Iowa State University

Digital Repository

1954

Mechanism of displacement of halogen from aromatic nuclei by nucleophilic reagents

Lawrence Roy Parks

Iowa State University

NOTE TO USERS

MECHANISM OF DISPLACEMENT OF HALOGEN

FROM AROMATIC NUCLEI BY NUCLEOPHILIC REAGENTS

by

Lawrence R. Parks

A Dissertation Submitted to the

Graduate Faculty in Partial Fulfillment of

The Requirements for the Degree of

DOCTOR OF PHILOSOPHY

Major Subject: Physical-Organic Chemistry

Approved:

In Charge of Major Work

Head of Major Department

Dean of Graduate College

Iowa State College

1954

UMI Number: DP12898

INFORMATION TO USERS

The quality of this reproduction is dependent upon the quality of the copy
submitted. Broken or indistinct print, colored or poor quality illustrations and
photographs, print bleed-through, substandard margins, and improper
alignment can adversely affect reproduction.

In the unlikely event that the author did not send a complete manuscript
and there are missing pages, these will be noted. Also, if unauthorized
copyright material had to be removed, a note will indicate the deletion.

UMI®

UMI Microform DP12898

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

TABLE OF CONTENTS (Continued)

INTRODUCTION

From a survey of the existing work in the literature it becomes immediately apparent that the vast field of aromatic nucleophilic substitution has received remarkably little attention during the development of theoretical organic chemistry in the last three decades. This field has received so little attention that the term, aromatic substitution, has become identified almost solely with electrophilic substitution. The ultimate object of this study is to contribute to the backlog of knowledge about theoretical organic chemistry.

Considerable attention has recently been directed toward the study of the nucleophilic displacement reactions of activated aryl halides. One of the striking features of the reaction is the regularity with which fluoride appears as a more reactive leaving group than the other members of the halogen family. The normal replacement order for this reaction is $F > Cl > Br$ with fluoride leaving considerably faster than the other two and little difference between chloride and bromide. This order stands in sharp contrast to the behavior of the halides in displacements at saturated carbon atoms where fluoride is almost impossible to replace. The primary object of this work was to gain more information about the mechanism by which the nucleophilic substitution of halogen is carried out.

To gain knowledge of the mechanism, the effect of factors such as steric requirement of nucleophile and changes in solvent on the replacement of halogen by nucleophiles were studied carefully. It was found that by increasing steric requirements in the nucleophile and changing to solvents with much lower solvating ability than those normally used, a complete reversal of the order of replacement of halogens could be achieved, that is $Br > Cl > F$. The kinetics of the reactions were followed by appropriate analytical methods, usually either titration of the excess nucleophile or displaced halide ion. The mechanism operating was then determined for each reaction by correlating the data with the proper rate expression.

The work reported should be of value as an aid to clarifying the mechanism of replacement of activated aryl halogens. The conclusions reached are based on kinetic evidence and are worthy of being drawn since they fall into a heretofore untouched phase of aromatic nucleophilic substitution.

HISTORICAL REVIEW

The Nucleophilic Displacement of Aromatic Halogens

It has long been known that nitro groups in the _ortho_ and _para_ positions activate the replacement of halogen from 1-halo-2,4-dinitrobenzenes by nucleophilic reagents. Pisani (1) recorded the attack by H_2O and NH_3 on picryl chloride in 1854. Bunnett and Zahler (2) reviewed the subject of aromatic nucleophilic substitution thoroughly in 1951. It is apparent from this excellent review or a search of the literature that the vast field of aromatic nucleophilic substitution has received only very slight attention in the development of theoretical organic chemistry compared to the more familiar electrophilic substitution.

The group displaced in nucleophilic substitution is almost never hydrogen in direct opposition to electrophilic substitution where hydrogen is nearly always the group displaced. Undoubtedly the most common and useful reaction involving nucleophilic displacement is the displacement of halogen by bases of various types. Replacement of halogen from 1-halo-2,4-dinitrobenzene has found many uses in preparative organic chemistry (2,p. 277). This is particularly true for the readily available 1-chloro-2,4-dinitrobenzene which has also been used extensively as a substrate for many and varied kinetic studies particularly in the past decade.

The Nucleophilic Displacement of Fluoride

Replacement of fluoride from 1-fluoro-2,4-dinitrobenzene has not received nearly so much study in the past as its chloro-, bromo-, and iodo-analogs. In the past few years, replacement of fluoride has become more important. Whalley (3) suggested the use of 1-fluoro-2,4-dinitrobenzene as a derivatizing agent for alcohols. The reaction is exothermic and proceeds readily with a trace of triethyl amine as catalyst. This reagent has the distinct advantages over more common derivatizing agents of not being hydrolyzed by small amounts of water and of not having to be stored under anhydrous conditions. 1-Fluoro-2,4-dinitrobenzene has recently found considerable use in biochemistry as a reagent for derivatizing amino groups. Porter and Sanger (4) devised a method for the identification of terminal amino-acids in protein in which the alpha-amino groups are free. The protein is treated with 1-fluoro-2,4-dinitrobenzene at room temperature and submitted to complete hydrolysis. Thereafter, the N-2,4-dinitrophenyl derivatives of the amino-acids are separated from each other and quantitatively estimated. Sanger (5) used this method to show that insulin contains glycine and phenylalanine in terminal positions, each present to the extent of two molecules per insulin molecule with molecular weight of 12,000. This very important work has caused 1-fluoro-2,4-dinitrobenzene to often be called Sanger's reagent.

The Use of Amines As Nucleophilic Reagents

Nucleophilic replacement of halogens from 1-halo-2,4-dinitro-benzenes by both aliphatic and aromatic amines has received a great deal of study. It is found that most primary and secondary amines replace halogens more rapidly than does ammonia. Piperidine is especially reactive and has been used to measure the replaceability of halogen in different situations (6). Brady and Cropper (7) covered the kinetics of the reaction of alkylamines and dialkylamines very thoroughly. They found remarkable differences between the rate constants for different amines which are not directly related to their basic strength. Amines with a number of alkyl groups on or near their nitrogen atoms are, in general, less reactive than amines with less branching near the nucleophilic center. Their argument, that the intrinsic nucleophilic activity of the amines is modified by the steric effects of their alkyl groups, is very convincing.

Of more interest to this thesis problem are the studies of nucleophilic attack on 1-halo-2,4-dinitrobenzenes by aromatic amines. Rheinlander's (8) investigation of the kinetics of the reaction between 1-bromo-, 1-chloro-, and 1-iodo-2,4-dinitrobenzenes and the two aromatic bases, aniline and methylaniline, in ethanol solvent is very closely related to this thesis problem. The kinetics of reactions of the same chemical systems (with substitution of 1-fluoro-2,4-dinitrobenzene for 1-iodo-2,4-dinitrobenzene) in nitrobenzene solution constituted a large part of the experimental section of this

thesis. Rheinlander's rate constants were confirmed experimentally for both aniline and N-methyl aniline with 1-chloro-2,4-dinitrobenzene and 1-bromo-2,4-dinitrobenzene and extended to include 1-fluoro-2,4-dinitrobenzene in ethanol solution. Methylaniline was found by Rheinlander and in this investigation to always react slower than aniline even though it is the stronger base. Rheinlander's specific objective was to ascertain whether the reactions were unimolecular or bimolecular and to obtain evidence for the existence or non-existence in appreciable quantities of intermediate additive compounds. He found that aniline bases react with 1-halo-2,4-dinitrobenzenes in a bimolecular fashion of a somewhat special type, in that the velocity coefficient varies slightly with the initial concentration. He reports no evidence for obtaining additive compounds in appreciable proportions. However, an increase in the concentration of base or halogeno-compounds diminishes the velocity coefficient appreciably, the effect of the former being the more marked. A recent publication by Ross (9) gives a very convincing explanation of the decrease in rate constants with increasing aniline concentration. Kinetic and spectroscopic evidence is given to show that the observed rate decreases are attributable to molecular compound formation between aniline and 1-chloro-2,4-dinitrobenzene in ethanol. In some solvents, for example ethyl acetate, complex formation occurs to a minor extent and no decrease in rate is observed.

Kinetic Studies of the Displacement of Fluoride

Singh and Peacock (10) and Van Opstall (11) have thoroughly
studied the kinetics of the reaction of primary aromatic amines
with 1-chloro-2,4-dinitrobenzenes in ethanol. The kinetics of
nucleophilic displacement of fluorine had received very little study
until Chapman (12, 13, 14, 15, 16, 17) began his extensive investi-
gation in the field about five years ago. Most organic fluorides
react very slowly with nucleophilic reagents and determination of
fluoride, in contrast to the other halide ions, does not lend itself
well to kinetic studies. The initial research in the area carried
out by Chapman was an attempt to correlate pharmacological activity
and chemical reactivity by replacing other primary alkyl halides
with fluoride. Work done by this group since that time has been
more physical-organic in nature with the primary objective being that
of determining the mechanism of nucleophilic displacement of halogens
in general. Kinetic studies carried out by Chapman show the nucleo-
philic displacement of fluoride from 1-fluoro-2,4-dinitrobenzene by
aniline in 99.8 per cent (by weight) ethanol to be approximately 56
times as fast as bromide and 42 times as fast as chloride from the
same aromatic nucleus. A difference in stoichiometry is observed in
the displacement of fluoride compared to the other halogens. The
amine hydrofluoride reacts almost as fast as the free amine but the
other amine hydrohalides will not react appreciably with the sub-
strate. The reaction of aniline with 1-fluoro-2,4-dinitrobenzene

obeys the rate law

(1) $\frac{dx}{dt} = k(a-x)(b-x)$

much better than

(2) $\frac{dx}{dt} = k(a-2x)(b-x)$,

which is followed by the 1-chloro-, 1-bromo-, or 1-iodo analogs.

Further kinetic studies by Chapman dealt with the interesting case of replacement of chloride from chloronitropyridines. It is commonly asserted that in aromatic systems the cyclic nitrogen atom and the substituent nitro group cause similar disturbances of the aromatic electron cloud. Aniline and pyridine were used as the nucleophiles. Aniline replaced chloride from 1-chloro-2,4-dinitrobenzene approximately 30 times faster than pyridine and from 2-chloro-5-nitropyridine about 10 times faster. This is the opposite from what would be expected from consideration of the basic strengths of the two bases, although basic strength is admittedly a very poor measure of nucleophilic power. To explain this anomaly Chapman proposes that there is important hydrogen bond formation in the transition state between the hydrogens on the nitrogen of the attacking aniline molecule and the oxygen of the ortho-nitro groups or the cyclic nitrogen in the substituted pyridine. This factor alone is not believed to entirely account for the differences in rate. The formation of the transition states for the reactions of primary amines is probably attended by a greater increase of solvation than with pyridine. This second factor, or other factors such

as steric hindrance, must be a great deal more important than

Chapman thought, because Dr. M. F. Hawthorne (18) has recently

completed a study in these laboratories of the replacement of

chloride from 1-chloro-2,4-dinitrobenzene by N-deuterated piperidine

and found no evidence for an isotope effect. Another facet of the

problem of replacement of fluoride that has been studied by the

kinetic method was the nucleophilic displacement of fluoride from

alkyl fluorides. With ethanolic sodium ethoxide, primary alkyl

fluorides undergo almost exclusive substitution at rates 10^3 to 10^4

times smaller than those for the corresponding bromides. The

reactions of primary fluorides and bromides differ little in energy

of activation, the lower rates with fluorides being due to low values

of A, the non-exponential parameter of the Arrhenius equation. Both

these facts are probably connected with a highly solvated transition

state for fluorides. Secondary and tertiary alkyl fluorides undergo

predominantly elimination at rates 10^5 to 10^6 times smaller than the

corresponding bromides. The most recent work published by Chapman

covers the kinetics of reaction of piperidine and morpholine with

ortho- and para-halogenonitrobenzenes in ethanol. For fluoro-

compounds, the rate law

(3) $\frac{dx}{dt} = k(b-x)(a-nx)$

is obeyed where $1 < n < 2$. A method is described for determining n by

successive approximations. One unusual feature of this paper is

that the explanation for the order of nucleophilic substitution in

activated systems, $F > Cl > Br > I$ is said to be due to "diminished

repulsion energy" in the formation of the transition state. All
previous explanations of this large increase in rate for fluoride
had been attributed to solvation of the fluoride in the transition
state.

