atom  $r$  to the mobile electron energy of a system can be shown to be  $2\beta\sum p_{rs}$ . If, during the course of a reaction, it is assumed that this atom is removed from the area of delocalization, then the energy change will have this value  $2\beta\sum p_{rs}$ , provided there is no rearrangement of the rest of the molecule. (This system may be com-

pared with the activated complex of Wheland, where a covalent bond is assumed to be formed between the radical and the atom attacked.) Thus, taking  $\beta$  as positive:

$$\Delta^x U_r = ({}^x E'_r - {}^x E') = 2\beta \Sigma p_{rs} = 2\beta(N_r - C_r) \quad (44)$$

$$\begin{aligned} &= 2\beta[N_{\max} - C_r - {}^x F_r] \\ &= \text{constant} - 2\beta F_r \end{aligned} \quad (45)$$

This equation is a mathematical statement of the fact that the greater the free valence available the greater the reactivity, since the larger  ${}^x F_r$ , the smaller  $\Delta^x U_r$ , and, by equation 28, the more reactive the position.

The rest of the molecule cannot remain unaffected when atom  $r$  is removed from the delocalization area and all the other mobile bond orders  $p_{mn}$  must change. Relationship 45 will therefore be correct only if the sum of these changes is zero. Brown (41) uses a modified equation:

$$\Delta^x U_r = \text{const.} - 2x\beta {}^x F_r \quad (46)$$

where  $x\beta$  is a similar change in all the resonance integrals  $\beta_r$  between atom  $r$  and its neighbor  $s$ , and where  $0 \leq x \leq 1$ .

Using calculated bond orders in conjunction with equations 41-43, the partial rate factors may be evaluated by equation 28. Thus,

$$\frac{{}^x k_r}{{}^H k_r} = \exp 2(x)\beta \frac{({}^x F_r - {}^H F)}{RT} \quad (47)$$

Tables 4 and 5 present some of the data, together with the calculated values of  ${}^x F_r$ ,  $\frac{{}^x k_r}{{}^H k_r}$ , and  $\frac{{}^x K}{{}^H K}$  (see Section IV,B).

It is seen that:

- (i) The  $({}^x F_r - {}^H F)$  values are very small, causing the predicted rates to

TABLE 4  
Free valence numbers  ${}^x F_r$

Aromatic Compound	Nuclear Position†			References
	Ortho or $\alpha$	Meta or $\beta$	Para or $\gamma$	
C <sub>6</sub> H <sub>6</sub> .....	0.398	0.398	0.398	(73, 176, 254)
C <sub>6</sub> H <sub>5</sub> F .....	0.412	0.398	0.404	(254)
C <sub>6</sub> H <sub>5</sub> Cl .....	0.410	0.400	0.404	(254)
C <sub>6</sub> H <sub>5</sub> Br .....	0.413	0.400	0.404	(254)
C <sub>6</sub> H <sub>5</sub> I .....	0.432	0.397	0.412	(254)
C <sub>6</sub> H <sub>5</sub> OH .....	0.422	0.395	0.406	(254)
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	0.431	0.396	0.412	(254; cf. 74)
C <sub>6</sub> H <sub>5</sub> N .....	0.420	0.394	0.412	(254)
C <sub>6</sub> H <sub>5</sub> N* .....	0.495	0.390	0.454	(74, 76)
C <sub>10</sub> H <sub>8</sub> .....	0.448	0.400	—	(254)
C <sub>10</sub> H <sub>8</sub> .....	0.452	0.404	—	(44, 74, 76)
C <sub>2</sub> H <sub>3</sub> C <sub>6</sub> H <sub>5</sub> * .....	0.535	0.395	0.412	(44; cf. 256, 257)

\* See Section IV,C,5, (iv).

† These values are calculated using  $N_{\max} = 3 + \sqrt{3}$  (equation 43). Provided the same value for  $N_{\max}$  is used in all the calculations its actual value is unimportant, as the difference  $({}^x F_r - {}^H F)$  is used (equation 43) to calculate the relative rates given in table 5.

TABLE 5

*Homolytic relative rate constants calculated from free valence numbers, assuming  $x = 1$ ,  $T = 353^\circ K.$ ,  $\beta = 17$  kcal. (equations 44-47)*

Aromatic Compound	$\frac{x_k}{H^k_o}$ or $\frac{x_k}{H^k_\alpha}$	$\frac{x_k}{H^k_m}$ or $\frac{x_k}{H^k_\beta}$	$\frac{x_k}{H^k_p}$ or $\frac{x_k}{H^k_\gamma}$	$\frac{x_k}{H^k}$
C <sub>6</sub> H <sub>5</sub> F.....	1.97	1.00	1.34	1.21
C <sub>6</sub> H <sub>5</sub> Cl.....	1.79	1.10	1.34	1.19
C <sub>6</sub> H <sub>5</sub> Br.....	2.07	1.10	1.34	1.28
C <sub>6</sub> H <sub>5</sub> I.....	5.12	0.95	1.97	2.35
C <sub>6</sub> H <sub>5</sub> OH.....	3.20	0.91	1.97	1.70
C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub> .....	4.95	0.91	1.97	2.28
C <sub>6</sub> H <sub>5</sub> N.....	2.91	0.82	1.97	1.57
C <sub>6</sub> H <sub>5</sub> N*.....	110.25	0.02	15.11	39.28
C <sub>10</sub> H <sub>8</sub> .....	11.29	1.10	—	8.26
C <sub>10</sub> H <sub>8</sub> .....	13.71	1.34	—	10.03
C <sub>7</sub> H <sub>7</sub> C <sub>6</sub> H <sub>5</sub> *.....	804.95	0.86	1.97	538.53

\* See Section IV,C,5,(iv).

be highly subject to the accuracy of evaluation of the individual  $F_r$  values.

- (ii) The possible fluctuation of the value of  $x$  in equations 44-47 and, indeed, the questionable validity of these equations, implies that no great reliance should be placed in the  $\frac{x_k}{H^k}$  figures. Strictly, this also applies to any qualitative predictions based on  $^x F_r$  values for positions within a single molecule for unless, in every case, the rest of the molecule either remains unchanged or alters to the same degree (i.e.,  $x = 1$  or is constant) during the reaction, the  $^x F_r$  sequence cannot be assumed to indicate the order of reactivities. In the past these assumptions have been rather too readily accepted.
- (iii) The dangers inherent in taking the summations of the  $^x F_r$  values (176) for comparing reactivities of molecules [see Section IV,B,6,(ii)] are demonstrated for the halogens. Thus, addition of the  $^x F_r$  values leads to the incorrect order of "reactivities" I > Br > Cl > F when compared with the sequence given by  $\frac{x_k}{H^k}$  of table 5. These orders should be compared with those for heterolytic reactions (222).
- (iv) The values for pyridine, naphthalene, and biphenyl are important, as the corresponding calculations can be made with some accuracy. There is no heteroatom in naphthalene, and consequently no arbitrary parameter need be introduced when calculating  $^x F_r$ , or, alternatively, to calculate  $^x F_r$ . It is noticed in these cases that the ortho positions give rise to very high values. Experimentally, these may not be observed, owing to steric hindrance at ortho sites. The values marked with an asterisk in tables 4 and 5 seem out of harmony, perhaps owing to the neglect of overlap integrals, and are rejected.
- (v) In all the cases quoted in tables 4 and 5 it is seen that the ortho and para positions are activated to a greater degree than the meta position, which, having an  $\frac{x_k}{H^k_m} \sim 1.0$ , is little different from any one position in benzene. The effect is an alternation in reactivity round the ring from the group X. Approximate treatment (76, 136) has shown the

possible reason for this selected activation. A hydrocarbon molecule is considered, e.g., benzene, and the Coulomb term  $\alpha_s$  of one atom  $s$  is changed; [this may be considered as being effected by replacement of a =CH group by a hetero =N atom or by the influence of group X on  $s$ ]. Neglecting any changes in the values of the bond integrals, the change in the bonding  $N_r$  of atom  $r$  is given by

$$\frac{dN_r}{d\alpha_s} = \frac{\partial N_r}{\partial \alpha_s} \cdot d\alpha_s + \frac{1}{2} \frac{\partial^2 N_r}{\partial \alpha_s^2} (d\alpha_s)^2 + \quad (48)$$

The first, and any other odd term, can be shown to be zero, and thus:

$$\frac{dN_r}{d\alpha_s} \sim \frac{1}{2} \frac{\partial^2 N_r}{\partial \alpha_s^2} (d\alpha_s)^2 \quad (49)$$

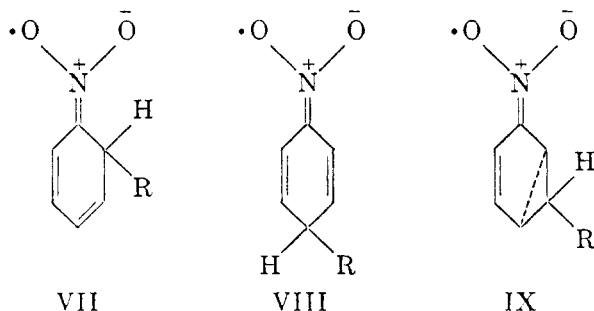
This implies that whatever the sign of  $d\alpha_s$ , the change in bonding of atom  $r$  will be determined by the sign of  $\partial^2 N_r / \partial \alpha_s^2$ . It was shown in addition that when  $r$  to  $s$  is odd,  $\partial^2 N_r / \partial \alpha_s^2$  is negative and ortho and para sites are activated, and when  $r$  to  $s$  is even,  $\partial^2 N_r / \partial \alpha_s^2$  is positive and meta sites are deactivated. The effects follow from the fact that a decrease in  $N_r$  causes an increase in  $F_r$  (equation 43) and hence an increase in the reactivity of atom  $r$ . The effect at the meta position is much dampened (76).

In view of the assumptions made, these results should be accepted with some reservation (75, 77), but they are nevertheless of considerable significance, as has recently been pointed out (136).

#### D. TRANSITION STATE (T.S.) APPROACH

##### 1. Resonance theory

In Section IV,C,2 an account has been given of how the resonance method is applied to heterolytic substitution, and how modification of the treatment enables the subject of homolytic reactions to be treated (Section IV,C,4). Wheland (290-291), breaking away from the then current treatment of the ground state alone, suggested that the reagent-molecule relationship should be studied. Thus, the ortho-para-directing effect of X in free-radical substitution was thought to be determined by the greater ease of formation of the *o*- and *p*-R-substituted  $C_6H_5X$  molecules, compared with that of the meta compound. The



meta complex (IX), containing a formal bond between the ortho and para positions, should possess greater energy than the corresponding ortho (VII) and para (VIII) structures.

This method again implies (see Section IV,C,4) attack in the ortho and para positions whatever the nature of the group X, provided some conjugation or hyperconjugation with the ring exists. This approach has been employed in a recent qualitative discussion (251).

### 2. Atom localization energy treatment

These considerations were also initiated by Wheland (290) and have been discussed and extended by many workers (34-41, 98, 99, 260, 286). The method is an attempt to calculate the height of the potential energy barrier which has to be surmounted in order that the reaction should take place (AB, figure 1) and is known as either the transition state or atom localization energy method. The possible relation between this method and the other treatments has been discussed (Sections IV,A, IV,B, and IV,C,5). It is not the charge distribution in the initial molecule or the difference between the ground state and an idealized state of bonding, but rather the difference between the ground state and the activated complex, which decides the products.

For electrophilic, radical, and nucleophilic substitution the assumption is made that the transition state is that in which 2, 1, or 0  $\pi$ -electrons, respectively, are completely localized at the point of attack  $r$  and are, therefore, effectively removed from conjugation. Figure 2 shows how the various quantities are derived for homolytic substitution of  $C_6H_5X$  by a radical  $R\cdot$  at the para position. Similar diagrams can be set up for substitution at any other position of  $C_6H_5X$ . The dot represents an odd electron and the area enclosed indicates the area over which the delocalization of the  $n$  or  $(n - 1)$  electrons takes place.

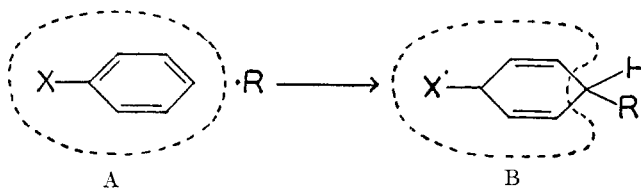


FIG. 2. Derivation of various quantities for homolytic substitution of  $C_6H_5X$  by a radical  $R\cdot$  at the para position. (A) Ground state; energy  ${}^x E$ . Delocalization over the whole molecule of its  $n$   $\pi$ -electrons. (B) Transition state for para substitution. Energy  ${}^x E_r$ . Restricted delocalization of the  $(n - 1)$  electrons.

The  $\pi$ -electron energy for each of these structures may be calculated by molecular orbital methods and the difference

$$({}^x E_r - {}^x E) = {}^x A_r = \Delta {}^x U_r \quad (50)$$

is taken to represent the variable portion of the heat of activation for the radical substitution (*cf.* Section IV,B). The atom localization energy  ${}^x A_r$  may be

TABLE 6  
*Electrophilic relative reaction rate calculated from atom localization energies*  
*(T = 291°K.)*

Aromatic Compound	$\frac{x}{H}k_o$ or $\frac{x}{H}k_\alpha$	$\frac{x}{H}k_m$ or $\frac{x}{H}k_\beta$	$\frac{x}{H}k_p$ or $\frac{x}{H}k_\gamma$	$\frac{x}{H}K$
C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> .....	0.088	0.821	0.454	0.38
C <sub>6</sub> H <sub>5</sub> Cl.....	1.068	0.059	0.268	0.42
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	42.43	13.87	34.83	24.57
C <sub>6</sub> H <sub>5</sub> OH.....	37 × 10 <sup>5</sup>	0.72	59 × 10 <sup>5</sup>	1.5 × 10 <sup>5</sup>
C <sub>6</sub> H <sub>5</sub> N.....	0.040	0.029	0.021	0.03
C <sub>10</sub> H <sub>8</sub> .....	99.2 × 10 <sup>4</sup>	37.2	—	4.46 × 10 <sup>5</sup>

identified with  $\Delta^x U_r$  (Section IV,B) and compared with the energy difference determined by the  $x F_r$  values (Section IV,C,5, equation 44).

The method is as easily applied to heterolytic substitution, and table 6 presents the relative rate values, calculated from the published  $x E_r$  data for electrophilic substitution (290). In the calculations the bond integral was taken to be equal to  $-38$  kcal., and the following parameters were used:  $\epsilon_1$  was included for C<sub>6</sub>H<sub>5</sub>Cl;  $\delta_1 = 0.2$ ,  $\delta_2 = 0.1$  for C<sub>6</sub>H<sub>5</sub>N, and  $\delta_\alpha = -0.1$  for C<sub>6</sub>H<sub>5</sub>CH<sub>3</sub>.

The figures in table 6 should be compared with the experimental ones of table 1, when the correspondence is seen to be rather poor. This lack of quantitative agreement was fully appreciated by Wheland. The high rate for phenol, or aniline, is predicted, but the very low values for other compounds, e.g., nitrobenzene, are not. Electrical perturbation, caused by the approach of the NO<sub>2</sub><sup>+</sup> ion, cannot account for this because this time-variable effect can only facilitate reaction (*cf.* Section IV,C,1), i.e., tend to increase the predicted figures.

For homolytic reaction, similar calculations have been made and the results are given in table 7.

Similar difficulties arise in these calculations to those already discussed (Section IV,C,5) in connection with the evaluation of free-valence numbers; e.g., the rate figures are again determined by small energy differences. The general prediction is again of slight activation with ortho-para direction. The figures for naphthalene, obtained without the use of any parameter, are very high (*cf.* table 5).

TABLE 7  
*Homolytic relative reaction rate calculated from atom localization energies*  
*(T = 353°K.)*

Aromatic Compound	$\frac{x}{H}k_o$ or $\frac{x}{H}k_\alpha$	$\frac{x}{H}k_m$ or $\frac{x}{H}k_\beta$	$\frac{x}{H}k_p$ or $\frac{x}{H}k_\gamma$	$\frac{x}{H}K$
C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> .....	2.25	0.85	8.74	2.49
C <sub>6</sub> H <sub>5</sub> Cl.....	5.81	1.42	1.92	2.73
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	2.51	0.86	2.14	1.48
C <sub>6</sub> H <sub>5</sub> OH.....	32.10	0.76	5.98	11.95
C <sub>6</sub> H <sub>5</sub> N.....	2.33	1.95	1.49	1.68
C <sub>10</sub> H <sub>8</sub> .....	87.79 × 10 <sup>3</sup>	19.71	—	4.39 × 10 <sup>4</sup>

## E. GENERAL DISCUSSION

The above survey is not complete; for example, it does not include suggestions, frequently made (160, 285-287), that all free radicals are electrophilic. Other treatments are the electron spin or "residual valency" concept of Moffitt (234), which is related to the ideas of free valence and valence libre, and the "frontier electron" method of Fukui (118, 119, 138), which attempts to treat all forms of substitution by consideration of the densities of the frontier electrons present in the isolated molecule.

