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THE CHLORINATION OF ANILINES; MECHANISM OF THE REARRANGEMENT
OF
N-CHLOROANILINES

by

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INTRODUCTION

1. General Statement

The chlorination of aniline was a topic of interest at the turn of this century.¹ Apparently, the very high reactivity of the system, the complexity of the product ratios, and often high yields of uncharacterized tarry materials drove researchers away from detailed studies of the reaction. Support for this proposition comes from the large volume of work that was reported from that time to the very recent past on the chlorination of anilides, and especially on the aspect of that study that is known as the Orton Rearrangement,^{2a,b,c} while a gap of about forty years existed between reports that show a serious attempt to study the mechanism of chlorination of anilines.^{1,3,4}

This thesis deals with a system of stable yet very reactive compounds. It deals with molecules that are "ambident"⁵ nucleophiles and at the same time quite strong bases which participate in an acid catalyzed reaction. Anilines can undergo substitution both on the nitrogen and on the ring, the products of the ring substitution are themselves bases and nucleophiles with basicities and nucleophilicities comparable to that of the reactants.

This thesis describes the synthesis and general properties of N-chloroanilines. A recent review lists eight other N-substituted compounds of similar structure,⁶ all of which undergo acid catalyzed rearrangement of a group attached to the nitrogen to yield ring substituted products. In seven of

these, the reviewer states that the principal product of the rearrangement arises from introduction of the migrating group into the para position of the aromatic ring. In these cases it has been shown that the rearrangement is an intermolecular process. The eighth compound, N-nitroaniline, rearranges by an intramolecular process and its principal product is o-nitroaniline.^{7,8} N-chloroanilines also rearrange to give very high but variable yields of o-chloroanilines. This suggests that there may be intramolecular processes involved in this rearrangement.

Much of the work described here, therefore, was directed towards an elucidation of the mechanism of rearrangement of N-chloroanilines. An exhaustive study has led to the conclusion that the major process taking place cannot be intramolecular.

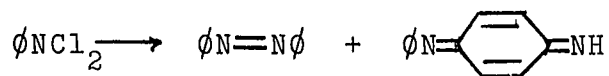
It will also be shown that N-chloroanilines are intermediates in the chlorination of anilines with certain chlorinating agents. This, therefore, is a study of the mechanism of chlorination of anilines by a detailed study of the N-chloroaniline intermediate.

2. N-Chloro Compounds

Proof of the existence of N-chloro derivatives of reactive anilines was presented in 1965.³ Before the presentation of that proof, there was much speculation in the literature that N-haloanilines were intermediates in the halogenation of anilines. These speculations were based on

the results of kinetic studies of the halogenation of anilines and what appeared to be unusually high yields of ortho substituted products especially from the chlorination reaction. The most recent of these specualtions came from Neale and his coworkers who observed o/p ratios in the chlorination of N-methylaniline that were always greater than 2.0, and a value of 1.85 for N-t-butylniline.⁴ They concluded that the product ratios provided circumstantial evidence for N-chloroanilines which were formed and rearranged under the conditions of the reaction. The authors did not define what the nature of the rearrangement process might be, but they suggested that certain variations in their results could be explained by a competition between the rearrangement of the N-chloroaniline and the direct attack of some chlorinating agent on the aniline. Their statements further implied that the major process was the rearrangement and not the direct attack pathway.

In 1913, Goldschmidt reported the preparation of N,N-dichloroaniline by the reaction of aniline with hypochlorous acid.¹ It was explosive on isolation and could not be analyzed but was identified by chemical reactions analogous to that of N,N,2,4,6-pentachloroaniline. It decomposed rapidly in the presence of water, and with bases, such as sodium hydroxide, aniline and ammonia, to give azobenzene and phenylquinone diimine.



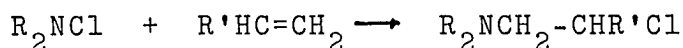
In the presence of acids rearrangement took place to give 2,4-dichloro-, and 2,4,6-trichloroaniline. Other evidence for N-haloanilines suggests that they are short-lived intermediates in the halogenation of anilines. For example, in 1925 Francis, Hill and Johnson showed that the results of kinetic studies on the bromination of anilines could best be interpreted by assuming that N,N-dibromoaniline was formed and rearranged to give mainly dibrominated products.⁹

In contrast to the very few references to N-chloroanilines, there is an extensive literature on the preparation and properties of other N-chloro compounds. The simplest member of the family, chloramine (NH_2Cl) is an important industrial chemical famous for its use in the Raschig synthesis of hydrazine.^{10,11} N-Chloro derivatives of aliphatic primary and secondary amines are well known compounds which can be prepared simply by mixing the amine or its salt with an aqueous hypochlorite solution.^{12a,b,c} Some reactions of N-chloroanilines are:

- 1) The Hofmann-Loeffler-Freytag reaction in which aliphatic N-chloroanilines cyclize in concentrated sulfuric acid to give pyrrolidine and substituted pyrrolidines.^{7c}



- 2) Beta-elimination of HCl to give imines which are then hydrolyzed in aqueous media to yield aldehydes and ketones.¹³
- 3) Free radical addition to alkenes.¹⁴



4. Reaction with ferrous ion to give nitrogen radicals.¹⁵

N-Chloroanilides are well known as the compounds studied in the Orton Rearrangement.² These compounds have been shown to rearrange by an intermolecular process in which chlorine is an intermediate. N-Chloroanilides and other N-chloroamides are also well known as chlorinating agents.⁴

The literature also contains some rather new and interesting work on N-chloro compounds. Recently, it has been shown that N-chloroaziridines have very high barriers to inversion about the nitrogen.¹⁶ In one case a barrier of about 21 kilocalories per mole has been estimated. It has not yet been shown that similar barriers exist in other N-chloro compounds, but this is one area where apparently work is continuing. Another recent area of interest is the solvolysis of N-chloroamines catalyzed by silver salts.^{17a,b} Only preliminary reports are available but it appears that rearrangements similar to that of carbonium ion rearrangements in the norbornyl series take place in these reactions.

Finally, all N-chloro compounds react with iodide ion in the presence of acids to form iodine.^{2,3,4,12} This is a very good method for detecting them, estimating them quantitatively by iodimetry, and for obtaining the parent compound.

3. Ring Chlorination of Anilines

It has been suggested that ring chlorination may arise either by direct attack of a chlorinating agent on the

aromatic ring, or by a rearrangement of the N-chloroaniline.⁴ This section of the discussion is an attempt to explain what is known of these possibilities. First a look will be taken at the possibilities for the rearrangement.

A rearrangement can take place by several pathways. There can be a dissociation-recombination sequence in which the electrophile becomes free and able to attack any electron-rich species in the medium. There also can be dissociation-recombinations in which the electrophile remains "caged" and only reacts with the molecule from which it was separated. This process cannot readily be distinguished from the case in which there may be a concerted intramolecular transfer of the electrophile from one part of the molecule to another. Of these possibilities, the one that seems to be generally accepted by most authors as a rearrangement is the concerted intramolecular transfer of the electrophile from one part of the molecule to another. The acid catalyzed rearrangement of N-nitroanilines is the reaction that is most commonly proposed to take place by this pathway, and the evidence that is cited to substantiate this proposal is summarized by Gould as the following:⁸

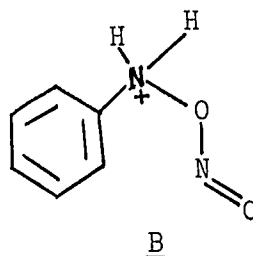
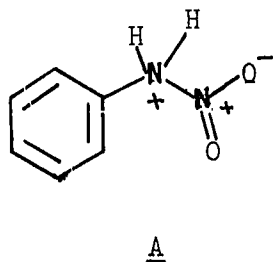
- 1) The rearrangement of N-nitroaniline in 85% sulfuric acid at 10°C gives almost exclusively o-nitroaniline.
- 2) Direct nitration of aniline gives a mixture of o,m,p nitroanilines in the ratio 1:6:10 respectively in 85% sulfuric acid at the same temperature.
- 3) When p,N-dinitroaniline undergoes rearrangement with N,N-dimethylaniline present in the medium, almost no nitration

of the dimethylaniline is observed.

4) Rearrangement of N-nitroaniline in the presence of N^{15} nitrate ion caused no incorporation of the label into the rearranged product.

From these observations, Gould,⁸ the original authors,⁷ and a number of other authors⁶ conclude that an intermolecular rearrangement may be ruled out as playing a significant role in the rearrangement of N-nitroanilines.

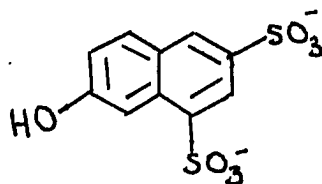
There is, however, some disagreement about the type of intramolecular process that can take place in this rearrangement. The original authors gave an extensive discussion to show that an oxygen-bridged intermediate such as B could not explain the observations. Gould, however, claims that the rearrangement from A to B is analogous to the Stevens rearrangement and should be capable of taking place. Other authors, Dewar for example,⁶ seem to prefer the view of Hughes and Jones⁷ and have proposed alternate explanations for the intramolecular pathway of the N-nitroaniline rearrangement. He described the rearrangement of the electrophile from the nitrogen to the ring very picturesquely in the following manner: (p 298 ref. 6) " In the pi complex $ArH \cdots X^+$



the group X^+ is held by the bond formed by the interaction with the pi electrons of the ring. Therefore, X should be able to move freely over the pi electron cloud, the latter providing a kind of electronic railroad over which X can move from one part of the molecule to another without ever being detached from the parent aromatic ring."

4. Nature of, and Evidence for, Pi Complexes

Evidence for the existence of pi complexes comes from the observation of charge transfer spectra between aromatic compounds and certain species that can act as electron acceptors.¹⁸ Zollinger has reported that in the bromination of G salt a certain absorption band appears in the uv which is neither present in the reactants nor the products. In the iodination of the same compound a similar band appears but even after one week no iodine is used up. He proposed that the intermediate formed is the pi complex, which because of the low reactivity and bulk of the iodine atom cannot go from the pi to a sigma complex. This observation was proposed by Olah as evidence for a pi complex intermediate in the bromination of G salt.



G Salt

Although there is much evidence for the existence of pi complexes, the strongest argument for their existence as intermediates in electrophilic substitutions is that they provide an explanation for observations that are otherwise difficult to explain.²⁰ When benzene and toluene are nitrated as a mixture with $\text{NO}_2^+ \text{BF}_4^-$, the ratio of rate constants (toluene/benzene), was observed to be 2.1, yet the positional selectivity on toluene was very high. The o/p ratio was 2.05, and only 2.3% m-chlorotoluene was formed. According to this author²⁰, aromatic compounds behave as pi bases towards the electrophile in forming the pi complex. i.e., the entire molecule rather than individual positions on the molecule reacts with the electrophile. The relative pi basicities of toluene and benzene are 0.91 and 0.61 respectively in the reaction with HCl .²¹ After the pi complex is formed in the rate-determining step the electrophile then moves into a sigma complex which determines the site at which the aromatic species is substituted.

Dewar insists that in a pi complex such as is formed in the rearrangement of N-nitroaniline, the bond holding the electrophile to the aromatic system is a dative covalent bond with strength that should approach that of normal covalent bonds.⁶ He adds that this point is misunderstood by many authors who refer to pi complexes as weak interactions of electrophiles and aromatic compounds.

The geometrical structure of pi complexes is a point about which there is some uncertainty. Brown claims from a study of the isomerization of certain alkyl benzenes with

Lewis acids, that pi complexes are not necessarily symmetrical but may be localized at sites where the electron density is greatest. Dewar asserts that for electrophiles in which the vacant orbital is of the p or d type, the most stable pi complex should be the one in which the electrophile is oriented about the six-fold axis of the ring.⁶

5. Nature of, and Evidence for, Sigma Complexes

Orientation in electrophilic aromatic substitution is generally explained by the relative stabilities of sigma complexes which are formed as high energy intermediates in the product-forming step of the reaction. These sigma complexes are sometimes called Wheland intermediates.²² Doering has shown that in the methylation of benzene with methylchloride and aluminum chloride 1,1,2,3,4,5,6-heptamethylbenzenonium tetrachloroaluminate is formed.²⁴ Brown and Pearsall have shown that at low temperatures aromatic hydrocarbons are protonated by HCl in the presence of aluminum chloride.²⁵ The protonated aromatic species and the benzenonium ion are sigma complexes similar in structure to the Wheland intermediate in electrophilic aromatic substitution. For a large number of electrophilic aromatic substitutions, the rate-determining step is believed to be the formation of the sigma complex, and these reactions generally show no primary deuterium isotope effect.^{26,27}

In conclusion, it should be pointed out that the N-nitroaniline rearrangement is, according to what can be seen in the

current literature, a good model for the rearrangement of N-chloroanilines. In a recent report Norman and Radda have indicated that nitration and chlorination of a variety of aromatic compounds with very reactive chlorinating and nitrating agents showed similar positional selectivities on the aromatic compounds²⁸ (see table 1) under conditions in which the chlorinating and nitrating agents showed similar reactivities. Furthermore, it has been shown that under those conditions which show very high reactivity, both nitration and chlorination of a variety of aromatic compounds take place through the formation of a pi complex intermediate in the rate-determining step of the substitutions.²⁷ These similarities suggest that the rearrangement of N-chloroanilines should be, like the rearrangement of N-nitroanilines, an intramolecular process.

Table I

Isomer Distribution in the Chlorination and Nitration of Monosubstituted Benzenes.²⁸

<u>Subst.</u>	<u>Chlorinated Products (%)</u>				<u>Nitration Products (%)</u>			
	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>o/2p</u>	<u>ortho</u>	<u>meta</u>	<u>para</u>	<u>o/2p</u>
NO ₂	17.6	80.9	1.5	5.9	6.4	93.2	0.3	11.0
CN	23.2	73.9	2.9	4.0	17.1	80.7	2.0	4.3
CHO	30.7	63.5	5.8	2.6	19	72	9	1.0
Br	39.7	3.4	56.9	0.35	36.5	1.2	62.5	0.3
Cl	36.4	1.3	62.3	0.29	29.6	0.9	69.5	0.21
CH ₃	74.7	2.2	23.1	1.6	58.4	4.4	37.2	0.78
OCH ₃	34.9	0	65.1	0.27	44.0	0	54.0	0.41

DISCUSSION OF RESULTS

1. Synthesis of N-Chloroanilines

Anilines may be expected to undergo covalency formation with nucleophiles both on nitrogen and on carbon.³ When the nucleophile is a chlorinating agent covalency formation has generally been reported to take place on carbon although there has been much speculation that this is preceded by covalency formation of nitrogen.^{4,30} We have already shown that covalency formation takes place exclusively on the nitrogen when N-methylaniline is chlorinated with calcium hypochlorite.³ This work has been extended to show that N-alkylanilines in general may be N-chlorinated with calcium hypochlorite as well as with N-chlorosuccinimide and N-chlorobenzanilide. (See exp. entry Nos. 21 & 33)*. Table II summarizes the results of this study.

