

Electrophilic Substitution

in Benzenoid Compounds

by R.O.C. Norman and R. Taylor

*Reaction Mechanisms in Organic Chemistry*

# ELECTROPHILIC SUBSTITUTION IN BENZENOID COMPOUNDS

BY

R. O. C. NORMAN, M.A., D.PHIL. (OXFORD), F.R.I.C.

*Fellow of Merton College, Oxford,  
and University Lecturer in Chemistry*

R. TAYLOR, B.SC., PH.D. (LONDON)

*Lecturer in Chemistry, University of Sussex*



ELSEVIER PUBLISHING COMPANY

AMSTERDAM / LONDON / NEW YORK

1965

**ELECTROPHILIC SUBSTITUTION  
IN BENZENOID COMPOUNDS**

## PREFACE

No single field of organic chemistry has received so much attention as that of the electrophilic substitutions of benzene and its derivatives, and in particular this field has long been a testing ground for theories of the mechanisms of organic reactions. It is indeed remarkable how much new material has appeared even during the last ten years and, with it, how theories have elaborated; but both these developments can be traced to the same principal cause: application of some of the newer physico-chemical techniques such as spectrophotometry has enabled aromatic reactivities to be measured with very much greater accuracy than was previously possible, and new data have necessitated refinements to an originally qualitative theory. It seems, therefore, an opportune time to review the subject.

The scope of this book is as follows. The principles of the electronic theory of organic chemistry, insofar as these are relevant to aromatic substitution, are set out in Chapter 1, while Chapter 2 presents a broad overall picture of the mechanistic processes of electrophilic substitution. In Chapters 3–10 individual reactions are described in detail, with especial reference to current theories of mechanism. Newer theories, particularly those concerned with quantitative structure–reactivity relationships, are discussed in Chapter 11. Finally, some of the synthetic applications of the reactions which have been described are briefly outlined in Chapter 12, and here an attempt is made to show how an understanding of mechanism can be usefully applied to the choice of a suitable preparative method.

Undergraduate readers should find that Chapters 1 and 2 provide an introduction to the subject and that any of the Chapters 3–10 can then be understood and read in order to acquire more detailed information. It frequently happens that students are interested in, and stimulated by, the theories of organic chemistry, but that they do not relate these theories to the practice of the subject in the

laboratory, and Chapter 12 has been included in an attempt to prevent this divorce. Research workers should find that Chapters 3-11 provide up-to-date reviews of theory and of specific processes.

Finally, a note of caution. Mechanistic theories in organic chemistry are never cut-and-dried. Repeatedly throughout this book the reader will find the statement that "this mechanism is consistent with the data" and there is little doubt that there is still considerable scope for alteration, modification, and refinement of the present theories. We hope that this will help the undergraduate to develop a critical approach to the subject, and will stimulate the research worker to explore further the many aspects of the subject where problems are apparent.

October, 1964

R. O. C. NORMAN  
R. TAYLOR

ELSEVIER PUBLISHING COMPANY  
335 JAN VAN GALENSTRAAT, P.O. BOX 211, AMSTERDAM

AMERICAN ELSEVIER PUBLISHING COMPANY, INC.  
52 VANDERBILT AVENUE, NEW YORK, N.Y. 10017

ELSEVIER PUBLISHING COMPANY LIMITED  
RIPPLESIDE COMMERCIAL ESTATE  
BARKING, ESSEX

LIBRARY OF CONGRESS CATALOG CARD NUMBER 64-18521

WITH 8 ILLUSTRATIONS AND 62 TABLES

ALL RIGHTS RESERVED  
THIS BOOK OR ANY PART THEREOF MAY NOT BE REPRODUCED  
IN ANY FORM, INCLUDING PHOTOSTATIC OR MICROFILM FORM,  
WITHOUT WRITTEN PERMISSION FROM THE PUBLISHERS