Reference to the above sections shows that the methods which are capable of a more than qualitative picture are based on the molecular orbital (M.O.) treatment. Although there is abundant evidence that these M.O. approximations (for the M.O. method is inherently an approximation) are consistent when applied to cyclic alternant hydrocarbon systems, it cannot be assumed that the same result will be obtained when they are applied to ionized systems, free radicals, or heteromolecules (41, 72).

Of the treatments available, the one most likely to be a reliable guide is Wheland's atom localization theory. Dewar (98, 100-105) believes this method to be the only valid one. The assumptions made about the transition state are reasonable, and the results, for any of the three forms of substitution, may be expressed directly in terms of an observable quantity: namely, the energy of activation. The method has been used very successfully by Brown (34-40) in attempts to predict the results of Diels-Alder and similar reactions.

Unfortunately, whenever heteromolecules are treated, whatever the theory employed (48, 290), certain parameters must be introduced into the mathematics. The choice of values for these is somewhat arbitrary, though in some cases rough figures are available (48), and in others attempts have been made to obtain the relevant experimental data (216-221). Since the number of parameters is usually three, then by suitable choice of values, the two types of substitution, heterolytic and homolytic, may be qualitatively described. For quantitative prediction, accurate values for the parameters are essential and the importance of possessing such data cannot be overemphasized. It is to be noted that the parameters used in the calculations for chlorobenzene (290) (table 6) had to be very carefully chosen in order to explain the ortho-para-directing, but deactivating, effect of the chlorine atom in electrophilic substitution (*cf.* table 1). The case of naphthalene is very important, for the predictions of the two methods (tables 5 and 7), each based on calculations which do not involve the use of arbitrary parameters, do not agree. Thus, free valence predicts a much lower reactivity than the method of Wheland. The reason for this may be that the partial fixation of the bonds in naphthalene (246, 259) was neglected, and all the carbon atoms were treated as if they were identical. Alternatively, it may be argued that the high reactivity predicted by the atom localization energy treatment is due to a gross exaggeration by this method of the degree of localization which takes place in the transition state and that a factor should be introduced to allow for this somewhat restricted localization. It is difficult to see, however, why this should affect only calculations on condensed nuclear systems.



The anticipated agreement among some of the theories has been demonstrated in a qualitative sense, although this correspondence does not prove any one of the theories correct. For all the cases considered, small energy differences are involved. Any small errors in the corresponding calculations, caused by neglect of overlap integrals, incorrect parameter values, etc., will be magnified in the evaluation of the reaction rate through the application of the exponential formula (equation 28). The employment of energy differences, however, has some recommendation, for consistent errors are eliminated when the differences are considered.

In all the treatments, particularly for homolytic reactions, the predictions have been made regardless of any other form of possible reaction. For example, the free-radical attack on a molecule could give rise to a heavily stabilized solvent radical, and nuclear substitution would then not take place at all. The figures obtained indicate the nuclear reactivities only and, although perfectly legitimate, are not to be assumed to indicate that the corresponding type of substitution will necessarily be observed.

It must also be pointed out that in none of the methods described above is any account taken of the influence of the reagent on the course of substitution reaction. Thus, for example, identical relative rates are predicted (table 6) for nitration, or chlorination, or, indeed, for any electrophilic substitution of a given compound. However, wide differences exist between the experimentally determined values of these rates (Section II). Since relative rates are under consideration, these differences cannot be due to variation in the  $P$ -factor (equation 27). This implies that the energies of activation for attack, at the same position  $r$  in  $C_6H_5X$ , by the entities causing nitration and chlorination, respectively, must be different. In the field of homolytic substitution, too, the relative rates and ratios of isomers have been found (51, 79, 146) to be dependent on the nature of the radical effecting substitution. Thus the introduction of substituents of an electron-attracting character into the para position of the phenyl radical results in the assumption by the radical of a measure of electrophilic character, while an electron-repelling substituent has the opposite effect of conferring upon the radical the properties of a nucleophilic reagent (*cf.* tables 12 and 13 in Section V,E and Section VI,A).

It is perhaps unfortunate that in testing quantitative theories of aromatic substitution attention has been directed largely to heterolytic reactions, since the homolytic reactions, being free from strong "Coulombic" effects, are probably more amenable to quantitative treatment. For homolytic substitution it is seen that all the treatments are in agreement in predicting that substitution by a neutral free radical into the nucleus of  $C_6H_5X$  (where there is no restriction on the group  $X$  within the previous relevant discussion) will be somewhat faster than the corresponding substitution in benzene, and that the activation is greatest in the ortho and para positions. In the following sections the recent experimental data are discussed in the light of these predictions, which could have been made largely before these data became available.

## V. COMPETITIVE REACTIONS

## A. THE COMPETITIVE METHOD

Relative rates of homolytic substitution are best determined by the competitive method, and a number of such determinations have been reported recently. The idea embodied in the use of the competitive technique (197) is to allow two molecular species to compete with each other for reaction with a grossly insufficient quantity of the reagent, and to determine the relative amounts of product formed from each compound. From this, the ratio of total reaction rates for the two compounds may be calculated (see Sections II and IV,B).

In order that the application and validity of the technique may be appreciated, it is necessary to consider the following points:

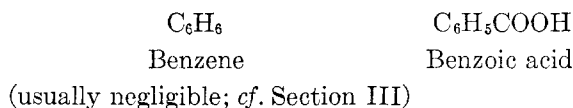
1. The foregoing evidence (Section III) shows that it may be assumed that in homolytic bimolecular aromatic substitution the substitution is effected by first-order attack of the phenyl radical upon the aromatic solvent molecule. The actual kinetics of this substitution step cannot be directly studied (5, 286), since in all the above D, G, H, and P reactions (Section III) this is not the observable rate-determining step. Thus, for example, in the H reaction the rate-determining stage is the intramolecular rearrangement (equation 11). The complicating circumstances of the production of the radical by preliminary change, either slow or reversible, or simultaneous interaction with other substances in mutually independent side reactions can be overcome by the competitive method. The essential requirement, which is satisfied, is that the attack of the active entity upon each of the two solvents should be of the same kinetic order (*cf.* Wegscheider's test for simultaneous reactions of the same order).

2. The reaction employed in the competitive experiments must be homogeneous, for otherwise physical or mechanical differentiation, e.g., the relative solubilities of the organic compounds in the phase where reaction takes place, may become important. This implies that the Gomberg reaction cannot be used and renders less reliable the only early experimental work available. This work is that of Hey (141), who found that nitrobenzene was approximately four times more reactive than toluene in phenylation.

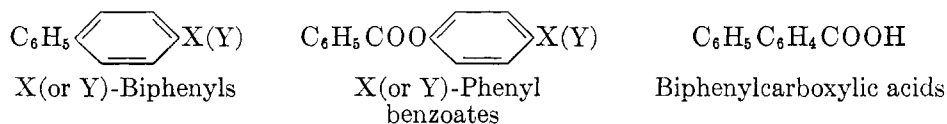
3. The decomposition of benzoyl peroxide (Section III,B) is the most useful reaction for competitive experiments, since the simple phenyl radical is ultimately produced, the reaction medium is homogeneous, the peroxide can be obtained in a good state of purity, and the reaction product is relatively clean. In the reaction mixture using the two solvents  $C_6H_5X$  and  $C_6H_5Y$ , the benzoyloxy, phenyl, and possibly solvent radicals can be expected to form some or all of the compounds shown in Chart I by successive substitution reactions:

*Chart I: Some possible products from competitive reaction*

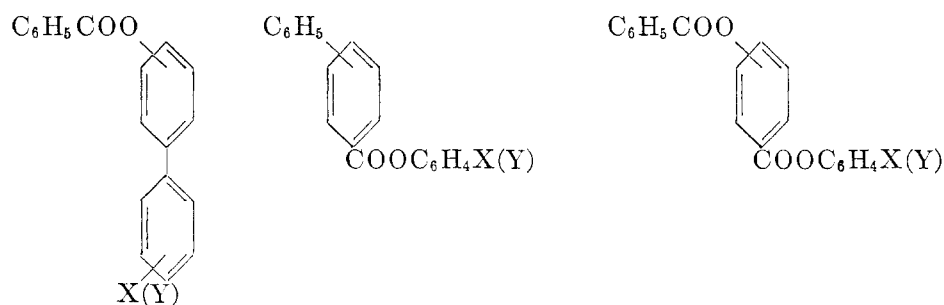
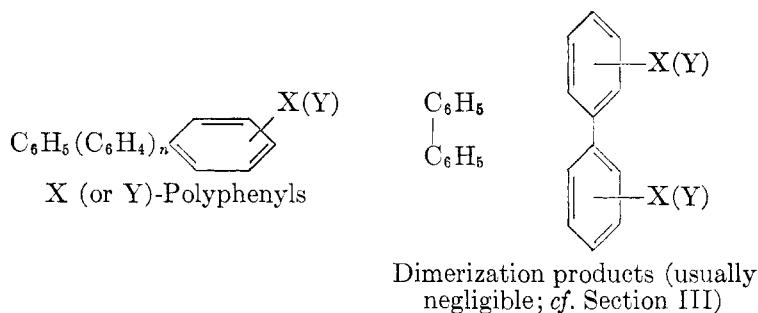
(a) *Simple products:*



(b) *Monosubstitution products:*



(c) *Polysubstitution products:*



Substituted esters

From a mixture of reaction products derived from the initially equimolecular mixture of solvents, the ratio of the weights of the monophenylated solvents, i.e., the ratio of X-biphenyl to Y-biphenyl, has to be obtained. This molecular ratio is not directly the ratio of the reaction velocities of the respective total substitutions, since the molar composition of the solution has changed during the course of the reaction. By using a large excess of mixed solvent, however, this error is minimized and the product ratio gives  $\frac{X}{Y}K$  directly.

The formation of large quantities of polysubstitution products like those shown under (c) above must be avoided, as differential removal of any one of the products of monophenylation may invalidate the value of  $\frac{X}{Y}K$  obtained. The dilution mentioned in the previous paragraph tends to minimize this occurrence but, if such highly substituted products are found in the product, their quantities must be determined and any necessary corrections applied. In the past, polysubstitution has been observed in many (1, 5, 169) free-radical reactions with the isolation of quaterphenyl and similar compounds. This was thought to be the reason for the production of large quantities of tar in these reactions and the low

TABLE 8  
 A. Relative rates of phenylation of compounds  $C_6H_5X$ 

X	(1)	(2)	(3)	X	(1)	(2)	(3)
	P Reaction 80°C.	P Reaction 70°C.	H Reaction 20°C.		P Reaction 80°C.	P Reaction 70°C.	H Reaction 20°C.
NO <sub>2</sub> .....	4.0		3.0	<i>i</i> -C <sub>3</sub> H <sub>7</sub> †.....	0.87		
F.....	1.35			<i>t</i> -C <sub>3</sub> H <sub>9</sub> .....	0.87		
Cl*.....	1.44	1.35	1.5	C <sub>6</sub> H <sub>5</sub> .....	4.0		3.0
Br.....	1.75	1.35	1.6	CH <sub>3</sub> O.....	2.5	1.2‡	2.0
I.....	1.80	1.65		SO <sub>2</sub> CH <sub>3</sub> .....		1.5	
CN.....		3.7		CF <sub>3</sub> .....		0.99‡	
CH <sub>3</sub> †.....	1.68		1.9	Si(CH <sub>3</sub> ) <sub>3</sub> .....		1.06‡	
C <sub>2</sub> H <sub>5</sub> †.....	1.24						

\* Approximate value (97) for  $\frac{Cl}{H}K \sim 2.0$ .

† Corrected for side-chain attack (cf. Section V,B,7).

‡ Data of Rondestvedt and Blanchard (251).

B. Relative rates of phenylation of miscellaneous compounds

Compound	(1)	(2)	(3)	Compound	(1)	(2)	(3)
	P Reaction 80°C.	P Reaction 70°C.	H Reaction 20°C.		P Reaction 80°C.	P Reaction 80°C.	H Reaction 20°C.
Pyridine.....	1.04	1.5	1.0	<i>p</i> -Di- <i>tert</i> -butylbenzene.....	0.63		
Naphthalene.....	24		20	<i>p</i> -Dichlorobenzene.....	2.69		
<i>p</i> -Xylene.....	3.29†		2.7	<i>s</i> -Trichlorobenzene.....	5.02		
Mesitylene.....	6.17†		6.7				

† See equation 56.

yields of biaryl obtained. The presence of such high-boiling residues has been typical of these reactions (Section III, D).

#### B. EXPERIMENTAL RESULTS AND DISCUSSION

1. The results of competitive reactions, using phenyl radicals, are shown in tables 8A and 8B.

The results obtained by Hey and his coworkers (1-6, 49-51, 161, 167, 168) are given in column (1). Two reference solvents, nitrobenzene and pyridine, were used and, in many cases, different indirect determinations of the relative rates by the method described in Section IV,B,6 (equation 33) served to check the values obtained and to demonstrate that the results obtained with solvent pairs in which one component was pyridine were not affected by complicating phenomena, e.g., solvent complexing (81). The benzoyl peroxide was allowed to decompose in dilute solution (6 g. per 200 g. of mixed solvent; mole fraction 0.01) at 80°C. for 72 hr. Procedures and analyses were independently checked as to their quantitative accuracy. The products isolated and identified generally accounted for about 85 per cent of the peroxide used.

Column (2) contains the results obtained by Dannley, Gregg, Phelps, and Coleman (80, 81) and by Rondestvedt and Blanchard (251), based on the use of pyridine as reference solvent and with rather higher peroxide concentrations (mole fraction 0.03-0.06) than those employed by Hey et al.

The results obtained by Huisgen and Sorge (186, 192), who employed the H and not the P reaction and who used pyridine as reference compound, are given in column (3).

2. The final reaction mixture for all column (1) experiments in which nitrobenzene was present as solvent was always dark-colored. This was never observed in any other case, e.g., using benzene and/or chlorobenzene as solvent, and indicates that reduction of the nitro group has taken place with further interaction of these reaction products with the peroxide to give colored nitrogen-containing compounds.

3. In certain column (1) reactions high-boiling residues were obtained in quantities approaching 50 per cent of the yield of biaryls (2, 5). These were identified as mixtures of terphenyls and quaterphenyls. Residues were not obtained in reactions in which one component of the mixture was nitrobenzene, except for the reactions with mixtures of nitrobenzene with anisole and naphthalene (1). Apart from these exceptions, which are considered separately below, it appears that polyphenylation products are produced only in the absence of a "fast" solvent, such as nitrobenzene (1, 50) ( $\frac{^N O_{\text{H}}}{\text{H}}K = 4$ ). Moreover, in Dannley's work (80, 81) high-boiling residues were always encountered when "slow" solvents were used. In the one case where a "fast" solvent was employed ( $\text{C}_6\text{H}_5\text{CN}$ ), only a small residue was obtained. The explanation of this is probably that in the presence only of relatively unreactive solvents ( $\frac{^X}{\text{H}}K \sim 1$ ), a phenyl radical collides with a sufficient number of molecules for there to be a fairly large probability of its eventual reaction with an already phenylated molecule, since, although such molecules are present only in low concentration, their reactivity is considerably greater than that of the solvents (*cf.* the relative rate for biphenyl itself,  $\frac{^C_6\text{H}_5}{\text{H}}K = 4.0$ ). However, in the presence of a "fast" solvent such as nitrobenzene, whose reactivity is equal to that of biphenyl, the probability of reaction of the phenyl radical with an already phenylated molecule is very much reduced. The nonoccurrence of polyphenylation products in the phenylation of biphenyl (49) (*cf.* Section V,B) further demonstrates that prohibition of polysubstitution is not confined to nitrobenzene but is dependent only on the relative rate of phenylation of the solvent. On this basis, the occurrence of a high-boiling resin in the product of the reaction with a mixture of pyridine and mesitylene (1) appears anomalous, since mesitylene is a "fast" solvent. Other considerations are relevant in this instance, however, which are considered below (Sections V,B,7 and V,B,8). However, simple polysubstitution is not a complete explanation of the formation of compounds of high molecular weight, as has been shown by Dannley (81), who isolated a very small quantity of a basic bromine-containing substance from a mixture of  $\text{C}_6\text{H}_5\text{Br}$  and  $\text{C}_6\text{H}_5\text{N}$ . This could be explained by the generation of small quantities of solvent radicals, a possibility which has already been discussed (Section III).

4. In those cases where resins are obtained, corrections should be made to allow for the possible differential removal of biphenyl-type products by further substitution (see Section V,B,3). This could be done in two ways: firstly, by accurate isolation and analysis of such residues to estimate the weights of the respective

biphenyls affected; and secondly, by measuring the ratio in which the biphenyls are removed from a solution by phenylation.

The first method was used in the determination of the figures in column (1) of table 8. It was found (1, 5) that, to a first-order approximation, the X- and Y-biphenyls were removed by further phenylation in that ratio in which they were formed by phenylation of  $C_6H_5X$  and  $C_6H_5Y$ , i.e.:

$$\frac{X}{Y}K \sim \frac{XC_6H_4}{YC_6H_4}K \quad (52)$$

If this were rigorously correct, then no correction need be applied to the value of  $\frac{X}{Y}K$  to allow for polysubstitution effects. Dannley made no correction to the column (2) figures for the selective removal of these compounds. It is, however, shown in Section VII,B,2 that this effect is present and that corrections are therefore necessary. The near equality for equation 52 which is observed in many cases is explained by the fact that resins are obtained only in mixtures of low reactivity, e.g.,  $C_6H_6$  and  $C_6H_5Cl$ , where the directing groups X and Y are of similar power (table 8).