2. Factors Affecting the Stability of N-Chloroanilines

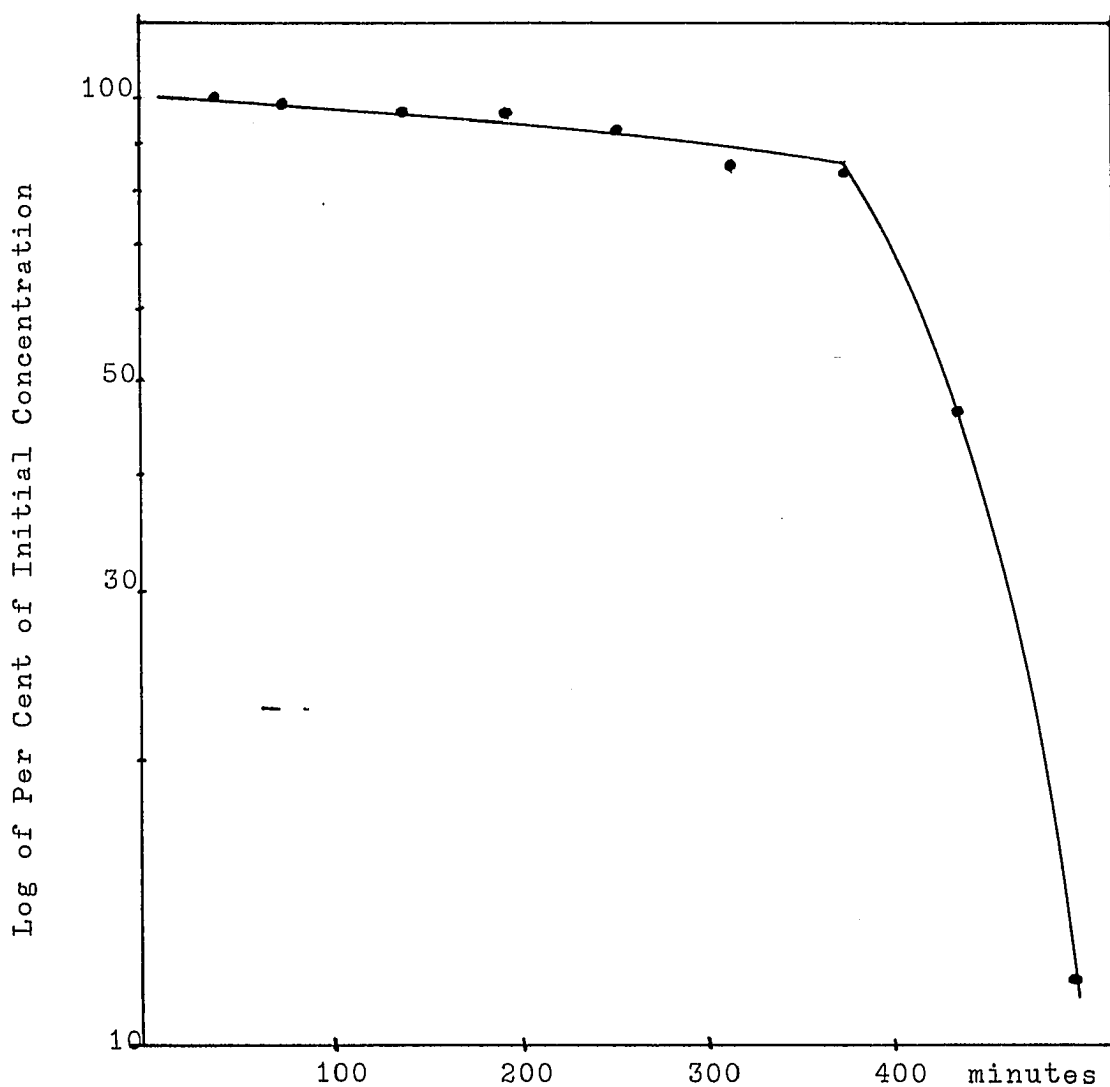
N-Chloroanilines undergo two major reactions that are responsible for their decomposition. The first of these is beta elimination of HCl, a reaction which aliphatic N-chloroanilines also undergo,¹³ and for which evidence has been found in the study of N-chloro-N-methylaniline (23). The

* Experimental entry numbers are given in the Table of Contents and title of the entry. In the future they will be inserted in parentheses at the end of statements whenever they apply.

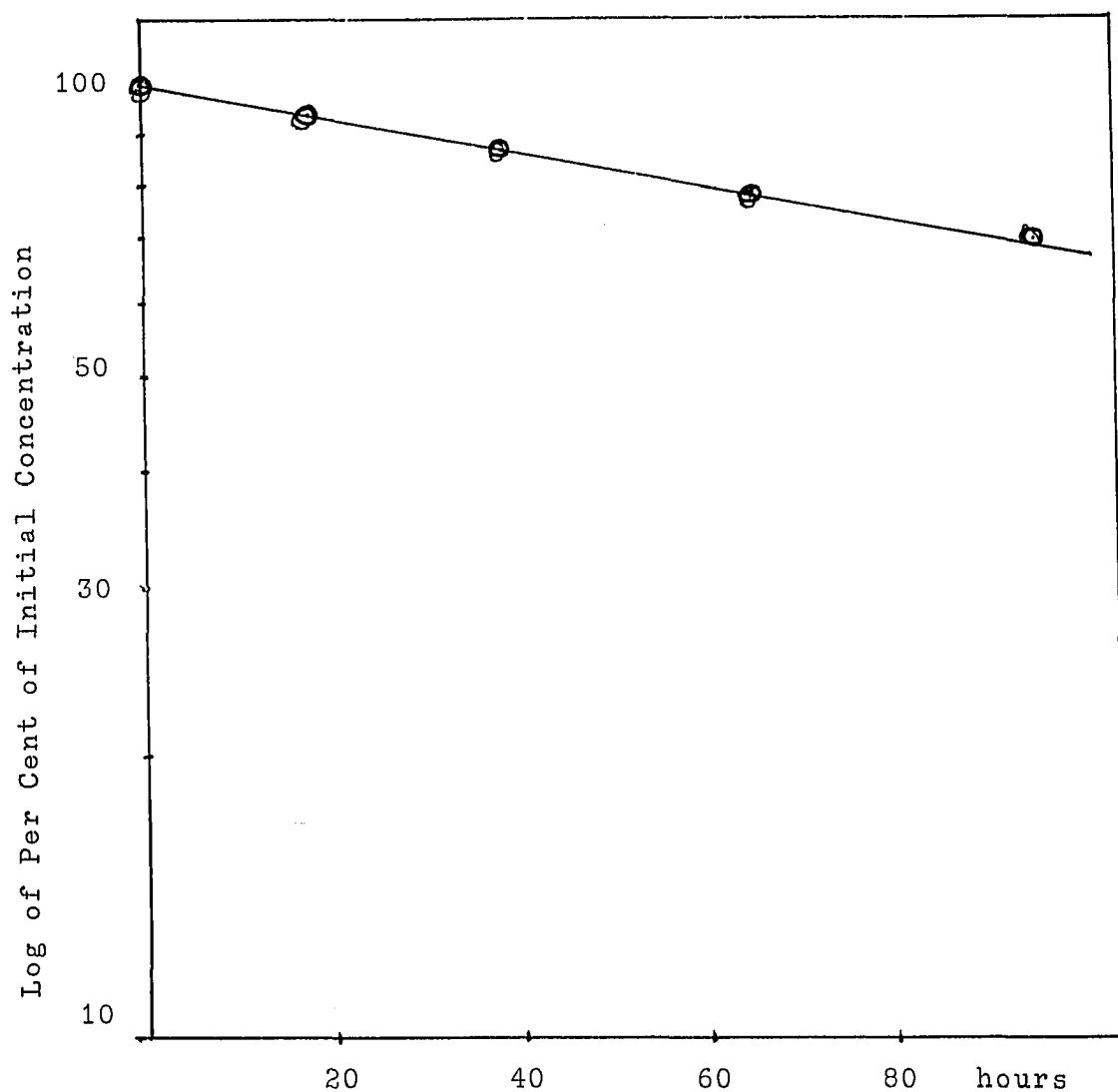
second reaction is a rearrangement to form ring chlorinated anilines (23, 31).

3. Effect of Acids on N-Chloroanilines

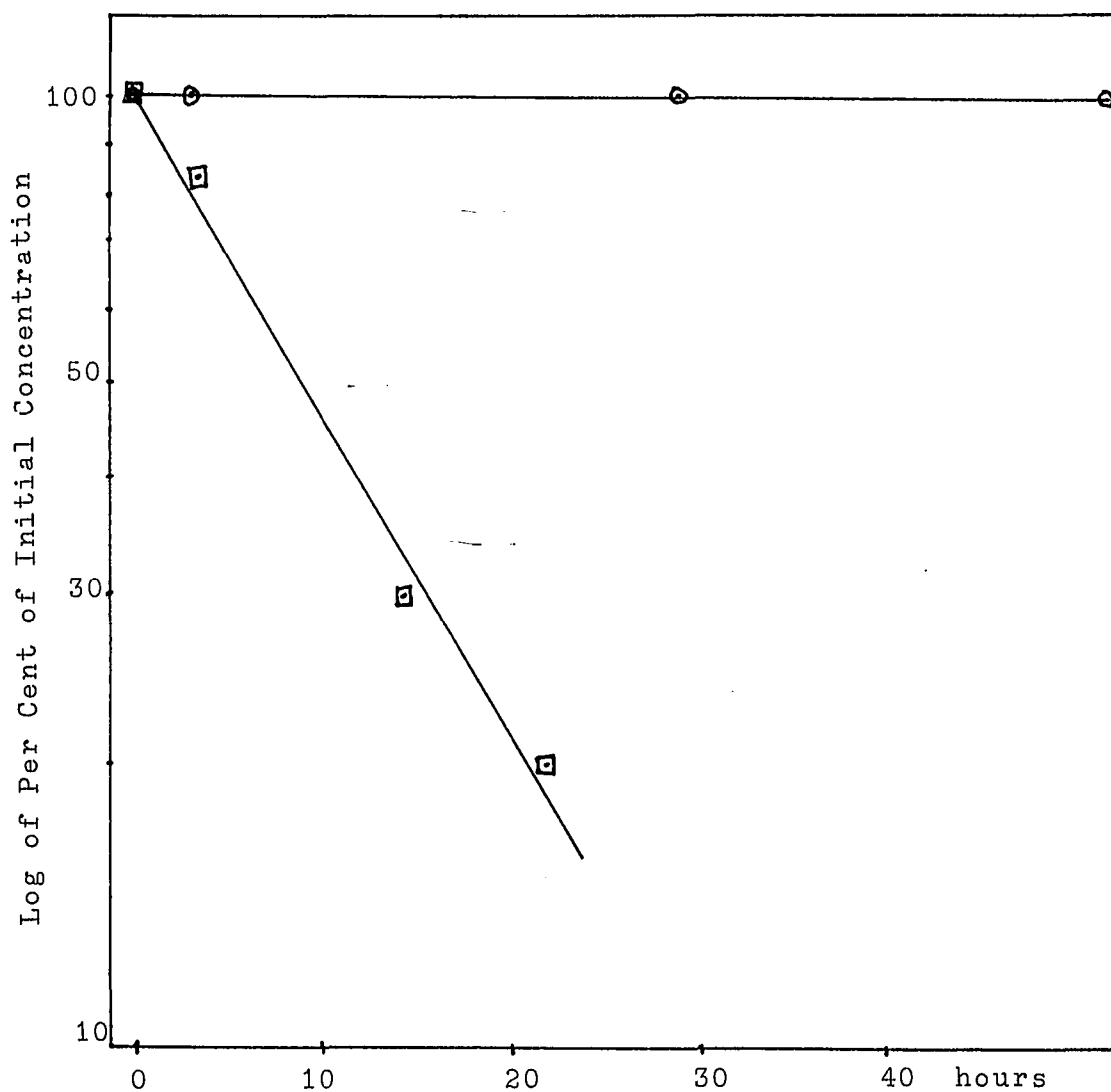
In a recent review Dewar states that eight "anilines" substituted on the heteroatom are known which undergo acid catalyzed rearrangement of the substituent from the heteroatom to the ring.⁶ His list of anilines contained such well known compounds as N-nitroaniline, N-nitrosoaniline, and N-chloroacetanilide. Evidence has been obtained that the rearrangement of N-chloroanilines is also an acid catalyzed process. The rearrangement of N-chloro-N-methylaniline is accompanied by the elimination of HCl. The rearrangement which is normally observed appears to have an induction period with a unimolecular rate constant of $10^{-6} - 10^{-5} \text{ sec}^{-1}$ in a 0.02 M solution in carbon tetrachloride at 0°C (22). The induction period is followed by a rise in the rate of rearrangement and the unimolecular rate constant $10^{-3} - 10^{-2} \text{ sec}^{-1}$ (see figure 1). This apparent induction period can be eliminated by the addition of traces of trichloroacetic acid to the solution of the compound (29), and the fast phase of the rearrangement can also be eliminated (see figure 2) by stirring the solution over sodium carbonate (30). In the case of N-t-butylniline there are no hydrogens on the carbon alpha to the nitrogen atom. Beta elimination of HCl cannot take place and there is no rate acceleration similar to that observed in the rearrangement of N-chloro-N-methylaniline (see figure 3).

Figure 1

Correlation between per cent of initial concentration and time in the rearrangement of 0.020 M solution of N-chloro-N-methylaniline at 0°C in carbon tetrachloride (20).

Figure 2

Correlation between log of per cent of initial concentration and time in the rearrangement of 0.020 M solution of N-chloro-N-methylaniline at 25°C in carbon tetrachloride stirred with sodium carbonate (30).

Figure 3

Correlation between log of per cent of initial concentration and time in the in the rearrangement of 0.10 M solution of N-chloro-N-t-butylaniline at 43°C in water-washed pyrex tubes (□) and in sodium carbonate washed pyrex tubes (○) (36).

Table II

List of Anilines Which Have Been N-Chlorinated, Solvent
and Chlorinating Agent

<u>Aniline</u>	<u>Solvent</u>	<u>Chlorinating Agent</u>	<u>Experimental Entry</u>
N-methyl	a, b, d	f, g, h	20,21
N-sec-butyl	a, b	f	20
N-ethyl	a, b	f	20
N-t-butyl	a, b, c,d	f, g	33
p-chloro- N-t-butyl	a	f	33

a = carbon tetrachloride

b = benzene

c = o-dichlorobenzene

d = pentane

f = calcium hypochlorite

g = N-chlorosuccinimide

h = N-chlorobenzanilide

4. Effect of Glass Surface and Oxygen on N-Chloroanilines

It was observed that samples of N-chloro-N-t-butylaniline rearranged in glass vessels that were washed with water (pH ca. 4.5) and baked dry. This rearrangement did not take place in polyethylene flasks nor in glass vessels which were washed with dilute solutions of sodium carbonate and baked dry to leave an invisible residue on the surface (36). Finally, it was observed that oxygen reacted with solutions of N-chloro-N-t-butylaniline to cause an enhancement of the rate of rearrangement (37). This rate enhancement can be nullified by the addition of small quantities of sodium carbonate to the reaction mixture. It appears, therefore, that oxygen produces acidic species in the system which can catalyze the rearrangement.

In the absence of acids and compounds capable of producing acids, N-chloroanilines are quite stable (32). N-Chloro-N-t-butylaniline has been kept for months at 0°C in a polyethylene flask at 0.40 M concentration in carbon tetrachloride with no observable rearrangement taking place. In the absence of oxygen, in a sodium carbonate treated, sealed glass tube at 60°C, the extent of rearrangement which took place was less than 5% at the end of 52 hours (36).

The reaction of N-chlorosuccinimide with anilines has been reported to yield the ring chlorinated aniline.⁴ Our work has shown that the addition of sodium carbonate to a mixture of an aniline and N-chlorosuccinimide results in the formation of the N-chloroaniline (21, 33) and that the rearrangement of

N-chloroanilines can be slowed down in the case of N-methylaniline (31) and stopped in the case of N-t-butylaniline (36). This would seem to indicate that in the presence of sodium carbonate, the N/C ratio of chlorination of aniline is at least of the order of 100 because although as little as 0.5% of any ring chlorinated product could have been detected in the preparation of N-chloro-N-t-butylaniline with N-chlorosuccinimide and sodium carbonate, none was observed (33). It seems that the addition of sodium carbonate merely allows the N-chloroaniline to accumulate rather than rearrange by removing acid from the solution. It is concluded, therefore, that N-alkylanilines react with N-chloroamides exclusively on the heteroatom, and that subsequent ring chlorination arises from a rearrangement of the N-chloroaniline.

5. Ortho/Para Ratios in the Rearrangement of N-Chloroanilines

The products of the rearrangement of N-chloroanilines in the absence of large quantities of acids and anilines were generally found to be o-chloro-, p-chloro- and 2,4-dichloroanilines (23, 34). In the case of N-chloro-N-methylaniline, a careful search for the meta isomer showed it to be absent under conditions in which as small a quantity as 0.1% (of the total product) could have been detected (15). Three outstanding features of the rearrangement in carbon tetrachloride are the absence of the meta isomer, presence of dichlorinated products, and an o/p ratio that is always larger than 2.0 .

Samples of a solution of N-chloro-N-methylaniline undergoing rearrangement at 25°C in carbon tetrachloride were

removed at intervals and the unrearranged N-chloro-N-methylaniline was converted to N-methylaniline with potassium iodide in 50% aqueous acetic acid (23). On analysis it was observed that the ratio of chlorinated products varied with the extent of rearrangement. The results are summarized in Table III.

Table III

Variation in Ratio of Chlorinated Products with Extent of Rearrangement of N-Chloro-N-methylaniline in Carbon Tetrachloride at 25°C (23).