PRINTED IN THE NETHERLANDS

## CONTENTS

PREFACE . . . . .	v
<i>Chapter 1. INTRODUCTION . . . . .</i>	1
1. The structure and stability of benzene . . . . .	1
2. Types of substitution . . . . .	5
3. The polar effects of substituents . . . . .	8
References . . . . .	23
<i>Chapter 2. THE MECHANISM OF ELECTROPHILIC SUBSTITUTION . . . . .</i>	25
1. Reaction of the reagent with the aromatic nucleus . . . . .	25
2. The theory of reaction rates . . . . .	34
3. The effects of substituents . . . . .	42
4. The effect of the reagent on orientation and reactivity . . . . .	56
5. Reversibility and rearrangement . . . . .	57
References . . . . .	58
<i>Chapter 3. REACTIONS INVOLVING ELECTROPHILIC NITROGEN . . . . .</i>	61
1. Nitration . . . . .	61
2. Nitrosation . . . . .	91
3. Diazonium coupling . . . . .	92
References . . . . .	95
<i>Chapter 4. REACTIONS INVOLVING ELECTROPHILIC SULPHUR AND OXYGEN . . . . .</i>	100
1. Sulphonation . . . . .	100
2. Sulphonylation . . . . .	108
3. Hydroxylation . . . . .	110
References . . . . .	117
<i>Chapter 5. ELECTROPHILIC HALOGENATION. . . . .</i>	119
1. Positive halogenation. . . . .	119
2. Molecular halogenation . . . . .	126
3. Substituent effects in halogenation . . . . .	134
References . . . . .	152
<i>Chapter 6. REACTIONS INVOLVING ELECTROPHILIC CARBON . . . . .</i>	156
1. Friedel-Crafts alkylation . . . . .	157
2. Friedel-Crafts acylation . . . . .	174

3. Chloromethylation . . . . .	182
4. The Gattermann-Koch reaction . . . . .	185
5. The Gattermann reaction . . . . .	187
6. The Hoesch reaction . . . . .	188
References . . . . .	190
<i>Chapter 7. ELECTROPHILIC METALLATION . . . . .</i>	194
1. Mercuration . . . . .	194
2. Thallilation . . . . .	199
3. Plumbylation . . . . .	199
References . . . . .	200
<i>Chapter 8. HYDROGEN-EXCHANGE . . . . .</i>	202
1. Mechanism . . . . .	203
2. Substituent effects . . . . .	207
References . . . . .	221
<i>Chapter 9. THE REPLACEMENT OF A SUBSTITUENT BY HYDROGEN . . . . .</i>	225
1. Protodemagnesation . . . . .	226
2. Protodemercuration . . . . .	226
3. Protodeboronation . . . . .	228
4. Protodecarbonylation . . . . .	229
5. Protodealkylation . . . . .	234
6. Protodesilylation . . . . .	234
7. Protodegermylation . . . . .	241
8. Protodestannylation . . . . .	243
9. Protodeplumbylation . . . . .	245
10. Protodesulphonation . . . . .	245
11. Protodehalogenation . . . . .	247
References . . . . .	248
<i>Chapter 10. THE REPLACEMENT OF A SUBSTITUENT, X, BY A SUBSTITUENT Y . . . . .</i>	251
1. Silylidelithiation . . . . .	251
2. Mercuridemercuration . . . . .	252
3. Mercurideboronation . . . . .	253
4. Hydroxydeboronation . . . . .	254
5. Halodeboronation . . . . .	255
6. Nitrodealkylation . . . . .	258
7. Halodealkylation . . . . .	259
8. Nitrodecabonylation . . . . .	260
9. Halodecarbonylation . . . . .	261
10. Mercuridesilylation . . . . .	264
11. Acylidesilylation . . . . .	267
12. Nitrodesilylation . . . . .	268
13. Sulphodesilylation and sulphodegermylation . . . . .	269
14. Halodesilylation . . . . .	270