However, from the point of view of the competitive experiments it is most desirable to keep polysubstitution to a minimum by the use of dilute solutions.

5. In general, the amount of benzoic acid formed in reactions with benzoyl peroxide corresponds roughly to one mole of benzoic acid per mole of peroxide (see table 9).

This is consistent with the simplest possible stoichiometric picture of the reaction. However, in certain cases such a simple picture is obviously not sufficient to explain the facts. The most notable of these exceptions is the case of naphthalene. In the competitive experiment in which benzoyl peroxide was decomposed in an equimolar mixture of nitrobenzene and naphthalene, and in decompositions of benzoyl peroxide in naphthalene alone (1), considerably more benzoic acid was formed after hydrolysis of esters than is required by the stoichi-

TABLE 9  
*Benzoic acid isolated from competitive reaction mixtures, using 6 g. of benzoyl peroxide*

Aromatic Compound	$C_6H_6$	$C_6H_5F$	$C_6H_5Cl$	$C_6H_5Br$	$C_6H_5I$	$C_6H_5NO_2$	$p-C_6H_4Cl_2$	Table 8 reference
*	grams	grams	grams	grams	grams	grams	grams	
$C_6H_5NO_2$ .....	3.0	2.60	2.8	2.8	3.5	—	2.7	} Column (1)† Column (2)‡
$C_6H_5N$ .....	3.3	—	3.2			3.3		
$C_6H_5N$ .....	3.6		3.9	4.2	3.9			
	$s-C_6H_4Cl_2$	$C_6H_5CH_3$	$p-C_6H_4(CH_3)_2$	$s-C_6H_4(CH_3)_2$	$C_6H_5C_6H_5$	$C_6H_5OCH_3$	$C_{10}H_8$	
	grams	grams	grams	grams	grams	grams	grams	
$C_6H_5NO_2$ .....	2.8	3.1	3.6	3.6	2.8	4.9	5.2	} Column (1)† Column (2)‡
$C_6H_5N$ .....								
$C_6H_5N$ .....								

\* Reference solvents used in competitive reaction.

† 80°C.; figures include free acid and acid resulting from the hydrolysis of esters (see chart I on page 156).

‡ 70°C.; only free acids included, containing about 7 per cent of phenylbenzoic acids.

ometry of the simple phenylation reaction. However, the excess of benzoic acid is accounted for by the acid present as 1- and 2-naphthyl benzoates, since a sufficient quantity of mixed naphthols was isolated after hydrolysis. Thus it appears that the very reactive solvent, naphthalene, is susceptible to attack by  $C_6H_5COO\cdot$  radicals (benzoyloxylation) which, though less active homolytic reagents than phenyl radicals, are probably present in higher concentration (*cf.* Section III,B,2). Again, a larger amount of benzoic acid is produced when pyridine is used as the reference solvent. This was thought (80, 81) to be due to the formation of reactive complexes between pyridine and benzoic acid or other substances present in the mixture. Variation in the quantity of phenylbenzoic acids isolated with different solvent pairs was also attributed to this complexing action but is, however, capable of simpler explanation. The amount of these compounds formed depends upon the reactivity of benzoic acid relative to that of the other substances present. From table 12, benzoic acid might be expected to have a rate value of  $\frac{COOH}{H}K \sim 3.7$ , and it follows, therefore, that in mixtures of solvents of low reactivity large amounts of phenylbenzoic acids will be formed. The problem is complicated with these mixtures, however, by the formation of high-boiling residues (Section V,B,3 and V,B,4).

Anisole is exceptional, for it gives rise to mutually untenable conclusions. According to table 9 and the foregoing, anisole should be a very reactive molecule, and this is contrary to the  $\frac{X}{H}K$  rate data of table 8. This is discussed further below (Section V,B,8).

6. The halogen series of relative rates (2)

$$\begin{array}{cccc} X = & F & Cl & Br & I \\ \frac{X}{H}K = & 1.35 & 1.44 & 1.75 & 1.80 \end{array} \quad (53)$$

illustrates the effect of moving down a group of the Periodic Table. Though the differences are small, the values have been obtained by cross-checked experiments and are confirmed by the various groups of workers. It would have been unwise to place complete reliance in the data, however, until the fluctuation in the amount of acid and resin obtained in each case had been explained and shown to have no effect on the  $\frac{X}{H}K$  value (see Sections V,B,5, V,B,7, and V,B,8). This series should be compared with the values predicted (tables 5 and 17) and related to the discussion in Section IV,C,5,(iii).

7. The methylbenzenes (1) are extremely interesting. The progressive introduction of methyl groups gives:

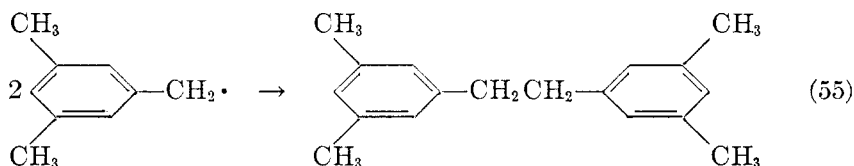
$$\begin{array}{ccc} X = & CH_3 & p-(CH_3)_2 & s-(CH_3)_3 \\ \frac{H}{X}K = & 1.85 & 3.29 & 6.17 \end{array} \quad (54)$$

but the situation is not clear-cut.

With nitrobenzene as the reference solvent it was found that nitro group analyses on the biphenyl fraction did not agree with those for elementary nitrogen from combustion analyses. This was attributed to the presence of already reduced nitrogen compounds not estimated by the former method, and this postu-

late was substantiated when a very small quantity of basic material was isolated from the  $s\text{-(CH}_3)_3\text{C}_6\text{H}_3/\text{C}_5\text{H}_5\text{NO}_2$  product-mixtures.

Investigation (1, 3) of the composition of the neutral reaction products resulting from the  $p\text{-(CH}_3)_2\text{C}_6\text{H}_4/\text{C}_5\text{H}_5\text{N}$  and  $s\text{-(CH}_3)_3\text{C}_6\text{H}_3/\text{C}_5\text{H}_5\text{N}$  reactions showed that they consisted of biphenyl fraction and resin. (From Section V,B,3 above, this resin should not have been formed, since  $\frac{\bar{x}}{\bar{H}}K > 4.0$ ; the explanation will become apparent in what follows.) The biphenyl fraction was observed to solidify partially and the crystals which formed were removed and identified as the dimers of the corresponding methyl-substituted benzyl radicals. Thus, for example, in the case of mesitylene the corresponding radical is stabilized by resonance, and the dimer 3,5,3',5'-tetramethyldibenzyl results:



The presence of this radical is the probable cause of resin formation in these compounds.

These results were the first to show side-chain attack by aryl radicals. The weights of the substances involved in the above cases allow the calculation of the percentages of side-chain attack to total attack. These figures are inherently approximate, owing to the experimental work and the assumptions which have to be made. Thus it has to be assumed that the substitution and hydrogen abstraction are effected by the same radical, i.e., free phenyl. This is somewhat justified, since the quantity of benzoic acid obtained from these experiments is normal. Moreover, mesitylene is known to behave as a typical aromatic molecule in peroxide decomposition, i.e., there is no induced decomposition of peroxide by the benzyl-type radical (see Section III,B and Section V,B,8). Furthermore, it is reasonably assumed that this dimerization also occurs in the competitive experiments using nitrobenzene as reference. Correction to the apparent relative rate values (equation 54) for the occurrence of side-chain attack gives the following figures:

$$\begin{array}{cccc}
 \text{X} = \text{CH}_3 & p\text{-(CH}_3)_2 & s\text{-(CH}_3)_3 & \\
 \frac{\bar{x}}{\bar{H}}K = 1.68 & 0.23 & 4.2 & \text{(56)}
 \end{array}$$

Thus, for the first time, a group X has been found which deactivates the nucleus for radical phenylation. Further work has since shown that *tert*-butylbenzene, *p*-di-*tert*-butylbenzene, and isopropylbenzene (50, 168) emulate this behavior. Explanations for both this order, assuming it to be a true one, and the effects observed with *tert*-butylbenzene and isopropylbenzene are given later (Sections VII,A,4 and VII,B,2).

Dannley and Zaremsky (83, 84) have confirmed the existence of simultaneous side-chain and nuclear reactions by using mixtures of a single solvent and peroxide. It is reported that both ethylbenzene and isopropylbenzene give



TABLE 10  
*Side-chain attack in the reaction of alkylbenzenes with benzoyl peroxide*

Alkylbenzene	Dannley and Zaremsky (83, 84)	Rondestvedt and Blanchard (250)	Hey, Pengilly, and Williams (167, 168)
	<i>per cent by weight</i>	<i>per cent by weight</i>	<i>per cent by weight</i>
Toluene .....	—	>15	13
Ethylbenzene.....	67	—	55
Isopropylbenzene.....	33	59	60.5

stabilized benzyl-type radicals which dimerize, but that toluene undergoes a unique reaction to form a very small quantity of diphenylmethane. This result has been disproved by the more recent work of Rondestvedt and Blanchard (250) and of Hey, Pengilly, and Williams (167, 168). Both groups of workers agree that no diphenylmethane is formed, but that a small quantity of bibenzyl (ca. 10 per cent) results from dimerization of benzyl radicals. In addition, all these groups of workers have measured the amount of side-chain attack which takes place in the phenylation of ethylbenzene and isopropylbenzene, resulting in the formation, respectively, of *dl*- and *meso*-2,3-diphenylbutane (in equal amounts) and 2,3-dimethyl-2,3-diphenylbutane (dicumyl). The results obtained for the relative amounts of side-chain and nuclear attack on these hydrocarbons are given in table 10. In addition, Rondestvedt and Blanchard measured the relative amounts of the products of side-chain and nuclear attack on toluene and isopropylbenzene by phenyl radicals derived from *N*-nitrosoacetanilide and 3,3-dimethyl-1-phenyltriazene. Substantially the same results were obtained with these sources, except in one case—the decomposition of *N*-nitrosoacetanilide in toluene—in which the temperature was maintained below 25°C. throughout. In this experiment no side-chain attack was observed.

It is seen from table 10 that, as might have been predicted, the substitution of methyl groups at the  $\alpha$ -carbon atom of the side chain renders hydrogen atoms attached to this atom more susceptible to removal by homolytic attack.

8. In the preceding discussion certain solvents have appeared to give rise to anomalous reaction products. The observations are difficult to explain and the possible suggestions conflicting. Table 11 presents the facts. The columns indicate in order the values of the total relative rate ( $K_{\text{calc.}}$ ) predicted by the mathematical theoretical treatments (Section IV) and the observed ( $K_{\text{obs.}}$ ) values of the free-radical reactivity for nuclear phenylation, the production of resins with the solvent mixtures using reference solvents  $\text{C}_6\text{H}_5\text{NO}_2$ ,  $\text{C}_6\text{H}_6$ , and  $\text{C}_5\text{H}_5\text{N}$ , whether or not induced decomposition is shown in the P reaction (Section III,B), and the quantity of benzoic acid which is recovered from the products. Phenol is included in the table as it is important in the discussion (see 300, 301).

In Section V,B,5 above, the acid-recovery figures were discussed, and it was pointed out that a high reactivity of the molecule in allowing benzyloxylation would give rise to a large amount of benzoic acid. Thus, the total recovery of acid from the reaction with phenol (table 11) could be explained by the very high solvent reactivity,  $K_{\text{calc.}}$ , facilitating benzyloxylation and inhibiting

TABLE 11  
*Anomalous behavior in reactions with benzoyl peroxide*

Aromatic Compound	$K_{\text{calc.}}$ (Table 7)	$K_{\text{obs.}}$ (Table 8)	Resin† in Solution with		P Reaction; Induced De- composition‡ (Section III,B)	$\text{C}_6\text{H}_4\text{COOH}\ddagger$ (Table 9)
			$\text{C}_6\text{H}_5\text{NO}_2$ (Sections V,B,3 and V,B,4)	$\text{C}_6\text{H}_6, \text{C}_6\text{H}_5\text{N}$ (Sections V,B,3 and V,B,4)		
$\text{C}_6\text{H}_5\text{OH}$ .....	11.95	?	?	?	++	++
$\text{C}_6\text{H}_5\text{Hal}$ .....	2.7	1.5	n(?)	+	n	-
$\text{C}_6\text{H}_5\text{OCH}_3$ .....	?	2.5	+	?	n	+
$6\text{-(CH}_3)_2\text{C}_6\text{H}_3$ .....	6.74*	4.2-6.2*	n(?)	+	n	n(+)
$\text{C}_{10}\text{H}_8$ .....	$4 \times 10^4$	23.9	+	?	?	+

\* See Sections VII,B,2 and V,B,7, equations 54 and 56.

† n denotes normal behavior, i.e., no resin, normal acid production, and very small induced rate of peroxide decomposition.

+ denotes increased behavior or production of correspondingly increased quantity.

- denotes decreased behavior or production of correspondingly decreased quantity.

? denotes unknown behavior.

decarboxylation of the  $\text{C}_6\text{H}_5\text{COO}\cdot$  radicals. This, however, neglects the fact that phenol does not behave as a typical aromatic solvent in the P reaction.<sup>5</sup> Owing to the production of stabilized aryloxy radicals (12, 65, 66, 235, 236) a very high rate of induced decomposition is exhibited. The presence of such solvent radicals is proved by the isolation of the corresponding dimerization products in certain instances (65, 66). These radicals possess a high specific activity in promoting the chain decomposition of the peroxide (steps (b) and (c), scheme IV, equation 24, are very fast). Thus, here the  $K_{\text{calc.}}$  value is misleading; some other reaction takes precedence over nuclear substitution (see Section IV,E).

Anisole, in distinction to phenol, does not show induced decomposition (235, 236). It does, however, produce resin and show high acid recovery in competitive reactions with nitrobenzene (1). It is suggested that an alkyl hydrogen atom is removed by  $\text{C}_6\text{H}_5\text{COO}\cdot$ , to give the acid and the stabilized aryloxy-alkyl radical  $\text{C}_6\text{H}_5\text{OCH}_2\cdot$ . It must be assumed that this radical does not promote induced decomposition of the peroxide, but does contribute to the formation of high-molecular-weight compounds. To some degree, the occurrence of resins when mesitylene is used in these experiments supports this viewpoint (Section V,B,7).

It is impossible, as yet, to suggest the reason for the occurrence of the resin with the  $\text{C}_{10}\text{H}_8/\text{C}_6\text{H}_5\text{NO}_2$  mixture (1). Using the former solvent alone in the P reaction, the resin has been shown to consist mainly of unidentified hydrocarbons. This suggests the formation of solvent radicals but is opposed to the known fact that this solvent has a high free-radical substitution reactivity, as evidenced by  $K_{\text{obs.}}$  and the fact that extensive benzoyloxylation occurs (79, 249).

### C. THE PRESENCE OF ACTIVE HYDROGEN

Previous discussion (Sections III and V) has indicated that hydrogen atoms, or other labile forms of hydrogen, may be formed in homolytic arylation. Much

<sup>5</sup> See references 300 and 301.

controversy has centered around this point (287, 288) and it is necessary to clarify the issue. The fact that molecular hydrogen was not evolved in the P reaction (78) gave some support to the solvent-radical decomposition mechanism (scheme II, equation 20), though this should have been rejected for other reasons (see Section III,B). The absence of hydrogen, however, does not preclude the presence of free hydrogen atoms which, being very reactive, would never be able to dimerize.

Confirmation for the existence of hydrogen atoms arises from the following:

- (i) The negative argument (Section III) based on the fact that no appreciable quantities of solvent radicals are formed in these reactions, the ratio of hydrogen-atom ejection to solvent-radical formation being about 120:1 (190) (equation 12).
- (ii) The isolation of quantities of quinhydrone from some of the typical free-radical reactions (Section III) when quinone was present in the mixture (59, 190, 293-298).
- (iii) The qualitative observation from competitive and preparative experiments (see Section V,B,2) that whenever nitrobenzene was used in the P reaction a very dark-colored reaction mixture was obtained, whereas relatively colorless products were obtained from a nitrogen-free solution, e.g., chlorobenzene or a  $C_6H_6/C_6H_5Cl$  mixture (1). This is attributed to reduction of the nitro group.
- (iv) Using the decomposition of benzoyl peroxide, with both nitrobenzene alone and the competitive mixture alkylbenzene/ $C_6H_5NO_2$ , the production of primary amine was suspected (see Section V,B,6). Furthermore, in a similar competitive experiment with  $C_{10}H_8/C_6H_5NO_2$ , aniline has been identified (1, 5).

Of these facts the last is vitally important, since it immediately aids the rejection of reaction scheme II (Section III). Moreover, reference to the proposed mechanism (scheme III, equation 21) and the relevant discussion indicates why the amine was found in reasonable quantity in this mixture and not in any other case (190, 192). In the normal situation, the most efficient acceptor of hydrogen atoms present in the reaction mixture is the benzoyloxy radical; hence, normally, the ejected hydrogen atoms appear in the product as benzoic acid. However, naphthalene is an unusually reactive compound and is therefore susceptible to benzoyloxylation. Since this reaction results in the consumption of benzoyloxy radicals with the production of the same number of hydrogen atoms, the nitrobenzene present in the mixture must be called into play as an oxidizing agent or acceptor for the excess of hydrogen atoms. This must result in an increased production of the products of reduction of nitrobenzene.