<u>Per Cent Rearranged</u>	<u>Per Cent of Chlorinated N-Methylaniline</u>				
	<u>o-chloro-</u>	<u>p-chloro-</u>	<u>2,4-dichloro-</u>	<u>o/p</u>	<u>o/p+2,4-</u>
38	25.8	7.9	4.5	3.3	2.1
56	41.3	8.9	5.9	4.6	2.8
77	56.5	10.3	10.1	5.5	2.8
100	66.4	9.4	10.3	7.0	3.4

A similar variation was also observed in the ratio of products when N-methylaniline was chlorinated with N-chlorosuccinimide in carbon tetrachloride at 25°C (24). The results are presented in Table IV. In both experiments, the ratio of p-chloro-N-methylaniline to o-chloro-N-methylaniline decreases and that of the 2,4-dichloroaniline to the o-chloroaniline increases as the extent of chlorination is increased. It can be seen also that despite large variations in the o/p ratio, the mean value of o/p+2,4- was in the range of 2.8-3.0 . It is

concluded, therefore, that the primary process taking place at 25°C in carbon tetrachloride yields o-chloro- and p-chloro-N-methylaniline in a ratio of 2.8, and the dichlorinated product arises principally from chlorination of p-chloro-N-methylaniline. Further evidence was obtained from the rearrangement of N-chloro-N-t-butylaniline which supports this conclusion. The products of the rearrangement of N-chloro-N-t-butylaniline in the absence of any additives (34) and with o-chloro-N-t-butylaniline (39) and p-chloro-N-t-butylaniline (40) added are compared in Table V.

As presented in Table V, the results are perhaps not sufficiently graphic. Let us assume that the 5% of 2,4-dichloro-N-t-butylaniline which is formed by the rearrangement with no added aniline is also formed when there is added monochlorinated aniline. The extra quantity of 2,4-dichloro-N-t-butylaniline formed by chlorination of the monochlorinated aniline can be found by subtracting 5% from the total quantity of dichlorinated product formed. The result of this operation is presented in Table VI. In this table the quantities have been normalized so that the N-chloroaniline is always at 100%.

Table IV

Variation in the Ratio of Chlorinated Products with Extent of Chlorination of N-Methylaniline by N-Chlorosuccinimide in Carbon Tetrachloride at 25°C (24)

<u>Ratio of N-Chlorosuccinimide to N-Methylaniline</u>	<u>Per Cent of Chlorinated N-Methylanilines</u>				
	<u>ortho</u>	<u>para</u>	<u>2,4-di-</u>	<u>o/p</u>	<u>o/p+2,4-</u>
0.78	58.5	12.7	0.0	4.6	4.6
0.91	55.8	13.7	3.4	4.1	3.3
1.04	72.5	15.3	7.2	4.8	3.2
1.30	77.0	7.6	19.7	10.1	2.8

Table V

Comparison of Products of the Rearrangements of N-Chloro-N-t-butylaniline with and without Added Monochloroanilines in Carbon Tetrachloride at 43°C (39)

<u>Sample Undergoing Rearrangement</u>	<u>% of Chlorinated N-t-Butylanilines</u>		
	<u>ortho</u>	<u>para</u>	<u>2,4-di-</u>
100% N-Chloro-N-t-butylaniline	83.2	6.9	5.0
52% N-Chloro-N-t-butylaniline and 48% o-Chloro-N-t-butylaniline	85.5	6.3	4.0
61% N-Chloro-N-t-butylaniline and 39% p-Chloro-N-t-butylaniline	48.0	27.2	12.0

Table VI

Comparison of Yields of 2,4-dichloro-N-t-butylaniline Obtained from the Rearrangement of N-Chloro-N-t-butylaniline with and without Added Chlorinated N-t-butylanilines.

<u>Sample Undergoing</u> <u>Rearrangement</u>	<u>Per Cent of 2,4-Dichloro-</u> <u>N-t-butylaniline</u>	<u>X</u>
100% N-chloro- N-t-butylaniline	5.0	0
100% N-chloro- N-t-butylaniline	7.8	2.8
96% o-chloro- N-t-butylaniline	-	
100% N-chloro- N-t-butylaniline	19.7	14.7
64% p-chloro- N-t-butylaniline		

The quantities in Column X are the extra 2,4-dichloro-N-t-butylaniline that may be attributed to the presence of o-chloro- and p-chloro-N-t-butylaniline in the medium of the rearrangement. It can be seen that 2.8/96 or 0.029 is the fraction of o-chloro-N-t-butylaniline while 14.7/64 or 0.23 is the fraction of p-chloro-N-t-butylaniline which is chlorinated. This suggests that p-chloro-N-t-butylaniline is about ten times as reactive as o-chloro-N-t-butylaniline. Thus the o/p+2,4- ratio is a reasonable approximation of the ratio of ortho and para chloroanilines that are formed as primary products of the rearrangement. The yield of p-chloro-N-t-butylaniline is not consistent from one run to another as shown in Table V. These runs were, however, carried out under

a variety of conditions and may reflect factors other than that which is being discussed. It will be shown later that changes in the dielectric constant of the reaction medium affects the ratio of products. Despite these, the results show that p-chloro-N-t-butylaniline is much more readily chlorinated to yield 2,4-dichloro-N-t-butylaniline than o-chloro-N-t-butylaniline.

6. Rearrangement of N-Chloroanilines with Added Anilines and with Sodium Carbonate

N-Chloro-N-methylaniline on standing rearranges to a mixture of ring chlorinated anilines. As was shown earlier (compare figures 1 and 2) the acceleration of the rearrangement due to HCl formation in the system can be reduced by addition of sodium carbonate to the solution of N-chloro-N-methylaniline. The rearrangement then is believed to be catalyzed mainly by acids which have been left on the water-washed glass surface as was shown for N-chloro-N-t-butylaniline (36). Irrespective of the source of the acid, the presence of sodium carbonate removes the rapid phase of the rearrangement and provides a more stable condition for studying the effect of added N-methylaniline on the rearrangement of N-chloro-N-methylaniline. Hexane was chosen as the solvent because it had been observed that N-methylaniline did not form a yellow color as rapidly in this solvent as it did with carbon tetrachloride.

The rearrangement of N-chloro-N-methylaniline was carried out with 0, 8, and 16 fold ratios of N-methylaniline to

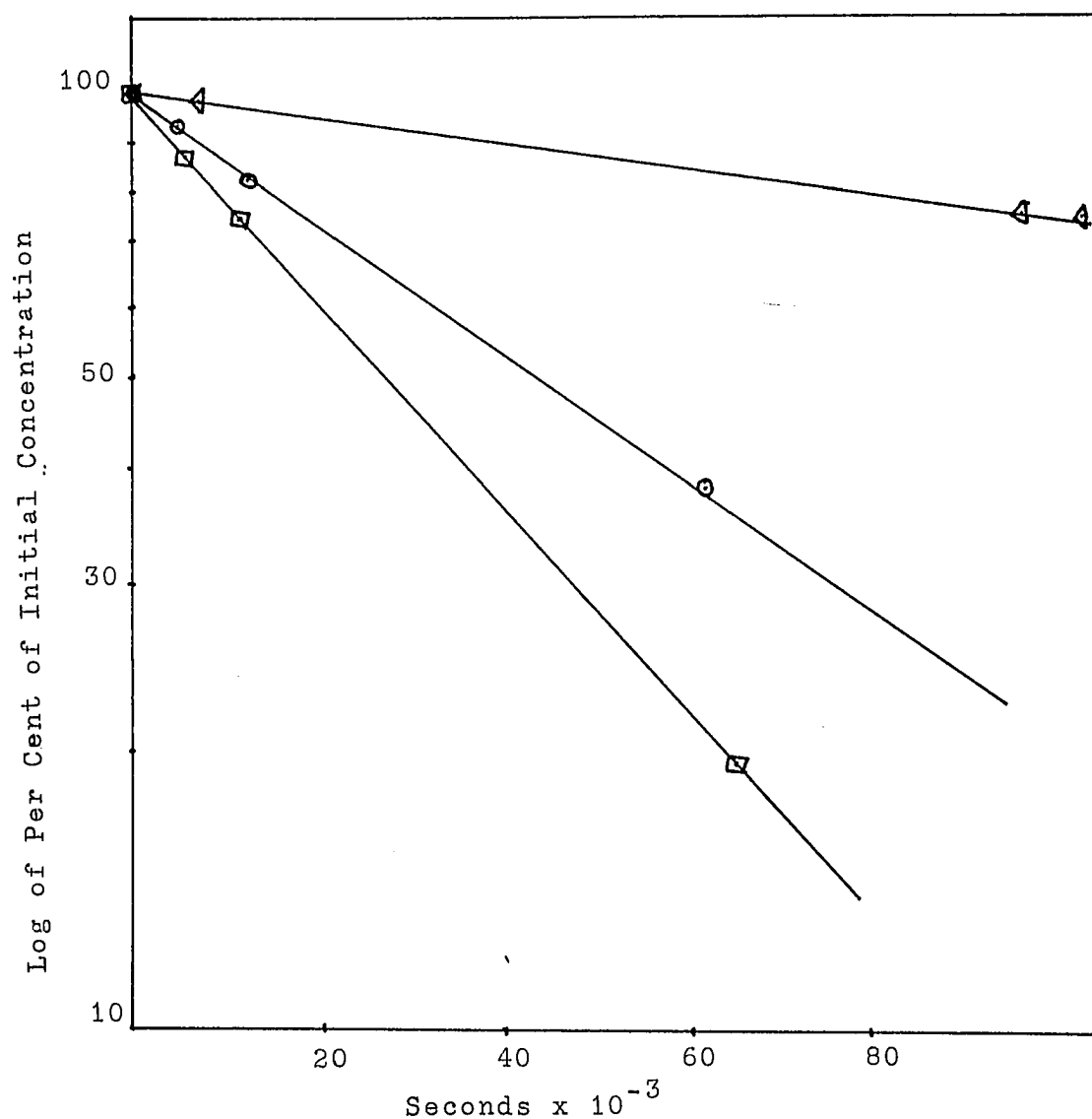
N-chloro-N-methylaniline at 25°C in an 0.02 M solution of the N-chloroaniline (31). The mixtures were stirred over sodium carbonate and samples were analyzed by titration at intervals for N-chloroaniline. Plots of the log of concentration versus time (figure 4) gave straight lines from which unimolecular rate constants were calculated for the disappearance of the chloroaniline.

Molar Ratio of Aniline to N-Chloroaniline	Unimolecular Rate Constant $\text{Secs}^{-1} \times 10^6$
0	1.1
8	5.6
16	9.6

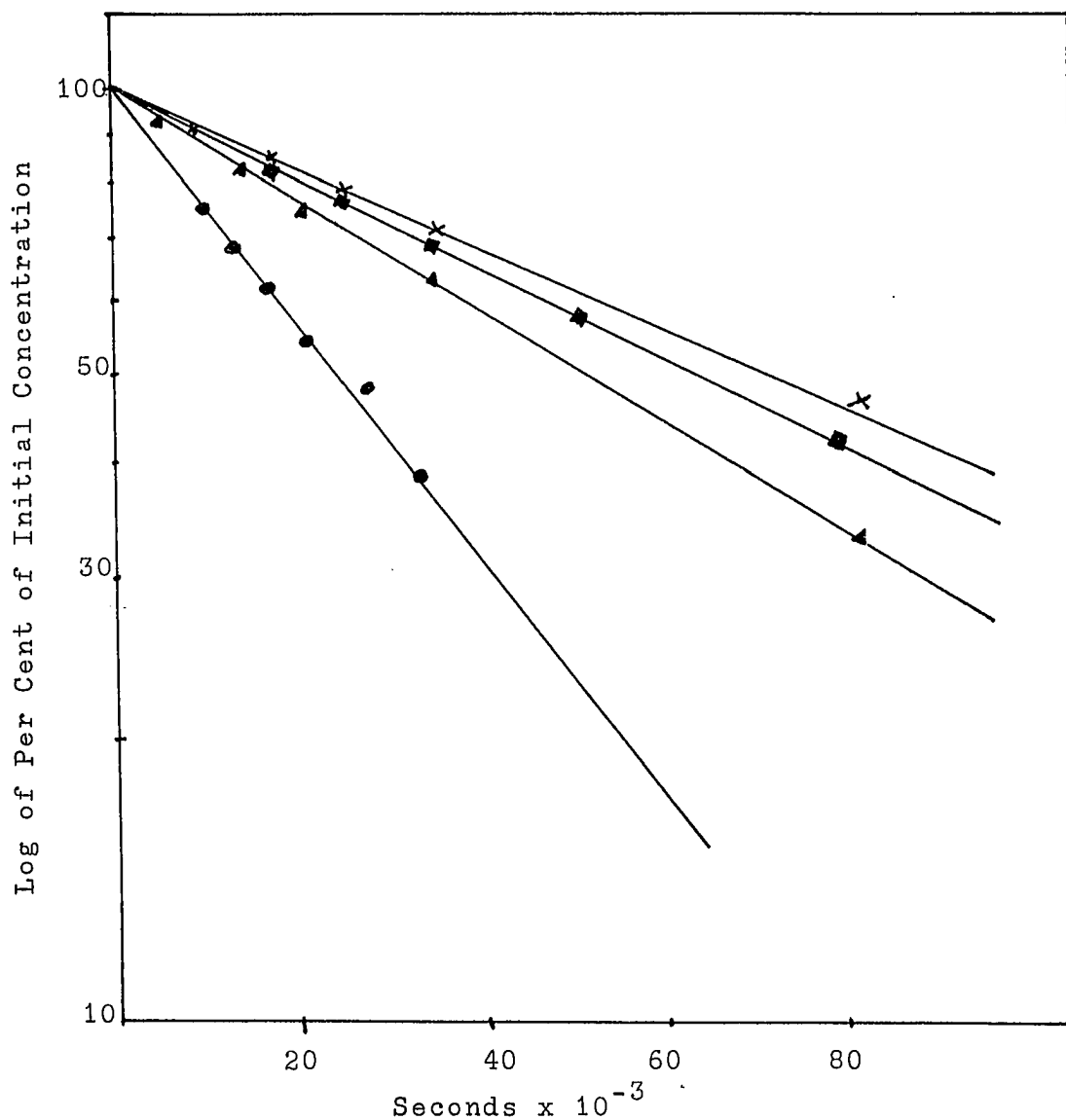
When another study was carried out at 43°C (38) in which the ratio of N-t-butylaniline to N-chloro-N-t-butylaniline in a 0.40 M solution of the latter was varied, the results obtained followed a similar pattern. Plots of the log of concentration of the chloroaniline versus time were straight lines beyond 50% of the rearrangement (figure 5). The unimolecular rate constant of the rearrangement showed a similar increase with increasing aniline concentration for ratios of aniline to chloroaniline 0.25 and greater, but showed a small decrease with a ratio of 0.10 (see page 29).

It has been observed that solutions of N-chloro-N-t-butylaniline prepared by the calcium hypochlorite chlorination of N-t-butylaniline have significantly less than 1.0% of N-t-butylaniline or any of the ring chlorinated anilines before the start of the rearrangements (32).

Figure 4



Correlation log of per cent of initial concentration and time in the rearrangement of 0.020 M solutions of N-chloro-N-methylaniline at 25°C in hexane stirred with sodium carbonate and with 0 (Δ), 8 ($\circ$), and 16 ($\square$) -fold ratios of N-methylaniline (31).

Figure 5

Correlation between per cent of initial concentration and time in the rearrangement of 0.40 M solutions of N-chloro-N-t-butylaniline at 42°C in carbon tetrachloride with 0 (■), 10 (x), 25 (▲), and 148 (●) mole per cent of N-t-butylaniline (38).

<u>Molar Ratio of N-t-butylaniline to N-chloro-N-t-butylaniline</u>	<u>Unimolecular Rate Constant Secs⁻¹ x 10⁶</u>
0	4.8
0.10	4.2
0.25	5.5
1.48	12.2

It is believed that a similar situation obtains for solutions of N-chloro-N-methylaniline. Therefore, the addition of enough N-t-butylaniline to make the ratio of N-t-butylaniline to N-chloro-N-t-butylaniline 0.10 constitutes a greater than ten-fold increase in the concentration of aniline in solution. This greater than ten-fold increase in aniline concentration is not matched by the rate increase which would be expected if the mechanism of ring chlorination was simply a bimolecular substitution of the aniline by the chloroaniline. The rearrangement, however, is catalyzed by acid and the addition of aniline should have an acid weakening effect. This acid weakening effect may be the cause of the apparent discontinuity in the rates of rearrangement of samples with no added aniline and others where aniline has been added. That is, the rearrangement in the absence of added aniline may be a process in which N-chloroaniline in the presence of an acid reacts with minute quantities of free aniline by an intermolecular transfer of chlorine. The discontinuity then on addition of aniline may be due to a decrease in the availability of protons.