The Mechanism for Nucleophilic Displacement of Halogen from Activated Aromatic Compounds

Chapman and his co-workers propose a straight forward bi-
molecular mechanism for nucleophilic replacement of halogen from
an activated position and are critical of a proposal of Berliner (19)
that the reaction may proceed through an intermediate. Berliner has
studied the nucleophilic displacement of halogens (bromine, chlorine,
and iodine) from the alpha- and beta-positions of naphthalenes. The
greater reactivity of the alpha-position in naphthalene, predicted
by modern theories of organic chemistry, is well substantiated by
substitution reactions, measurements of physical constants, and
quantum mechanical calculations. The alpha-position should also be
more reactive toward nucleophilic displacements but experimental
evidence points out very clearly that the beta-position is the more
reactive, but both alpha and beta halogens are more reactive than
the corresponding halobenzenes. Although the reaction appears to
be preferred electronically (and therefore energetically) at the
alpha-position, the probability for reaction is greater in the un-
hindered beta-position. Substitution of the halonaphthalenes with
a nitro group ortho to the halogen (the nitro group always in the

1- or the 2- position) gave the opposite result. The alpha-halogen with an activating beta-nitro group was replaced considerably faster than beta-halogen activated by an alpha-nitro group. This is best explained on the basis of steric inhibition of resonance of the nitro group in the alpha-position. If the nitro group is not coplanar with the naphthalene ring, because of interference with the peri hydrogen, the beta-halogen will be less activated and the rate will fall off accordingly.

The reactions without nitro activators are presumably S_N2* displacements and the transition state is subject to steric hindrance. If the same mechanism is assumed for the nitro activated reactions, it is difficult to see why the alpha-halogen flanked by an ortho-nitro group would not be in an even more stericly hindered position. Berliner proposed a two-step mechanism for the reaction with halogenonitronaphthalenes. The first step leads to the formation of either a fairly stable intermediate or actually an intermediate compound. In either case this intermediate would represent a "valley" in the potential energy diagram. The second step in the reaction is the breaking of the carbon halogen bond with a characteristic energy of activation of its own. There is no way Berliner's proposed two-step mechanism can be distinguished from a one-step mechanism on the basis of data available at the present time.

_____

*Substitution, nucleophilic, second order.

The Comparison of Aromatic Substituents As Activators
for Nucleophilic Substitution

A more recent work by Berliner (20) was an important contri-
bution to the study of the effect of substituents on nucleophilic
displacement. This subject has also received a great deal of study
the past five years by Bunnett and co-workers and by Miller.
Berliner's work includes nucleophilic displacement of bromide from
4-substituted-2-nitrobromobenzenes with groups in the 4 position
which are deactivators, such as methoxy. Very few investigations
of this type have been made since the reactions are very slow.
Berliner was able to get a good Hammett (21) equation fit for the
nucleophilic displacement of bromide from 4-substituted-2-nitro-
bromobenzenes with piperidine. A <u>rho</u> value of 4.95 was obtained.
The standard compound was <u>ortho-nitrobromobenzene</u>. This is of
interest because of all the reactions listed by Hammett none
involves direct nucleophilic attack on the ring. All are side
chain reactions.

Bunnett has been by far the most prolific American contributor
to the field of nucleophilic displacement in the past decade. A
large portion of his work has dealt with the comparative activation
of groups toward nucleophilic substitution in 4-substituted-2-
nitrochlorobenzenes (22, 23). The following order of activating
power was found: $NO_2 > CH_3SO_2 > (CH_3)_3N^+ > CN > CH_3CO > Cl > H$. It
should be noted that $(CH_3)_3N^+$ deactivates nitration more strongly

than nitro but it activates nucleophilic displacement less strongly.
Bunnett explains the anomaly as being a consequence of the different
polarization and polarizability of the two groups. Deactivation is
principally caused by polarization effects and the $(CH_3)_3N^+$ group
evidently polarized the ring somewhat more strongly than the nitro
group. Activation results not only from the polarization effects
of groups but also from their polarizability effects; that is, from
the capacity of the groups to accommodate a positive or negative
charge in the transition state. A plot of log k _versus_ _sigma_ for
replacement of chloride from 4-substituted-2-nitrochlorobenzenes
with methanolic sodium methoxide (where the 4-substituents are the
ones whose order of reactivity was compared above) gave a _rho_ value
of 3.9. This is a very high value but not so high as the 4.95
value reported by Berliner and Monack (20). Other information
regarding the activating effects of various groups has been summariz-
ed in the review by Bunnett and Zahler (2,p. 307).

The principal interest of a later work by Bunnett and Davis (24)
was to compare the reactivity of nucleophilic reagents. The rate of
reaction with 1-chloro-2,4-dinitrobenzene with hydroxide ion, phen-
oxide ion, piperidine, methoxide ion and thiophenoxide ion fell off
in the following order: thiophenoxide ion > piperidine > methoxide
ion > hydroxide ion. A comparison was made between the pair of
ions, hydroxide and methoxide, and ammonia and methylamine. In each
case, as a hydrogen was replaced with a methyl group, the increase

in strength as a nucleophile, as exemplified by a large increase
in rate constant for the reaction with 1-chloro-2,4-dinitrobenzene,
was a great deal more than would be expected. Methylamine reacts
800 times as fast as ammonia and methoxide ion reacts 33 times as
fast as hydroxide ion.

The most recent investigation by Bunnett and co-workers (25)
extends the study of activation by different substituents of nu-
cleophilic displacement of chlorine from 4-substituted-2-nitrochloro-
benzenes and 4-substituted-2,6-dinitrochlorobenzenes by methoxide
ion. The 2,6-dinitro-compound provides enough activation to permit
the substitution of deactivating groups in the 4 position and still
obtain a rate rapid enough to make kinetic study feasible. New
4 substituents used in addition to those mentioned above were CF_3
and phenylazo. The phenylazo group does not fall on the straight
line of a Hammett plot and this is explained quite convincingly as
being due to an exceptionally low entropy of activation. This un-
expectedly low entropy of activation is attributed to two effects.
In the transition state quinoid type structures such as the follow-
ing must play a fairly important role.
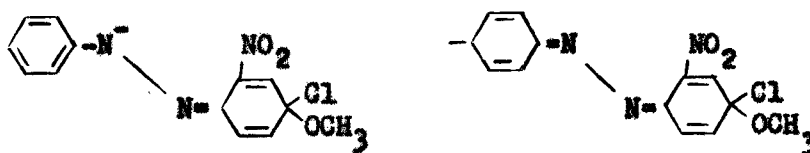
The restriction of rotation about carbon-nitrogen bonds entails a

loss of entropy which no small group such as nitro could approach. The second effect takes into account the large size of the phenylazo group and the exceptional opportunity for stabilization of the negative charge in the transition state.

Joseph Miller and his co-workers at the University of Western Australia have done considerable work on the problem of activation of groups toward nucleophilic substitution by different substituents. The activating or deactivating power of substituents has been defined and measured in the form of substituent rate factors which Miller abbreviates, S. R. F. The substituent rate factor is defined as the ratio of the rate of reaction of a substituted halobenzene to the rate of an unsubstituted halobenzene. By definition the S. R. F. of hydrogen = 1. In the first paper (26) of the series, S. R. F.'s are calculated for the following substituents: $o\text{-}NO_2$, $p\text{-}NO_2$, $p\text{-}CO_2Me$, $p\text{-}CO_2^-$, $p\text{-}CH_3$, $p\text{-}Cl$, and $p\text{-}NH_2$. A following investigation (27) of the reaction of 1-halogeno-2,4-dinitrobenzenes with sodium methoxide or sodium p-nitrophenoxide in dry methanol found the usual order of replacement, $F > Cl > Br > I$. This order is explained by Miller as follows.

A nucleophilic substitution reaction will generally be facilitated by variation of the replaced group, X, so that (a) X is more electronegative and more able to go off as X^-, and (b) the bond Ar-X is as weak as possible. These two factors are opposing for the halogens. The first varies $F > Cl > Br > I$ and the opposite order is obtained

for the second factor. The bond energy factor (a) is the more important one in most nucleophilic displacements and causes the order of replacement of halogens to be $F > Cl > Br > I$, but Miller predicts it might not be if 1. the differences in electronegativity were small, 2. there is little activation by other groups, and 3. the nucleophilic power of the reagent is small. This thesis contains the study of the case where a weak nucleophile N-methyl-aniline was used and the opposite order of replacement of halogen from 1-halo-2,4-dinitrobenzene was found to be $Br > Cl > F$. A weak, non-ionizing solvent, nitrobenzene, makes the rate of replacement of fluoride much slower in comparison to chloride and bromide than a hydroxylic solvent such as alcohol. The same order is found in ethyl alcohol but the rates of reaction converge considerably.

A further study (28) of substituent effect on nucleophilic displacement dealt with ortho-effect and para-effect. ortho-Effects were shown to exhibit considerable variation in both magnitude and character. This is to be expected since a substituent in the ortho-position has a good chance of having a steric factor superimposed on its normal polar behavior which usually reduces its effect as compared to the same substituent in the para-position (19). The evidence presented in this work shows that the ortho-effects are mainly polar and not geometrical in origin for a number of substituents. para-Effects vary much less, and variations are associated with a change in the extent of conjugation of the substituent group

and the ring. The most recent investigation of the series (29) determined the activating power of the halogens in a group of nucleophilic substitution reactions. The order of decreasing activating strength was found to be $I > Br > Cl > F$ with fluorine approximately equal to hydrogen.

The Mechanism for Displacement of Halogen from Mono-halobenzenes

Displacement of halogens from mono-halobenzenes with powerful nucleophiles are usually difficult reactions requiring rather drastic experimental conditions and often give the order of reactivity $Br > Cl > F$ (30, 31, 32). These reactions must go by a mechanism other than direct displacement. One reaction of this type, the reaction of aryl halides with amide ion in liquid ammonia (33), has been shown to go through an elimination addition mechanism involving at least transitory existence of an electrically neutral "benzyne" intermediate. Tracer study using C^{14} provides very convincing evidence for a mechanism that proceeds through a symmetrical intermediate.

EXPERIMENTAL*

The Displacement of Halogen from 1-X-2,4-Dinitrobenzenes
by N-Methylaniline

Preparation of reagents

1-Fluoro-2,4-dinitrobenzene (Eastman Kodak Co.) was recrystallized from absolute ethanol, m.p. 25 to 26°.

1-Chloro-2,4-dinitrobenzene was prepared by adding 100 ml. of chlorobenzene cautiously to a well stirred mixture of 200 ml. fuming nitric acid and 100 ml. of concentrated sulfuric acid. Upon completion of the addition of the chlorobenzene, the reaction mixture was heated carefully for five minutes, just warm enough to avoid the formation of dense brown fumes, and poured into two liters of ice water. A 56 per cent yield of light yellow, crystalline material was obtained after six recrystallizations from 80 per cent ethanol, m.p. 51 to 52°.