#### D. THE SUBSTITUTION STEP

The "RH scheme" of Gelissen and Hermans (122-129) (Section III,B; equation 13) was the first clear attempt to explain the substitution step in the arylation of aromatic solvents with acyl peroxides. The same scheme was advocated subsequently by other workers (26, 112, 297, 298). More recently,



solvents,  $C_6H_5X$ , and hydroxyl radicals are employed, the favored reactions are (a) and (c), and we have seen that aryl radicals react via (b). This behavior can be explained by a consideration of the stabilities of the solvent radicals it is possible to form and the strengths of the bonds involved.

Szwarc has shown (199, 271-274, 277) by a study of the bond-dissociation energies involved, that although the biphenyl-coupling resonance energy is gained in the phenylation reaction (b) (additional energy amounting to 14-25 kcal. relative to  $CH_3CH_3$  is obtained), this is still not sufficient to explain the substitution. Szwarc postulated a hot-complex  $C_6H_5-Ar-H$  (*cf.* the intermediate in equation 7) with ( $\pi-\pi$ ) electron interaction in the  $C_6H_5-Ar$  "bond" and another radical taking off the hydrogen atom. It is difficult to explain the nuclear arylation of toluene, rather than exclusive side-chain attack (a) (equation 57; *cf.* Section V,B,7), without invoking the presence of this second radical. It is significant that, in most substitution reactions with benzoyl peroxide, the yield of benzoic acid accounts for half of the original peroxide (table 9). This implies a pseudo-termolecular collision, wherein the phenyl radical effects substitution and the "liberated" hydrogen atom combines with the  $C_6H_5COO\cdot$  radical remaining (see Section II,B). Returning to reaction scheme III (Section III,B), which describes the observed kinetic and preparative work, it is seen that this process is the one described. If the solvent readily induces substitution (e.g., naphthalene) and sufficient hydrogen-atom acceptors in the form of radicals  $R'\cdot$  (equation 57), and in particular  $C_6H_5COO\cdot$ , are not available, then the solvent may take up this role with the production of reduced compounds in the mixture (Section V,C). Whether or not the "liberated" hydrogen atom is ever free, as such, it is impossible to say (*cf.* the "kryptoradical" theory (192)). Stockmayer and Peebles (268), Bickel and Kooyman (20), and Boozer and Hammond (24) have concluded that the formation of a radical-solvent complex, associated with a small activation energy, takes place. This formation of the complex must, in any case, be the slow stage in the substitution reaction, since Sheppard (258) has shown that there is no isotope effect when tritiated benzene is allowed to react with benzoyl peroxide and triphenylmethyl. This indicates that the removal of hydrogen from the complex is a fast stage, to which no kinetic significance may be attached, and that, therefore, the activated process must be the formation of the complex.

The favored reaction of the methyl radical would be expected to be that of hydrogen-atom abstraction (a) with the formation of methane (276, 280). This is observed (275) with aliphatic-type solvents but not with benzene or pyridine (131, 275, 276, 280). Here the main reaction appears (275) to be substitution (b) with some double addition to form unsaturated compounds of type (c), but these have not been isolated. The methyl radical has been reported not to attack the side chain of toluene (*cf.* Section V,B,7; 275). These results point to the fact that the addition complex for this reaction may have some stability and therefore a finite life in solution, so that addition of a further radical can take place. If the activating group were of stronger power, e.g., as in nitrobenzene (115), then direct substitution by the first methyl radical would be facilitated.

On the other hand, if the attacking radical, instead of methyl were more nucleophilic, e.g.,  $\cdot\text{OH}$ , then hydrogen abstraction would be favored. The reaction of polycyclic hydrocarbons and certain other aromatic compounds with methyl radicals has recently been studied by Levy and Szwarc (211), and their results have been discussed by Hey and Williams (177) and by Coulson (71). These results are further discussed in Section V,E.

Mayo (229) has indicated that solvent-radical complexes may be formed between a styrene polymer molecule and bromobenzene. This is not relevant to the case under review, for the benzyl-type radical of the polymer is able to resonate among various forms (*cf.* equation 55) and will possess a smoothed free valence over the whole molecule. This radical might, therefore, be expected to form a loose  $p$ - $\pi$  complex with aromatic molecules, e.g., bromobenzene. With a more highly reactive solvent, e.g., *m*-dinitrobenzene, the polymer radical may be induced to react, and such a solvent should show a moderately good inhibition effect, as observed (139).

The evidence must be carefully assessed before any concrete conclusion can be arrived at concerning the nature of the substitution stage in the phenylation of an aromatic molecule. By analogy with nitration (230), where the addition mechanism is known to occur, and acceptance of gradation between radical and solvent natures and interactions (see Section VI,D), it may be said that the substitution is most probably effected by the addition process. This is consistent with the lack of a kinetic isotope effect. Within this statement are included the various possibilities dependent on the extreme properties of the reactants. Thus, with phenyl radicals, phenol reacts via equation 57a, owing to the stability of aryloxy radicals, whilst chlorobenzene acts via equation 57b.

## E. OTHER RADICALS

### 1. Radicals other than aryl radicals

Competitive experiments using radicals other than aryl radicals are summarized in table 12.

*Column (1):* Dannley and Gippin (79) used a series of  $\alpha$ -X-substituted naph-

TABLE 12  
Relative rates of reaction with radicals other than aryl (79, 109, 139, 211)

Aromatic Compound	$\frac{k}{k^0}$			
	(1) $\text{C}_6\text{H}_5\text{COO}\cdot$ , 70°C.	(2) $\text{CH}_3\cdot$ , 100°C.	(3) Polystyryl, 100°C.	(4) $\text{CH}_3\cdot$ , 85°C.
$\text{C}_6\text{H}_5\text{CH}_3$ .....	1.4	19.2	3.6	
$\text{C}_6\text{H}_5\text{COOCH}_3$ .....	3.7	1.6		
$\text{C}_6\text{H}_5\text{NO}_2$ .....	7.0			
$\text{C}_6\text{H}_5\text{COC}_6\text{H}_5$ .....				11
$\text{C}_6\text{H}_5\text{OC}_6\text{H}_5$ .....				2
$\text{C}_6\text{H}_5\text{C}_6\text{H}_5$ .....				5
$\text{C}_6\text{H}_5\text{N}$ .....	1.7			3
$\text{C}_{10}\text{H}_8$ .....				22

thalenes in reaction with benzoyl peroxide. Substitution is effected by the benzoyloxy radical and results in the production of 2-, 4-, or 5-substituted naphthalene derivatives. The esters were isolated semiquantitatively and the ratios of the hetero- and homonuclear substituted compounds were determined. This was assumed to represent the activation of one half of the molecule relative to the other, i.e.,  $\frac{X}{H}K$  is found for benzoyloxylation at 70°C. Owing to the fact that the group X will affect both rings, and that there appears to be some peculiarity of the naphthalene molecule itself (*cf.* Sections IV,C and IV,D), these values should be accepted with reserve. It might appear that the COOCH<sub>3</sub> group has about half the activating effect of the nitro group, and from table 8 this would result in a relative rate of  $\frac{COOCH_3}{H}K = 2.0$  for phenylation. This value seems to be not unreasonable (*cf.* Section V,B,5).

*Column (2):* These figures were obtained (109) using methyl radicals from diacetyl peroxide. Owing to the fact that free methyl will tend to abstract a hydrogen atom rather than effect substitution, the high rate for toluene is reasonable, since free benzyl radicals are formed.

*Column (3):* Polymerization work using styrene (139) allows the ratio of rates of (chain transfer to solvent)/(chain propagation) to be measured. Nitrobenzene and *m*-dinitrobenzene are known to be good inhibitors and, on the results of table 8, naphthalene or *s*-trichlorobenzene should be as effective (see Section V,C). The efficiency of polynuclear hydrocarbons as inhibitors has been observed (25).

*Column (4):* Levy and Szwarc (211) have measured the affinities of a number of compounds, particularly polynuclear hydrocarbons, for methyl radicals. Selected results from this work are included in table 12. The compounds investigated which are not included in table 12 are polynuclear hydrocarbons, which gave very high values for the relative rate. In further discussion of these results (177) it has been shown that a high degree of correlation exists between them and the corresponding results for phenylation (*cf.* table 8). In addition, Coulson (71) has shown that for the condensed nuclear hydrocarbons considered (including naphthalene) a straight-line relationship exists between the logarithm of the methyl affinity and the maximum free valence in the molecule. The absolute values of the free valence numbers are also of the correct order of magnitude. A similar straight-line relationship exists with the atom localization energies; here the absolute values are not of the correct order of magnitude but result in the production of reactivities which are much too high, as in the case of naphthalene (Section IV,E). Thus, a similar error seems to be incurred in all calculations of localization energies in condensed nuclear hydrocarbons.

## 2. Aryl radicals other than phenyl

Recently determined values for relative rates of arylation of a number of compounds C<sub>6</sub>H<sub>5</sub>X with substituted phenyl radicals are given in table 13. The same techniques were employed in the determination of these relative rates as were employed by Augood, Hey, and Williams (6) in the determination of the figures listed in table 8, and the same comments therefore apply to them.

TABLE 13

*Relative rates of arylation with substituted phenyl radicals at 80°C. (6, 51, 146, 167, 168)*

Radical	$\frac{\text{NO}_2 K}{\text{H}K}$	$\frac{\text{Cl}K}{\text{H}K}$	$\frac{\text{CH}_3 K}{\text{H}K}$
<i>p</i> -NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> .....	0.94	1.17	2.61
<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> .....	1.53	1.02	1.32
<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> .....	2.92	1.56	—
C <sub>6</sub> H <sub>5</sub> .....	4.0	1.49	1.63*
<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> .....	5.13	2.05	1.03

\* Approximate value.

Some of these results were measured directly, and others obtained by the cyclic procedure outlined previously (Section IV,B,6, equation 33). The results demonstrate clearly the effect on the relative rates of arylation of electron-attracting and electron-repelling substituents in the para positions of the radicals. The groups NO<sub>2</sub>, Cl, and CH<sub>3</sub>O attract electrons, and the magnitude of the effect varies in the order NO<sub>2</sub> > Cl > CH<sub>3</sub>O. The methyl group repels electrons. Thus, the first three radicals of table 13 would be expected to possess some measure of electrophilic character, since the withdrawal of electrons by the substituent groups must result in a deficit of electrons at the position which carries the odd electron. It is conventional to regard hydrogen as the zero for effects of electron attraction and repulsion; following the same convention, the phenyl radical is assumed to be neither electrophilic nor nucleophilic. By similar argument it is seen that the *p*-tolyl radical possesses some nucleophilic character, and therefore that the radicals in table 13 are listed in order of decreasing electrophilic power or increasing nucleophilic power.

The nitro group is known to deactivate the aromatic nucleus towards electrophilic substitution, and to activate it towards nucleophilic substitution. It is to be expected, therefore, that the relative rate  $\frac{\text{NO}_2 K}{\text{H}K}$  for arylation with an electrophilic radical should be less than its value for phenylation, and similarly that it should be greater for arylation by a nucleophilic radical than for phenylation. The second column of table 13 shows that this prediction is borne out, and that the magnitude of the effect varies in the order predicted from the magnitude of the electron attraction of the groups concerned. Reference to the third column shows that the rate ratio  $\frac{\text{Cl}K}{\text{H}K}$  is dependent on the nature of the attacking radical in a similar manner. (The slightly anomalous value obtained for  $\frac{\text{Cl}K}{\text{H}K}$  with *p*-anisyl radicals is possibly due to experimental inaccuracy.) In the last column, the order of variation of the relative rates is reversed, since the methyl group is an activating substituent for electrophilic substitution and a deactivating substituent for nucleophilic substitution.

It has been shown (Section V,B,7) that in the phenylation of toluene some side-chain attack takes place. This results in the abstraction of a hydrogen atom with the consequent production of bibenzyl. This process is also observed in the arylation of toluene with the radicals under discussion, and the values given in table 13 for the relative rate  $\frac{\text{CH}_3 K}{\text{H}K}$  are those obtained after a correction for the side-chain attack has been applied. They refer, therefore, only to attack on the



TABLE 14  
*Side-chain attack in the arylation of toluene (146)*

Radical.....	<i>p</i> -O <sub>2</sub> NC <sub>6</sub> H <sub>4</sub>	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	C <sub>6</sub> H <sub>5</sub>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>
Per cent bibenzyl.....	0	10	13*	42

\* Approximate value.

nucleus of toluene. The various proportions of side-chain attack which were determined in the evaluation of these corrections are of interest as they, too, reflect the influence of the substituent groups in the radicals. It is clear that with toluene nuclear substitution should be favored by electrophilic radicals, while side-chain attack should be favored by nucleophilic radicals. The relevant data are given in table 14 and clearly demonstrate the influence of the polar character of the radical.

## VI. RATIO OF ISOMERS

### A. RECENT RESULTS

Only very recently have reliable figures become available for the proportions in which the substituted C<sub>6</sub>H<sub>5</sub>X isomers are formed in homolytic reactions. Reference to table 3 and the corresponding discussion indicates the situation prior to 1951, when it was accepted that the para isomer was the compound usually produced in greatest quantity in these reactions. At this time the work of Hey and his collaborators (164) showed that the meta isomer, which had rarely been isolated before could, in fact, account for approximately 10 per cent of the isomer mixture in some reactions, and further results followed quickly. All the published data concerning isomer percentages are given in table 4 of the accompanying paper (92).

From these data, only those values obtained in very careful experiments should be considered in quantitative argument. The best figures are, undoubtedly, the ones derived from spectroscopic analysis of complete isomer mixtures, where mechanical separation of the isomers has been minimized, if not eliminated, in the working-up procedure. Unfortunately, in one or two cases, e.g., naphthalene, the relevant information is not available and the quoted figures, possibly inaccurate, have to be used in the evaluation of the partial rate factors. Moreover, those data obtained by use of single solvents are preferred compared with those obtained when the solvent concerned has been used with pyridine in competitive experiments (see Section V,B). The data used in the evaluation of the partial rate factors for phenylation are presented in table 15 (*cf.* table 4 of reference 92).

In the following discussion on isomer ratios in general, two important facts must be borne in mind: (1) the effect caused by change of the radical and (2) the effect of the temperature at which the reaction is carried out.

### B. PHENYLATION: SUBSTITUTION BY PHENYL

Important conclusions have been based upon the fact that similar isomer ratios have been found to be produced by all of the main homolytic reactions (see Section III). Thus the results of the Gomberg reaction at 5°C. have been com-

TABLE 15

*Ratios of isomers used in the calculation of partial rate factors for phenylation at 80°C.*

Aromatic Compound	Isomer Percentage			Reference (cf. Table 4 in reference 92)
	Ortho or $\alpha$	Meta or $\beta$	Para or $\gamma$	
$C_6H_5NO_2$ .....	58	10	32	(5, 164)
$C_6H_5N^*$ .....	58	28	14	(80, 81)
$C_6H_5F$ .....	54.1	30.7	15.2	(4)
$C_6H_5Cl$ .....	60.3	25.9	13.8	cf. table 16
$C_6H_5Br$ .....	49.3	33.3	17.4	(2)
$C_6H_5I$ .....	51.7	31.6	16.7	(2)
$C_6H_5CN^*\dagger$ .....	60	10	30	(80)
$C_6H_5CH_3$ .....	66.5	19.3	14.2	(168)
$C_6H_5C_2H_5$ .....	53	28	19	(168)
$C_6H_5C_6H_7-4$ .....	31	42	27	(168)
$C_6H_5C_6H_9-4$ .....	24	49	27	(50)
$C_6H_5C_6H_5$ .....	48.5	23.0	28.5	(49)
$C_{10}H_8\dagger$ .....	33.4	16.6	—	(192; cf. 232)
$C_6H_5SO_2CH_3^*\dagger$ .....	53	33	14	(80)
$C_6H_5CF_3$ .....	20	40	40	(32, 251)
$C_6H_5Si(CH_3)_3$ .....	31	45	24	(251)

\* Reaction carried out at 70°C.

† Mixture from competitive reaction with pyridine.

‡ Product of H reaction and possibly inaccurate.

pared (5, 161) with, and found equal to, those of the peroxide reaction at 80°C. However, the difference in temperatures at which these reactions have been conducted has been neglected, and such a comparison is unjustified and invalid. Reference to the reported data for chlorobenzene (5) gives the appropriate figures [(a) and (b), table 16] for the two cases under discussion. [Note: This splitting of the published data, formerly considered together (reference 5 and table 4 of reference 92) increases the experimental accuracy in the groups (a) and (b)]. Additional reported work (80, 81) is also tabulated [(c) and (e)].