An alternate explanation of the discontinuity may be that there are two processes taking place by which chlorine enters the ring. The first occurs in the absence of free aniline and is an unimolecular, intramolecular process involving a protonated N-chloroaniline. The second process is a bimolecular transfer of chlorine from a protonated N-chloroaniline to an aniline molecule, or a bimolecular transfer from the N-chloroaniline to a protonated aniline. The latter possibilities are kinetically indistinguishable. If the two processes are simultaneous, the rate of rearrangement, R, is

$$R = ck_1 + nc^2k_2 \quad (\text{Equation 1})$$

where c = concentration of N-chloroaniline

n = ratio of aniline to N-chloroaniline

k_1 = unimolecular rate constant

k_2 = bimolecular rate constant

Thus, in the absence of added anilines, the principal process or only process would be the unimolecular rearrangement.

From equation 1, the observed unimolecular rate constant, k_{obs} , is found to be:

$$k_{\text{obs}} = k_1 + nck_2 \quad (\text{Equation 2})$$

k_{obs} has been tabulated for N-chloro-N-methylaniline and N-chloro-N-t-butylaniline (see pp 26 & 29).

Substitution of values for N-chloro-N-t-butylaniline into equation 2 gives:

$$5.5 = k_1 + 0.25 (0.40)k_2$$

$$12.2 = k_1 + 1.48 (0.40)k_2$$

and solving these equations simultaneously yields:

$$k_1 = 3.9 \times 10^{-6} \text{ sec}^{-1}$$

$$k_2 = 15.7 \times 10^{-6} \text{ M}^{-1} \cdot \text{sec}^{-1}$$

For N-chloro-N-methylaniline, using the data on the eight-fold and sixteen-fold ratios of N-methylaniline, one calculates as above:

$$k_1 = 1.6 \times 10^{-6} \text{ sec}^{-1}$$

$$k_2 = 25.0 \times 10^{-6} \text{ M}^{-1} \cdot \text{sec}^{-1}$$

The quantity of products which would be expected to be formed by each process may be estimated for the two N-chloro compounds. The integrated expression for the first order process is:

$$\ln C_0/C = k_1 t \quad (\text{Equation 3})$$

where C_0 is the initial concentration of the N-chloroaniline, and C is the concentration after t seconds. For N-chloro-N-methylaniline in this case $C_0 = 0.020 \text{ M}$ (31). The quantity of it which would rearrange by the unimolecular process in 10^5 seconds may be calculated by substituting into equation 3:

$$\ln 0.020/C = 1.6 \times 10^{-6} \times 10^5$$

$$\text{or } 0.020/C = e^{0.16}$$

$$C = 0.017 \text{ M}$$

This indicates that 15% of the N-chloroaniline would have rearranged by the unimolecular process if it were the only available mechanism of rearrangement.

The bimolecular process for the chlorination of N-methylaniline by N-chloro-N-methylaniline is a reaction of the type:



If B is the N-chloroaniline, then

$$\frac{-d(B)}{dt} = k_2 (A) (B)$$

$$\frac{-d(B)}{(B)} = k_2 (A) dt.$$

Since (A) is constant in the system,

$$- \int \frac{d(B)}{(B)} = k_2 (A) dt$$

$$\ln \frac{(B_o)}{(B)} = k_2 (A) t. \quad \text{(Equation 4)}$$

In the case of N-methylaniline, if the concentration of aniline equals that of the N-chloroaniline, substitution into equation 4 for $t = 10^5$ secs yields:

$$\ln 0.020/(B) = 25.0 \times 10^{-6} \times 10^5 (0.020)$$

$$0.020/(B) = e^{-.05}$$

$$(B) = 0.0190 \text{ M}$$

This indicates that in 10^5 seconds 5% of the N-chloroaniline would rearrange by the bimolecular process if it alone were taking place in the system. A more exact analysis would demand a simultaneous solution of the unimolecular and bimolecular processes. However, it can be seen that if two processes are taking place, the addition of an equivalent quantity of methylaniline would cause about one fourth of the initial product to be formed by an intermolecular chlorination of aniline. When a similar analysis is done on the N-t-butylaniline rearrangement (38) it is observed that in 2×10^4 seconds

7% of the N-chloro-N-t-butylaniline would rearrange by an independent unimolecular process and 12% would be obtained by an independent bimolecular process. The change in the relative contributions of the unimolecular and bimolecular processes is due mainly to the difference in the concentrations at which the reactions are carried out. At 0.02 M the unimolecular process for N-chloro-N-t-butylaniline should yield 14% product in 4×10^4 seconds and 1% by the independent bimolecular process. This is quite like the results observed with N-chloro-N-methylaniline at the same concentration. The products obtained from rearrangements of these chloroanilines with varying ratios of the respective anilines are given in table VII. Ratios of t-butylaniline to N-chloro-N-t-butylaniline greater than 1.48 were not studied because the high concentration of aniline would make the medium quite different from other systems studied.

The product ratio in the rearrangement of N-chloro-N-methylaniline can support the two mechanism hypothesis only if one assumes that the unimolecular process yields a low ortho/para ratio of products and the bimolecular process yields a high ratio of products. The product ratios in the case of N-t-butylaniline shows no variation in the o/p+2,4-ratio. This seems to suggest that there is no change in mechanism. But a rate enhancement could only have been observed if the addition of aniline introduced a new process of lower energy than that which already existed, or if the concentration of one of the species in a

Table VII

Yields of Products Obtained From the Rearrangement of N-Chloroanilines with and without Added Anilines in Carbon Tetrachloride Solutions*

<u>Aniline</u>	<u>Ratio of Aniline to N-Chloroaniline</u>	<u>Per Cent Yields of Chlorinated Products</u>				<u>Experimental Reference</u>
		<u>ortho</u>	<u>para</u>	<u>2,4-di-</u>	<u>o/p+2,4-</u>	
N-Methyl-	0	57.5	12.4	7.4	2.9	23
N-Methyl-	1	78.0	19.8	0.0	3.9	26
N-Methyl-	10	92.0	8.0	0.0	11.5	26
N-t-Butyl-	0	94.0	6.0	0.0	16.0	38
N-t-Butyl-	0.10	94.0	6.0	0.0	16.0	38
N-t-Butyl-	0.25	93.0	7.0	0.0	13.0	38
N-t-Butyl-	1.48	93.0	7.0	0.0	13.0	38

* Temperature: 25°C for N-methylaniline and 43°C for N-t-butylaniline.

bimolecular reaction was increased. It must be concluded, therefore,

1) The major process taking place in the absence of added anilines, and with catalytic concentrations of acids present, is a bimolecular (intermolecular) transfer of chlorine from the N-chloroaniline to the carbon of an aniline molecule.

2) An intramolecular rearrangement, if it exists, requires a higher activation energy than the intermolecular transfer of chlorine to another aniline molecule.

7. Chlorination of N,N-Dimethylaniline by N-Chloro-N-t-butylaniline

Further evidence that anilines are chlorinated by transfer of chlorine from N-chloroanilines comes from the observation that addition of N,N-dimethylaniline to a sample of N-chloro-N-t-butylaniline under conditions in which the rearrangement takes place leads to both chlorination of the dimethylaniline and rearrangement of the N-chloroaniline (44). Table VIII lists the per cent of available chlorine which is transferred when various mixtures of the two compounds undergo reaction. A close look at the data shows that at the start of the reaction the major process is the chlorination of dimethylaniline (see figures 6 & 7). As dimethylaniline is chlorinated, the concentration of N-t-butylaniline is increased and the ratio of the chlorine that goes into the ring of

Per Cent of Available Chlorine Transferred to N,N-Dimethylaniline When Various Quantities of It Are Placed in Samples of N-Chloro-N-t-Butylaniline Undergoing Rearrangement (43, 44)

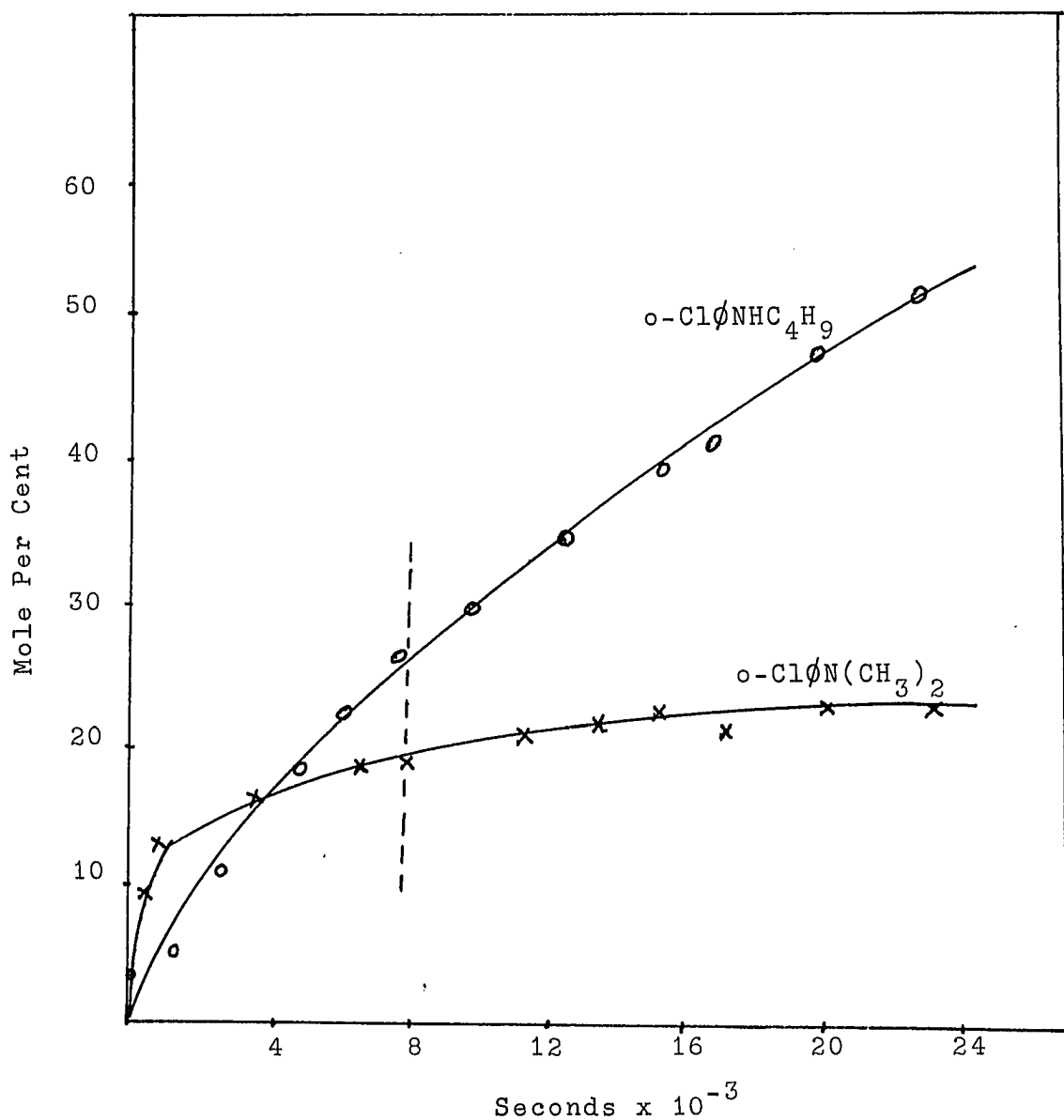
<u>Molar Ratio of Dimethylaniline to N-Chloro-N-t-butylaniline</u>	<u>Per Cent of Available Chlorine Transferred to Dimethylaniline</u>
0.354	26.5 ^a
1.25	42.7 ^a
1.60	60.0 ^b

a) Catalyzed by trichloroacetic acid in sodium carbonate treated glass vessel.

b) Catalyzed by residual acids in water-washed glass vessels.

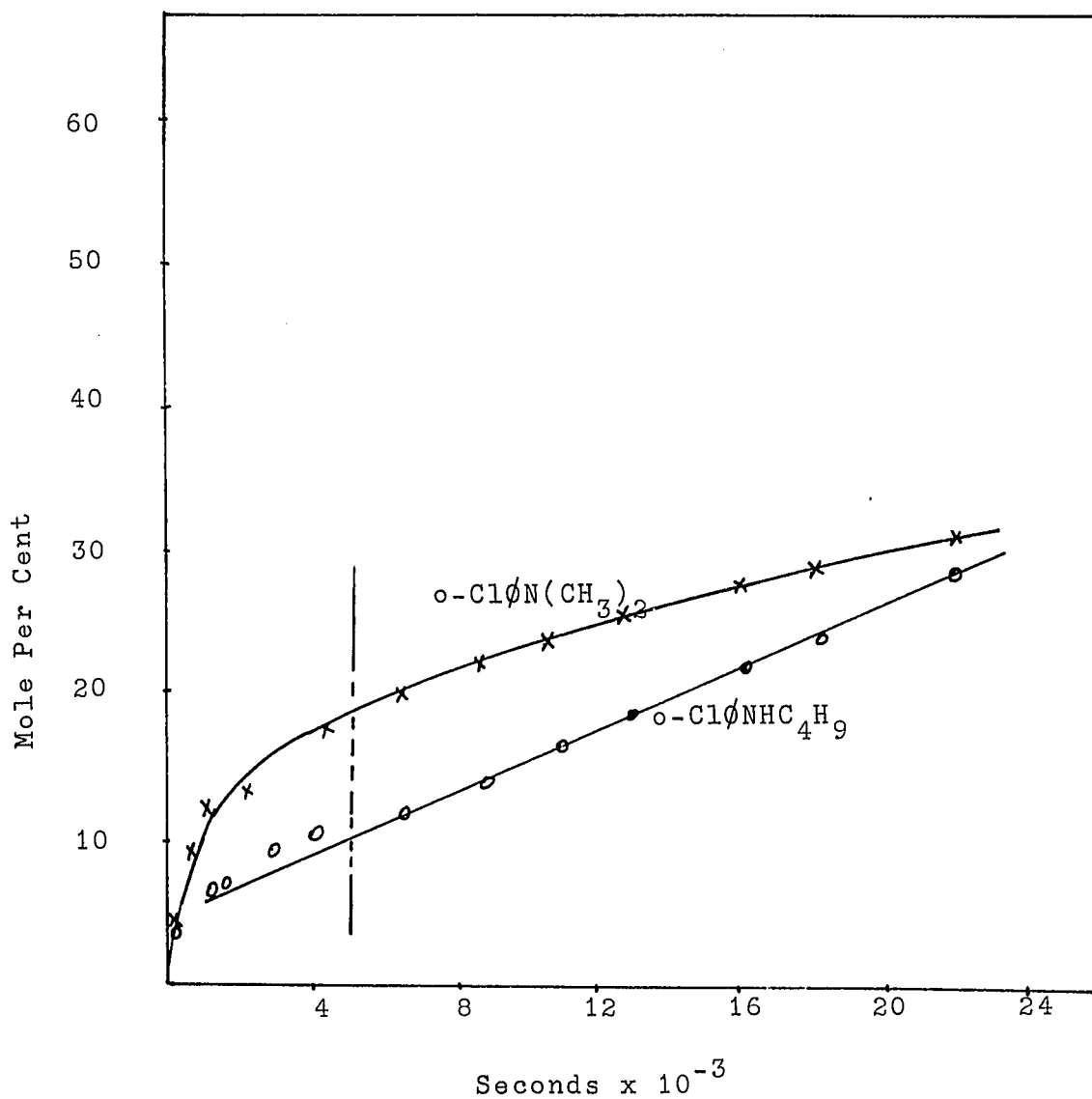
N-t-butylaniline to that going into the N,N-dimethylaniline is increased. This kinetic behavior suggests the following reactivity sequence for the formation of ring chlorinated products: (1) chlorination of N-t-butylaniline is a faster reaction than chlorination of N,N-dimethylaniline. A look at the data in table XXXI shows that at 7.92×10^3 seconds the concentration of N-t-butylaniline is approximately equal to the concentration of N,N-dimethylaniline, yet the slope of the curve for the formation of o-chloro-N-t-butylaniline (figure 6) is steeper than that for the formation of o-chloro-N,N-dimethylaniline. Again, a look at table XXXII shows that at 4.98×10^3 seconds the ratio of N-t-butylaniline to N,N-dimethylaniline is $1.79/11.7$ or 0.15 and figure 7 shows that the slopes of the curves at that time are almost parallel.