1-Bromo-2,4-dinitrobenzene (Eastman Kodak Co.) was recrystallized from 80 per cent ethanol, m.p. 71 to 72°.

N-Methylaniline (Eastman Kodak Co.) was purified by acetylation followed by recrystallization of the acetyl derivative from water to

---

*All melting points and boiling points in this section are uncorrected. Unless otherwise noted, the reagents were reagent grade and were used without further purification.

a constant melting point, 101° to 102°. Hydrolysis by aqueous hydrochloric acid followed by fractional distillation gave a pure, colorless product, b.p. 81° to 82° (14 mm.).

Ethanol was purified by drying commercial absolute ethanol by the method of Lund and Bjerrum (34). The product obtained gave a negative test with aluminum ethoxide in benzene indicating that the material contained less than 0.05 per cent water (35).

Kinetics of the displacement of halogen from 1-X-2,4-dinitrobenzenes in nitrobenzene solvent

The tertiary amine product formed by the reaction of N-methylaniline and 1-X-2,4-dinitrobenzenes is a red crystalline material which forms highly colored solutions. The first method of analysis which was tried as a means of following the above reaction was an attempt to follow formation of the colored product spectrophotometrically. Solutions were made up and the ultra-violet and visible spectra of all products and reactants were run in a Carey recording spectrophotometer. All of the compounds were shown to obey Beer's law and a wave length of 540 millimicrons was found to give appreciable adsorption by the product and almost no adsorption by any of the reactants in ethanol. The highly colored complex formed between N-methylaniline and nitrobenzene (36) (discussed below) adsorbs to some extent at 540 millimicrons. N-methylaniline hydrohalides and the tertiary amine products tend to settle out of the cold nitrobenzene solution in the spectrophotometer cells

causing serious errors in determination of the optical densities and thus making the analytical method worthless.

The rate of displacement of halogen was followed by potentiometric titration of excess N-methylaniline with perchloric acid in glacial acetic acid. A Beckmann pH meter, Model G, was used as a potentiometer with glass and silver-silver chloride electrodes.

When N-methylaniline is added to nitrobenzene a deep red color forms due to complex formation. This is an often-observed phenomenon with poly nitro compounds and the complexes are stabilized by amino groups in the second molecule (36). Since second order kinetics were observed throughout the run in every case studied in nitrobenzene, the amount of material complexed with the substrate must have been very small.

Samples prepared from 4 ml. of 0.5 M N-methylaniline and 2 ml. of 0.5 M 1-X-2,4-dinitrobenzene dissolved in nitrobenzene were sealed in ampules and placed in a well insulated thermostat. Samples were removed at regular intervals and frozen to quench the reaction. After rapid filtration of the sample, the unreacted amine in the samples was titrated potentiometrically with 0.1 N perchloric acid in glacial acetic acid. N-methylaniline hydrochloride and hydrobromide did not interfere with this analysis, and the hydrofluoride was insoluble in cold nitrobenzene and was removed quantitatively by the filtration procedure.

The reactions of all three halo compounds with N-methyl-aniline have the same stoichiometry in nitrobenzene solvent.
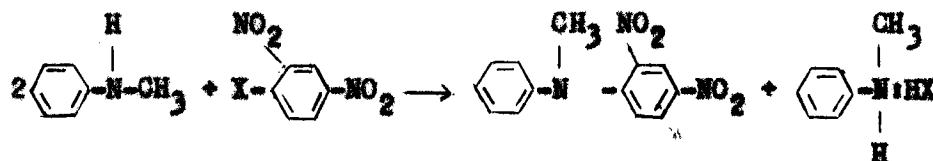
The rate law,

$$(4) \quad \frac{dx}{dt} = k(a-2x)(b-x),$$

a = Amine concentration

b = 1-X-2,4-dinitrobenzene concentration

which simplifies to

$$(5) \quad k = \frac{1}{2t} \quad \frac{x}{b(b-x)}$$

if a = 2b, gave good second order rate constants in all three cases. Typical runs are summarized in Table I. The temperatures at which reactions were run and the rate constants obtained are found in Table II.

Some difficulty was encountered when the reaction of N-methylaniline with 1-fluoro-2,4-dinitrobenzene was carried out in glass tubes at low temperatures which necessitated long time intervals. The rate constant dropped consistently. The trouble was found to be due to the action of hydrogen fluoride on glass and the consequent release of N-methylaniline. This could be corrected by using copper tubes which were carefully cleaned with hydrofluoric acid before use. The tubes were sealed before being placed in the thermostat.

Table I

Rate Constants for the Reaction of N-methylaniline
with 1-X-2, 4-dinitrobenzene in Nitrobenzene Solvent at 120°

Time increment hours	X = F $k \times 10^5$ l.mole^{-1} sec.$^{-1}$	X = Cl $k \times 10^4$ l.mole^{-1} sec.$^{-1}$	X = Br $k \times 10^4$ l.mole^{-1} sec.$^{-1}$
1		2.70	9.02
2		2.78	
3		2.80	8.55
4		2.80	8.11
5	2.00	2.70	8.62
6		2.79	7.75
7		2.78	8.71
10	1.72		
25	1.97		
50	1.73		
75	1.54		
100	2.00		
Average	1.82	2.75	8.45

Kinetics of the displacement of halogen from 2,4-dinitrobenzene
in 99.8 per cent ethanol solvent

The reaction of N-methylaniline with 1-bromo and 1-chloro-
2,4-dinitrobenzene was followed by determining the amount of
halogen displaced by the Volhard Method. Ten ml. of 0.2 M
N-methylaniline was mixed with 10 ml. of 0.1 M halo compound in
individual stoppered tubes which were immersed in a thermostat.

At regular intervals samples were removed and poured into a separatory funnel containing 30 ml. of benzene and 20 ml. of silver nitrate and the mixture was shaken thoroughly. The aqueous layer containing the excess silver nitrate was drawn off and the benzene layer was washed twice with distilled water. The unreacted starting materials and the tertiary amine product remained in the benzene layer. The silver bromide or silver chloride remained at the boundary between the two layers causing no difficulty in the analysis. The excess silver nitrate was titrated with standard potassium thiocyanate using ferric ammonium sulfate as the indicator. Good second order rate constants were obtained using the same rate law that was used for the bromo and chloro compounds in nitrobenzene solvent.

The reaction of N-methylaniline with 1-fluoro-2,4-dinitrobenzene was followed by bromination of excess N-methylaniline as described by Siggia (37). Ten ml. of 0.2 M N-methylaniline and 10 ml. of 0.2 M 1-fluoro-2,4-dinitrobenzene were mixed thoroughly and immersed in the thermostat in tightly stoppered tubes. The samples were removed at regular intervals and poured into a preparatory funnel containing 30 ml. of benzene and 25 ml. of concentrated hydrochloric acid which stopped the reaction by converting all the free amine to the anilinium ion. The separatory funnel was shaken, allowed to stand, and the aqueous layer was removed. The benzene layer was washed twice with water. Excess 0.1 N bromate-bromide solution was added to the aqueous layer and after

the solution had been allowed to stand for 12 minutes an excess of potassium iodide was added. The iodine liberated was titrated with standard sodium thiosulfate. The excess bromate-bromide solution was never allowed to exceed 3 ml. of 0.1 N solution. Under these conditions it was shown by Chapman (15) that none of the other substances present, particularly ethanol, was oxidized or brominated.

A summary of the temperatures at which reactions were run and the rate constants obtained can be found in Table II.

The Displacement of Halogen from 1-X-2,4-Dinitrobenzenes
by Aniline

Kinetics of the displacement of halogen from 1-X-2,4-dinitro-
benzene by aniline in nitrobenzene solvent

Ten ml. of 0.5 M aniline in nitrobenzene and 5 ml. of 0.5 M of 1-X-2,4-dinitrobenzene in nitrobenzene, both warmed to 26.5°, were added to a large test tube. The tightly stoppered test tube was shaken thoroughly and placed in a thermostat at 26.5°. The initial reaction time was taken as the time of mixing the reactants. At regular time intervals, samples were removed and the reaction was followed by nonaqueous titration of the unreacted amine with perchloric acid in glacial acetic as described on page 18. An identical run was made at 50.0° and the rate constants for both runs and the energies of activation are found in Table III.

Table II

Rates of Displacement of Halogen from 1-X-2,4-Dinitrobenzenes
by N-Methylaniline

Halogen displaced	Solvent	Temp. °C.	$k \times 10^{-7}$ l.mole^{-1}sec.$^{-1}$	$\Delta H^{\ddagger}$ kcal./ mole[a]	$\Delta S^{\ddagger}$ in e.u.
F	Nitrobenzene	131.5	267 ± 10		
F	Nitrobenzene	120	182 ± 20	10	-56
Cl	Nitrobenzene	131.5	4400 ± 40		
Cl	Nitrobenzene	120	2750 ± 50	12	-48
Cl	Nitrobenzene	25	15 ± 4	12	
Cl	Nitrobenzene	0	7 ± 3	10	
Br	Nitrobenzene	131.5	13000 ± 50		
Br	Nitrobenzene	120	8450 ± 350	11	-44
Br	Nitrobenzene	25	54.7 ± 1.6	12	
F	Ethanol	50	4.53 ± 0.7		-68
F	Ethanol	77	12.4 ± 0.7	7	
Cl	Ethanol	50	6.22 ± 2		-62
Cl	Ethanol	76	16.6 ± 2	8	
Br	Ethanol	50	13.7 ± 2		-50
Br	Ethanol	76	51.0 ± 1	12	

[a]The values listed were calculated using the values for the rates at the particular temperature and at the highest temperature. This procedure was adopted because the low precision of the low temperature rate constants was compensated by the very large temperature intervals.

Table III

Rate Constants for Displacement of Halogen
from 1-X-2,4-Dinitrobenzene by Aniline in Nitrobenzene Solution

Tempera-ture	Halogen displaced	$k \times 10^6$ $l.mole^{-1}sec.^{-1}$	H Kcal./mole
26.5	F	23.3	
26.5	Cl	2.49	
26.5	Br	4.70	
50.0	F	135	14.3
50.0	Cl	10.5	11.8
50.0	Br	21.4	12.4

The comparison of rate constants in this table with those

obtained by Chapman and Parker (38) in Table IV show clearly the

large decrease in rate when the solvent is changed to nitrobenzene

from ethanol. But of greater importance is comparison of the

ratio of the rate constants of 1-bromo-2,4-dinitrobenzene and

1-fluoro-2,4-dinitrobenzene in ethanol with the ratio of the

respective rate constants in nitrobenzene.

The stoichiometry of the reaction of aniline with 1-X-2,4-

dinitrobenzene is evidently the same in nitrobenzene as the same

reaction with N-methylaniline, page 19. Two moles of base are

used up for each mole of halo compound. The rate law

$$(4) \quad \frac{dx}{dt} = k(a-2x)(b-x),$$

a = amine concentration

b = 1-X-2,4-dinitrobenzene concentration

which integrates to give

(5) $k = \frac{1}{2t} \quad \frac{x}{b(b-x)}$

if a = 2b, gave good second order rate constants in all three cases.

Chapman and Parker (38) ran the displacement of halogen from 1-X-2,4-dinitrobenzenes by aniline in ethanol. The results are summarized in Table IV.