Employing equation 39, which was developed in Section IV,B,8, the (a) (G. 278°K.) figures are operated upon to ascertain the values that would be expected from this reaction if it could be carried out at 80°C., i.e., (d) in table 16. It is

TABLE 16

*Phenylation of chlorobenzene: spectroscopic values*

Method	Temperature	Isomer Percentage			Reference
		Ortho	Meta	Para	
	°K.				
(a) G	278	64.6	21.7	13.7	(5)
(b) P	353	60.3	25.9	13.8	(5)
(c) P	343	64	23	13	(80)
(d) G(a)	353	59.6	25.2	15.2	Calculated from equation 39
(e) P	343	54	31	15	(81)

(c) From competitive experiment using  $C_6H_5Cl$  and  $C_6H_5SO_2CH_3$ .

(e) From competitive experiment using  $C_6H_5Cl$  and  $C_6H_5N$ .

seen that the ortho position, having the smallest energy of activation, becomes less important on increase in temperature, as expected from first principles. The agreement between the (d) and (b) figures, one set observed experimentally at 80°C. and the other calculated as described, is extremely good. Thus, due recognition of the temperature effect has improved the observations and strongly substantiates the conclusions reached in Section III,C. It will be noted that in table 15, which gives isomer ratios for 80°C., some determinations at 70°C. are included. It is now apparent that this difference in reaction temperature has only a small effect on the isomer ratios.

When the  $C_6H_5Cl/C_5H_5N$  solvent mixture was used in a competitive experiment, it was found (81) [(e), table 16] that the chlorobenzene gave rise to another set of values for the isomer percentages, i.e., other than the mean between (a) and (b) or the further set of values (c). This led to the suggestion that solvent association was responsible for these deviations (*cf.* Section V,B,5); this is now shown to be very unlikely. Firstly, as presented in table 16, the true isomer percentages for 80°C. are given by (b) or (d) and not, as reported, by the mean of (a) and (b). This does not, however, shorten the gap between (c) and (e). Secondly, evidence is now available (2, 81) for the other halogenobenzenes (92, table 4) and it is seen that, whether pyridine is present or not, there are insignificant variations in the isomer ratios obtained. If complexing of the pyridine occurred with chlorobenzene, it might be expected to occur with the other halogenobenzenes, and these figures do not support this view. For benzoic acid the situation is different, as salt formation with pyridine might be expected. This is shown well in table 4 of the accompanying paper (92) (*cf.* Section V,B,5).

The above discussion shows that, if experiments are conducted at the same temperature, then for a given solvent all sources of phenyl radicals give identical mixtures of isomers in the product. This principle has been applied (169) to show that the decomposition of lead tetrabenzoate in nitrobenzene at 125°C. proceeds via a homolytic mechanism to yield phenyl radicals. In addition, isomer percentages have been determined recently (170) for the phenylation of nitrobenzene (at 125°C.) and pyridine (at 105°C.) with phenyl radicals derived from phenyl iodosobenzoate, *N*-nitrosoacetanilide, and phenylazotriphenylmethane. These results are given in table 17. Although the values for the H reaction are admittedly inaccurate, the figures demonstrate clearly the independence of the

TABLE 17  
*Comparison of radical sources: isomer percentages obtained (170)*

Radical Source	Nitrobenzene (125°C.)			Pyridine (105°C.)		
	Ortho	Meta	Para	$\alpha$	$\beta$	$\gamma$
$(C_6H_5COO)_2$ .....	56.3	15.7	28.0	54	32	14
$Pb(C_6H_5COO)_4$ .....	55	16	29	52	32.5	15.5
$C_6H_5I(OCOC_6H_5)_2$ .....	57.5	14	28.5	58	28	14
$C_6H_5N(NO)COCH_3$ .....				46	43	11
$C_6H_5N_2C(C_6H_5)_3^*$ .....				53	31	16

\* Corrected values (see text).

isomer ratio on the source from which the phenyl radicals are derived. In the case of the reaction of phenylazotriphenylmethane with pyridine, different isomer percentages were obtained, and a solid compound was isolated which was shown to be derived from  $\alpha$ -phenylpyridine by reaction with triphenylmethyl. This process therefore resulted in the selective removal of  $\alpha$ -phenylpyridine from the isomer mixture, and when the measured isomer percentages were corrected for this, a set of values was obtained which corresponded closely with those obtained using the other radical sources.

Finally, in connection with the validity of the determination of the isomer ratio, it is important to establish that the isomers are not selectively removed by further phenylation.

In a competitive reaction mixture the possibility of selective removal of the X- and Y-biphenyls to form resins was shown to be important in the determination of the relative total rate constant  $\frac{\sum k}{\sum K}$  (Sections V,B,3 and V,B,4). Moreover, any such differential reaction between the isomers of either X- or Y-biphenyl will produce an incorrect set of isomer percentage values. Dannley (81) has investigated this point in the following way. A mixture of isomeric phenylpyridines was phenylated, and the isomer percentages determined both before and after reaction. Since no observable change was found, the conclusion was drawn that there was no preferential removal of any of the isomers. It will be shown later (Section VII,B,2), that this deduction is untenable and that these experiments were not sensitive enough to detect the change. Although this effect is usually less important than in the case of competitive experiments (Section V,B,2), the most reliable figures are still those which were obtained under conditions (of high dilution) wherein the incidence of polyphenylation is minimized. With only a few exceptions it is these figures which are used in the calculation of partial rate factors (Section VII).

#### C. ARYLATION: SUBSTITUTION BY ARYL RADICALS OTHER THAN PHENYL

It has been pointed out (Section V,E,2) that when aryl radicals other than phenyl are employed, the course of reaction is profoundly influenced by the electrophilic or nucleophilic character conferred on the radicals by the polar effects of the substituent groups. It is emphasized that the primary effect of a charge at site  $r$  in the compound  $C_6H_5X$  now becomes that of attracting or repelling that portion of the radical where the odd electron resides, thereby either assisting or inhibiting reaction. The charges are not ultimately responsible for the reaction, as in heterolytic substitution, and the reaction remains a homolytic process.

This effect is well documented in so far as it is illustrated by relative rates of substitution (Section V,E,2), and some data are also available for its influence on isomer ratios. The work of Dannley and Sternfeld (82) on the arylation of benzotrichloride with phenyl,  $p$ -nitrophenyl, and  $p$ -chlorophenyl radicals (92, table 4) is relevant in this connection. The reaction of  $p$ -nitrophenyl radicals with benzotrichloride is influenced by the following: steric hindrance at the ortho positions due to the bulk of the  $-CCl_3$  group; ortho-para substitution according

to the homolytic rules (see Sections VII and VIII); and meta reaction according to the electrophilic rules, since  $-\text{CCl}_3$  is a meta-directing group. It is seen (92, table 4) that steric hindrance is prominent, as arylation is completely prevented at the ortho sites, and the electrical effect is such that reaction takes place only at the meta position. With phenyl radicals it is seen that there is a greater steric effect with the  $-\text{CCl}_3$  group than with the  $-\text{CF}_3$  group, as would be expected. (This steric effect is also illustrated (*cf.* table 15) by the data for isopropylbenzene (168) and *tert*-butylbenzene.) Finally, the radicals  $\text{C}_6\text{H}_5$ , *p*- $\text{ClC}_6\text{H}_4$ , and *p*- $\text{NO}_2\text{C}_6\text{H}_4$  present a sequence of increasing electrophilic nature, and hence would be expected to show increasing meta substitution of  $\text{C}_6\text{H}_5\text{CCl}_3$ , assuming steric hindrance to remain constant in the series; this is strikingly demonstrated by the reported data (see table 4 of reference 92).

For substitution in nitrobenzene the influence of the attacking radical was demonstrated by Hey, Nechvatal, and Robinson (164), who showed that while reaction with *p*-tolyl radicals gave rise to a mixture containing 9 per cent of 4'-methyl-3-nitrobiphenyl, this proportion was increased to about 12 per cent when *p*-bromophenyl radicals were used. These tendencies, which are in agreement with the theory of substituted radicals which has been developed, are confirmed by more recent measures of the ratio of isomers obtained in the arylation of nitrobenzene. Thus, it has been shown (146) that with *p*-nitrophenyl radicals the isomers are formed in the proportions ortho 57.5 per cent, meta 15.2 per cent, para 27.3 per cent. With *p*-bromophenyl radicals (55), the ratio of isomers is ortho 58.8 per cent, meta 13.4 per cent, para 27.8 per cent.

For aryl radicals other than phenyl the overall reaction is determined, therefore, by the relative electron charge configurations of both the reactants, as well as the corresponding homolytic reactivities of the individual solvent positions. In comparison of theoretical predictions based on quantum-mechanical calculations with experimental data for homolytic reactions, the only investigations which have any significance are those in which nearly neutral radicals participate, *i.e.*, the phenylation reactions. Even here, some electrical effects may be present (251, 281), but it is the best case that can be treated experimentally. It is regrettable that simple alkyl radicals have not so far proved amenable to quantitative investigations of this type, as these, too, should be almost neutral. Most other radicals, such as trichloromethyl and other substituted alkyl radicals and hydroxyl radicals, must be highly polarized, and hence entirely unsuitable for the determination of the factors influencing the reactions of neutral free radicals.

#### D. HYDROXYLATION

The interpretation of the results of hydroxylation experiments (67, 203, 213-215, 231, 261-266), which are very complicated and somewhat uncertain, is extremely difficult (288). The isomer ratios obtained in apparent substitution of aromatic compounds seem to be dependent on experimental conditions, *e.g.*, the pH of the solution, and often the simple monohydroxylated compound comprises only a minor portion of the total product (213, 214). The relevant isomer ratios are given in tables 8 and 9 of the accompanying paper (92).

TABLE 18\*

*Partial and total relative rate factors for phenylation at 80°C.*

Aromatic Compound	$\frac{x}{H}k_o$ or $\frac{x}{H}k_\alpha$	$\frac{x}{H}k_m$ or $\frac{x}{H}k_\beta$	$\frac{x}{H}k_p$ or $\frac{x}{H}k_\gamma$	$\frac{x}{H}K$
C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub> .....	6.86	1.20	7.68	4.00
C <sub>6</sub> H <sub>5</sub> N.....	1.81	0.87	0.87	1.04
C <sub>6</sub> H <sub>5</sub> F.....	2.19	1.50	1.23	1.35
C <sub>6</sub> H <sub>5</sub> Cl.....	2.60	1.12	1.19	1.44
C <sub>6</sub> H <sub>5</sub> Br.....	2.09	1.80	1.83	1.75
C <sub>6</sub> H <sub>5</sub> I.....	2.08	1.71	1.80	1.80
C <sub>6</sub> H <sub>5</sub> CN.....	6.48	1.08	6.48	3.60
C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub> .....	3.5	1.0	1.4	1.68
C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> .....	1.97	1.04	1.41	1.24
C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> - <i>i</i> .....	0.81	1.1	1.41	0.87
C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub> - <i>t</i> .....	0.63	1.28	1.41	0.87
C <sub>6</sub> H <sub>5</sub> C <sub>6</sub> H <sub>5</sub> .....	2.91	1.38	3.42	4.00
C <sub>7</sub> H <sub>8</sub> .....	29.90	5.48	—	23.90
C <sub>6</sub> H <sub>5</sub> SO <sub>2</sub> CH <sub>3</sub> .....	2.39	1.49	1.26	1.50
C <sub>6</sub> H <sub>5</sub> CF <sub>3</sub> .....	0.59	1.2	2.4	0.99
C <sub>6</sub> H <sub>5</sub> Si(CH <sub>3</sub> ) <sub>3</sub> .....	0.99	1.4	1.5	1.06

\* Competitive results from table 8; ratios of isomers from table 15.

## VII. PARTIAL RATE FACTORS FOR PHENYLATION AT 80°C.

## A. RESULTS AND DISCUSSION

1. In the preceding sections the nature of the recent experimental work has been discussed. It has been found possible to determine the relative rates of phenylation of certain molecules C<sub>6</sub>H<sub>5</sub>X, and the proportions in which the corresponding isomers XC<sub>6</sub>H<sub>4</sub>C<sub>6</sub>H<sub>5</sub> have been formed at the reaction temperature of 80°C. From these data the partial rate factors are evaluated (see Sections IV,B,6, V, and VI). Table 18 presents the results; the reader is referred to the immediately preceding sections for the arguments whereby the validities of the experiments are considered.

For all the cases investigated, except where steric hindrance is important (see Section VII,A,4), it is seen that the introduction of the X group has activated the nucleus for homolytic substitution of the near-neutral phenyl radical. The ortho and para positions display the effect better than the meta position, which is relatively unaffected by the presence of the directing group X and is, therefore, in all cases, similar in reactivity to any position in benzene. These results indicate the reason why the meta isomer was rarely observed in the early work (see table 3). It is seen that this isomer does, in fact, form a considerable fraction of the product, even when electrical and steric hindrance effects are absent (see Section VI,C), but not enough to rival the production of ortho isomer. The para isomer is generally by far the least soluble and hence is very easily isolated.

The very large proportion of ortho isomer (*cf.* tables 15 and 18) is in complete contrast to the situation as known before 1951, when only on careful investigation (*cf.* table 3) is the isomer shown to be present in any significant quantity, and then only in two or three cases. Examination of the data given in tables 5 and 7 reveals that, with one or two exceptions, the high values of  $\frac{x}{H}k_o$  are predicted by both theoretical methods. However, Rondestvedt and Blanchard

(251) have suggested an alternative explanation based on the inductive effects of the groups X. These workers postulated that in the formation of the preliminary  $\pi$ -complex which they envisage as the precursor of the  $\sigma$ -complex (*cf.* Section V,D), the phenyl radical tends to become associated with sites of high electron density, i.e., that the phenyl radical is somewhat electrophilic. In compounds  $C_6H_5X$ , in which X is a  $-I$  group (e.g.,  $C_6H_5NO_2$ ), the greatest electron density is at the substituent itself, and if the postulate is accepted, the incoming radical becomes associated in the  $\pi$ -complex largely with the substituent X, giving a complex which can most readily rearrange to the ortho  $\sigma$ -complex. With  $+I$  groups (e.g.,  $CH_3$ ), the greatest electron density is thought to be at the ortho position, and it is considered that, for this reason, the ortho  $\sigma$ -complex is the most easily formed in these compounds. The low value of  $\frac{x}{H}k_o$  for benzotrifluoride (*cf.* table 18) is thought to be due to the fact that in this compound the inductive effect of the trifluoromethyl group is considered to cause the electron densities to decrease in the order  $p > m > o$ . Steric hindrance cannot be responsible in this case, since the trifluoromethyl group is of the same size as the methyl group.

Closer examination, however, reveals certain inconsistencies in this explanation. Thus with  $-I$  directing groups not only is a negative charge induced on the group itself, but also a positive charge is induced at the ortho position, and this must tend to deter the electrophilic phenyl radical from attacking this position. Again, with  $+I$  directing groups, the positive charge is induced on the group X, and a corresponding deterrence must exist towards association of the radical with this position. Thus it is implicit in Rondestvedt and Blanchard's explanation that with  $-I$  directing groups the charge induced at the directing group is more important than that induced at the ortho position, while with  $+I$  groups, the charge induced at the ortho position is more important than that induced at the substituent itself. This is acceptable only if the  $\pm I$  effects of the directing groups are largely inductomeric in nature, i.e., they are called into play by the approaching reagent and can assist, but never hinder, reaction (*cf.* Section II,C,1).

2. The magnitude of the  $\frac{x}{H}K$  value for phenylation should be compared with that for heterolytic nitration (*cf.* table 1). It is seen that the term never assumes the proportion observed in nitration, i.e., powers of ten are absent. This indicates the absence of strong Coulombic effects in the phenylation reaction.

3. The good agreement between the predicted  $\frac{x}{H}k$  values of tables 5 and 7 and the above experimental ones (table 18) is open to the criticism that, as free-radical  $\frac{x}{H}k$  values differ only slightly from unity, any set of parameters may be used in the evaluation of the predicted data. This may be true, but it is equally true that this comment is somewhat out of context. The most striking thing about these predictions is the fact that they were largely made at a time when no experimental evidence whatever was available for the rates of homolytic substitution in the molecule  $C_6H_5X$  (see Section IV). The parameters were chosen to describe qualitatively the ionic forms of substitution, and the results for homolytic reaction were purely supplementary. Now, experiment has shown the prediction to be correct to a high degree of accuracy in suggesting the activating

influence of group X in all cases. This remarkable correspondence between molecular orbital theory and experiment has also been noted recently in connection with the Diels–Alder (34–41) reaction and methylation experiments (71). It would be expected that relative reactivities between different positions within a given molecule might be qualitatively assessed, but to be able to predict the actual rate of reaction of any position relative to a standard is a noteworthy achievement, particularly in view of the number of assumptions that it is necessary to accept (*cf.* Section IV).

4. (i) The comparison of the actual with the calculated partial rate factors is worthy of comment. For the case of chlorobenzene Wheland (290) found considerable difficulty in choosing parameters which would correctly predict ortho–para nitration in a deactivated nucleus. If it is assumed that this correctly limits the numerical values of the parameters, then a better correspondence in the homolytic figures (tables 7 and 18), would be expected.

(ii) The experimental results for pyridine seem somewhat low; this may be due to the fact that too low a value for  $\frac{x}{H}K$  has been taken (*cf.* columns (1) and (2) of table 8). It is apparent that there is not much activation in the molecule.

(iii) The experimental values for nitrobenzene show some differences from the calculated figures, but these could be minimized by correct choice of parameters and/or more accurate determination of the isomer percentages (Section VI,A).