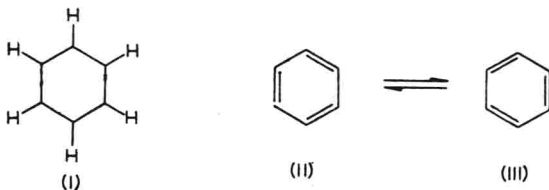
15. Iododestannylation . . . . .	273
16. Nitrodesulphonation . . . . .	276
17. Halodesulphonation . . . . .	277
18. Nitrodehalogenation . . . . .	278
References . . . . .	279
<i>Chapter 11. RECENT DEVELOPMENTS IN THE THEORY OF</i>	
ELECTROPHILIC AROMATIC SUBSTITUTION . . . . .	283
1. Quantitative treatments of structure-reactivity relationships . . . . .	283
2. The ortho:para ratio . . . . .	301
References . . . . .	310
<i>Chapter 12. PREPARATIVE ASPECTS OF ELECTROPHILIC AROMATIC</i>	
SUBSTITUTION . . . . .	313
1. Nuclear reactivities . . . . .	313
2. Techniques for the preparation of derivatives with specific orientations . . . . .	325
References . . . . .	331
SUBJECT INDEX . . . . .	335

## Chapter 1

### INTRODUCTION

#### 1. The Structure and Stability of Benzene

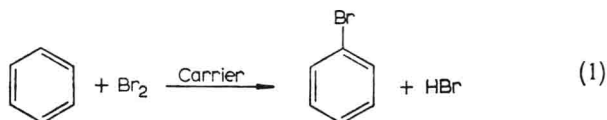
The problems raised by the reactions of benzene and its derivatives have received wide attention ever since the isolation of benzene by MICHAEL FARADAY in 1825. Historically, the first of these problems was the formulation of a satisfactory structure for benzene. Its molecular formula,  $C_6H_6$ , and many of its reactions and those of its derivatives, notably those which demonstrated the equivalence of the six carbon atoms, necessitated a cyclic structure and, furthermore, one possessing six-fold symmetry. A structure based on (I) satisfies these conditions but leaves one valency of each carbon atom to be accounted for; but the attempt to satisfy the classical valency rules, by inserting three double bonds into the ring, as in (II), immediately destroys the six-fold symmetry.



To resolve this difficulty, KÉKULÉ made the brilliant suggestion in 1865 that benzene consists of two structures, (II) and (III), in dynamic equilibrium [1]. Yet this theory, while accounting for the observed structural features of benzene—for example, that there is only one *ortho*-disubstituted compound,  $C_6H_4X_2$ , and not two—could not account for the differences in properties between benzenoid compounds and the formally similar olefins.

This aspect of the problem can be illustrated simply by comparing

the bromination of ethylene with that of benzene. Ethylene reacts by *addition* to give 1,2-dibromoethane, whereas benzene does not react except in the presence of a catalyst (a halogen carrier; Chap. 5) such as iron filings, and in these conditions it undergoes *substitution*, eqn. (1).



The understanding of the comparative unreactivity of benzene and its tendency to undergo substitution rather than addition made little progress until the present theories of molecular structure began to develop from wave-mechanical theory in the nineteen-twenties. It then became clear that the reactivity of benzene and the substitutions which are characteristic of it are determined by the remarkable thermodynamic stability of the benzene nucleus; and this in turn can be understood in terms of the current theories of the structure of benzene. It is therefore necessary briefly to review these theories.

Benzene has a very much greater thermodynamic stability than would be expected for a compound which possesses three C—C, three C=C, and six C—H bonds. Experimentally, the stability is demonstrated by measurements of heats of hydrogenation: that of the double bond in cyclohexene is 28.6 kcal per mole and that of benzene, which contains formally three double bonds, is 49.8 kcal per mole [2]. The latter value is 36 kcal per mole less than three times the former, so the heat of formation of benzene is greater by this amount than the value predicted by comparison with an aliphatic system. Theoretically, the stability of benzene may be understood in terms of both the Molecular Orbital and the Valence Bond theories

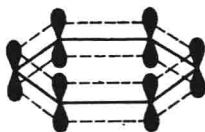
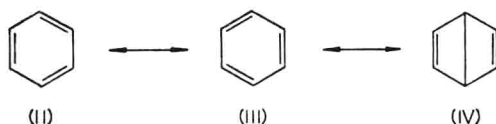


Fig. 1. Diagrammatic representation of *p*-orbital overlap in benzene.