Table IV

Rates of Displacement on 1-X-2,4-Dinitrobenzenes by Aniline in 99.8 Per Cent Ethanol[a]

Halogen dis- placed	$k_{50} \times 10^{4}$ $1.\text{mole}^{-1}\text{sec.}^{-1}$	$\Delta H^{\ddagger}\text{-kcal./mole}$[b]	$\Delta S^{\ddagger}\text{-in e.u.}$
F	168	5.8	-49
Cl	2.69	10.6	-43
Br	4.05	10.6	-42

[a]From the summary by Chapman and Parker (38).

[b]The value of RT has been subtracted from the values of E listed by Chapman and Parker to effect the conversion to heats of activation.

Investigation of the Cleavage
of 2,2',4,4'-Dinitro-6-s-butyldiphenylether
by Weak Nucleophiles

Preparation of 2,2',4,4'-dinitro-6-s-butyldiphenylether

2,4-Dinitro-6-s-butylphenol (Dow Chemical Co.) was re-
crystallized from n-pentane until pure, m.p. $40°$ to $41°$. The
sodium salt was made by stirring the substituted phenol with
excess aqueous NaOH and collecting and drying the red insoluble
material formed. The first attempt to prepare the ether was by
reaction of the sodium salt with 1-fluoro-2,4-dinitrobenzene in
absolute ethanol solution. This reaction gave an excellent yield
of the undesired 2,4-dinitro-6-s-butylphenyl ethyl ether by
attack of the ethoxide ion formed by the equilibrium below.
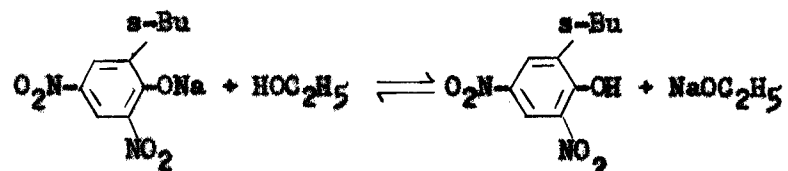
The reaction could not be made to go in nitrobenzene solvent at
$125°$. The preparation was finally accomplished with the phenol
itself as solvent. Stiochiometric amounts of the reactants,
26.22 grams (0.1 mole) of the sodium salt and 18.61 grams
(0.1 mole) of 1-fluoro-2,4-dinitrobenzene, were mixed with an
excess of the phenol in a sealed tube. The materials were care-
fully dried before use. The sealed tube was heated for 48 hours
at $110°$ in an oil bath. The melting point of the ether is much
below this temperature ($40°$ to $41°$) and fortunately both the

sodium salt and 1-fluoro-2,4-dinitrobenzene dissolved in the
molten phenol. At the end of the heating period the reaction
mixture was allowed to cool and the caked mass was dissolved in
a chloroform, carbon tetrachloride and water mixture and extracted
with 2 per cent sodium carbonate solution until the water layer
no longer became red from the sodium salt of the phenol. The
chloroform, carbon tetrachloride solution was evaporated to dry-
ness and the grayish solid was recrystallized from 95 per cent
ethanol. Four recrystallizations and a treatment with animal
charcoal gave 8.32 grams (19.9 per cent) of white crystalline
material, m.p. 180° to 182°. Elemental analysis gave the follow-
ing results: H, calculated 3.473 per cent, found, 3.475 per cent;
C, calculated 47.295 per cent, found, 47.40 per cent.

Preparation of 1-chloro-2,4-dinitro-6-s-butylbenzene

This compound had been previously prepared by Hawthorne and
Gram (39). A mixture of 4.6 grams (0.019 mole) of 2,4-dinitro-
6-s-butylphenol, 8.3 grams (0.053 mole) of benzene sulfonyl
chloride and 20 ml. of freshly distilled N,N-diethylaniline was
sealed in a pressure tube and heated at 100° for 18 hours. The
tube was cooled, opened, and the dark blue tar was dissolved in
150 ml. of benzene. The benzene solution was washed twice with
excess 6 N sulfuric acid, twice with water, twice with 10 per cent
sodium carbonate solution and was dried over potassium carbonate.
No unreacted phenol was recovered by acidification of the basic

extract. The benzene solution was evaporated to an oil under

aspirator pressure at room temperature. The residual oil was

dissolved in 40 ml. of pentane and put on a 40 x 2 cm. activated

alumina column and was eluted with pentane. Evaporation of

eluate gave an oil which was dissolved in 50 ml. of methanol. The

solution was heated to boiling and water was added until the solu-

tion became turbid. When cooled the solution deposited 3.5 grams

(73 per cent) of the desired chloro compound as long white

needles, m.p. 54° to 54.5°.

This procedure is very efficient for making small, very pure

portions of 1-chloro-2,4-dinitro-6-s-butylbenzene. When larger

amounts of the product were desired, it was found to be easier to

extract the tarry reaction product many times with n-pentane and

evaporate the solvent and recrystallize the impure material

several times from methanol water. This avoids the long,

tedious chromatographic procedure necessary to pass a large amount

of material through a column.

Preparation of N-2,4-dinitro-6-s-butylphenylaniline

To a large excess of freshly distilled aniline was added

2.60 grams (.01 mole) of 1-chloro-2,4-dinitro-6-2-butylbenzene.

The mixture was placed in a sealed tube in a 100° oil bath for

48 hours. At the end of this time the tube was opened and

extracted with dilute hydrochloric acid solution which removed the

excess aniline leaving 2.08 grams (65.2 per cent) of finely divided blood red crystals of N-2,4-dinitro-6-s-butylphenyl aniline. Recrystallization from ethanol gave a pure material, m.p. 148° to 149°.

Preparation of N-2,4-dinitrophenylaniline

A quantitative yield of N-2,4-dinitrophenylaniline was obtained by combining 2.60 grams (.01 mole) of 1-chloro-2,4-dinitrobenzene and an excess of aniline. The mixture was warmed gently and went to completion almost immediately. Extraction of the dilute hydrochloric acid removed the excess aniline and left a reddish tar which recrystallized from ethanol to give long, soft needles, m.p. 148° to 149°.

Cleavage of 2,2',4,4'-dinitro-6-s-butyldiphenyl ether with weak bases

The weak nucleophiles, N-methylaniline, p-chloroaniline and p-nitroaniline were heated with 2,2',4,4'-dinitro-6-s-butyldiphenyl ether in ethanol and in excess base as its own solvent. Reactions were attempted in sealed tubes placed in an oil bath at 120° for as much as three days. Upon removal of the aniline base with aqueous hydrochloric acid the original ether reprecipitated unchanged.

Cleavage of 2,2',4,4'-dinitro-6-s-butyldiphenyl ether with aniline

When aniline was used as the attacking agent, the ether was cleaved at temperatures as low as 25°. The reaction went to completion in 12 days. The reaction mixture was poured in dilute (3N) hydrochloric acid and a reddish oil formed on standing. Two recrystallizations from ethanol gave a red crystalline material, m.p. 148° to 149°. A mixed melting point with the original ether gave a deep depression to 118° to 125°. When mixed with a pure sample of N-2,4-dinitrophenylaniline (preparation, page 29) no depression of melting point was observed. Therefore, it was concluded that cleavage by aniline occurs by attack at the less hindered position.

The Kinetics of Displacement of Chloride from 1-Chloro-2,4-dinitrobenzene with Benzoate Ion

Preparation of silver benzoate

Forty grams (.33 mole) of benzoic acid was treated with 11.7 grams (.33 mole) of ammonium hydroxide in 300 ml. of water. Addition of 56.7 grams (.33 moles) silver nitrate to the mixture gave a heavy white crystalline material which was filtered, washed with water and methanol, and dried in an oven at 70°. The product weighed 39 grams (53 per cent) and did not darken with age. The use of ammonium hydroxide seemed very superior to the more commonly used sodium hydroxide which gives products that darken

badly. Further purification by recrystallization was done with acetonitrile as solvent. The process is a bit tedious due to the insolubility of the silver salt in acetonitrile.

Reaction of silver benzoate with 1-chloro-2,4-dinitrobenzene in acetonitrile

The insolubility of silver benzoate in acetonitrile limited the concentration to less than .005 M. Five ml. of .005 M silver benzoate was added to 5 ml. of .005 M 1-chloro-2,4-dinitrobenzene in acetonitrile in a tightly stoppered tube. The contents were frozen in a dry ice bath, evacuated, and sealed off. The sealed ampules were placed in an oil bath at 77°. The desired displacement reaction did not proceed cleanly and the reaction mixture became filled with a heavy, black, tarry deposit. Analysis of the mixture for halide ion gave very erratic results. It was decided to use potassium benzoate as benzoate ion source rather than silver benzoate.

Kinetics of the reaction of potassium benzoate with 1-X-2,4-dinitrobenzenes in 60 per cent dioxane solution

Potassium benzoate was prepared by adding slightly less than a stoichiometric amount of potassium hydroxide to a well stirred slurry of benzoic acid and heating. The water was then evaporated off and the solid was recrystallized several times from ethanol and dried in an oven at 70°. A nice white crystalline product was obtained.

The dioxane for use as solvent was purified by the method of Beste and Hammett (40). Solid sodium hydroxide was added to the refluxing dioxane at intervals until no red tarry material coated the freshly added sodium hydroxide pellets. After filtering, the dioxane was refluxed with metallic sodium for several hours until no discoloration of molten freshly added sodium was noted. The system was protected from atmospheric moisture by a calcium chloride tube filled with drierite. At the end of the reflux period, the dioxane was subjected to fractional distillation and the middle fraction boiling at 101.8° was retained. The first and last quarters were discarded. Distilled water was added to make a solution 60 per cent (by volume) dioxane which was used as a solvent in the following reactions.

Five ml. of 0.1 M potassium benzoate and 5 ml. of 0.1 M 1-chloro-2,4-dinitrobenzene were placed in a constricted tube and immediately frozen in a dry ice bath. The tubes were evacuated and sealed off. The sealed ampules were placed in a bath at 93°. Individual tubes were removed at intervals, opened, and poured into small separatory funnels containing 10 ml. of benzene, 4 ml. of nitrobenzene, 5 ml. of 1 M nitric acid, and a carefully measured quantity of standard silver nitrate. The separatory funnel was shaken thoroughly and the aqueous layer was collected. The silver chloride is wet by the nitrobenzene and remains at the boundary between the two layers and this avoids the necessity of filtering it off. The benzene layer was washed carefully twice

with 10-ml. portions of distilled water, and the three aqueous layers containing the excess silver nitrate were combined for analysis. The excess silver nitrate was determined by titration with potassium thiocyanate. The normal Volhard technique of using ferric alum as indicator was not sensitive enough to give good results. The end point could be found much more accurately potentiometrically using a Beckmann pH meter, Model G, as a potentiometer with a silver electrode in the titration cell and a standard calomel electrode connected by a salt bridge filled with potassium chlorate.

A typical rate run with equal concentrations of benzoate ion and 1-chloro-2,4-dinitrobenzene is shown in Table V.