(iv) Naphthalene presents the most interesting result. Both theoretically and experimentally this case must be further examined. It is clear, from all sides, that the molecule is very reactive. The formation of unexpected products in the phenylation reaction (1) (*cf.* Section V,B,8) casts some doubt on the meaning of the experimental results. Theoretically, the free-valence treatment (*cf.* table 5) predicts rate values of the correct magnitude, whereas that of Wheland (table 7) gives values much too large (this also applies to the prediction of electrophilic reactivity by this method; *cf.* table 6). These anomalies might be due to the neglect in the mathematical treatment of the differences between the C<sub>9</sub> and C<sub>10</sub> atoms and the other carbons (*cf.* Sections IV,C, D, and E).

(v) The case of *tert*-butyl is especially interesting (50). Earlier it was shown that *p*-xylene, in undergoing side-chain attack, became less reactive in nuclear phenylation when compared with benzene (see Sections V,B,6 and VII,B,2). The single *tert*-butyl group shows the same effect but for entirely different reasons. Firstly, since the hyperconjugation of the *tert*-butyl group with the ring is very small, the activating effect of this group for homolytic substitution should likewise be small (*cf.* Sections IV,C,4 and IV,D,1), and the total relative rate would be expected to be of the order of  ${}^t\text{-C}_4\frac{x}{H}K \sim 0.9\text{--}1.1$ . Secondly, no side-chain attack of the kind observed with the other alkylbenzenes can take place (139, 204), since there are no  $\alpha$ -hydrogen atoms and benzyl-type radicals cannot be formed under any circumstances. Thus, the competitive experiments are directly valid and there is no need, as shown experimentally, to correct for this alternative reaction. Lastly, the large size of the *tert*-butyl group might be expected to give rise to a steric effect, which in mainly affecting the generally most reactive ortho positions should cause the total relative rate to decrease. The presence of



TABLE 19  
*Isomer percentages obtained in nitration and phenylation of alkylbenzenes*  
 (31, 50, 168, 196, 240)

Reaction	Isomer	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> C <sub>2</sub> H <sub>5</sub>	C <sub>6</sub> H <sub>5</sub> C <sub>3</sub> H <sub>7-i</sub>	C <sub>6</sub> H <sub>5</sub> C <sub>4</sub> H <sub>9-i</sub>
Nitration	Per cent ortho	57	55	30	11.8
	Per cent meta	3	0	7.7	8.7
	Per cent para	40	45	62.3	79.5
Phenylation	Per cent 2-phenyl	66.5	53	31	24
	Per cent 3-phenyl	19.2	28	42	49
	Per cent 4-phenyl	14.3	19	27	27

these effects has been demonstrated by the fact that substitution in benzene by the ortho *tert*-butyl radical can be effected only with great difficulty, as hydrogen abstraction is the preferred reaction (50). The combination of these processes leads to the observations (*cf.* table 18) that the ortho positions are apparently unreactive for substitution and that the total relative rate is less than unity, i.e.,  ${}^{t\text{-C}_4\text{H}_9\text{K}}_{\text{H}} < 1.0$ .

The effect of steric hindrance is also apparent in the phenylation of phenyl-trimethylsilane (251), though here it is less apparent, owing to the fact that the methyl groups are held further from the ring and consequently exert a smaller steric influence in this compound.

(vi) Similar considerations apply to the case of isopropylbenzene (168, 250) except that, in this case, side-chain attack proceeds to a considerable extent. When due allowance has been made for the side-chain attack it again becomes clear that steric hindrance to substitution at the ortho position results in a relative rate of less than unity (*cf.* table 8). A comparison (table 19) of the isomer percentages for phenylation of the alkylbenzenes with those for nitration of these compounds (31, 196) reveals a striking similarity between the steric effects observed in these reactions. In both reactions the steric effect is absent in toluene and ethylbenzene and important in isopropylbenzene and *tert*-butylbenzene.

5. An important conclusion arising from the agreement between the data of tables 5 and 18 is that there appears to be some support for assuming the value of  $x = 1$  in Section IV,C,5 (equations 46 and 47), i.e., the  $r^{\text{th}}$  atom is completely removed from the  $\pi$ -bonding of the molecule and a covalent bond can be assumed to be formed in the transition complex (figure 2). This also adds weight to the decision to regard the substitution as being effected via an addition process (Sections III, IV, and VI,D).

## B. ADDITIVITY OF ENERGIES OF ACTIVATION

### 1. Experimental verification

In Section IV,B,7 it was shown that experiments made with mono-, di- and trisubstituted benzene would allow, via equations 31, 36, and 37, the individual partial rate factors  $\frac{x}{\text{H}}k_o$ ,  $\frac{x}{\text{H}}k_m$ , and  $\frac{x}{\text{H}}k_p$  to be obtained, provided it was assumed that the energy of activation for phenylation at any position was com-

posed of the summation of the energies dictated by each of the X groups and their relative positions.

Owing to the doubtful validity of the methylbenzene experiments (see Sections V,B,7 and VII,B,2), this series of compounds cannot be used. The chlorobenzene sequence, however, is free from these objections, as far as is known (6), and the  $\frac{X}{H}K$  values recorded in table 8 are substituted into the appropriate equations mentioned above. Unfortunately, no positive root to the derived cubic equation is obtained but, by assuming separate errors of ca. 20 per cent in  $^{s-Cl_3}K$ , 10 per cent in  $^{p-Cl_3}K$ , or 3 per cent in  $\frac{Cl}{H}K$ , or simultaneous smaller errors in each, the curve can be displaced vertically to give a positive root. This is not an unreasonable assumption, since the single error of 3 per cent required in the value of  $\frac{Cl}{H}K$  is within the limits of accuracy of the determination. Solution of the cubic equation then gives:

$$\frac{Cl}{H}k = 2.7; \quad \frac{Cl}{H}k_m = 1.49; \quad \frac{Cl}{H}k_p = 1.05 \quad (58)$$

These results illustrate the fact that small experimental deviations may prevent any answer from being obtained. In the light of the assumptions made, however, the results are good. The figures of equation 58, when compared with the partial rate factors of table 18, suggest that the important assumption, made above, as to the additivity of the energies of activation, is correct (6). This might have been expected by analogy with heterolytic substitution (27, 200, 201, 246). Other methods for checking these conclusions for the homolytic case are available but have not so far been applied.

### 2. Application of principle

If the above conclusion is accepted, the principle of the additivity of the energies of activation may be employed in useful explanation and prediction. If the partial rate factors for groups X and Y are available, then for the molecule  $r\text{-YC}_6\text{H}_4\text{X}$  the reactivity of any position, or the total reactivity, may be obtained by the method described in Section IV.

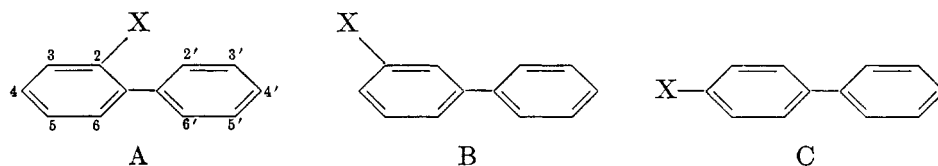
(i) Returning to the methylbenzenes (1) (Section V,B,7), and using this principle in the form of equations 36 and 37 with the  $\frac{CH_3}{H}k_r$  values for toluene from tables 7 and 18, the calculated values for the total relative rates are:

$X = \text{CH}_3$	$p\text{-(CH}_3)_2$	$s\text{-(CH}_3)_2$	}	(59)	
$\frac{X}{H}K = 1.48$	1.44	6.74			value of $\frac{CH_3}{H}k_r$ taken
$\frac{X}{H}K = 1.85$	2.53	11.60			value of $\frac{CH_3}{H}k_r$ taken
				from table 18	

These series should be compared with the observed sequence (equation 56), which makes allowance for side-chain attack. This observed order, if it is a true one, can be explained by the following. It is seen from equation 59 that the methyl group in toluene slightly activates the five nuclear positions and nuclear substitution is statistically favored. Xylene is only slightly more active than toluene, since every position is meta to a methyl group and  $\frac{X}{H}k_m$  values are usually

of the order of unity (*cf.* table 18). Hydrogen removal is encouraged by the methyl groups owing to their size, and since the nucleus is not sufficiently activated, this side-chain attack predominates. In mesitylene, the introduction of the third methyl group has caused the nucleus to become highly reactive as each position is both ortho and para to a methyl group, and direct substitution is again favored but has to compete with side-chain attack (see Section V,B,7). Similar argument is applied to the case of *p*-di-*tert*-butylbenzene (50).

(ii) The above technique may be applied to molecules containing dissimilar directing groups X and Y and is very important in permitting predetermination of experiment. Consider molecules of the type  $r\text{-C}_6\text{H}_5\text{C}_6\text{H}_4\text{X}$ , e.g., the isomeric phenylpyridines or nitrobiphenyls (80). Using the known partial rate factors for chlorobenzene, nitrobenzene, pyridine, and biphenyl (*cf.* table 18), and making the reasonable assumptions given in the footnote to table 20, the figures given in tables 20 and 21 may be evaluated for the reactivities of the isomers shown in formulas A, B, and C:



It is seen that the difference in reactivities of the phenylpyridines is small. Any experiment using a mixture of such compounds, e.g., that which is formed on phenylation (*cf.* table 15: A = 58 per cent, B = 28 per cent, and C = 14 per cent), designed to study whether or not such isomers are selectively removed by further

TABLE 20\*  
Composite partial rate factors for phenylation at 80°C.

X	Isomer A				Isomer B				Isomer C	
	$k_3$	$k_4$	$k_5$	$k_6$	$k_2$	$k_4$	$k_5$	$k_6$	$k_2$ or $k_5$	$k_3$ or $k_6$
Hetero nitrogen .....	2.66	3.03	1.48	2.58	5.51	6.46	1.25	3.07	2.58	2.66
Chlorine .....	3.64	3.81	1.67	3.25	7.54	8.84	1.57	3.45	3.25	3.64
Nitro .....	9.74	4.08	10.75	3.48	20.18	23.66	1.68	22.27	3.48	9.74

\* Assuming that the group  $\text{XC}_6\text{H}_4$ —is similar to an unsubstituted group in its effect on the nucleus to which it is attached, the partial rate factors for positions 2'–6' (formulas A, B, and C above) have the same values as the partial rate factors for these positions in biphenyl (table 18). The data of table 21 may then be obtained by addition.

TABLE 21  
Calculated relative rates of phenylation of isomeric X-biphenyls at 80°C.

X	$\text{XC}_6\text{H}_4\text{K}$ for A	$\text{XC}_6\text{H}_4\text{K}$ for B	$\text{XC}_6\text{H}_4\text{K}$ for C
Hetero nitrogen .....	3.62	4.71	3.75
Chlorine .....	4.06	5.57	4.30
Nitro .....	6.68	13.30	6.57

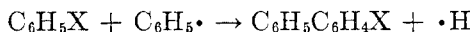
phenylation, must consequently be capable of high accuracy. Thus, the reported work (80) indicating no such effect (see Sections V,A,3, V,B,4, and VI,B), wherein 22 per cent of the original mixture of phenylpyridines was phenylated, should have been capable of working to an accuracy of better than 1.5 per cent on the percentages of isomers A and B if it were to yield the required information. This was not the case, and the experiment is therefore inconclusive. On the other hand, the employment of a similar mixture of nitrobiphenyls, artificially enriched in the meta isomer B, would have allowed an experimental accuracy of 5 per cent, a result which is feasible.

### VIII. CONCLUSIONS

Throughout the previous sections the various conditions upon which the significance of the developed partial rate factors depend have been analyzed and discussed.

The topic of homolytic aromatic substitution is a large one. Theoretical techniques are capable of only very approximate results, and the practical difficulties encountered in experimental work are many and formidable. Owing to the delicate fashion in which the reactions appear to be balanced, such that almost any reaction has some probability of fulfilment, the subject has to be carefully broken down and any discussion carefully qualified.

The competitive method has been used to obtain total relative rate values for phenylation. In certain cases, where steric and other effects become important, it is necessary to declare the results invalid for comparison with mathematical theory, e.g., the methylbenzenes and phenol. The results of different workers are in agreement. From the classification of aromatic solvents into orders of reactivity, it is possible to explain the variation in product quantities and the appearance of reduction products in the mixture. These phenomena concur with the observed kinetics of benzoyl peroxide decomposition. The mechanism of this decomposition is discussed with reference to the nature of the solvent present. Except for specific cases (phenols, amines, methylbenzenes, and anisole), the predominance of the reaction:



as initially suggested by Hey, is shown to be substantiated. Substitution is effected by the radical  $\text{C}_6\text{H}_5\cdot$  itself, probably through an addition mechanism. It is impossible to say whether or not the hydrogen atom is ever free. The alternative reaction involving hydrogen-atom abstraction from the aromatic nucleus occurs only very rarely, but hydrogen-atom removal from a side chain may take place (particularly with phenol and alkylbenzenes), sometimes to the exclusion of the nuclear substitution reaction. The first examples of side-chain attack by aryl radicals in solution are presented.

Together with recent accurate data concerning the proportions in which the isomers are formed in the phenylation of  $\text{C}_6\text{H}_5\text{X}$ , the competitive reaction results allow the partial relative rate factors for phenylation to be derived. These values are probably the nearest that can be obtained to those representing true homo-

lytic attack of a neutral free radical upon the molecule  $C_6H_5X$ . The data presented confirm the existence of homolytic substitution and place the treatment upon a quantitative basis.

A review of the more recent theories of aromatic substitution has shown that the difficulties which these methods encountered were to some extent due to the fact that they had to operate upon experimental data which were representative only of heterolytic reactions. The modifications which have been made, and the new treatments which have been devised in order to describe free-radical phenomena, have been described and presented in a critical manner. Although they were developed at a time when the relevant experimental data were not available, certain of these treatments allow the quantitative behavior of homolytic phenomena to be predicted. These predictions are discussed.

A comparison between the experimental partial relative rate factors for phenylation and those predicted for homolytic substitution shows a high degree of agreement. The evidence is in favor of the formation of a covalent bond in the transition state of the reaction, with the consequent removal of the attacked site from the delocalization area of the solvent molecule. All theories have indicated that, for true free-radical attack, provided complicating effects are absent, the nucleus of  $C_6H_5X$  is always activated relative to benzene, with ortho substitution predominating. This has been verified experimentally by the phenylation experiments, carried out in systems relatively free from any electrical, steric, and other complicating effects. This, therefore, presents a guiding rule for neutral homolytic substitution. Meta-substituted compounds are produced, the position being only slightly more active than any one position in benzene, unless complicating effects are present when meta-substituted compounds may form the majority of the product mixture. The observed activations are compared with those observed in electrophilic reactions and are found to be of a lower order of magnitude.

The radical-environment relationship has been discussed. The consideration of other radicals, i.e., aryl (not phenyl), acyloxy, and hydroxyl, must include a study of the demands of the reagent, for these may determine the form of the reactions with any of the typically aromatic solvents. Electrical effects have been shown to be present, and it is possible to speak of electrophilic and nucleophilic free radicals. Here the effects due to electrical polarization and to the odd electron are superimposed.

The need for much further theoretical and experimental work is apparent and certain lines of research have been suggested in the presentation. A concentration of effort upon reactions of homolytic nature will, undoubtedly, allow theoretical interpretations to be adequately tested. Studies of this nature will permit further investigation of the electrical effects in the substitution and this may, by extrapolation, be related to the case of heterolytic substitution.

While the ultimate goal of investigations of this type must be the complete understanding of the substitution reaction in aromatic systems, it is unlikely that precise prediction of the course of the reaction will become possible, on account of the extreme difficulties of accurate mathematical treatment.