[2,3]. According to the former, benzene consists of a planar ring of six carbon atoms each of which is bonded to two other carbons and to one hydrogen by  $sp^2$ -hybridized bonding orbitals; these three bonds lie in a plane and make angles of  $120^\circ$  with each other, while the fourth valency electron of each carbon is in a p-orbital perpendicular to this plane. Because of the planarity of the molecule, the p-orbitals can overlap laterally (Fig. 1) to give extended molecular orbitals in which the six p-electrons are situated in three bonding pairs. It is the delocalization of these pairs of electrons (which are termed  $\pi$ -electrons) which gives rise to the increased stability of benzene compared with a system containing isolated double bonds. Alternatively, according to the Valence Bond theory, benzene's stability is understood in terms of the concept of resonance. Its structure is represented as a hybrid of several canonical structures of which the two considered by KÉKULÉ, (II) and (III), are the most important and the three Dewar structures of the type (IV) are somewhat less important. It is recognized that benzene is not correctly represented by any one of these structures but rather has a structure "in between" the extremes; the symbol  $\longleftrightarrow$  represents this intermediate character and does not indicate an oscillation or equilibrium between the structures as envisaged by KÉKULÉ. Further, the stability of benzene is greater than that expected for any of the canonical structures.



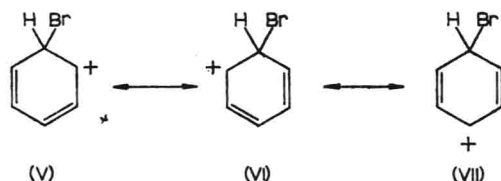
The molecular-orbital description of benzene gives an immediate pictorial idea of the source of the stability of the aromatic ring and is in this sense more satisfying than the valence-bond description. Nevertheless, it is usually easier to describe and discuss the reactions of benzenoid compounds in terms of the Kekulé structures providing it is remembered that one such structure does not give a true picture of the molecule.

The thermodynamic stability possessed by benzene which would not be possessed in the absence of delocalization or resonance is

termed *delocalization energy* or *resonance energy* and may be approximately equated with the experimentally derived value of 36 kcal per mole. It is, however, perhaps better to regard the measured value as the *stabilization energy* of benzene, since it is not necessarily entirely attributable to the phenomenon of resonance [4]. The reactions of benzene can now be examined in the light of the fact that it possesses this considerable stabilization energy.

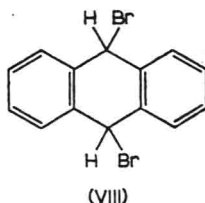
The first consequence is that addition reactions, which result in the loss of this stability, are rendered energetically unfavourable relative to addition to olefins. In fact, the addition of one mole of hydrogen to benzene is endothermic while the reduction of ethylene is exothermic by 32.8 kcal per mole [2]. Substitution in benzene does not, however, result in the loss of the stabilization energy.

The second consequence depends on the fact that the path of lowest energy for substitution in benzene involves first the addition of the reagent to the nucleus, to give, in the case of bromination, an intermediate which is represented as the hybrid of three canonical structures (V-VII) (Chap. 2). Again, therefore, the stabilization



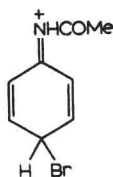
energy of the benzene ring is lost, although the loss is offset to some extent by the resonance energy of the resulting carbonium ion. Nevertheless, this has the effect of causing this addition to benzene to be slower than the corresponding addition to ethylene.

Although this discussion has revealed the cause of the principal



differences between benzene and ethylene, two qualifications are necessary. First, whereas benzene and its monosubstituted derivatives are relatively inert to addition, systems in which two or more benzene rings are fused together are often quite susceptible to addition. For example, anthracene reacts with bromine to give 9,10-dibromo-9,10-dihydroanthracene (VIII) which slowly loses hydrogen bromide at room temperature to form the substitution product, 9-bromoanthracene [5]. The reason is that the stabilization energy of anthracene, 83.5 kcal per mole [2], is much less than three times that of benzene: the adduct (VIII) has a stabilization energy of 72 kcal per mole derived from two benzene rings, so that the loss of stabilization energy is only about 11 kcal per mole, which is much less than that lost on addition to benzene.