Table V

Rate Constants for Reaction of Potassium Benzoate
with 1-Chloro-2,4-dinitrobenzene in 60 Per Cent Dioxane at 93°

Time increment minutes	$k \times 10^5$ l.mole^{-1}sec.$^{-1}$
720	4.27
960	4.37
1440	4.20
1680	4.21
2760	4.30
7650	4.03
Average	4.23

A second run was made with samples containing 0.1 M benzoic acid (concentration of the two reactants, 0.05 M) to see if the equilibrium

$$\text{C}_6\text{H}_5\text{-}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{-O K} + \text{H}_2\text{O} \rightleftharpoons \text{C}_6\text{H}_5\text{-}\underset{\underset{\text{O}}{\|}}{\text{C}}\text{-O H} + \text{K}^+ + \text{OH}^-$$
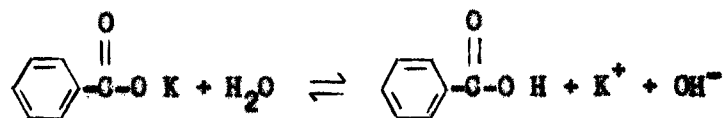
were important and if the attacking agent could have been hydroxide ion and not benzoate ion. The rate constant obtained (3.67 x 10^{-5} l.mole^{-1}sec.$^{-1}$) was close enough to that obtained with no benzoic acid added to almost rule out the possibility of the above equilibrium's being important. To further establish this point a run was made with the concentration of potassium benzoate twice that of the substrate. The rate constant, 4.23 x 10^{-5} l.mole^{-1}sec.$^{-1}$, was the same as that obtained in the first run. The concentrations used and the rate constants obtained are summarized in Table VI.

Table VI

Rate Constants for Reaction of Potassium Benzoate
with 1-Chloro-2,4-dinitrobenzene with Varying Concentrations
of Reactants

Run	Conc. potassium benzoate moles/liter	Conc. 1-Cl-2,4- dinitrobenzene moles/liter	Conc. benzoic acid moles/liter	K_{93} x 10^5 l.mole^{-1}sec.$^{-1}$
1	0.0500	0.0500		4.23
2	0.0500	0.0500	0.1000	3.67
3	0.0667	0.0333		4.23

The reactions of potassium p-methoxy benzoate and p-nitro-benzoate with 1-chloro-2,4-dinitrobenzene were carried out in an identical manner with that described above for the potassium salt of the unsubstituted benzoic acid. The rate constants are summarized in Table VII. A plot of log $\frac{k}{k^0}$ versus sigma gave a surprisingly low value of -0.207 for rho for the reaction.

The displacement of iodide from methyl iodide by benzoate ions

To compare the displacement of halogen from an alkyl halide by benzoate ion to displacement from an activated aromatic position, the potassium salts of p-methoxy benzoic acid, benzoic acid, and p-nitrobenzoic acid were reacted with methyl iodide. The reaction conditions and method of analysis were identical with those in the preceding section. It was unnecessary to use nitro-benzene to wet the silver halide, since silver iodide does not interfere with Volhard determinations. The reaction

$$AgX + KCNS \longrightarrow AgCNS + KX$$

does not occur if X^- is bromide or iodide (41). The reaction was first run at 93° in sealed ampules and proceeded to completion in a few hours. A sample without the benzoate attacking agent showed a considerable amount of displaced iodide after a few hours of heating at 93°. This was attributed to hydrolysis at the high temperature. The reaction was then run at a lower temperature of 25.5° where hydrolysis is much slower but still not negligible. Corrections for the amount of hydrolysis were applied by running

blanks. The rate constants obtained are listed in Table VII. The reaction of methyl iodide with substituted benzoate ions is less sensitive to substituent effects (rho value of -0.120) than in the case where attack was made on an aromatic carbon where rho has a value of -0.207.

Table VII

Rate Constants for Reaction of 1-Chloro-2,4-dinitrobenzene and Methyl Iodide with Potassium Salts of p-Methoxy, p-Nitro, and Unsubstituted Benzoic Acid in 60 Per Cent Dioxane Solution

Halo compound	Potassium salt	Temp. °C.	$k \times 10^{-6}$ l.mole^{-1} sec.$^{-1}$	rho
1-Cl-2,4-Dinitrobenzene	Potassium p-Methoxy Benzoate	93	47.6	
1-Cl-2,4-Dinitrobenzene	Potassium Benzoate	93	41.7	
1-Cl-2,4-Dinitrobenzene	Potassium p-Nitro-benzoate	93	22.8	-0.207
Methyl Iodide	Potassium p-Methoxy Benzoate	25.5	14.7	
Methyl Iodide	Potassium Benzoate	25.5	14.5	
Methyl Iodide	Potassium p-Nitro-benzoate	25.5	9.47	-0.120

The Kinetics of Nucleophilic Displacement of Chloride
from 1-Chloro-2,4-dinitrobenzene by Hydroxide
in 60 Per Cent Dioxane

Bunnett and Davis (24) ran the reaction of sodium hydroxide with 1-chloro-2,4-dinitrobenzene in 60 per cent dioxane at 25.2° and found a bimolecular rate constant of 6.62×10^{-2} l.mole^{-1}sec.$^{-1}$. The extent of reaction in all samples was estimated by potentiometric titration of chloride liberated using a silver electrode vs. glass electrode cell. It was desired to duplicate these results and to compare the rate constant for the reaction of hydroxide ion in 60 per cent dioxane-water with the rate constant for deuteroxide ion in 60 per cent dioxane-D_2O.

Samples containing 10 ml. of 0.045 M sodium hydroxide and 5 ml. of 0.045 M 1-chloro-2,4-dinitrobenzene were placed in tightly stoppered tubes and immersed in a well regulated water bath at 25.5°. At regular time intervals the tubes were removed and the contents were analyzed for chloride ion by the same procedure described on page 32.

The reaction involves two moles of sodium hydroxide for each mole of 1-chloro-2,4-dinitrobenzene as can be seen from the following equation:
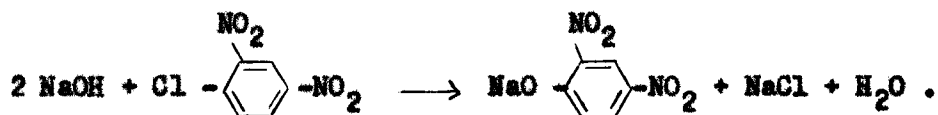
Therefore, the rate constant should be given by Equation 4
(page 19):

$$k = \frac{x}{2t \cdot b \cdot (b-x)}$$

b = concentration of the
1-chloro-2,4-dinitrobenzene

The average rate constant found was $6.32 \times 10^{-2} 1.\text{mole}^{-1}\text{sec.}^{-1}$.
The small difference between this value and Bunnett and Davis'
value is probably due to differences in technique.

The Kinetics of Nucleophilic Displacement of Chloride
from 1-Chloro-2,4-dinitrobenzene by Deuteroxide
in 60 Per Cent Dioxane

Sodium deuteroxide was prepared by weighing rapidly a small
piece of sodium metal of about the desired weight and then plac-
ing a freshly cut portion of comparable size in 60 per cent
dioxane in D_2O. The resulting solution was standardized by
titration with standard acid.

The rate run was made using conditions, technique, and
analysis identical to that described above for hydroxide ion. An
average rate constant of $11.1 \times 10^{-2} 1.\text{mole}^{-1}\text{sec.}^{-1}$ was found by
this method which is indicative of an isotope effect which will
be discussed later.

The Displacement of Chloride from 1-Chloro-2,4-dinitrobenzene
by Phenol and Triethylamine in Benzene Solution

This reaction of phenol with 1-chloro-2,4-dinitrobenzene in
benzene was first tried without the presence of triethylamine. As

was expected, no evidence of reaction could be found after heating
at 77° for 72 hours. When a trace of amine was added, displaced
chloride was found in measurable quantities after 72 hours, but
the reaction was too slow to determine an accurate rate constant.
Reactions run with equimolar amounts of phenol, triethylamine, and
1-chloro-2,4-dinitrobenzene proceeded at an easily followed rate
but gave complicated kinetics.

The procedure and method of analysis was the same as that
used in the reaction of hydroxide ion with 1-chloro-2,4-dinitro-
benzene (page 37). Runs were made with all three reagents at
equal concentrations, 0.25 M and 0.125 M, and with the phenol and
1-chloro-2,4-dinitrobenzene concentrations both 0.125 M in the
presence of 0.25 M amine.

When samples were removed from the oil bath for analysis,
triethylamine hydrochloride precipitated from the reaction
mixture as it cooled. A series of samples were run as before but
containing a carefully weighed quantity of the amine hydrochloride
to determine the effect on the rate of having this product of the
reaction present initially in sizable amounts. Attempts to add
the salt as a benzene solution failed due to its almost complete
insolubility in benzene. The presence of phenol in benzene in-
creases the solubility considerably. Excess amine hydrochloride
was used in all cases to maintain a saturated solution. The
presence of the large amount of amine hydrochloride made analysis

for displaced chloride much more difficult. It was necessary to filter carefully the water layer from the separatory funnel, since the amount of silver chloride formed was large and not all retained by the benzene-nitrobenzene layer. Large amounts of silver chloride in the titration beaker gave poor end points and erratic, low values for chloride ion replaced. The extra filtration necessitated a large amount of washing and the solution to analyze was quite dilute, but surprisingly sharp end points and very consistent results were obtained.

Infra-red spectra of solutions of phenol and triethylamine of the same concentrations used for kinetic studies were run to determine the amount of effect the amine has on the O-H bond stretching frequency of the phenol. The spectrum of a phenol in benzene solution saturated with triethylamine hydrochloride was run to determine the same effect by the salt. These spectra are found on pages 42 and 44 of this thesis.

Instantaneous rate constants were determined by plotting x (the amount of reaction) vs. t (time) and finding $\frac{dx}{dt}$ by the mirror method. A mirror was placed on the curve at each experimentally determined point and turned until the line seemed to continue through the mirror. A line drawn along the bottom of the mirror is a normal to the curve and is perpendicular to the tangent. The negative reciprocal of the slope of the normal is the slope of the tangent and the value of $\frac{dx}{dt}$ at the point on the curve.

Figure 1

#7163 — 0.25 M Phenol.
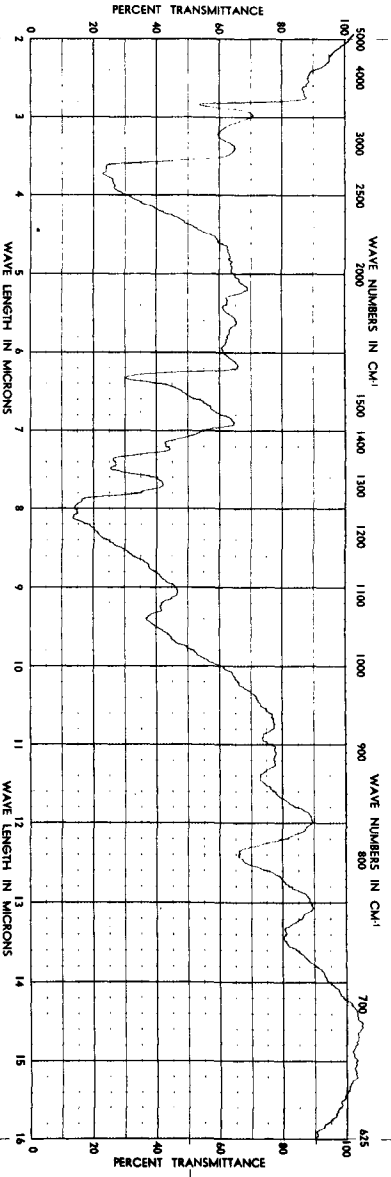
#7159 — 0.25 M Phenol and 0.25 M Triethylamine.

#7164 — 0.25 M Phenol and Saturated with Triethylamine Hydrochloride.

PERCENT TRANSMITTANCE

WAVE LENGTH IN MICRONS

WAVE NUMBERS IN CM⁻¹

PERCENT TRANSMITTANCE

Figure 2

#7162 — 0.125 M Phenol and 0.125 M Triethylamine.