Figure 6



Correlation between per cent of available chlorine transferred to N,N-dimethylaniline (x) and rearranged to o-chloro-N-t-butylaniline in the rearrangement of N-chloro-N-t-butylaniline (0.4 M) in carbon tetrachloride at 43°C with a 0.147 M concentration of N,N-dimethylaniline. The vertical line indicates the time when concentration of anilines were equal (44).

Figure 7

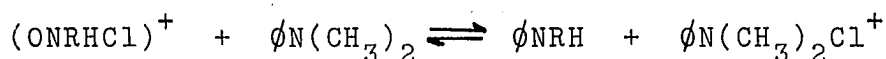


Correlation between per cent of available chlorine transferred to N,N-dimethylaniline (x) and rearranged to o-chloro-N-t-butylaniline (o) in the rearrangement of N-chloro-N-t-butylaniline at 43°C in carbon tetrachloride. The vertical line indicates time when the ratio of concentrations (t-butyl/dimethyl) was 0.15 (44).

The higher reactivity of N-t-butylaniline may be a reflection of factors which make it about 100 times a stronger base than N,N-dimethylaniline (see table XI). But this is unlikely. Weaker conjugation of the electrons on the nitrogen with those in the ring for steric reasons, should make the nitrogen in N-t-butylaniline a stronger base than that in dimethylaniline, but should decrease the reactivity of the ring of the former as compared to the ring of the latter. Therefore, the higher reactivity of N-t-butylaniline is attributed to the fact that it is a secondary amine while N,N-dimethylaniline is a tertiary amine. The reason for this difference will be shown in section 11 of the Discussion.

2) This kinetic behavior also suggests that if N-Cl-N-t-butylaniline also rearranges by an intramolecular process it must be slower than the intermolecular chlorination of dimethylaniline in the systems discussed. This conclusion is considered to be based on more reliable evidence than that obtained in the rearrangement of N-chloro-N-t-butylaniline with added N-t-butylaniline because in this system the acid strength and concentration are fixed while in the study with varying concentrations of N-t-butylaniline, variations in the availability of the proton may exist from one mixture to another. The reactivity sequence obtained here is also very important because it shows that transfer of chlorine from a chloroaniline molecule to the ring of another aniline molecule is preferred to transfer to the ring of the chloroaniline itself. A possible intramolecular pathway may also be proposed for chlorination of N,N-dimethylaniline. The N,N-dimethyl-N-chloroanilinium

ion, $\phi\text{N}(\text{CH}_3)_2\text{Cl}^+$, is electronically quite similar to that of the protonated N-chloro-N-methylaniline. In order to explain the observed results it has to be assumed that the concentration of $\phi\text{N}(\text{CH}_3)_2\text{Cl}^+$ is governed by an equilibrium such as:

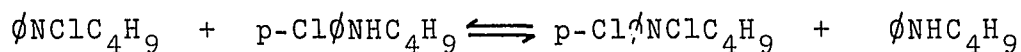


At the beginning of the reaction when the concentration of aniline is low, the concentration of chlorodimethylanilinium ion will be greatest and the rate of formation of chlorinated dimethylaniline will be greatest.

This objection although apparently quite logical has certain flaws. It may be asked, for example, why is an intramolecular pathway the lower energy process for the chlorination of dimethylaniline when the bimolecular transfer is preferred by N-methylaniline and N-t-butylaniline? Furthermore, analysis of the products obtained from these mixtures shows that in the sample where the o/p ratio was low, i.e., 3.0 for t-butylaniline, it was low, i.e., 2.2 for N,N-dimethylaniline (43), and in the others, when p-chloro-N-t-butylaniline is not observed p-chloro-N,N-dimethylaniline is also not observed (44, see also section 13 of the Discussion). This suggests that the mechanism of chlorination is the same for both anilines. It is concluded, therefore, that in the presence of added N,N-dimethylaniline, the principal pathway is transfer of chlorine from the N-chloroaniline to the ring of another aniline molecule.

8. Rearrangement of N-chloro-N-t-butylaniline with Added Rind Chlorinated N-t-Butylanilines

To pursue the use of added anilines as probes of the mechanism of the rearrangement of N-chloroanilines, the rearrangement of N-chloro-N-t-butylaniline with added p-chloro-N-t-butylaniline (40) and with added o-chloro-N-t-butylaniline was examined. When carbon tetrachloride solutions of N-chloro-N-t-butylaniline and p-chloro-N-t-butylaniline were mixed in a sodium carbon treated vessel, no reaction took place until trichloroacetic acid was added. On the introduction of a small quantity of acid there was a rapid transfer of chlorine between the anilines as shown below:



This equilibrium was attained in less than four minutes, and was maintained for the duration of the run. Table IX shows values of the equilibrium constant at various times in the rearrangement of a sample at 43°C.

Table IX

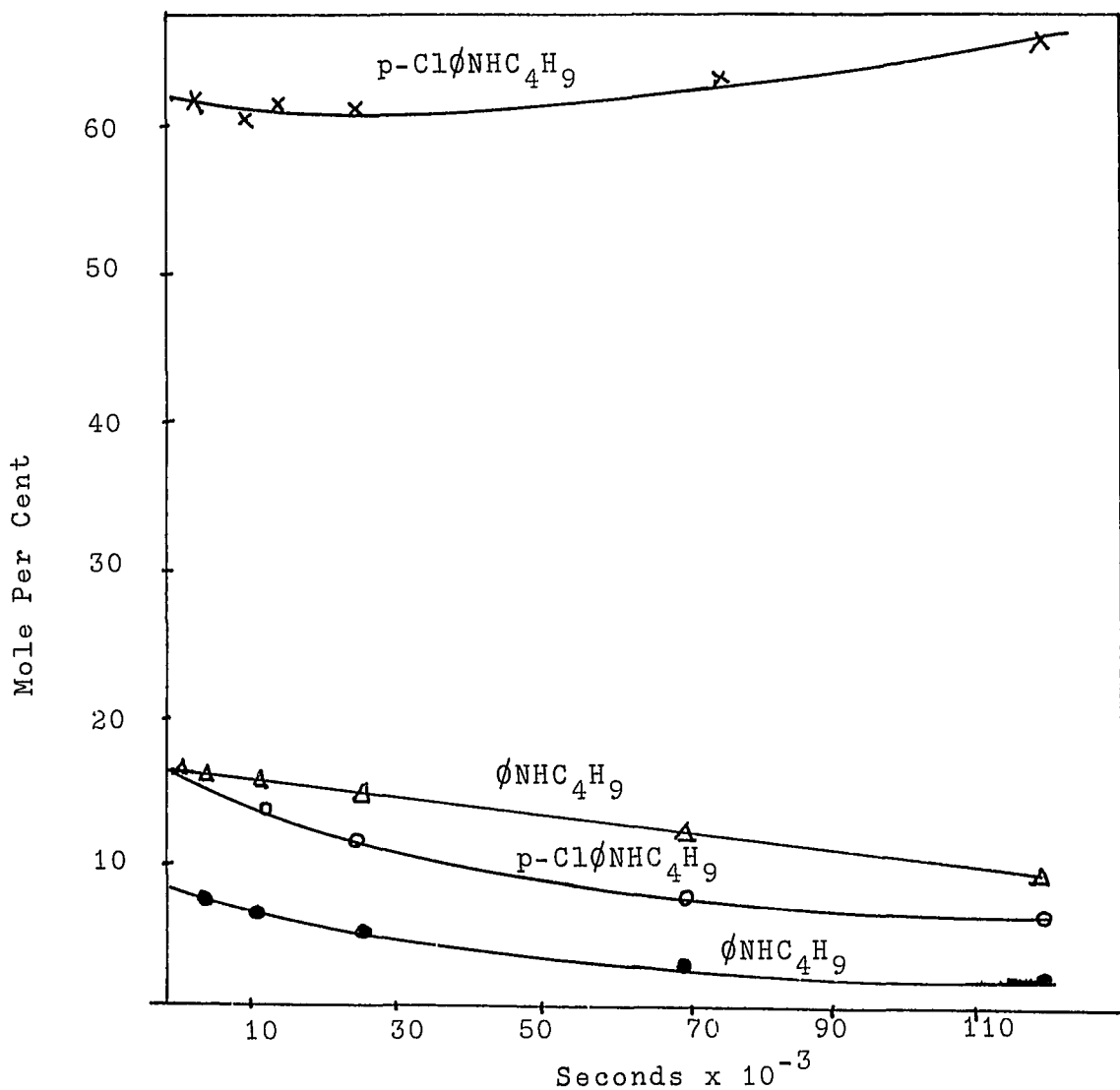
Mole Per Cent of N-t-Butylanilines in Reaction of N-Chloro-N-t-butylaniline and p-Chloro-N-t-butylaniline in Carbon Tetrachloride at 43°C

<u>Time Sec x 10⁻³</u>	<u>$\phi\text{NHC}_4\text{H}_9$</u>	<u>$p\text{-Cl}\phi\text{NClC}_4\text{H}_9$</u>	<u>$\phi\text{NClC}_4\text{H}_9$</u>	<u>$p\text{-Cl}\phi\text{NHC}_4\text{H}_9$</u>	<u>K</u>
20	16.0	15.5	47.0	9.5	0.56
40	15.5	14.0	39.0	10.0	0.56
60	15.5	12.5	33.0	10.5	0.56
80	15.5	11.5	27.0	11.0	0.58
100	15.0	10.0	24.0	11.5	0.56
120	14.5	9.5	21.0	12.0	0.55

Because of this equilibrium, the concentration of an N-chloroaniline is not independent of the concentration of the other species present in the reaction medium (see figures 8 & 9). Therefore, one cannot tell from this study whether the formation of product 2,4-dichloro-N-t-butylaniline, for example, is kinetically dependent on the concentration of p-chloro-N-t-butylaniline alone or on the product of the concentrations of p-chloro-N-t-butylaniline and the N-chloroanilines present in the reaction medium.

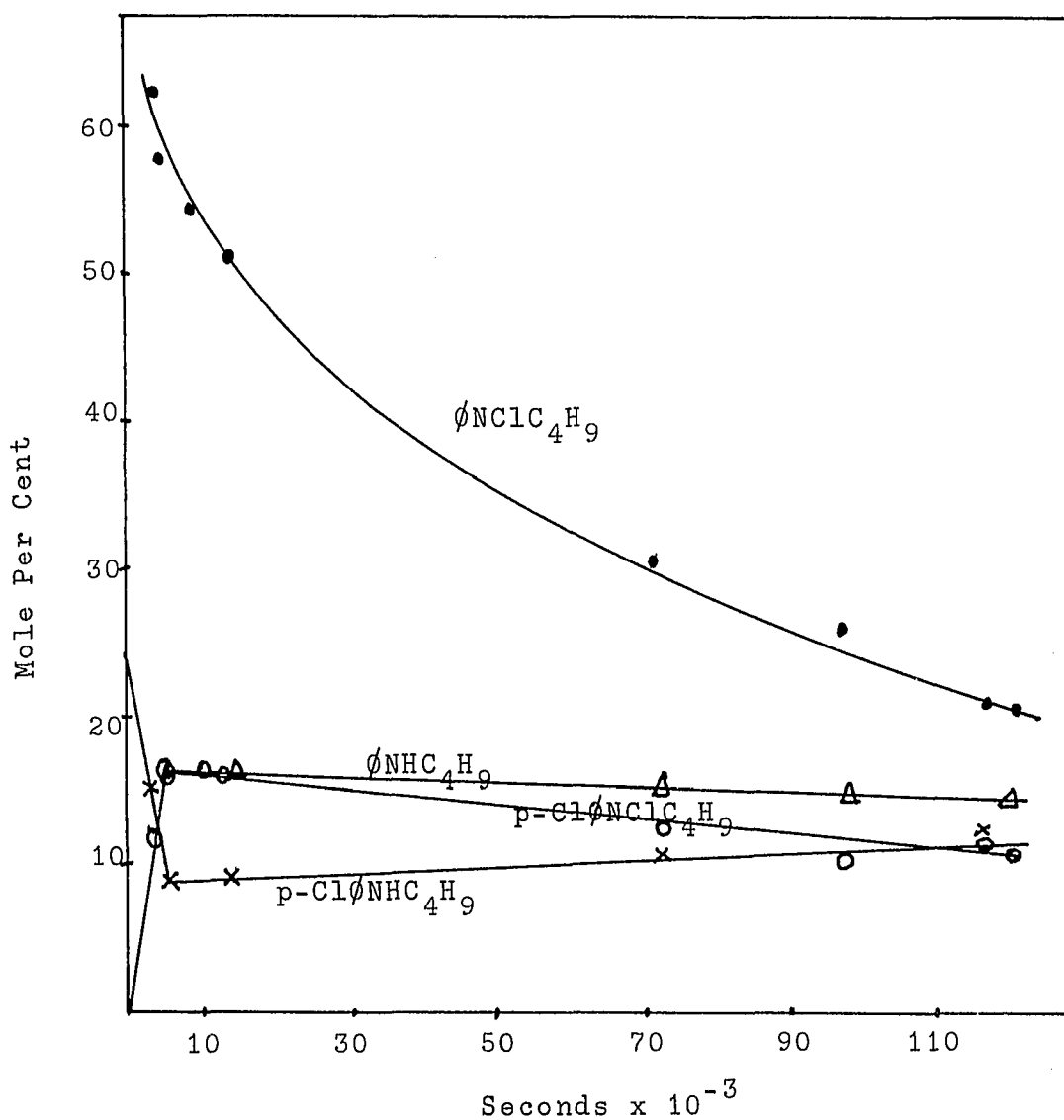
When o-chloro-N-t-butylaniline was mixed with N-chloro-N-t-butylaniline, rearrangement took place with no evidence for the formation of o,N-dichloro-N-t-butylaniline (30). A careful search of the nmr spectrum in the region of 50-100 cps downfield from TMS showed no evidence for absorptions that could be ascribed to o,N-dichloro-N-t-butylaniline. Furthermore,

Figure 8



Correlation between mole per cent of N-chloro-N-t-butylaniline ($\bullet$), p,N-dichloro-N-t-butylaniline (o), N-t-butylaniline (Δ), p-chloro-N-t-butylaniline (x) and time in the rearrangement of N-chloro-N-t-butylaniline, 0.40 M in carbon tetrachloride at 43°C with a 1.3 M concentration of p-chloro-N-t-butylaniline. (Mixture M, Exp. No. 40).

Figure 9



Correlation between the mole per cent of N-chloro-N-t-butylaniline ($\bullet$), p,N-dichloro-N-t-butylaniline ($\circ$), N-t-butylaniline (Δ), p-chloro-N-t-butylaniline ($\times$), and time in the rearrangement of N-chloro-N-t-butylaniline, 0.40 M in carbon tetrachloride at 43°C with a 0.052 M concentration of p-chloro-N-t-butylaniline (Mixture H, Exp. No. 40).

analysis of the product indicated that less than 3.0 per cent of the o-chloro-N-t-butylaniline was chlorinated at 100% conversion (see section 5, p 24, of the Discussion).

This concludes the portion of the study in which anilines were added to the medium of the rearrangement to act as probes of the mechanism. The most outstanding conclusion of this part is that transfer of the electrophilic chlorine species from an N-chloroaniline molecule to the ring of an aniline is a lower energy process than intramolecular rearrangement to the ring of the N-chloroaniline. This observation suggests that even in cases where no aniline is added a significant portion of the rearrangement may be a rapid intermolecular chlorination of low concentrations of anilines. The facile equilibration of chlorine between the N-chloroaniline and the p-chloroaniline formed in the reaction, assures the formation of some of the aniline from which the N-chlorination was made.

From the results obtained in this study, it is possible to set up a reactivity scheme for the bimolecular chlorination of anilines by N-chloroanilines. In the case of N-t-butylanilines, the fastest process which takes place is the transfer of the anilines (see p 41). This exchange is expected to take place with o-chloro-N-t-butylaniline, but if it occurred, the equilibrium concentration of o,N-dichloro-N-t-butylaniline must be less than 5% of the total N-chloro concentration.