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## IX. REFERENCES

- (1) AUGOOD, D. R.: Ph.D. Thesis, London (1952).
- (2) AUGOOD, D. R., CADOGAN, J. I. G., HEY, D. H. AND WILLIAMS, G. H.: *J. Chem. Soc.* **1953**, 3412.
- (3) AUGOOD, D. R., HEY, D. H., NECHVATAL, A., ROBINSON, T. S., AND WILLIAMS, G. H.: *Research* **4**, 386 (1951).
- (4) AUGOOD, D. R., HEY, D. H., NECHVATAL, A., AND WILLIAMS, G. H.: *Nature* **167**, 725 (1951).
- (5) AUGOOD, D. R., HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1952**, 2094.
- (6) AUGOOD, D. R., HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1953**, 44.
- (7) BACHMANN, W. E. AND HOFMANN, R. A.: *Organic Reactions*, Vol. II, p. 224. John Wiley and Sons, Inc., New York (1944).
- (8) BADGER, G. M.: *Structure and Reactions of Aromatic Compounds*. Cambridge University Press, Cambridge (1954).
- (9) BAMBERGER, E.: *Ber.* **28**, 403 (1895).
- (10) BAMBERGER, E.: *Ber.* **29**, 446 (1896).
- (11) BARTLETT, P. D., AND ALTSCHUL, R.: *J. Am. Chem. Soc.* **67**, 812 (1945).
- (12) BATTEN, J. J., AND MULCAHY, M. F. R.: *Nature* **172**, 72 (1953).
- (13) BAWN, C. E. H., AND MELLISH, S. F.: *Trans. Faraday Soc.* **47**, 1216 (1951).
- (14) BENNETT, G. M., BRAND, J. C. D., JAMES, M. C. D., SAUNDERS, T. G., AND WILLIAMS, G.: *J. Chem. Soc.* **1947**, 474.
- (15) BENNETT, G. M., BRAND, J. C. D., AND WILLIAMS, G.: *J. Chem. Soc.* **1946**, 869.
- (16) BERLINER, E., AND BERLINER, FRANCES J.: *J. Am. Chem. Soc.* **71**, 1195 (1949).
- (17) BERLINER, E., AND BONDUS, FRANCES J.: *J. Am. Chem. Soc.* **68**, 2355 (1946).
- (18) BERLINER, E., AND BONDUS, FRANCES J.: *J. Am. Chem. Soc.* **70**, 854 (1948).
- (19) BERLINER, E., AND MONACK, L. G.: *J. Am. Chem. Soc.* **74**, 1574 (1952).
- (20) BICKEL, A. F., AND KOOYMAN, E. C.: *Rec. trav. chim.* **71**, 1137 (1952).
- (21) BIRD, M. L., AND INGOLD, C. K.: *J. Chem. Soc.* **1938**, 918.
- (22) BLUMQUIST, A. T., AND BUSELLI, A. J.: *J. Am. Chem. Soc.* **73**, 3883 (1951).
- (23) BÖESEKEN, J., AND HERMANS, P. H.: *Ann.* **519**, 133 (1935).
- (24) BOOZER, C. E., AND HAMMOND, G. S.: *J. Am. Chem. Soc.* **76**, 3861 (1954).
- (25) BOVEY, F. A., AND KOLTHOFF, I. M.: *Chem. Revs.* **42**, 491 (1948).
- (26) BOWEN, E. J., AND ROHATGI, K. K.: *Discussions Faraday Soc.* **14**, 146 (1953).
- (27) BRADFIELD, A. E., AND JONES, B.: *Trans. Faraday Soc.* **37**, 726 (1941).
- (28) BRANCH, S. J., AND JONES, B.: *Research* **5**, 334 (1952).
- (29) BRAUDE, E. A.: *Ann. Repts. on Progress Chem. (Chem. Soc. London)*, **46**, 114 (1949).
- (30) BROWN, D. J.: *J. Am. Chem. Soc.* **62**, 2657 (1940).
- (31) BROWN, H. C., AND BONNER, W. H.: *J. Am. Chem. Soc.* **76**, 605 (1954).
- (32) BROWN, H. C., AND NELSON, K. L.: *J. Am. Chem. Soc.* **73**, 5605 (1951).
- (33) BROWN, R. D.: *J. Am. Chem. Soc.* **70**, 1208 (1948).
- (34) BROWN, R. D.: *J. Chem. Soc.* **1950**, 691.
- (35) BROWN, R. D.: *J. Chem. Soc.* **1950**, 2730.
- (36) BROWN, R. D.: *J. Chem. Soc.* **1950**, 3249.
- (37) BROWN, R. D.: *J. Chem. Soc.* **1951**, 1612.
- (38) BROWN, R. D.: *J. Chem. Soc.* **1951**, 1950.
- (39) BROWN, R. D.: *J. Chem. Soc.* **1951**, 3129.
- (40) BROWN, R. D.: *J. Chem. Soc.* **1952**, 2229.
- (41) BROWN, R. D.: *Quart. Revs.* **6**, 63 (1952).
- (42) BUNNETT, J. F., DRAPER, F., RYASON, P. R., NOBLE, P., TONKYN, R. G., AND ZAHLER, R. E.: *J. Am. Chem. Soc.* **76**, 4525 (1954).

- (43) BUNNETT, J. F., AND ZAHLER, R. E.: *Chem. Revs.* **49**, 273 (1951).
- (44) BURKITT, F. H., COULSON, C. A., AND LONGUET-HIGGINS, H. C.: *Trans. Faraday Soc.* **47**, 553 (1951).
- (45) BUTTERWORTH, E. C., HEILBRON, I. M., AND HEY, D. H.: *J. Chem. Soc.* **1940**, 355.
- (46) BUTTERWORTH, E. C., HEILBRON, I. M., HEY, D. H., AND WILKINSON, R.: *J. Chem. Soc.* **1938**, 1386.
- (47) BUTTERWORTH, E. C., AND HEY, D. H.: *J. Chem. Soc.* **1938**, 116.
- (48) BUU-HOI, N. P., DAUDEL, P., DAUDEL, R., AND MARTIN, M.: *Bull. soc. chim. France* **15**, 1202 (1948).
- (49) CADOGAN, J. I. G., HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1954**, 794.
- (50) CADOGAN, J. I. G., HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1954**, 3352.
- (51) CADOGAN, J. I. G., HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1955**, 1425.
- (52) CASE, F. H.: *J. Am. Chem. Soc.* **60**, 424 (1938).
- (53) CASS, W. E.: *J. Am. Chem. Soc.* **68**, 1976 (1946).
- (54) CHALVET, O.: *Bull. soc. chim. France* **17**, 66 (1950).
- (55) CHANG SHIH, HEY, D. H., AND WILLIAMS, G. H.: To be published.
- (56) CHATTERJEE, N.: *J. Indian Chem. Soc.* **12**, 410 (1935).
- (57) CHATTERJEE, N.: *J. Indian Chem. Soc.* **12**, 690 (1935).
- (58) COHEN, M. D., LEFFLER, J. E., AND BARBATO, L. M.: *J. Am. Chem. Soc.* **76**, 4169 (1954).
- (59) COHEN, S. G.: *J. Polymer Sci.* **2**, 511 (1947).
- (60) COHN, H., HUGHES, E. D., JONES, M. H., AND PEELING, M. G.: *Nature* **169**, 291 (1952).
- (61) CONDON, F. E.: *J. Am. Chem. Soc.* **70**, 1963 (1948).
- (62) CONDON, F. E.: *J. Am. Chem. Soc.* **74**, 2528 (1952).
- (63) COOPER, W.: *J. Chem. Soc.* **1951**, 3106.
- (64) CORSE, W. M., NORRIS, J. F., AND MACINTYRE, B. G.: *Am. Chem. J.* **29**, 121 (1903).
- (65) COSGROVE, S. L., AND WATERS, W. A.: *J. Chem. Soc.* **1949**, 3189.
- (66) COSGROVE, S. L., AND WATERS, W. A.: *J. Chem. Soc.* **1951**, 388.
- (67) COSGROVE, S. L., AND WATERS, W. H.: *J. Chem. Soc.* **1951**, 1726.
- (68) COULSON, C. A.: *Trans. Faraday Soc.* **42**, 265 (1946).
- (69) COULSON, C. A.: *Discussions Faraday Soc.* **2**, 9 (1947).
- (70) COULSON, C. A.: *Research* **4**, 307 (1951).
- (71) COULSON, C. A.: *J. Chem. Soc.* **1955**, 1435.
- (72) COULSON, C. A., AND DEWAR, M. J. S.: *Discussions Faraday Soc.* **2**, 54 (1947).
- (73) COULSON, C. A., AND LONGUET-HIGGINS, H. C.: *Proc. Roy. Soc. (London)* **192A**, 16 (1947).
- (74) COULSON, C. A., AND LONGUET-HIGGINS, H. C.: *Rev. sci.* **85**, 929 (1947).
- (75) COULSON, C. A., AND LONGUET-HIGGINS, H. C.: *Trans. Faraday Soc.* **43**, 87 (1947).
- (76) COULSON, C. A., AND LONGUET-HIGGINS, H. C.: *J. chim. phys.* **45**, 243 (1948).
- (77) CRAWFORD, V. A., AND COULSON, C. A.: *J. Chem. Soc.* **1948**, 1990.
- (78) CUTHBERTSON, A. C., MCCLURE, J. H., AND ROBERTSON, R. E.: *Can. J. Research* **20B**, 103 (1942).
- (79) DANNLEY, R. L., AND GIPPIN, M.: *J. Am. Chem. Soc.* **74**, 332 (1952).
- (80) DANNLEY, R. L., AND GREGG, E. C.: *J. Am. Chem. Soc.* **76**, 2997 (1954).
- (81) DANNLEY, R. L., GREGG, E. C., PHELPS, R. E., AND COLEMAN, C. B.: *J. Am. Chem. Soc.* **76**, 445 (1954).
- (82) DANNLEY, R. L., AND STERNFELD, M.: *J. Am. Chem. Soc.* **76**, 4543 (1954).
- (83) DANNLEY, R. L., AND ZAREMSKY, B.: Abstracts of Papers Presented at the 124th Meeting of the American Chemical Society, Chicago, Illinois, September, 1953, p. 36-O.
- (84) DANNLEY, R. L., AND ZAREMSKY, B.: *J. Am. Chem. Soc.* **77**, 1588 (1955).
- (85) DAUDEL, P., AND DAUDEL, R.: *J. Chem. Phys.* **16**, 639 (1948).
- (86) DAUDEL, R., AND PULLMAN, A.: *Compt. rend.* **220**, 888 (1945).
- (87) DAUDEL, R., AND PULLMAN, A.: *Compt. rend.* **222**, 663 (1946).

- (88) DAUDEL, R., AND VROELANT, C.: Bull. soc. chim. France **16**, 217 (1949).
- (89) DAVIS, P., EVANS, M. G., AND HIGGINSON, W. C. E.: J. Chem. Soc. **1951**, 2563.
- (90) DERBYSHIRE, D. H., AND WATERS, W. A.: J. Chem. Soc. **1951**, 73.
- (91) DERBYSHIRE, D. H., AND WATERS, W. A.: J. Chem. Soc. **1951**, 564.
- (92) DERMER, O. C., AND EDMISON, M. T.: Chem. Revs. **57**, 77 (1957).
- (93) DE TAR, D. F.: J. Am. Chem. Soc. **72**, 1028 (1950).
- (94) DE TAR, D. F., AND HOWARD, J. C.: J. Am. Chem. Soc. **77**, 4393 (1955).
- (95) DE TAR, D. F., AND RELYEA, D. I.: J. Am. Chem. Soc. **76**, 1202 (1954).
- (96) DE TAR, D. F., AND SAGMANLI, S. V.: J. Am. Chem. Soc. **72**, 965 (1950).
- (97) DE TAR, D. F., AND SCHIEFELE, H. J.: J. Am. Chem. Soc. **73**, 1442 (1951).
- (98) DEWAR, M. J. S.: J. Chem. Soc. **1949**, 463.
- (99) DEWAR, M. J. S.: Ann. Repts. on Progress Chem. (Chem. Soc. London) **48**, 112 (1951).
- (100) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3341 (1952).
- (101) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3345 (1952).
- (102) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3351 (1952).
- (103) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3353 (1952).
- (104) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3355 (1952).
- (105) DEWAR, M. J. S.: J. Am. Chem. Soc. **74**, 3357 (1952).
- (106) DIETRICH, W.: Helv. Chim. Acta **8**, 149 (1925).
- (107) DRESEL, E., AND HINSHELWOOD, C. N.: J. Chem. Soc. **1944**, 649.
- (108) DUNSTAN, W. J., AND HUGHES, G. K.: J. Proc. Roy. Soc. N. S. Wales **80**, 77 (1946).
- (109) EDWARDS, F. G., AND MAYO, F. R.: J. Am. Chem. Soc. **70**, 1265 (1950).
- (110) ELKS, J., HAWORTH, J. W., AND HEY, D. H.: J. Chem. Soc. **1940**, 1284.
- (111) ELKS, J., AND HEY, D. H.: J. Chem. Soc. **1943**, 441.
- (112) ERLNMEYER, H., AND SCHOENAUER, W.: Helv. Chim. Acta **19**, 338 (1936).
- (113) FERGUSON, L. N.: Chem. Revs. **50**, 47 (1952).
- (114) FICHTER, F., AND STENZL, H.: Helv. Chim. Acta **22**, 970 (1939).
- (115) FIESER, L. F., CLAPP, R. C., AND DAUDT, W. H.: J. Am. Chem. Soc. **64**, 2052 (1942).
- (116) FRANCE, H., HEILBRON, I. M., AND HEY, D. H.: J. Chem. Soc. **1938**, 1364.
- (117) FRANCE, H., HEILBRON, I. M., AND HEY, D. H.: J. Chem. Soc. **1939**, 1283.
- (118) FUKUI, K., YONEZAWA, T., NAGATA, C., AND SHINGU, H.: J. Chem. Phys. **22**, 1433 (1954).
- (119) FUKUI, K., YONEZAWA, T., AND SHINGU, H.: J. Chem. Phys. **20**, 722 (1952).
- (120) GAMBARJAN, S.: Ber. **58B**, 1775 (1925).
- (121) GAMBARJAN, S.: J. Gen. Chem. (U.S.S.R.) **3**, 222 (1933).
- (122) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 285 (1925).
- (123) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 476 (1925).
- (124) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 479 (1925).
- (125) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 764 (1925).
- (126) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 765 (1925).
- (127) GELISSEN, H., AND HERMANS, P. H.: Ber. **58**, 770 (1925).
- (128) GELISSEN, H., AND HERMANS, P. H.: Ber. **59**, 63 (1926).
- (129) GELISSEN, H., AND HERMANS, P. H.: Ber. **59**, 662 (1926).
- (130) GLASSTONE, S., LAIDLER, K. J., AND EYRING, H.: *The Theory of Rate Processes*. McGraw-Hill Book Company, Inc., New York (1941).
- (131) GOLDSCHMIDT, S.: Ber. **87**, 956 (1954).
- (132) GOMBERG, M.: Ber. **33**, 3150 (1900).
- (133) GOMBERG, M., AND BACHMANN, W. E.: J. Am. Chem. Soc. **46**, 2339 (1924).
- (134) GOMBERG, M., AND PERNERT, J. C.: J. Am. Chem. Soc. **48**, 1372 (1926).
- (135) GRAEBE, C., AND SCHESTAKOW, P.: Ann. **284**, 306 (1895).
- (136) GREENWOOD, H. H.: Trans. Faraday Soc. **48**, 585 (1952).
- (137) GREENWOOD, H. H.: Trans. Faraday Soc. **48**, 677 (1952).
- (138) GREENWOOD, H. H.: J. Am. Chem. Soc. **77**, 2055 (1955).
- (139) GREGG, R. A., AND MAYO, F. R.: Discussions Faraday Soc. **2**, 328 (1947).



- (140) GRIEVE, W. S. M., AND HEY, D. H.: *J. Chem. Soc.* **1932**, 1888.  
(141) GRIEVE, W. S. M., AND HEY, D. H.: *J. Chem. Soc.* **1934**, 1797.  
(142) GRIEVE, W. S. M., AND HEY, D. H.: *J. Chem. Soc.* **1938**, 108.  
(143) GYOERFFY, M. E.: *Compt. rend.* **230**, 2106 (1950).  
(144) HALFPENNY, E., AND ROBINSON, P. L.: *J. Chem. Soc.* **1952**, 928.  
(145) HALFPENNY, E., AND ROBINSON, P. L.: *J. Chem. Soc.* **1952**, 939.  
(146) HAMBLING, J. K., HEY, D. H., AND WILLIAMS, G. H.: To be published.  
(147) HAMMOND, G. S.: *J. Am. Chem. Soc.* **72**, 3737 (1950).  
(148) HAMMOND, G. S., RUDESILL, J. T., AND MODIC, F. T.: *J. Am. Chem. Soc.* **73**, 3929 (1951).  
(149) HARLEY-MASON, J., AND MANN, F. G.: *J. Chem. Soc.* **1940**, 1379.  
(150) HARTMAN, P. F., SELLERS, H. G., AND TURNBULL, D.: *J. Am. Chem. Soc.* **69**, 2416 (1947).  
(151) HAWORTH, J. W., HEILBRON, I. M., AND HEY, D. H.: *J. Chem. Soc.* **1940**, 349.  
(152) HAWORTH, J. W., HEILBRON, I. M., AND HEY, D. H.: *J. Chem. Soc.* **1940**, 372.  
(153) HAWORTH, J. W., AND HEY, D. H.: *J. Chem. Soc.* **1940**, 361.  
(154) HEACOCK, R. A., AND HEY, D. H.: *J. Chem. Soc.* **1952**, 1508.  
(155) HEACOCK, R. A., AND HEY, D. H.: *J. Chem. Soc.* **1952**, 4059.  
(156) HEILBRON, I. M., HEY, D. H., AND LAMBERT, A.: *J. Chem. Soc.* **1940**, 1279.  
(157) HEILBRON, I. M., HEY, D. H., AND WILKINSON, R.: *J. Chem. Soc.* **1938**, 113.  
(158) HEY, D. H.: *J. Chem. Soc.* **1932**, 2636.  
(159) HEY, D. H.: *J. Chem. Soc.* **1934**, 1966.  
(160) HEY, D. H.: *Ann. Repts. on Progress Chem. (Chem. Soc. London)* **45**, 139 (1948).  
(161) HEY, D. H.: *J. Chem. Soc.* **1952**, 1974.  
(162) HEY, D. H., AND LAWTON, S. E.: *J. Chem. Soc.* **1940**, 374.  
(163) HEY, D. H., AND MULLEY, R. D.: *J. Chem. Soc.* **1952**, 2276.  
(164) HEY, D. H., NECHVATAL, A., AND ROBINSON, T. S.: *J. Chem. Soc.* **1951**, 892.  
(165) HEY, D. H., AND OSBOND, J. M.: *J. Chem. Soc.* **1949**, 3164.  
(166) HEY, D. H., AND OSBOND, J. M.: *J. Chem. Soc.* **1949**, 3172.  
(167) HEY, D. H., PENGILLY, B. W., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1955**, 6.  
(168) HEY, D. H., PENGILLY, B. W., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1956**, 1463.  
(169) HEY, D. H., STIRLING, C. J. M., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1954**, 2747.  
(170) HEY, D. H., STIRLING, C. J. M., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1956**, 1475.  
(171) HEY, D. H., STUART-WEBB, J., AND WILLIAMS, G. H.: *Research* **4**, 385 (1951).  
(172) HEY, D. H., STUART-WEBB, J., AND WILLIAMS, G. H.: *J. Chem. Soc.* **1952**, 4657.  
(173) HEY, D. H., AND WALKER, E. W.: *J. Chem. Soc.* **1948**, 2213.  
(174) HEY, D. H., AND WATERS, W. A.: *Chem. Revs.* **21**, 169 (1937).  
(175) HEY, D. H., AND WATERS, W. A.: *J. Chem. Soc.* **1948**, 882.  
(176) HEY, D. H., AND WILLIAMS, G. H.: *Discussions Faraday Soc.* **14**, 216 (1952).  
(177) HEY, D. H., AND WILLIAMS, G. H.: *J. Chem. Phys.* **23**, 757 (1955).  
(178) HIRSCH, R.: *Ber.* **23**, 3705 (1890).  
(179) HIRSCH, R.: *Ber.* **25**, 1973 (1892).  
(180) HODGSON, H. H.: *J. Chem. Soc.* **1948**, 348.  
(181) HODGSON, H. H., AND MARSDEN, E.: *J. Chem. Soc.* **1940**, 208.  
(182) HOLLEMAN, A. F.: *Chem. Revs.* **1**, 200 (1925).  
(183) HORNER, L., AND STÖHR, H.: *Ber.* **86**, 1073 (1953).  
(184) HOWARD, J. C.: Ph.D. Thesis, Cornell University, Ithaca, New York (1954).  
(185) HUGHES, E. D., INGOLD, C. K., AND REED, R. I.: *J. Chem. Soc.* **1950**, 2400.  
(186) HUISGEN, R.: Private communication.  
(187) HUISGEN, R.: *Ann.* **573**, 163 (1951).  
(188) HUISGEN, R.: *Ann.* **574**, 171 (1951).  
(189) HUISGEN, R.: *Ann.* **574**, 184 (1951).  
(190) HUISGEN, R., AND HORELD, G.: *Ann.* **562**, 137 (1949).  
(191) HUISGEN, R. AND NAKATEN, H.: *Ann.* **574**, 181 (1951).