#7160 — 0.125 M Phenol and 0.125 M Triethylamine.

#7161 — 0.0833 M Phenol and 0.0833 M Triethylamine.

NO.		DATE			INDEX
		11-2-33		SAMPLE	

FROM
II.

SAMP. CELL-1   MM   CMS.
REF. CELL   2   3MM   CMS.
CHEM.   MG.   MG.
SOLV.   C₆H₆
VOL.   C.C.   %   C.C.   %
F.S. SOLID   C₁ GAS   MM

PERCENT TRANSMITTANCE

WAVE NUMBERS IN CM⁻¹

WAVE LENGTH IN MICRONS

PERCENT TRANSMITTANCE

NO.		DATE			INDEX
		11-2-34		SAMPLE	

FROM
II.

SAMP. CELL-1   MM   CMS.
REF. CELL   2   MM   CMS.
CHEM.   MG.   MG.
SOLV.   C₆H₆
VOL.   C.C.   %   C.C.   %
F.S. SOLID   C₁ GAS   MM

PERCENT TRANSMITTANCE

WAVE NUMBERS IN CM⁻¹

WAVE LENGTH IN MICRONS

PERCENT TRANSMITTANCE

NO.		DATE			INDEX
I.		11-2-34		SAMPLE	

FROM
II.

SAMP. CELL-1   MM   CMS.
REF. CELL   2   MM   CMS.
CHEM.   MG.   MG.
SOLV.
VOL.   C.C.   %   C.C.   %
F.S. SOLID   C₁ GAS   MM

PERCENT TRANSMITTANCE

WAVE NUMBERS IN CM⁻¹

WAVE LENGTH IN MICRONS

PERCENT TRANSMITTANCE
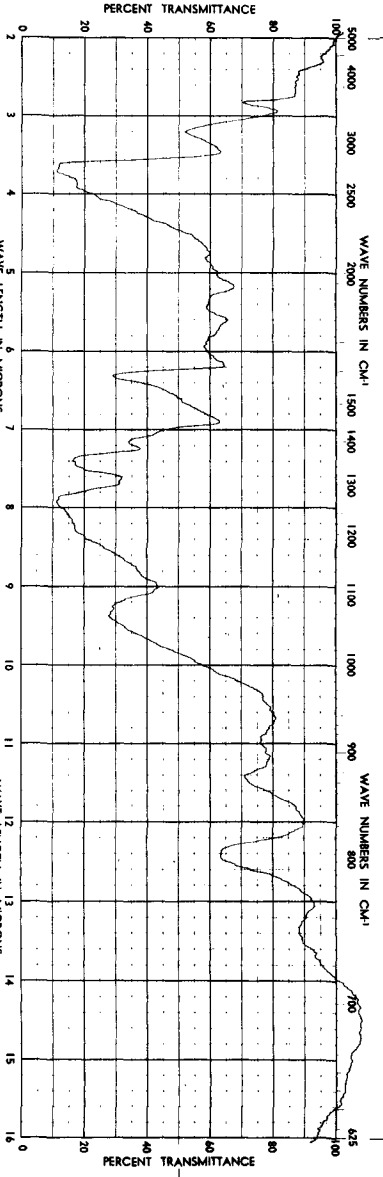
The data obtained for the reactions of phenol, triethylamine, and 1-chloro-2,4-dinitrobenzene at varying concentrations of reactants and with or without added triethylamine are summarized in Table VIII.

The mechanisms whose rate expressions were attempted to fit with the experimental data obtained were as follows:

1. Prior equilibrium with much tight complexing between the products of the equilibrium.

$$\text{C}_6\text{H}_5\text{—OH} + \text{NEt}_3 \underset{K}{\rightleftharpoons} \text{C}_6\text{H}_5\text{—O}^- + \text{HNEt}_3^+$$
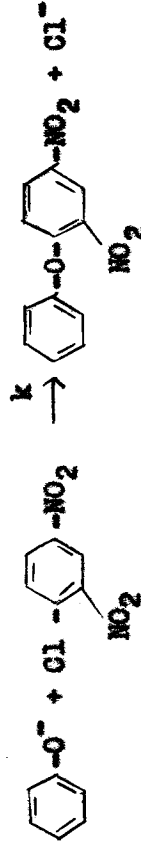
(6) $\dfrac{dx}{dt} = kK \ (a-x)(b-x)(c-x)$

  a = amine concentration

  b = phenol concentration

  c = 1-chloro-2,4-dinitrobenzene concentration

2. Same as 1 except amount of complexing of equilibrium products is small.

(7) $\dfrac{d\left[\text{Cl}^-\right]}{dt} = kK \dfrac{\left[\text{C}_6\text{H}_5\text{—OH}\right]\left[\text{NEt}_3\right]\left[\text{Cl—C}_6\text{H}_3(\text{NO}_2)_2\right]}{\left[\text{HNEt}_3^+\right]}$

3. Termolecular

(8) $\dfrac{dx}{dt} = k(a-x)(b-x)(c-x)$

Table VIII

Data Obtained for the Reactions Phenol, Triethylamine,
and 1-Chloro-2,4-dinitrobenzene

Time min.	Concentrations (mole/l.)			x Concentration chloride ion (mole/l.)	$\dfrac{dx}{dt}$
	1-chloro-2,4-dinitrobenzene	phenol	triethyl-amine		
900	0.25	0.25	0.25	0.0376	4.33 x 10^-5
1200	0.25	0.25	0.25	0.0396	3.85
1500	0.25	0.25	0.25	0.0405	3.50
2400	0.25	0.25	0.25	0.0572	3.08
990	0.125	0.125	0.125	0.0093	7.84 x 10^-6
1230	0.125	0.125	0.125	0.01125	7.42
2640	0.125	0.125	0.125	0.0187	6.54
4500	0.125	0.125	0.125	0.0266	4.48
1085	0.125	0.125	0.250	0.0144	10.0 x 10^-6
1380	0.125	0.125	0.250	0.0162	9.68
1685	0.125	0.125	0.250	0.0196	8.75
2480	0.125	0.125	0.250	0.0281	7.60
3060	0.125	0.125	0.250	0.0297	7.23
3930	0.125	0.125	0.250	0.0335	6.43
7155	0.125	0.125	0.250	0.0530	6.34
2220	0.0833	0.0833	0.0833	0.00534	1.78 x 10^-6
2790	0.0833	0.0833	0.0833	0.00610	1.55
3630	0.0833	0.0833	0.0833	0.00713	1.44
3810	0.0833	0.0833	0.0833	0.00753	1.26
4290	0.0833	0.0833	0.0833	0.00805	1.24
5640	0.0833	0.0833	0.0833	0.00976	1.16

DISCUSSION

The Kinetic Study of Displacement of Halogen
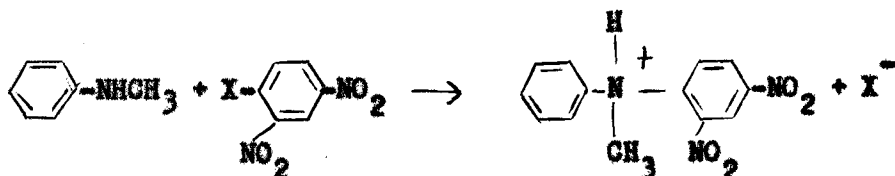from 1-X-2,4-Dinitrobenzenes by N-Methylaniline

The rate constants for the reactions of N-methylaniline with

1-fluoro-, 1-chloro-, and 1-bromo-2,4-dinitrobenzenes in both

nitrobenzene and 99.8 per cent ethanol solvent, which are summar-

ised in Table II, clearly show that a reversal of the usual order

for nucleophilic displacement of halogen, $F > Cl > Br$ has been

accomplished. The order found in both solvents is $Br > Cl > F$.

If only the electronegativity of the halogens is considered, the

order of ease of displacement should definitely be $F > Cl > Br$.

Not only is fluorine the most electronegative and most able to go

off as a negative ion, but it also renders the ring atom to which

it is attached more positive and facilitates attack by a nucleo-

philic reagent. However, the carbon-fluorine bond is stronger

than the carbon-chlorine or carbon-bromine bond and this factor

acts in direct opposition to the electronegativity factor. The

electronegativity difference is dominant in most aromatic,

nucleophilic substitution reactions giving the order $F > Cl > Br$,

but the bond energy becomes of much greater importance when the

nucleophile is weak. The high reactivity of activated aryl

fluorides compared to other similarly activated aryl halides is

an indication that bond breaking is not nearly so important in the

transition states as in the case of nucleophilic displacement of

halogen from an aliphatic carbon. The order of displacement at aliphatic carbons is always found to be Br > Cl > F.

The transition state for the replacement of halogen from an aromatic carbon must approach a configuration in which the carbon atom undergoing substitution is nearly tetrahedral. There is not enough evidence available to definitely determine the timing of the reaction nor to prove the presence or absence of reaction intermediates. If the free energy of formation of the new bond between the nucleophile and the carbon holding the halogen to be replaced determines the rate of reaction, the normal order of displacement F Cl Br would be expected. If the rate controlling step can be made to involve stretching the old bond beyond normal covalent distances, the inversion noted above is possible. The amount of bond breaking in the transition state was increased by using a weak nucleophile and relatively non-polar solvent, nitrobenzene.

In the case chosen the effect of the weak nucleophile must be the more important than the solvent effect since change to a more polar hydroxylic solvent, ethanol, did not change the order back to the "normal" one of F > Cl > Br as it was anticipated that it might. It will be noted, however, in Table II that the rate of replacement of fluoride is much nearer the rates of replacement of chloride and bromide in ethanol than in nitrobenzene. This is undoubtedly due to the greater solvation of fluoride in ethanol than in nitrobenzene and subsequent ease of removal of the fluoride ion.

The rate determining step for the reaction of N-methylaniline with activated aryl halides must be represented by the following equation since the reaction is first order with respect to both the nucleophile and the halo compound.

$$\text{C}_6\text{H}_5\text{-NHCH}_3 + \text{X-C}_6\text{H}_3(\text{NO}_2)\text{-NO}_2 \rightarrow \text{C}_6\text{H}_5\text{-N}^+(\overset{\text{H}}{\underset{\text{CH}_3}{|}})\text{-C}_6\text{H}_3(\text{NO}_2)\text{-NO}_2 + \text{X}^-$$

This reaction may proceed in two steps with the formation of an intermediate with a tetrahedral configuration at the carbon attached to the halogen. Two transition states would then be found on either side of the unstable intermediate. Since bond breaking is so important in the rate determining step of reactions with N-methylaniline, if it is a two-step mechanism, the second step must be rate determining. Existing data do not enable one to distinguish between a one and two-step process.

The reaction illustrated by the equation above is probably endothermic so a decrease in the stability of the products of this step would shift the transition state configuration toward that of the reaction products. This was accomplished by using a nucleophile with considerable steric requirements and a very poor solvating solvent, nitrobenzene.

The activation energies and entropies listed in Table II are not highly accurate because the accurately measured rate constants span only relatively small temperature intervals. The

very slow rates of reaction at low temperatures in nitrobenzene were not measured with high accuracy but give reasonably accurate values for the thermodynamic parameters when compared with high temperature rates. The heats of activation may be in error by one or two K.cal. which would cause an uncertainty in ΔS values of as much as six entropy units.