In mixture H (40) in which the average concentration of N-t-butylaniline is approximately equal to that of p-chloro-

N-t-butylaniline, 3% of o-chloro-N-t-butylaniline is formed in 7×10^3 seconds and 3% of 2,4-dichloro-N-t-butylaniline is formed in 70×10^3 seconds. This suggests that the N-t-butylaniline is ten times more reactive than p-chloro-N-t-butylaniline (see table XXVI p 120).

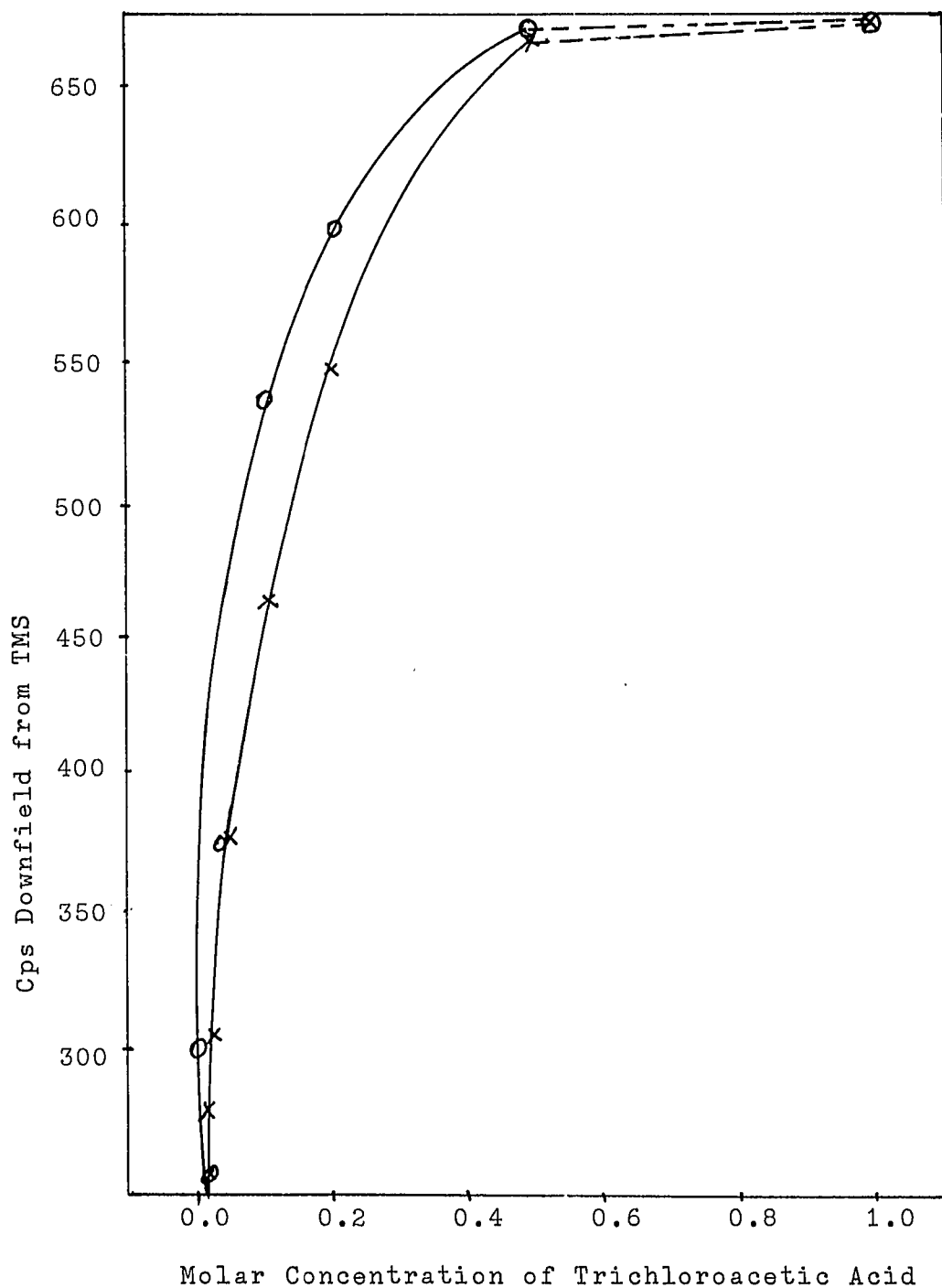
It is interesting that no o,N-dichloro-N-t-butylaniline is observed. Its low equilibrium concentration (assuming some is formed) cannot be due to a rapid rearrangement to give 2,4-dichloro-N-t-butylaniline because as was shown in section 5 of the Discussion, the presence of o-chloro-N-t-butylaniline does not lead to significant increase in the yield of 2,4-dichloro-N-t-butylaniline. This does not however, rule out the formation of o,N-dichloro-N-t-butylaniline. It merely shows that it is unstable and will transfer chlorine rather than "rearrange" by an intramolecular process. This is a key conclusion as will be shown later. Furthermore, it was shown earlier that o-chloro-N-t-butylaniline is at least about 10 times less reactive than p-chloro-N-t-butylaniline. This relative reactivity towards the electrophilic chlorine is, as will be shown later, quite different from the relative basicities of the anilines in carbon tetrachloride. It will be shown also that the ratio of the basicities of N-methylaniline to o-chloro-N-methylaniline is about 1.0 at 43°C (see section 9 of the Discussion).

9. Acid-Base Behavior of Anilines with Trichloroacetic Acid in Carbon Tetrachloride

This study was carried out as part of the development of techniques for studying anilines in non-aqueous solutions. Solutions of many of the anilines reported in the experimental part had to be prepared with varying concentrations of acid. It was therefore necessary to know how they would behave. A look at figure 10 shows that the position of absorption of the amino proton is extremely sensitive to the presence of relatively small concentrations of acid (42). In a 0.2 M solution of N-methylaniline, addition of a 10% molar quantity of trichloroacetic acid causes the amino proton to shift by more than 100 cps downfield. This downfield movement is evidence for a rapid chemical exchange between the amino and the carboxyl protons. Evidence for this rapid exchange has been presented by Grunwald and Price who also showed that the amino protons of N-methylaniline exchange at a significant rate only if carboxyl protons are present.³¹

This study shows also that as the concentration of acid is increased there is a shift in the position of the methyl absorption downfield. This downfield shift is evidence of rapid exchange of the proton between the anilinium ion and the aniline. An example of proton exchange between such a conjugate pair has been studied by Gutowsky who showed that the position of observed absorption is linearly related to the relative concentrations of the two species undergoing exchange.³² In going from the neutral solution to a 1.0 M acid solution, the

Figure 10



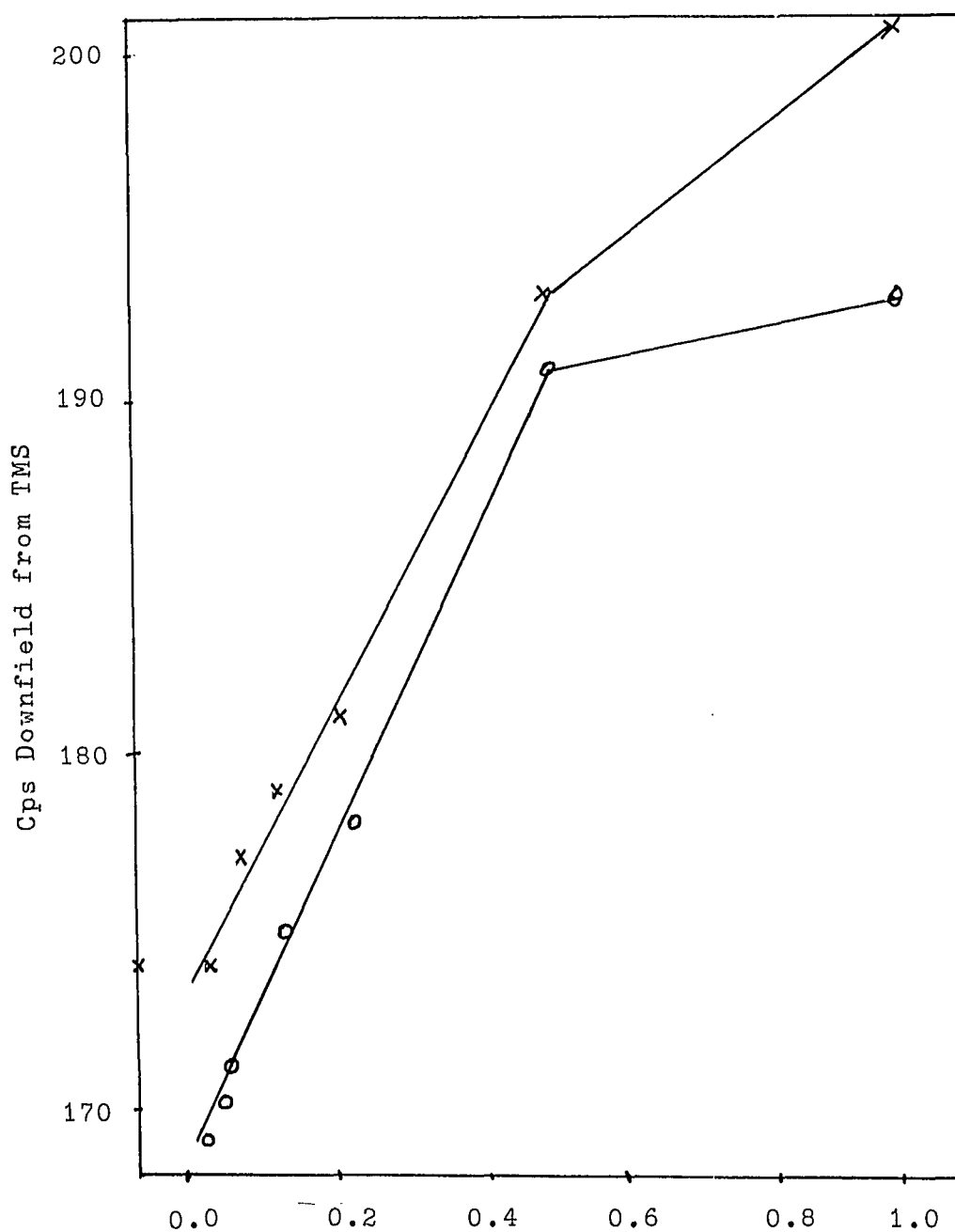
Correlation of position of absorption of amino proton of N-methylaniline (o) and o-chloro-N-methylaniline (x) with concentration of acid in carbon tetrachloride at 43°C (Concentration of each aniline is 0.2 M).

absorption of the methyl protons of N-methylaniline (0.2 M) shifts downfield by as much as 24 cps. This is a very large change and should be significant as an analytical technique for studying alkyanilines (see figure 11). If it is assumed that the protonated aniline shows a methyl resonance at the highest point observed on the curve, then it can be seen that at 0.2 M acid concentration, a significant portion of the N-methylaniline (also 0.20 M) is not protonated.

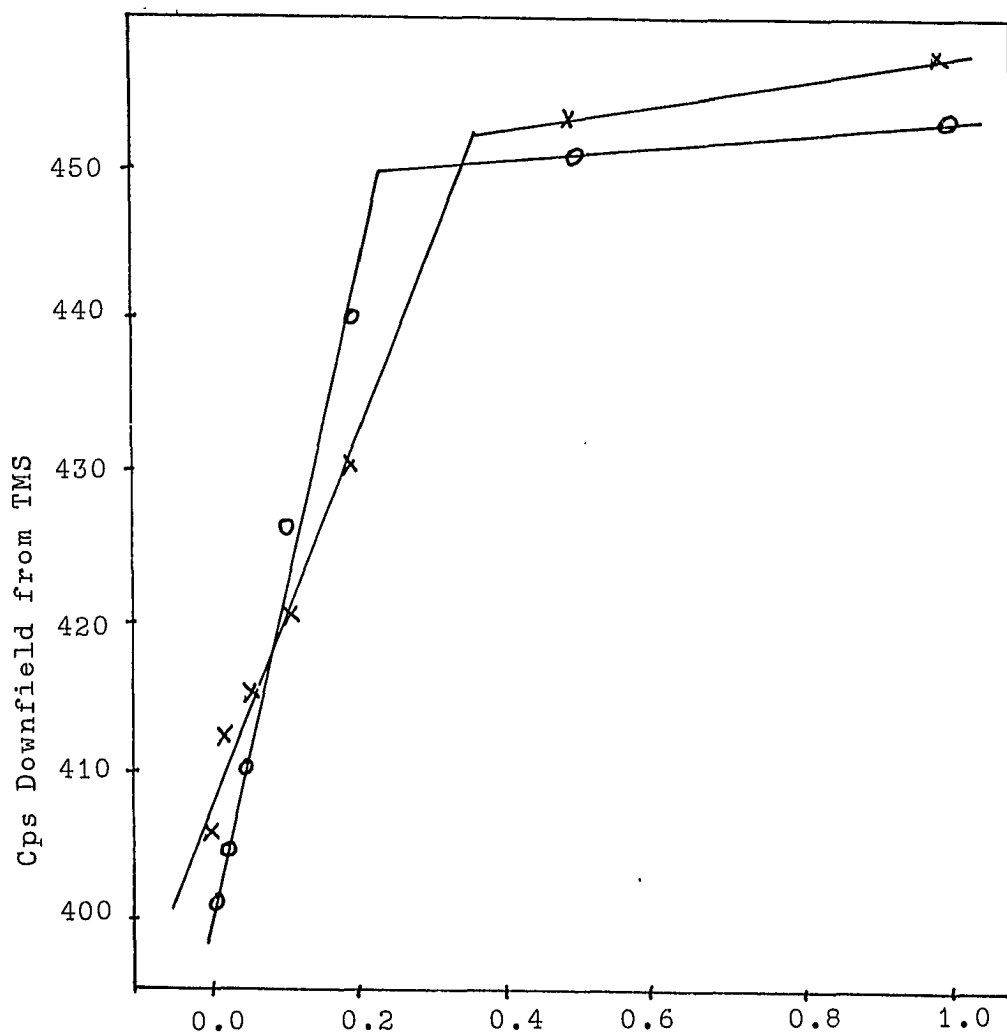
Another interesting feature of the study comes from observation of the aromatic protons (see figure 12). As the acid concentration is increased there is a gradual downfield shift of the center of the aromatic band. This is accompanied by a narrowing of the absorption band which eventually collapses to a singlet in the case of N-methylaniline. This is further evidence for the formation of the anilinium ion. It has been shown that the differences in the position of absorption in the nmr of the aromatic protons is due chiefly to differences in the charge distribution around the ring.

$$d_{\text{ArH}} = d_{\phi\text{H}} + 10z \quad (\text{Equation 7})$$

Here, d_{ArH} is the position of absorption of an aromatic proton in ppm, $d_{\phi\text{H}}$ is the position of absorption of a proton in benzene, and z is the charge on the carbon to which the aromatic proton is attached.⁴⁷ Using equation 7, the charge on a carbon atom in the ring of N-methylanilinium salt may be calculated by substituting 7.55 ppm for the aromatic protons in ArH and 7.27 for the protons in benzene.⁴⁸ The value of 7.55 (453 cps downfield from TMS) was chosen as the point at

Figure 11

Correlation of position of absorption of methyl protons of N-methylaniline (o) and o-chloro-N-methylaniline (x) with concentration of trichloroacetic acid in carbon tetrachloride at 43°C (Concentrations of anilines equal 0.2 M each).

Figure 12

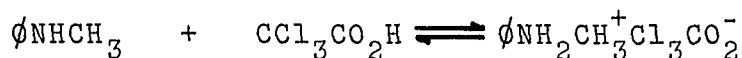
Correlation of center of absorption of aromatic protons of N-methylaniline (o) and o-chloro-N-methylaniline (x) with concentration of trichloroacetic acid in carbon tetrachloride at 43°C. (Concentration of each aniline is 0.2 M)

which the aromatic proton signal collapsed into a singlet (42). For N-methylanilinium salt a value of 0.03 is obtained for z . This means that in the entire ring there is a total charge of 0.18 and it is equally distributed over all carbon atoms. In the case of o-chloro-N-methylanilinium substituting 7.62 ppm for d_{ArH} yields a z value of 0.035 which corresponds to a total charge of 0.21 on the ring. This higher charge on the ring is consistent with the presence of an additional electron withdrawing group.