- (192) HUISGEN, R., AND SORGE, G.: *Ann.* **566**, 162 (1950).  
(193) HUNTRESS, E. H., AND SEIKEL, M. K.: *J. Am. Chem. Soc.* **61**, 1066 (1939).  
(194) INGOLD, C. K.: *Chem. Revs.* **15**, 225 (1934).  
(195) INGOLD, C. K.: *Trans. Faraday Soc.* **34**, 227 (1938).  
(196) INGOLD, C. K.: *Structure and Mechanism in Organic Chemistry*, p. 258. Cornell University Press, Ithaca, New York (1953).  
(197) INGOLD, C. K., LAPWORTH, A., ROTHSTEIN, E., AND WARD, D.: *J. Chem. Soc.* **1939**, 1959.  
(198) INGOLD, C. K., AND SMITH, M. S.: *J. Chem. Soc.* **1938**, 905.  
(199) JAQUISS, H. T., AND SZWARC, M.: *Nature* **170**, 312 (1952).  
(200) JONES, B.: *J. Chem. Soc.* **1942**, 418.  
(201) JONES, B.: *J. Chem. Soc.* **1942**, 676.  
(202) KLEGL, A., AND HUBER, H.: *Ber.* **53**, 1646 (1920).  
(203) KONECNY, J. O.: *J. Am. Chem. Soc.* **76**, 4993 (1954).  
(204) KOOYMAN, E. C.: *Discussions Faraday Soc.* **10**, 163 (1951).  
(205) KOOYMAN, E. C., AND FARENHORST, E.: *Nature* **169**, 153 (1952).  
(206) KOOYMAN, E. C., AND FARENHORST, E.: *Trans. Faraday Soc.* **49**, 58 (1953).  
(207) KUHLING, O.: *Ber.* **28**, 41 (1895).  
(208) KUHLING, O.: *Ber.* **28**, 523 (1895).  
(209) KUHLING, O.: *Ber.* **29**, 165 (1896).  
(210) LEFFLER, J. E.: *J. Am. Chem. Soc.* **72**, 67 (1950).  
(211) LEVY, M., AND SZWARC, M.: *J. Chem. Phys.* **22**, 1621 (1954).  
(212) LIPPMAN, E.: *Monatsh.* **7**, 521 (1886).  
(213) LOEBL, H., STEIN, G., AND WEISS, J.: *J. Chem. Soc.* **1949**, 2074.  
(214) LOEBL, H., STEIN, G., AND WEISS, J.: *J. Chem. Soc.* **1950**, 2704.  
(215) LOEBL, H., STEIN, G., AND WEISS, J.: *J. Chem. Soc.* **1951**, 405.  
(216) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5243 (1950).  
(217) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5248 (1950).  
(218) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5250 (1950).  
(219) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5252 (1950).  
(220) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5256 (1950).  
(221) MATSEN, F. A.: *J. Am. Chem. Soc.* **72**, 5260 (1950).  
(222) DE LA MARE, P. B. D.: *J. Chem. Soc.* **1949**, 2871.  
(223) DE LA MARE, P. B. D., HUGHES, E. D., AND VERNON, C. A.: *Research* **3**, 192 (1950).  
(224) DE LA MARE, P. B. D., HUGHES, E. D., AND VERNON, C. A.: *Research* **3**, 242 (1950).  
(225) DE LA MARE, P. B. D., AND ROBERTSON, P. W.: *J. Chem. Soc.* **1943**, 279.  
(226) DE LA MARE, P. B. D., ROBERTSON, P. W., AND SWEDLUND, B. E.: *J. Chem. Soc.* **1953**, 782.  
(227) DE LA MARE, P. B. D., AND VERNON, C. A.: *J. Chem. Soc.* **1951**, 1764.  
(228) DE LA MARE, P. B. D., AND WATERS, W. A.: *Ann. Repts. on Progress Chem. (Chem. Soc. London)* **50**, 124 (1953).  
(229) MAYO, F. R.: *Discussions Faraday Soc.* **14**, 250 (1952).  
(230) MELANDER, L.: *Nature* **163**, 599 (1949).  
(231) MERZ, J. H., AND WATERS, W. A.: *J. Chem. Soc.* **1949**, 2427.  
(232) MÖHLAU, R., AND BERGER, R.: *Ber.* **26**, 1196 (1893).  
(233) MÖHLAU, R., AND BERGER, R.: *Ber.* **26**, 1994 (1893).  
(234) MOFFITT, W.: *Trans. Faraday Soc.* **45**, 373 (1949).  
(235) NOZAKI, K., AND BARTLETT, P. D.: *J. Am. Chem. Soc.* **68**, 1686 (1946).  
(236) NOZAKI, K., AND BARTLETT, P. D.: *J. Am. Chem. Soc.* **69**, 2299 (1947).  
(237) OVERHOFF, J., AND TILMAN, G.: *Rec. trav. chim.* **48**, 993 (1929).  
(238) DE PAOLINI, I., AND RIBET, G.: *Gazz. chim. ital.* **62**, 1041 (1932).  
(239) PAULING, L.: *The Nature of the Chemical Bond*. Cornell University Press, Ithaca, New York (1949).

- (240) PENGILLY, B. W.: Ph.D. Thesis, London (1955).
- (241) PRAY, H. A. H.: J. Phys. Chem. **30**, 1417 (1926).
- (242) PRAY, H. A. H.: J. Phys. Chem. **30**, 1477 (1926).
- (243) PRICE, C. C.: Chem. Revs. **29**, 37 (1941).
- (244) PULLMAN, A.: Rev. sci. **84**, 489 (1946).
- (245) PULLMAN, A.: Ann. chim. **12**, 2 (1947).
- (246) REMICK, A. E.: *Electronic Interpretations of Organic Chemistry*, 2nd edition. John Wiley and Sons, Inc., New York (1949).
- (247) ROBERTS, J. D., SANFORD, JANET, K., SIXMA, F. L. T., CERFONTEIN, H., AND ZAGT, R.: J. Am. Chem. Soc. **76**, 4525 (1954).
- (248) ROBERTS, J. S., AND SKINNER, H. A.: Trans. Faraday Soc. **45**, 339 (1949).
- (249) ROITT, I. M., AND WATERS, W. A.: J. Chem. Soc. **1952**, 2695.
- (250) RONDESTVEDT, C. S., AND BLANCHARD, H. S.: J. Am. Chem. Soc. **77**, 1769 (1955).
- (251) RONDESTVEDT, C. S., AND BLANCHARD, H. S.: J. Org. Chem. **21**, 229 (1956).
- (252) RUST, F. F., SEUBOLD, F. H., AND VAUGHAN, W. E.: J. Am. Chem. Soc. **70**, 95 (1948).
- (253) SANDIN, R. B., AND BROWN, R. K.: J. Am. Chem. Soc. **69**, 2253 (1947).
- (254) SANDORFY, C.: Bull. soc. chim. France **16**, 615 (1949).
- (255) SAUNDERS, K. H., AND WATERS, W. A.: J. Chem. Soc. **1946**, 1154.
- (256) SEEL, F.: Z. Naturforsch. **3a**, 35 (1948).
- (257) SEEL, F.: Z. Elektrochem. **52**, 191 (1948).
- (258) SHEPPARD, W. A.: Ph.D. Thesis, Massachusetts Institute of Technology (1954).
- (259) SINCLAIR, V. C., ROBERTSON, J. M., AND MATHIESON, A.: Acta Cryst. **3**, 251 (1952).
- (260) SIXMA, F. L. J.: Rec. trav. chim. **72**, 273 (1953).
- (261) STEIN, G., AND WEISS, J.: J. Chem. Soc. **1949**, 3245.
- (262) STEIN, G., AND WEISS, J.: J. Chem. Soc. **1949**, 3254.
- (263) STEIN, G., AND WEISS, J.: J. Chem. Soc. **1951**, 3275.
- (264) STEIN, G., AND WEISS, J.: J. Chem. Soc. **1951**, 3265.
- (265) STEIN, G., AND WEISS, J.: Nature **161**, 650 (1948).
- (266) STEIN, G., AND WEISS, J.: Nature **166**, 1104 (1950).
- (267) STEPHENSON, O., AND WATERS, W. A.: J. Chem. Soc. **1939**, 1796.
- (268) STOCKMAYER, W. H., AND PEEBLES, L. H.: J. Am. Chem. Soc. **75**, 2278 (1953).
- (269) STUBBS, F. J., WILLIAMS, C. D., AND HINSHELWOOD, C. N.: J. Chem. Soc. **1948**, 1065.
- (270) SVARTHOLM, N.: Arkiv Kemi, Mineral. Geol. **15**(13), 1 (1941).
- (271) SZWARC, M.: Nature **160**, 403 (1947).
- (272) SZWARC, M.: Nature **161**, 890 (1948).
- (273) SZWARC, M.: Discussions Faraday Soc. **14**, 236 (1952).
- (274) SZWARC, M.: Discussions Faraday Soc. **14**, 246 (1952).
- (275) SZWARC, M., LEVY, M., AND STEINBERG, M.: J. Am. Chem. Soc. **76**, 3429 (1954).
- (276) SZWARC, M., AND ROBERTS, J. S.: Trans. Faraday Soc. **46**, 625 (1950).
- (277) SZWARC, M., AND WILLIAMS, D.: J. Chem. Phys. **20**, 1171 (1952).
- (278) VICARY, W. R., AND HINSHELWOOD, C. N.: J. Chem. Soc. **1939**, 1372.
- (279) WADSWORTH, K. D., AND HINSHELWOOD, C. N.: J. Chem. Soc. **1944**, 469.
- (280) WALKER, O. J., AND WILD, G. L. E.: J. Chem. Soc. **1937**, 1132.
- (281) WALSH, A. D.: Discussions Faraday Soc. **2**, 18 (1947).
- (282) WARING, C. E., AND ABRAMS, J. R.: J. Am. Chem. Soc. **63**, 2757 (1941).
- (283) WATERS, W. A.: J. Chem. Soc. **1937**, 113.
- (284) WATERS, W. A.: J. Chem. Soc. **1939**, 864.
- (285) WATERS, W. A.: Trans. Faraday Soc. **37**, 770 (1941).
- (286) WATERS, W. A.: J. Chem. Soc. **1948**, 727.
- (287) WATERS, W. A.: *The Chemistry of Free Radicals*. Oxford University Press, London (1948).
- (288) WATERS, W. A.: Ann. Repts. on Progress Chem. (Chem. Soc. London) **49**, 110 (1952).
- (289) WATERS, W. A.: Discussions Faraday Soc. **14**, 247 (1952).

- (290) WHELAND, G. W.: *J. Am. Chem. Soc.* **64**, 900 (1942).  
(291) WHELAND, G. W.: *The Theory of Resonance*. John Wiley and Sons, Inc., New York (1945).  
(292) WHELAND, G. W., AND PAULING, L.: *J. Am. Chem. Soc.* **57**, 2086 (1935).  
(293) WIELAND, H.: *Ann.* **514**, 145 (1934).  
(294) WIELAND, H., AND MAYER, A.: *Ann.* **551**, 249 (1942).  
(295) WIELAND, H., PLOETZ, T., AND INDEST, H.: *Ann.* **532**, 166 (1937).  
(296) WIELAND, H., POPPER, E., AND SEEFRIED, H.: *Ber.* **55B**, 1816 (1922).  
(297) WIELAND, H., AND RAZUVAEV, G.: *Ann.* **480**, 157 (1930).  
(298) WIELAND, H., SCHAPIRO, S., AND METZGER, H.: *Ann.* **513**, 93 (1934).  
(299) WILSON, R. H.: *J. Appl. Chem.* **3**, 37 (1953).

## ADDENDUM

This review was completed in February, 1956. The articles referred to in references 168 and 170 have since then appeared in print. Other recently published work relevant to the subject is noted below. Some of these papers, especially those of Batten (300) and Batten and Mulcahy (301), are of particular importance to the main discussion.

- (300) BATTEN, J. J.: *J. Chem. Soc.* **1956**, 2959.  
(301) BATTEN, J. J., AND MULCAHY, M. F. R.: *J. Chem. Soc.* **1956**, 2948.  
(302) BAVIN, P. M. G., AND DEWAR, M. J. S.: *J. Chem. Soc.* **1956**, 164.  
(303) BECKWITH, A. L. J., AND WATERS, W. A.: *J. Chem. Soc.* **1956**, 1108.  
(304) BENKESER, R. A., AND GOSNELL, R. B.: Abstracts of Papers Presented at the 130th Meeting of the American Chemical Society, Atlantic City, New Jersey, September 16, 1956, p. O-24.  
(305) BROWN, R. D.: *J. Chem. Soc.* **1956**, 272.  
(306) DANIELS, M., SCHOLES, G., AND WEISS, J.: *J. Chem. Soc.* **1956**, 832.  
(307) DE LA MARE, P. B. D., AND HARVEY, J. T.: *J. Chem. Soc.* **1956**, 36.  
(308) DE TAR, D. F.: *J. Am. Chem. Soc.* **78**, 3911 (1956).  
(309) DE TAR, D. F., AND BALLENTINE, A. R.: *J. Am. Chem. Soc.* **78**, 3916 (1956).  
(310) DE TAR, D. F., AND KWONG, S.: *J. Am. Chem. Soc.* **78**, 3921 (1956).  
(311) DE TAR, D. F., AND TURETZKY, M. N.: *J. Am. Chem. Soc.* **78**, 3925, 3928 (1956).  
(312) DEWAR, M. J. S., AND MOLE, T.: *J. Chem. Soc.* **1956**, 1441.  
(313) DEWAR, M. J. S., MOLE, T., URCH, D. S., AND WARFORD, E. W. T.: *J. Chem. Soc.* **1956**, 3572.  
(314) DEWAR, M. J. S., AND WARFORD, E. W. T.: *J. Chem. Soc.* **1956**, 3570, 3576, 3581.  
(315) IMOTO, M., AND TAKEMOTO, K.: *J. Polymer Sci.* **19**, 579 (1956).  
(316) MCBAY, H. C., AND GROVES, P. T.: *J. Org. Chem.* **21**, 691 (1956).  
(317) MORRISON, R. T., AND SWEENEY, R. F.: Abstracts of Papers Presented at the 130th Meeting of the American Chemical Society, Atlantic City, New Jersey, September 16, 1956, p. O-74.  
(318) SMID, J., AND SZWARC, M.: *J. Am. Chem. Soc.* **78**, 332 (1956).