The very large negative values for the entropy of activation are not unusual for reactions of the charge type produced by the initial attack of N-methylaniline on 1-halo-2,4-dinitrobenzene (42). It has been previously noted (17) that the superiority of fluoride in most displacements from activated aromatic positions by nucleophiles is due to low energies of activation which are partially compensated by large negative activation entropies. If, as was suggested by Chapman and Parker, this is correlated with the large heat and negative entropy of solvation of the fluoride ion, the fact that the entropies are increased when N-methylaniline is substituted for aniline in ethanol solution is in good agreement with the hypothesis introduced above that bond breaking has become more important to the activation process and the transition state has a configuration closer to products.

The Displacement of Halogen from 1-X-2,4-Dinitrobenzene
by Aniline

When a stronger nucleophile such as aniline is used to replace halogens from activated aryl positions the "normal" order

of replacement, $F > Br > Cl$ is found in nitrobenzene. The rate constants found in Table III show fluoride to be 6.3 times as fast as bromide which is replaced roughly twice as fast as chloride. In this reaction the transition state must have a configuration very similar to products and bond forming must be much more important than the bond breaking step.

It is instructive to compare the rates in nitrobenzene with those in 99.8 per cent ethanol (Table IV). The reaction is much faster in the latter solvent as would be expected. Also, as was expected, the fluoride replacement is a great deal faster in comparison to the bromide, 41.5 times, and chloride, 62.5 times, than it is in nitrobenzene solvent. This is in line with the results observed with N-methylaniline even where a reversal of order was found. In every case, the rate of displacement of fluoride is markedly increased when the solvent is changed from nitrobenzene to ethanol. This is due to the greater energy of solvation of fluoride in the hydroxylic solvent ethanol.

In both ethanol and nitrobenzene, the reaction of aniline with 1-halo-2,4-dinitrobenzene reverses the position of fluoride from slowest to fastest but bromide is still replaced about twice as fast as chloride just as it is when N-methylaniline is the nucleophilic reagent. This can probably be attributed to the greater polarizability of the bromide ion and increased steric effects of the larger atom.

The Cleavage of a Sterically Hindered Ether
with Weak Nucleophiles

It was hoped that by using a weak nucleophile, attack on
the carbon at the more hindered end of the oxygen bridge of the
$2,2',4,4'$-dinitro-6-s-butyldiphenyl ether could be obtained. If
in the reaction of N-methylaniline or other weak base with the
ether, the intermediate

R_1 = phenyl

R_2 = methyl or hydrogen
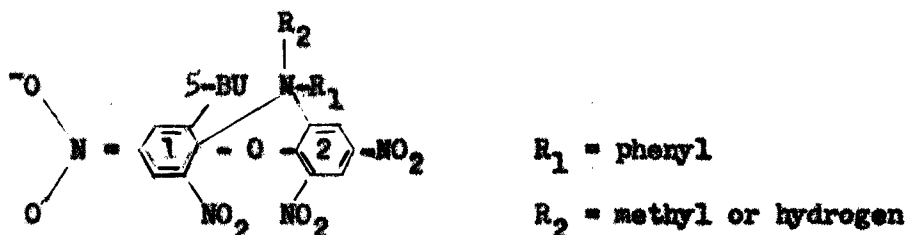
could exist long enough to allow ring 2 to become perpendicular
to ring 1, the formation of the quinoid type intermediate
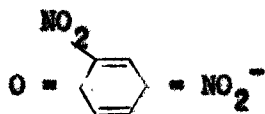
could provide a low energy path for the breakdown of the inter-
mediate which would have a structure very similar to products.
This would be the reversal of normal cleavage where attack always
occurs on the less hindered position (43).

The successful reversal of the displacement order of
halogens by increasing the importance of bond breaking in the
transition state leads one to believe that the cleavage of the
highly hindered $2,2',4,4'$-dinitro-6-s-butyldiphenyl ether might
be made to go by an analogous mechanism. If a weak nucleophile

could be found that would attack the hindered carbon, the bond breaking step would be easier than if the base had attacked the carbon at the less hindered end of the oxygen bridge.

R_1 = phenyl

R_2 = methyl or hydrogen
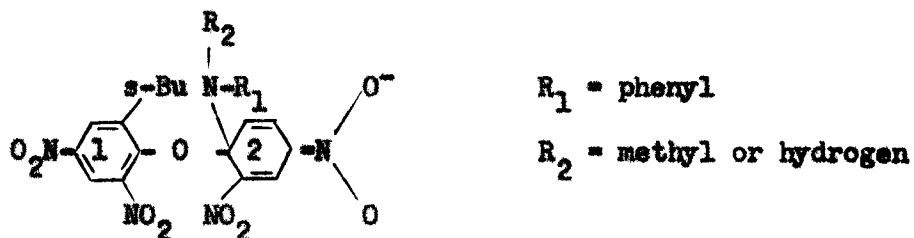
It is impossible for ring 1 to become perpendicular to ring 2 without interference between the _ortho_ nitro group on ring 2 and _ortho_ nitro or the secondary butyl group on ring 1.

The weak nucleophiles tried, N-methylaniline, p-chloroaniline and p-nitroaniline, would not cleave the highly hindered ether even in excess base as solvent and with prolonged periods of heating in a pressure tube at high temperature.

The stronger nucleophile, aniline, cleaved the ether at temperatures as low as $25°$ in excess base as solvent. Cleavage also occurred in ethanol solvent, but in both solvents the secondary amine obtained was the one produced by attack at the less hindered position.

The Nucleophilic Displacement of Halogens by Benzoate Ions

Only one case has been reported in the literature of the preparation of an ester by replacement of an activated aromatic

halogen with carboxylate ion. Kym (44) reports the preparation
of 2,4-dinitrophenylbenzoate by reaction of sodium benzoate with
1-chloro-2,4-dinitrobenzene. No kinetic studies of reactions
with carboxylate ions as nucleophiles are to be found in the
literature. It was decided to carry out some reactions of this
type and to follow the kinetics, if possible, and perhaps gain
some knowledge of the carboxylate ion as a nucleophile. The
benzoate ion was of particular interest since its strength as a
nucleophile could be varied by adding electron withdrawing and
repelling substituents. It was also hoped that attack on the
labile 1-halo-2,4-dinitrobenzene system might prove an easy path
for preparation of esters.

Silver benzoate was the first compound used as a source of
benzoate attacking agent. Many silver salts are soluble in
acetonitrile and this solvent was preferred to hydroxylic
solvents, such as water, which might hydrolyse the reagent and
provide hydroxyl ion which could in turn attack the substrate.
Silver benzoate also provides the attractive possibility of added
driving force for the reaction due to electrophilic attack by the
silver ion on the displaced halogen and subsequent precipitation
of the silver halide. As mentioned on page 31 of this thesis,
silver benzoate was very sparingly soluble in acetonitrile and
the reaction with 1-chloro-2,4-dinitrobenzene in acetonitrile
solvent did not proceed cleanly. The reaction mixture became

filled with a heavy, black, tarry deposit and no reasonable analysis for displaced halide ion could be made.

Potassium benzoate proved a much superior source of benzoate ion. It was extremely insoluble in acetonitrile so 60 per cent dioxane-water was chosen as solvent. The reaction proceeds at an easily followed rate at 93° and gave good second order kinetics. Runs were made with varying amounts of benzoate ion and added benzoic acid to see if hydroxide ion formed by reaction of potassium benzoate with water could be the real attacking species. The same second order rate constant was found for all runs so benzoate ion must be the attacking agent. A rough analysis of the reaction products showed that an almost stoichiometric amount of 2,4-dinitrophenol was obtained. A prepared sample of the ester, m.p. 132° to 133°, was hydrolyzed almost completely in a 60 per cent dioxane solution when heated at 93° for 48 hours.

The rate of reaction of the potassium salt of p-methoxy-benzoic acid with 1-chloro-2,4-dinitrobenzene was just slightly faster than that of the potassium salt of the unsubstituted acid. The electron releasing ability of the p-methoxy group would be expected to increase the nucleophilic strength of the carboxylate anion. When the p-nitro substituent is added, the rate of reaction drops by approximately a factor of two. This is, of course, the predicted behavior. A positive substituent in a

conjugated position should decrease the strength of nucleophilic center. A plot of log $\frac{k}{k_0}$ versus sigma gave a surprisingly low value of -0.207 for rho for the replacement of activated aryl chloride with benzoate ion.

The low value of rho for the replacement of activated aryl halogens with substituted benzoate ions made it of interest to compare this reaction with replacement of halogen from an alkyl halide by these same anions. Methyl iodide was chosen as the substrate. Iodide is more easily replaced from an alkyl carbon than the other members of the halogen family due to its greater polarizability. The replacement of iodide by benzoate ions proceeded at a rapid rate at 93° in 60 per cent dioxane solution but a large portion of the replacement was due to hydrolysis at this rather high temperature. The reaction was carried out at 25° where hydrolysis was very slow and could be accounted for by running blanks. The rate of reaction at this low temperature was quite slow and rather difficult to follow. The rates of reaction of the p-methoxy, p-nitro, and unsubstituted benzoate ions with methyl iodide fall in the same general order as for replacement of the activated aryl chloride. p-Methoxy and the unsubstituted benzoate ions react at almost equal rates with the p-methoxy slightly faster. The p-nitrobenzoate ion reacts noticeably slower than the other two. The rho value for the reaction is -0.120.

Neither of the two cases studied, replacement of an activated aryl halide nor an alkyl halide, gave a large value for rho.

Replacement of the chloride from the aromatic position was some-
what more sensitive to substituent effect in the nucleophile then
replacement of the alkyl halide. The surprisingly low sensi-
tivity to nucleophilic strength in both reactions points to a
transition state that is very close to reactants. If the transi-
tion states were of such a nature that the new bond had become
completely covalent, the magnitude of the _rho_ values should
approach or exceed that for the ionization of the corresponding
acids instead of being smaller. This is the opposite of the
reaction of N-methylaniline with 1-chloro-2,4-dinitrobenzene in
both ethanol and nitrobenzene where the transition state configura-
tion lies very close to products and bond breaking is rate
determining.

**The Replacement of Chloride from 1-Chloro-2,4-dinitrobenzene
by Deuteroxide Ion in 60 Per Cent Dioxane Solution**

The evidence presented by Bunnett and Davis (24) proves
quite conclusively that hydroxide ion is a very weak nucleophile
in spite of its high base strength. It reacts with 1-chloro-
2,4-dinitrobenzene approximately 20,000 times as slowly as thio-
phenoxide ion which is a very weak base. This is just one of
many examples pointing out the fact that great caution must be
observed in extending the unusual parallelism between nucleophilic
reactivity and basicity beyond comparison of reagents of very
similar types.

Methoxide ion reacts 33 times as fast with 1-chloro-2,4-dinitrobenzene as hydroxide ion and an interesting close parallel is observed in the low nucleophilic reactivity of ammonia as compared to methylamine. With 1-chloro-2,4-dinitrobenzene in ethanol, methylamine reacts 800 times as fast as ammonia. Ammonia is a weaker base than methylamine, but this vast difference in nucleophilic reactivity must relate to some special effect of replacing a hydrogen atom by an alkyl group. Whatever this effect is, it no doubt is also responsible for the high reactivity of methoxide as compared to hydroxide.

Since the most obvious difference between a hydrogen and a methyl group is the difference in mass, it seemed of interest to see if an isotope effect could be found. This was done by measuring the rate of the reaction of deuteroxide ion with 1-chloro-2,4-dinitrobenzene and then comparing it to the rate of reaction of hydroxide ion with the same substrate. Unfortunately, it is not possible to use exactly the same solvent for the two reactions. The deuteroxide reaction was carried out in 60 per cent dioxane and 40 per cent deuterium oxide, and the hydroxide reaction was in 60 per cent dioxane and 40 per cent water solvent.