Since there is rapid exchange between the aniline and the anilinium salt, the observed absorption is an average which is observed as a downfield shift of the band as was explained earlier for the methyl group.

For both the methyl protons and the aromatic protons there is a leveling off of the downfield shift beyond 0.5 M trichloroacetic acid. This leveling off is consistent with the observation that for both anilines (shown in figures 11 & 12) significant quantities are not protonated by an equivalent quantity of trichloroacetic acid.

Kolthoff and Bruckenstein have shown that the reaction of acids and bases in media of low dielectric constant produces ion pairs.³³ They refer to this reaction as the ionization reaction. e.g.,



is the ionization of N-methylaniline in trichloroacetic acid. The ionization constant for this reaction is:

$$k_1 = \frac{(\phi\text{NH}_2\text{CH}_3^+\text{Cl}_3\text{CO}_2^-)}{(\phi\text{NHCH}_3)(\text{Cl}_3\text{CO}_2\text{H})} \quad (\text{Equation 5})$$

The ionization constant of N-methylaniline in trichloroacetic acid can be determined from experiments like the ones described here.

The fraction of aniline that is not protonated at a given acid concentration can be determined from Gutowsky's relationship;³²

$$d_{\text{obs}} = d_1 p_1 + d_2 p_2 \quad (\text{Equation 6})$$

d_{obs} is the observed position of the signal of the aniline undergoing rapid exchange, d_1 and d_2 the positions of the aniline and the anilinium signals respectively, and p_1 and p_2 are the mole fractions of the aniline and anilinium ion respectively. It is assumed that the extreme position of absorption of the methyl protons as acid concentration is increased may be chosen as the position of absorption of the anilinium ion. The value cannot be very much higher than those observed (42) because the curves are leveling off in that region. Table X presents a collection of data from which ionization constants may be calculated. Substituting these values into equation 6 for N-methylaniline yields:

$$178 = 169 p_1 + 193 (1-p_1)$$

$$\text{i.e., } p_1 + p_2 = 1$$

$p_1 = .62$ where p_1 is the fraction of the aniline that is not protonated.

Table XPosition of Resonance of Methyl Group in the nmr Spectra of Various N-Methylanilines in Trichloroacetic Acid Solutions

<u>Compound</u>	<u>Position of Resonance Cps Downfield from TMS</u>		
	<u>Neutral</u>	<u>0.2 M Acid</u>	<u>Anilinium Ion</u>
N-Methylaniline	169	178	193
o-chloro-N-methylaniline	174	182	201
p-chloro-N-methylaniline	163	182	202

Substituting into equation 5 yields:

$$k_1 = \frac{0.38}{0.62 \times 0.62} = 0.99$$

A calculation over all points (42) yielded $0.9 \pm .2$ for k_1 . By similar methods k_1 for o-chloro-N-methylaniline has been calculated to be $0.8 \pm .2$ and for p-chloro-N-methylaniline $2.0 \pm .3$. When the data obtained for the center of the aromatic band (see figure 12) is used to calculate ionization constants, a value of 7.7 ± 5.0 is obtained for N-methylaniline and 3.3 ± 1.5 for o-chloro-N-methylaniline. The low reliability, and the poor correlation of this method with the similar analysis using the methyl shift is due principally to the large uncertainty in determining the "true" center of absorption. A better method for obtaining the center would be to use the half-way point of the integral scan of the band. This scan was not recorded when the experiments were carried out.

These results show that all three anilines have quite similar basicities towards trichloroacetic acid as the reference acid. This is not very surprising because, although Popovych has shown that for a series of methyl pyridines in hydrocarbon solvents, the relative ionization constants paralleled the basicity constants in water,³⁴ it has been shown that in water pyridine is more basic than aniline, but in glacial acetic acid that aniline is more basic than pyridine.³⁵ The base strengths of a number of anilines in water as measured by their pK_B are given in Table XI.³⁶ It can be seen that o-chloro-N-methylaniline is missing from the collection but the variation in basicities between chlorinated anilines and between aniline and N-methylaniline would suggest that o-chloro-N-methylaniline should be at least 10 times less basic than N-methylaniline in water. The high value obtained for the basicity of p-chloro-N-methylaniline may be an indication of the uncertainty of the experimental point for the 0.2 M acid solution.

10. Rearrangement of N-Chloroanilines in Varying Concentrations of Trichloroacetic Acid

As was shown in the previous section N-methylaniline, ortho- and para-chloro-N-methylaniline show moderate base strengths towards trichloroacetic acid in carbon tetrachloride and, very significantly, all three anilines are of similar base strengths. It was also shown earlier that the introduction of anilines into the reaction medium initiated intermolecular

Table XI

Dissociation Constants of Some Anilines in Water at 25°C.³⁶

<u>Compound</u>	<u>pk_B</u>
Aniline	4.62
2-Chloroaniline	2.65
4-Chloroaniline	3.98
N-Methylaniline	4.84
4-Chloro-N-methylaniline	4.395
N-t-Butylaniline	7.0
N,N-Dimethylaniline	5.15
N-iso-Propylaniline	5.77
N,N-di-iso-Propylaniline	7.37

Where k_B is defined as $(BH^+) (OH^-) a^{\pm} / (B) a_b$
 and (B) and (BH⁺) are the molar concentrations of the base
 and its conjugate acid, and a is the activity coefficient.

processes which made it difficult to detect any unimolecular processes which may exist. In the absence of added anilines, a mechanistic pathway exists, namely, exchange of the electrophilic chlorine between the N-chloroaniline and the nitrogen of the para chlorinated aniline in solution, for generating the aniline from which the original N-chloroaniline was prepared. It was therefore concluded that any attempt to observe the unimolecular process should begin with a method for removing the anilines from solution, and that protonation by an acid could be an appropriate method for doing this.

Removal of the anilines by addition of acid seemed to be interesting because it would at the same time increase the concentration of protonated N-chloroaniline, thereby increasing the fraction of products that should be formed by the intramolecular process. It had one principal drawback, *i. e.*, acids which were strong enough to protonate the anilines almost quantitatively were either not soluble in carbon tetrachloride or had other undesirable properties.

It was decided, therefore, that trichloroacetic acid could be used in an experiment in which its concentration was varied and a trend in the product ratios should be observable. According to the current theory of electrophilic substitution and especially of electrophilic aromatic rearrangement, one would expect that increasing the unimolecular process should be indicated by an increasing yield of ortho-chlorinated products.⁶ Therefore, as the concentration of acid is increased, the ortho/para ratio should increase. Table XII

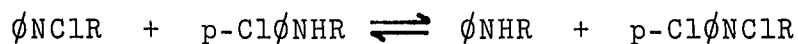
Table XII

Per Cent Yields of Products in the Rearrangement of N-Chloro-N-t-butylaniline (0.25 M) with Varying Concentrations of Trichloroacetic Acid in Carbon Tetrachloride (39).

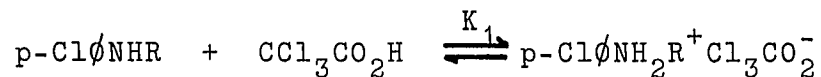
Molar Ratio of Acid to N-chloro- aniline	<u>Per Cent of Products</u>			
	$\phi\text{NHC}_4\text{H}_9$	$o\text{-Cl}\phi\text{NHC}_4\text{H}_9$	$p\text{-Cl}\phi\text{NHC}_4\text{H}_9$	$2,4\text{-diCl}\phi\text{NHC}_4\text{H}_9$
0.20	3.9	86.5	3.9	3.9
0.40	4.9	82.6	5.3	6.1
0.80	14.2	65.5	5.7	14.2
2.00	37.3	20.8	8.4	33.6
4.00	42.4	10.5	13.4	33.6

shows trends in the product ratios in the rearrangement of N-chloro-N-t-butylaniline (41) which suggests the need for a more rigorous approach to the problem.

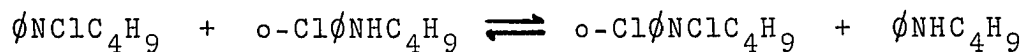
The products which are formed in the early stages of the rearrangement can participate in acid-base equilibria. They can also participate in an exchange of the electrophilic chlorine moiety between their nitrogen atoms. For Example:



It was shown that when R was t-butyl, k_{eq} was equal to 0.56 at 43°C in carbon tetrachloride.



It was shown that for $R = \text{CH}_3$, K_1 , K_2 , and K_3 (for o-chloro-N-methylaniline) all had a value in the range of 1.0. This suggests that there is very little selectivity in protonation of the anilines, and in a system in which the total aniline and acid concentrations were equal about one half of each aniline will be protonated. On the other hand it has been shown that N-chlorination is a highly selective process. It has been shown that the equilibrium concentration of o,N-dichloro-N-t-butylaniline is well under 5% of the N-chloroaniline concentration when there are approximately equal concentrations of N-chloro-N-t-butylaniline and o-chloro-N-t-butylaniline in a mixture (39). This means that for the exchange



the equilibrium constant is less than 0.003. The value of 0.003 is obtained by assuming that 5% of o,N-dichloro-N-t-butylaniline was actually formed in the reaction medium. By substituting into the equation for the equilibrium constant,

$$K_{\text{eq}} = \frac{(\phi\text{NHC}_4\text{H}_9) (\text{o-Cl}\phi\text{NClC}_4\text{H}_9)}{(\phi\text{NClC}_4\text{H}_9) (\text{o-Cl}\phi\text{NHC}_4\text{H}_9)}$$

and assuming that equal concentrations of N-chloro-N-t-butylaniline and o-chloro-N-t-butylaniline were mixed at the start of the reaction. The equilibrium constant then is

$$K_{\text{eq}} = \frac{(0.05) (0.05)}{(0.95) (0.95)} \quad \text{which is less than 0.003 .}$$

- -

Therefore, in a system containing, initially, approximately equal concentrations of N-chloroaniline and trichloroacetic acid, the only species which never will exist in a significant concentration is o,N-dichloro-N-t-butylaniline. The data shows that as acid concentration is increased, the yield of o-chloro-N-t-butylaniline decreases and 2,4-dichloro-N-t-butylaniline increases. If it is assumed that the early stages of rearrangement with a four-fold ratio of acid is similar to that with only small quantities of acid, then large quantities of o-chloro-N-t-butylaniline should have been formed. Its absence in the final product could only have been due to further chlorination to yield 2,4-dichloro-N-t-butylaniline, but this is unlikely because of the low reactivity of o-chloro-N-t-butylaniline. Therefore, it seems more reasonable to assume that in high concentrations of acid the major process yields mainly p-chloro-N-t-butylaniline. This would mean that as the concentration of N-t-butylaniline is decreased by protonation the process changes from mainly o-chlorination to p-chlorination. Therefore, that which yielded mainly o-chloro-N-t-butylanilines is a process which depended on the presence of N-t-butylaniline and is, therefore, not an intramolecular process.

In the absence of N-t-butylanilines, the most nucleophilic species should be the N-chloro-N-t-butylaniline itself. It has already been shown that the formation of o,N-dichloro-N-t-butylaniline is a very unfavorable process (39). The same factors which disfavor N-chlorination of o-chloro-N-t-butyl-

aniline may also disfavor o-chlorination of N-chloro-N-t-butylaniline. Thus under conditions in which the reaction should either be an intramolecular rearrangement of a protonated or unprotonated N-chloroaniline or a bimolecular chlorination of an N-chloroaniline by a protonated N-chloroaniline, products differ dramatically from those in which only catalytic amounts of acid are present.

This clearly indicates that in the process involving catalytic amounts of acids, aniline or protonated aniline must be a participant. Since the other participant must be the N-chloroaniline the reaction with catalytic amounts of acid must be bimolecular.

The rate-determining step in the intramolecular rearrangement of N-chloro-N-t-butylaniline must be the formation of a pi complex.⁶ An intermolecular transfer can either form a pi complex such as that expected from the intramolecular process or it can go directly into the sigma complex. Since it is doubtful that the formation of a pi complex with o-chloro-N-t-butylaniline can be a lower energy process than the formation of a similar complex with N-t-butylaniline, it must be assumed that the rate-determining step in the intermolecular reaction is the formation of a sigma complex. Although a sigma complex can be formed by chlorine transfer from the nitrogen to the ring of another molecule, such a complex cannot be formed directly by transfer from the nitrogen to the ring of the same molecule without the electrophile becoming free during the transfer.

11. Solvent and Temperature Effects on the Rearrangement of N-Chloroanilines

Evidence has been obtained that the rearrangement of N-chloro-N-t-butylaniline in water-washed glass vessels becomes increasingly faster as the dielectric constant of the solvent is increased (35). In glass tubes with surfaces that were uniformly prepared, rearrangement of 0.40 M solutions of N-chloro-N-t-butylaniline was complete, first in nitrobenzene then in o-dichlorobenzene and finally in benzene. Since it is not known how the concentration of the protonated N-chloroaniline varies in the different solvents, it seems unwise to attribute this rate enhancement solely to reduction of the energy of the transition state leading to the products. Yet the products obtained in nitrobenzene are in quite a different ratio from those obtained in benzene or carbon tetrachloride. As the dielectric constant of the medium is increased there is a decrease in the o/p ratio of products formed in the rearrangement. Similarly, as the temperature is increased in a given solvent there is also a reduction of the o/p ratio of products. The greatest change in this temperature effect is seen in the solvents of lowest polarity. A summary of the results is given in table XIII.

These results show that factors which affect the ratio of products in chlorination are not all dependent on the intrinsic properties of anilines but may be to some extent controlled by the medium in which the reaction takes place. Similar variations would be expected if the direct chlorination

Table XIII

Changes in the o/p+2,4- Ratio of Products Obtained from the
Rearrangement of N-Chloro-N-t-butylaniline (0.40 M) with
Changes in Solvent and Temperature in Water-Washed Glass Vessels

<u>Solvent</u>	<u>Dielectric Constant</u> ⁴⁹	<u>Temp. °C</u>	<u>o/p+2,4-</u>
Carbon tetra- chloride	2.2	43	7.0
Benzene	2.3	43	4.3
Benzene	2.3	60	1.1
o-Dichlorobenzene	9.9	43	0.59
o-Dichlorobenzene	9.9	60	0.44
Nitrobenzene	35.7	43	0.57
Nitrobenzene	35.7	60	0.54

were carried out in these solvents with N-chlorosuccinimide because the ring chlorination step is a rearrangement of N-chloroanilines.

The increase in yield of p-chlorinated products as the dielectric constant of the medium of the rearrangement changes suggests that the transition states for ortho and para substitution are different in respect to charge distribution. More precisely, it indicates that para substitution demands greater separation of charge than ortho substitution. Furthermore, it has already been shown that the transition state of the substitution on the ring may be the formation of a sigma complex (see part 10 of the Discussion).

In figure 13 some possibilities for the transition state for ortho and para substitution both by an intermolecular process and by an intramolecular process are indicated. If it is assumed that the energy of the transition state is determined chiefly by that of the most highly conjugated resonance contributor and that the greatest density of charge will be on the nitrogen atom, then it can be seen that in substitution by the intermolecular process the anion associated with the protonated N-chloroaniline is furthest away from the center of highest positive charge density. This charge separation in a solvent of low polarity is a very unfavorable process. In table XIV is given the difference in activation energy between the transition state for ortho and para substitution calculated from the observed o/p+2,4- ratios. It can be seen that in polar solvents para substitution is favored by almost one kilocalorie per mole while in non-polar solvents such as carbon tetrachloride at 43°C, ortho substitution is favored by about one kilocalorie and is very sensitive to changes in temperature.