Secondly, substituted benzenes are often further substituted very readily: *e.g.*, acetanilide reacts with bromine to form mainly *p*-bromoacetanilide in the absence of a halogen carrier, and aniline is so reactive that it gives 2,4,6-tribromoaniline immediately. This is the result of stabilization by the substituent of the unstable intermediate through which addition occurs. For acetanilide, this is represented by the contribution of (IX) to the intermediate which enables the positive charge to be delocalized over nitrogen as well



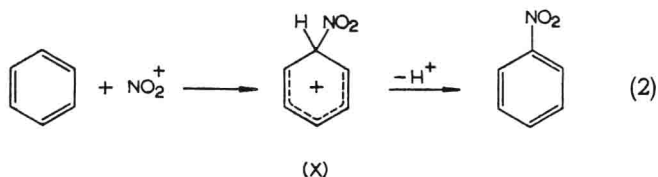
(IX)

as three of the nuclear carbon atoms [*cf.* (V-VII)]. Since the rate of formation of these intermediates is related to their stabilities (Chap. 2), acetanilide is brominated faster than benzene and reacts in the absence of a carrier.

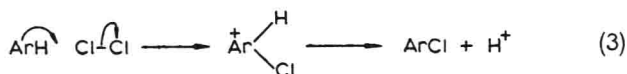
## 2. Types of Substitution

Substitution in benzenoid compounds may be brought about by three types of reagent: electrophiles, nucleophiles, and free radicals.

In electrophilic substitution, the two electrons which form the covalent bond between the aromatic compound and the reagent are both supplied by the former. This may be illustrated by the nitration of benzene by the nitronium ion,  $\text{NO}_2^+$  (Chap. 3, sect. 1). The aromatic ring supplies two electrons to form a covalent bond with the nitrogen atom of the reagent, causing a temporary electron-deficiency which is accommodated in the  $\pi$ -orbitals of the residual aromatic system [structure (X)], and reaction is completed by the removal of a proton from the nucleus, eqn. (2).

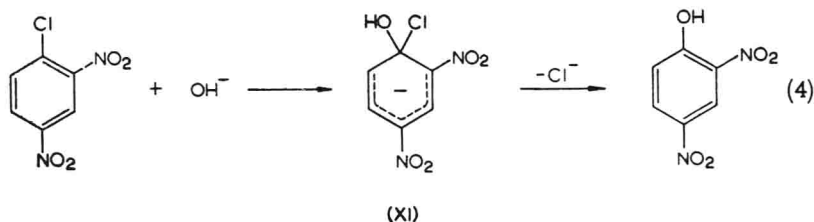


In this example the reagent is clearly electron-deficient, *i.e.*, electrophilic. Neutral species may also be electrophilic. For instance, in the reaction of chlorine with a benzene ring the new C—Cl bond is formed by the supply of two electrons from the aromatic compound, eqn. (3), molecular chlorine behaving as an electrophile because of the ability of one chlorine atom to be displaced as chloride ion. It is to be noted that this reaction could equally well be described as the

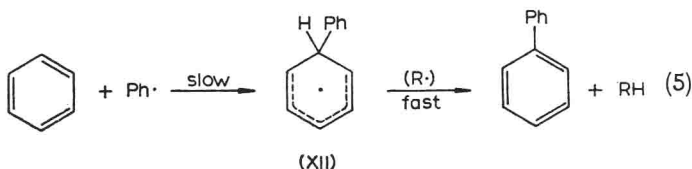


nucleophilic displacement by the aromatic compound on chlorine; in this sense the categorisation of reactions is an arbitrary one.

In nucleophilic substitution, two electrons are supplied for the



formation of the new bond by the reagent, as in the amination of pyridine by amide ion [6] or the hydrolysis of 2,4-dinitrochlorobenzene, eqn. (4). Here, the nucleus accommodates a negative charge in the intermediate (XI). Free-radical substitution may be illustrated by the phenylation of benzene by the phenyl radical derived from the thermal decomposition of dibenzoyl peroxide, eqn. (5) [7]. The aromatic compound accommodates an unpaired electron in its  $\pi$ -orbitals in the intermediate (XII).