As can be seen by comparing rate constants for the two reactions, there is an increase in rate of approximately 76 per cent (from 6.32×10^{-2} l.mole^{-1}sec.$^{-1}$ to 11.1×10^{-2} l.mole^{-1}sec.$^{-1}$) when the hydrogen of a hydroxide ion is replaced by a deuterium

atom. It is not clear just how this isotope effect arises. It seems quite possible that the change from 40 per cent water to 40 per cent deuterium oxide in the solvent could have more effect on the rate than the change from hydrogen to deuterium in the attacking species. Deuterium oxide is the superior solvating agent for the displaced halide ion. It is possible that deuterium may form a stronger "hydrogen" bond with the displaced chloride ion than hydrogen or deuterium oxide may do a better job of solvating the displaced anion. Either of these effects or both working together would provide a lower energy path for decomposition of the transition state than in water solution and give rise to a faster rate.

It would be of interest to compare the rate of ND_3 with ammonia for the same reaction. However, lack of time and materials make it impossible to carry out the experiment and include it in this thesis.

Nucleophilic Displacement of Chloride
from l-Chloro-2,4-dinitrobenzene
by Phenol and Triethylamine in Benzene

Phenol will not replace chloride from l-chloro-2,4-dinitro-benzene in benzene solution. The presence of a small amount of amine forms phenoxide ion which is known to be a fairly strong nucleophile (24) and the reaction proceeds. This is directly analogous to the reaction of alcohols with l-fluoro-2,4-dinitro-benzene in the presence of a tertiary amine which was proposed by Whalley (3) as a means of derivatizing alcohols.

The kinetics of the reaction are complicated and the rate definitely depends on the concentration of the amine. The rate expression which gives the most nearly constant constant with varying concentrations of reactants is Equation 7 on page 45. The more expected rate expression, the prior equilibrium with tight complex formation gave a two-fold increase in rate constant when the reactants' concentrations were doubled as can be seen in Table II.

The addition of an initial amount of triethylamine hydrochloride sufficient to saturate the reaction mixture decreased the rate approximately 41 per cent. This fact and the smaller decrease in rate constant when the amine concentration is doubled with respect to the other two reactants points to a mechanism such as number 2 on page 33. The assumption made to obtain this rate expression is that the prior equilibrium of the phenol and triethylamine lies on the left (toward reactants) and only a small amount of phenoxide ion is available to replace the chloride. The triethylamine hydrohalide concentration appears in the denominator and decreases the rate constant. The rate constants listed in Table II undoubtedly include an equilibrium constant as a factor but the equilibrium constant must be small or the above assumption is not valid.

The decrease in third order rate constant upon addition of excess triethylamine hydrochloride may be a result of complex

Table II

Rate Constants Obtained for the Reaction of Phenol, Triethylamine, and 1-Chloro-2,4-dinitrobenzene in Benzene Solution

Mechanism	Triethylamine Conc. in moles/l.	1-Chloro-2,4-dinitrobenzene conc. in moles/l.	Phenol conc. in moles/l.	Rate Constant
Termolecular	0.250	0.250	0.250	5.4×10^{-3} l.moles^{-2}min.$^{-1}$
Termolecular	0.125	0.125	0.125	5.1×10^{-3}
Termolecular	0.250	0.125	0.125	4.5×10^{-3}
Prior Equilibrium	0.250	0.250	0.250	10.6×10^{-4} l.moles^{-1}min.$^{-1}$
Prior Equilibrium	0.125	0.125	0.125	5.8×10^{-4}
Prior Equilibrium	0.250	0.125	0.125	5.5×10^{-4}
Prior Equilibrium (with high conc. of NEt$_3$·HCl added initially)	0.0833	0.0833	0.0833	3.2×10^{-3}

formation between the phenol and the salt. This could lower the amount of phenol available for reaction with the free amine and then with the substrate as phenoxide ion. There is no way of distinguishing between the two mechanisms experimentally.

The infra-red spectra show considerable effect on the OH bond stretching of the phenol by both triethylamine and triethylamine hydrochloride. The spectrum of 0.25 M phenol in benzene shows the characteristic strong OH adsorption at 2.85 microns. The spectrum containing 0.25 M phenol and 0.25 M triethylamine and the one containing 0.25 M phenol and saturated with 0.25 triethylamine hydrochloride both show a much less intense adsorption by the OH at 2.85 microns. The deep, broad adsorption at four microns is characteristic of quaternary ammonium ions and is present in both the spectra. Therefore, it seems obvious that phenol and triethylamine do complex or ionize appreciably in benzene solution. This is particularly obvious from comparison of the spectrum of the benzene solution containing 0.125 M phenol and 0.125 M triethylamine with the one containing 0.125 M phenol and 0.25 M triethylamine. The per cent transmittancy for the OH peak changes from 57 per cent to 70 per cent upon doubling the amine concentration.

SUMMARY

Evidence is presented for the reversal of the normal order of nucleophilic replacement of activated aromatic halogens. This was achieved by greatly increasing the importance of bond breaking in the transition state. The increase in importance of the bond breaking step was brought about by (a) increasing the steric requirement of the nucleophile and (b) decreasing the solvating power of the solvent. The former is exemplified by the use of N-methylaniline rather than aniline and the latter by substituting nitrobenzene for ethanol. An increase in the importance of the bond breaking step is synonymous with a shift of the transition state toward products.

A study was made of substituted and unsubstituted benzoate ions as nucleophiles. Substituents were found to have surprisingly little effect on the strength of the benzoate ion as a nucleophile. Replacement of activated aromatic halogens was more sensitive to substituents in the benzoate ion than was replacement of aliphatic halogens. This points to a transition state located very close to reactants for this reaction.

The reaction of 1-chloro-2,4-dinitrobenzene with deuteroxide ion in 60 per cent dioxane - 40 per cent deuterium oxide is faster than the corresponding reaction of hydroxide ion in 60 per cent dioxane - 40 per cent water. It is not perfectly clear whether this is an isotope effect in the attacking species or a change in

the solvating power of the solvent. The latter seems the more logical possibility.

Replacement of halogen from 1-chloro-2,4-dinitrobenzene with phenol and triethylamine in benzene solution gave complicated kinetics. The rate depends on the concentration of all three reactants and is inhibited by added amounts of the triethylamine hydrochloride, one of the reaction products. A mechanism is proposed involving a prior equilibrium between the amine and the phenol which provides a small amount of phenoxide ions. The phenoxide ion then attacks the substrate and replaces the aromatic halogen.

BIBLIOGRAPHY

(1) L. Pisani, Compt. rend., 39, 852 (1854).

(2) J. F. Bunnett and R. E. Zahler, Chem. Revs., 49, 273 (1951).

(3) W. B. Whalley, J. Chem. Soc., 2241 (1950).

(4) R. R. Porter and F. Sanger, Biochem. J., 42, 287 (1948).

(5) F. Sanger, Biochem. J., 45, 563 (1949).

(6) A. Brewin and E. E. Turner, J. Chem. Soc., 332 (1928).

(7) O. L. Brady and F. R. Cropper, J. Chem. Soc., 507 (1950).

(8) A. H. Rheinlander, J. Chem. Soc., 3099 (1923).

(9) S. D. Ross and I. Kuntz, J. Am. Chem. Soc., 76, 3000 (1954).

(10) A. Singh and D. H. Peacock, J. Chem. Soc., 1410 (1935).

(11) H. J. Van Opstall, Rec. Trav. chim., 52, 901 (1933).

(12) M. B. Chapman and J. W. James, Chem. and Ind., 633 (1951).

(13) M. B. Chapman and R. E. Parker, J. Chem. Soc., 3301 (1951).

(14) R. R. Bishop, E. A. Cavell and N. B. Chapman, J. Chem. Soc., 437 (1952).

(15) N. B. Chapman and J. L. Levy, J. Chem. Soc., 1673 (1952).

(16) E. A. Cavell and N. B. Chapman, J. Chem. Soc., 3392 (1953).

(17) N. B. Chapman, R. E. Parker and P. W. Soanes, J. Chem. Soc., 2109 (1954).

(18) M. F. Hawthorne. Unpublished research. Iowa State College, Ames, Iowa. 1954.

(19) E. Berliner, M. J. Quinn and P. J. Edgerton, J. Am. Chem. Soc., 72, 5305 (1950).

(20) E. Berliner and L. C. Monack, J. Am. Chem. Soc., 74, 1574 (1952).

(21) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., New York (1940), p. 186.

(22) J. F. Bunnett and A. Levitt, J. Am. Chem. Soc., 70, 2778 (1948).

(23) J. F. Bunnett, F. Draper, P. Ryason, P. Noble, R. Tonkyn and R. E. Zahler, J. Am. Chem. Soc., 75, 642 (1953).

(24) J. F. Bunnett and G. T. Davis, J. Am. Chem. Soc., 76, 3013 (1954).

(25) J. F. Bunnett, H. Moe and D. Knutson, J. Am. Chem. Soc., 76, 3936 (1954).

(26) Joseph Miller, J. Chem. Soc., 3550 (1952).

(27) A. Beckwith, J. Miller and G. Leahy, J. Chem. Soc., 3552 (1952).

(28) J. Miller and V. Williams, J. Chem. Soc., 1475 (1953).

(29) R. L. Heppolette and J. Miller, J. Am. Chem. Soc., 75, 4265 (1953).

(30) B. V. Tronov and F. A. Kruger, J. Russ. Phys. Chem. Soc., 58, 1270 (1926).

(31) F. W. Bergstrom, R. E. Wright, C. Chandler and W. A. Gilker, J. Org. Chem., 1, 170 (1936).

(32) F. W. Bergstrom and C. H. Horning, J. Org. Chem., 11, 34 (1946).

(33) J. D. Roberts, H. E. Simmons, L. A. Carlsmith and C. W. Vaughan, J. Am. Chem. Soc., 75, 3290 (1953).

(34) H. Lund and J. Bjerrum, Ber., 64, 210 (1931).

(35) F. Henle, Ber., 53, 719 (1920).

(36) G. W. Wheland, "Advanced Organic Chemistry," John Wiley and Sons, Inc., New York (1949), p. 62.

(37) S. Siggia, "Quantitative Organic Analysis Via Functional Groups," John Wiley and Sons, Inc., New York (1949), p. 111.

(38) N. B. Chapman, R. E. Parker and P. W. Soanes, Chem. and Ind., 148 (1951).

(39) M. F. Hawthorne and D. J. Cram, J. Am. Chem. Soc., 74, 5864 (1952).

(40) G. Beste and L. Hammett, _J_. _Am_. _Chem_. _Soc_., _62_, 2481 (1940).

(41) H. H. Willard and N. H. Furman, "Elementary Quantitative
        Analysis," D. Van Nostrand Co., New York (1940),
        p. 185.

(42) A. A. Frost and R. G. Pearson, "Kinetics and Mechanism,"
        John Wiley and Sons, Inc., New York (1953), Chap. 7.

(43) Y. Ogato and M. Okano, J. Am. _Chem_. _Soc_., _71_, 3211 (1949);
        ibid., _71_, 3214 (1949).

(44) O. Kym, _Ber_., _32_, 3539 (1899).

ACKNOWLEDGMENTS

The author wishes to express his sincerest appreciation to Professor George S. Hammond for his continual inspiration and unfailing enthusiasm without which this work could never have been completed.

Sincere thanks are due Dr. M. F. Hawthorne for many helpful and stimulating discussions.

The author also wishes to express gratitude to his wife, Earline, for her understanding and assistance while this work was in progress.