The last two types of reaction are of far less general importance than the electrophilic substitutions of benzene and its derivatives and they have been investigated less comprehensively. In general, as is apparent from the examples mentioned, there are mechanistic similarities in the three types.

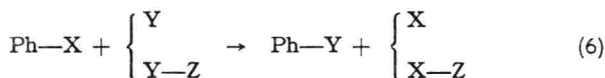
Electrophilic substitutions in benzene may be generalized as in eqn. (6) where Y may or may not carry a formal positive charge. Four classes of reaction may be distinguished:

(a) Both X and Y are hydrogen atoms but in different isotopic forms. For example, if X is tritium and Y—Z is an acid (Y=H) the process corresponds to acid-catalyzed protodetritiation.\* Such reactions are generally known as hydrogen-exchanges (Chap. 8).

\* The method of naming substitution reactions used throughout this book is that recommended in the Editorial Report on Nomenclature, *J.Chem.Soc.*, 4718(1954), and is as follows:

The name is composed of the following parts: the name of the incoming group, the syllable "de", the name of the departing group, and the suffix "ation"; suitable elision of vowels or introduction of consonants is sometimes necessary for euphony. The protium isotope of hydrogen is described as "proto" in reactions in which it is introduced or displaced, though its participation in reactions is often understood, the term "proto" being then omitted. The term following the syllable "de" usually identifies, in the leaving substituent, only the atom bonded to the aromatic ring; thus the removal of the  $\text{SiMe}_3$  and  $\text{SiEt}_3$  groups are both desilylation reactions.





(b)  $\text{X}=\text{H}$ ,  $\text{Y} \neq \text{H}$ . This constitutes the substitutions of widest applicability including nitration, sulphonation, halogenation, and Friedel-Crafts reactions.  $\text{Y}$  (or  $\text{Y-Z}$ ) may be any of a large number of species some of which are cations such as  $\text{NO}_2^+$ ,  $\text{ArN}_2^+$ , and  $\text{Hg}^{2+}$ , and others of which are covalent species such as  $\text{Cl}_2$ ,  $\text{Br}_2$ , and  $\text{SO}_3$ .

(c)  $\text{X} \neq \text{H}$ ,  $\text{Y}=\text{H}$ . Many substituents may be removed from the aromatic ring by protolytic displacements: *e.g.*,  $\text{X} = \text{SiMe}_3$  (protodesilylation) (Chap. 9).

(d)  $\text{X} \neq \text{H}$ ,  $\text{Y} \neq \text{H}$ . Since both  $\text{X}$  and  $\text{Y}$  may be one of a number of groups there is a large number of reactions of this type, *e.g.*,  $\text{X} = \text{B(OH)}_2$ ,  $\text{Y-Z} = \text{Br}_2$  (bromodeboronation) (Chap. 10).

### 3. The Polar Effects of Substituents

In reactions on monosubstituted benzenes the substituent present usually influences strongly both the reactivity of the compound relative to benzene and the proportions of the three possible isomeric monosubstitution products. For example, under commonly used conditions toluene is nitrated about 25 times faster than benzene, and gives the *o*-, *m*-, and *p*-nitro-derivatives in the relative proportions 15:1:10. (These figures vary slightly according to the conditions of nitration; see Chap. 3, sect. 1.) Chlorobenzene, on the other hand, reacts only at about one-hundredth of the rate of benzene, giving the three nitrochlorobenzenes in the approximate ratios *o*:*m*:*p* = 30:1:70.

In many cases there is evidence that substitution at the *ortho*-position is hindered or facilitated by the substituent which is already present by an effect which is steric in origin, but steric effects cannot be invoked to account for the marked variations in the ease of reaction at *meta*- and *para*-positions. Since the reactions involve electrophilic reagents polar effects are of importance, and it is therefore necessary first to examine the polar effects of substituents to see how they may play a part in determining aromatic reactivities.

Polar effects can usually be satisfactorily treated by dividing them into two main categories: (a) those which are transmitted along