This temperature effect on the products of the rearrangement is evidence for a large entropy difference for substitution in the ortho and para positions in non-polar solvents. A negative entropy of activation is generally taken as evidence that the reactants are more highly ordered in the transition state than they are in the ground state.⁸ The negative values obtained for $\Delta S_o - \Delta S_p$ (see table XIV) is evidence that the transition state for ortho substitution is more ordered than

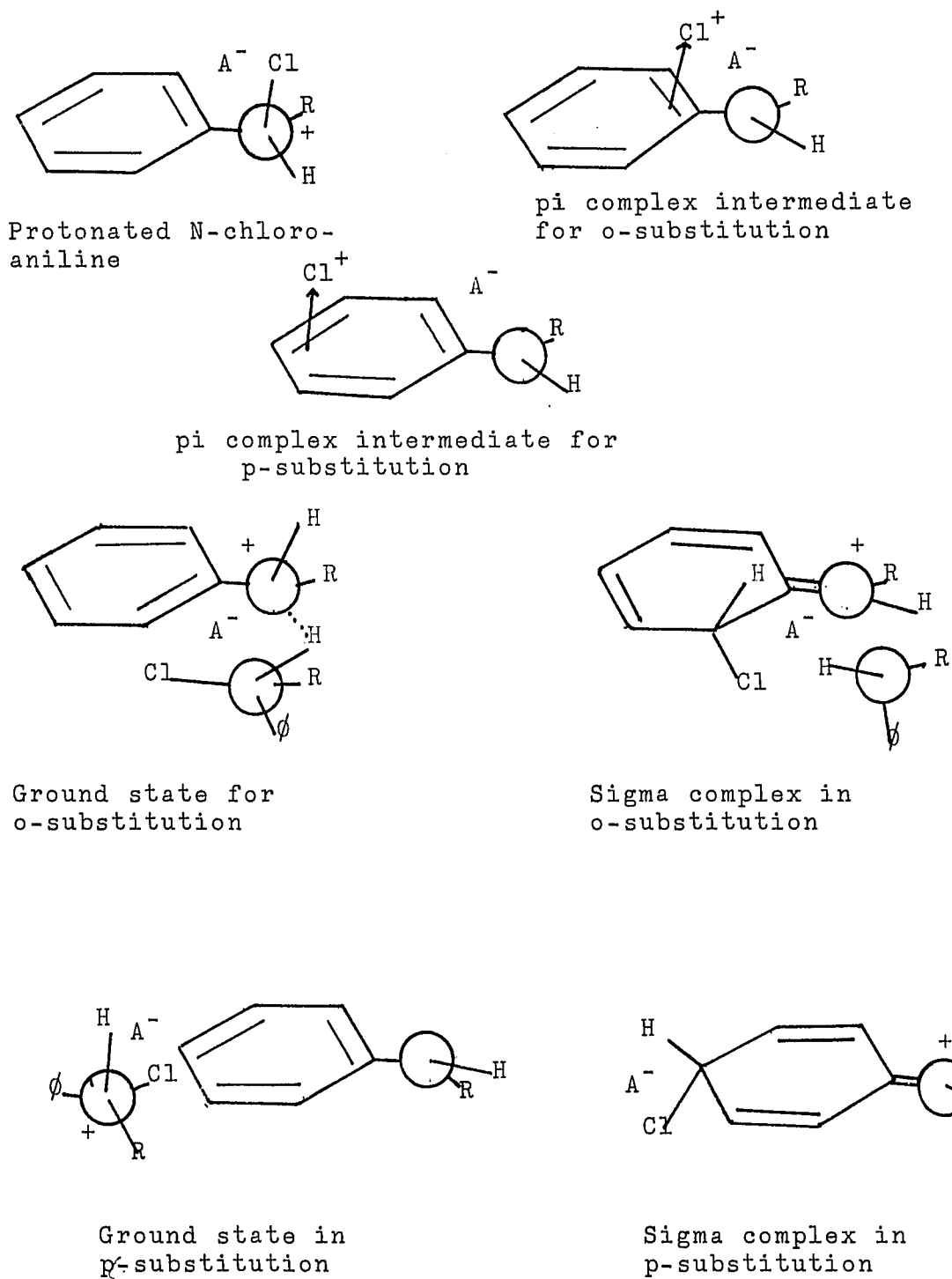
Figure 13

Table XIV

Activation Free Energy, Enthalpy and Entropy Differences for ortho and para Substitution in the Rearrangement of N-Chloro-N-t-butylaniline with Changes in Solvent and

<u>Solvent</u>	<u>Temp. °C</u>	<u>Temperature</u>		
		$G_o^* - G_p^* \text{ (cals)}$	$H_o^* - H_p^* \text{ (cals)}$	$S_o^* - S_p^* \text{ (cals/°C)}$
Carbon Tetrachloride	43	-785		
Benzene	43	-450		
Benzene	60	390	-16500	-50
o-Dichlorobenzene	43	750		
o-Dichlorobenzene	60	990	-6300	-22
Nitrobenzene	43	780		
Nitrobenzene	60	860	-620	-4.4

for para substitution, and that this ordering is greatest in non-polar solvents. Note should be taken however, that this ordering of the transition state is a factor which decreases the activation free energy for ortho substitution as compared to para substitution. Table XIV shows that ortho substitution requires 16 kilocalories per mole less than para substitution in order to raise the reactants to the transition state in benzene. The order in the reactants which lowers the activation energy for ortho substitution appears as a negative entropy factor which almost cancels the large energy difference. Stated otherwise, there is something about the structure of anilines in non-polar solvents which makes ortho substitution more favored than para substitution.

There is evidence that in non-polar solvents anilinium salts exist as dimers.⁴⁷ One may surmise that when anilinium salts are in mixtures with anilines in non-polar solvents, the dimer may consist of an anilinium salt and a free aniline. The geometry of the complex is such that the N-chloroaniline is in an excellent position for transfer of the chlorine to the ortho position of the aniline. Such a position is shown in figure 13. As can be seen in table XIV, increasing solvent polarity is accompanied by a decrease in the activation entropy difference between ortho and para substitution. This is to be expected because the number of dimers should be decreasing as the polarity of the solvent is increased.

Sample Calculations of Activation Free Energy, Enthalpy, and Entropy Differences for Ortho and Para Substitution Given in Table XIV

$$\Delta G^* = 2.301 RT \left(\frac{\log k'T}{h} - \log k \right)$$

Where T = temperature in $^{\circ}\text{K}$, k' is the Boltzmann constant, h is Planck's constant, k is the rate constant of the reaction, and ΔG^* is the activation free energy of the reaction. The activation free energy difference for ortho and para substitution,

$$\begin{aligned} \Delta G_o^* - \Delta G_p^* &= -2.301 RT (\log k_o/k_p) \\ &= -1.51 \times 10^3 \log\left(\frac{o/p+2,4-}{2}\right) \text{ cal at } 60^{\circ}\text{C}, \end{aligned}$$

$$\text{and} \quad = -1.44 \times 10^3 \log\left(\frac{o/p+2,4-}{2}\right) \text{ cal at } 43^{\circ}\text{C}$$

if it is assumed that the ratio of products is proportional to the ratio of the rate constants. Substituting the $o/p+2,4-$ values given in table XIII into the above equation yields the $G_o^* - G_p^*$ values given in table XIV.

$$E_a = \frac{2.301 RT_2 T_1}{T_2 - T_1} \log k_2/k_1$$

k_2 and k_1 are respectively the rate constants for the formation of a given product at T_2 and T_1 . In this study $T_2 = 333^{\circ}\text{K}$ and $T_1 = 316^{\circ}\text{K}$.

Therefore,

$$\begin{aligned}
 E_a &= 2.82 \times 10^4 \log k_2/k_1 \text{ cal/s} \\
 E_{ao} - E_{ap} &= 2.82 \times 10^4 (\log k_{2o}/k_{1o} - \log k_{2p}/k_{1p}) \\
 &= 2.82 \times 10^4 \log (k_{2o}/k_{2p}) (k_{1p}/k_{1o}) \\
 &= 2.82 \times 10^4 \log \left(\frac{o/p+2,4- \text{ at } 333^\circ\text{K}}{o/p+2,4- \text{ at } 316^\circ\text{K}} \right)
 \end{aligned}$$

Substitution of the values given in table XIII into the above equation provides values for $H_o^* - H_p^*$ since

$$\begin{aligned}
 E_a &= \Delta H^* - RT, \\
 E_{ao} - E_{ap} &= \Delta H_o^* - \Delta H_p^* . \\
 \Delta S^* &= \frac{\Delta H^* - \Delta G^*}{T} \\
 S_o^* - S_p^* &= \frac{(\Delta H_o^* - \Delta H_p^*) - (\Delta G_o^* - \Delta G_p^*)}{T}
 \end{aligned}$$

Substituting the values for $\Delta H_o^* - \Delta H_p^*$

and $\Delta G_o^* - \Delta G_p^*$

gives the $\Delta S_o^* - \Delta S_p^*$

which are listed in table XIV.

12. Effect of Chloride Ion on the Rearrangement of N-Chloro-anilines

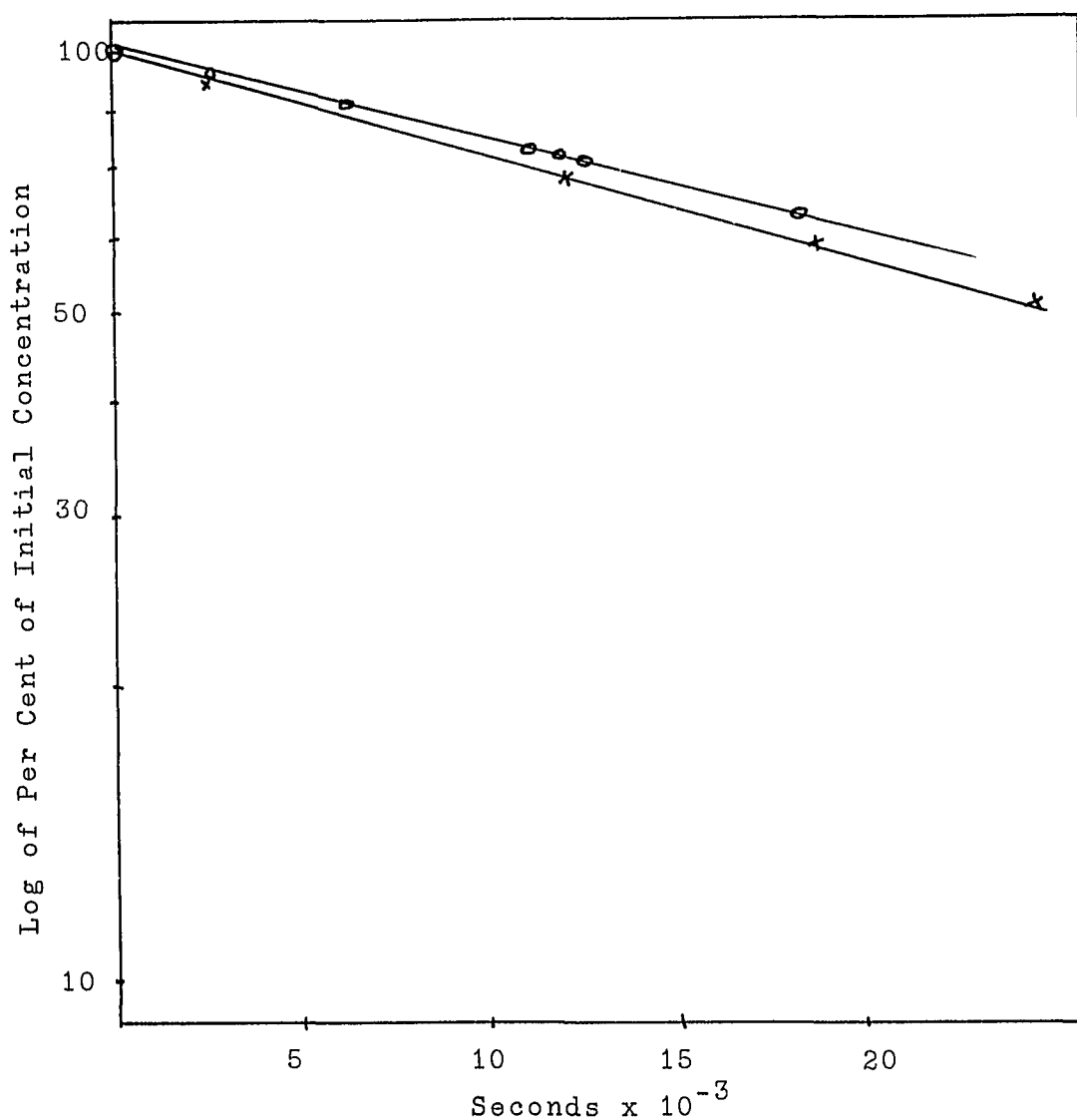
A convenient method for the introduction of chloride ion into the medium of the rearrangement was by use of the hydrochloride salt of N-methylaniline (27). In order to be sure that this salt did not introduce other factors into the rearrangement, similar runs were made with the p-toluene sulfonic acid (28) and the trichloroacetic salts of N-methylaniline (29 F). The yield of 2,4-dichloro-N-methylaniline was in each case less than 1.0%. Chlorination with chlorine (25) gave an o/p+2,4- of 1.6 in carbon tetrachloride at 25°C.

<u>Anion in Rearranging Sample</u>	<u>o/p Ratio</u>
Toluene sulfonate	2.8
Trichloroacetate	3.0
Chloride	2.3

These rearrangements were carried out in carbon tetrachloride at 25°C. It has been observed that some HCl is formed from N-chloro-N-methylaniline under conditions of the rearrangement (23). The maximum quantity that is estimated for most of the rearrangements described is believed not to exceed 10% because 96% of the starting chlorine can be accounted for with an uncertainty not greater than $\pm 5\%$ (see table III). If the addition of chloride ion causes the introduction of a pathway for chlorination involving chlorine as an intermediate, then it can be shown that the quantity of the chlorine process observed is insignificant.

If the process going purely by chlorine gives an o/p+2,4- of 1.6 (25) and the rearrangement gives an o/p+2,4- of 2.8 (23), then $2.3 = 1.6 + (1-x) 2.8$ where $x = 0.4$ or 40% and is the fraction of the process going by the chlorine mechanism. If one equivalent of chloride ion causes 40% of the process to be chlorinated by chlorine then one can estimate that about 4% of this process will take place when HCl (to an extent of 10% of the N-chloroaniline concentration) is formed in the reaction medium.

Further evidence for the absence of a chlorine mechanism comes from a study in which the rearrangement of N-chloro-N-t-butylaniline was catalyzed by equal concentrations of trichloroacetic acid and by hydrochloric acid (34). The rates obtained for the two samples at 43°C in carbon tetrachloride differed by an insignificant quantity. For the hydrochloric acid sample, the unimolecular rate constant for the rearrangement was $1.94 \times 10^{-6} \text{ sec}^{-1}$ and for the trichloroacetic acid catalyzed sample it was $2.02 \times 10^{-6} \text{ sec}^{-1}$. The log of concentration versus time for both rearrangements were straight lines beyond the 50% point (see figure 14). The product ratios were also almost exactly the same. The o/p+2,4- for the hydrochloric acid catalyzed sample was 11.0 and for the trichloroacetic acid sample it was 12.0. It appears, therefore, that the rearrangement does not involve chlorine as an intermediate.

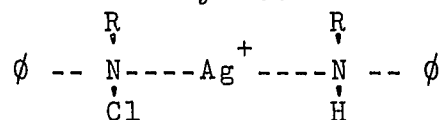
Figure 14

Correlation between per cent of the initial concentration and time in the rearrangement of N-chloro-N-t-butylaniline, 1.66 M, in carbon tetrachloride at 43°C catalyzed by hydrochloric acid (o) and by trichloroacetic acid (x) (34).

13. Catalysis of Rearrangement of N-Chloroanilines by Silver Salts; Effect of Various Acids on the o/p+2,4- Ratio

When rearrangement of N-chloro-N-methylaniline was carried out in carbon tetrachloride in heterogenous mixtures with silver tosylate (29) a marked increase was observed in the o/p+2,4- ratio of products. The ratio observed when N-chloro-N-methylaniline was rearranged with a 1.0 M ratio of N-methylaniline was 4.0 (26). When an equivalent quantity of silver tosylate was added to such a mixture the o/p+2,4- ratio of products jumped to 15.5 (29 D). When acid, silver salt, N-methylaniline and N-chloro-N-methylaniline were allowed to react in an equimolar ratio, the o/p+2,4- ratio dropped down to 3.4 (29 G). This is the same product ratio observed with equimolar quantities of N-methylaniline, N-chloro-N-methylaniline and acid (29 F). It is apparent, therefore, that in strong acid, the effect of the silver ion on the rearrangement is destroyed. This means that under these conditions the proton, rather than the silver ion, is the catalyst.

The structure of the silver complex is different from that of the protonated N-chloroaniline. First, the atomic radii of silver atom and hydrogen atom are 1.34 and 0.37 respectively.³⁷ The silver complex is therefore a much bulkier chlorinating agent. In addition, the silver complex of an aniline in water coordinates with two aniline molecules.³⁷ A possible structure of this complex with the N-chloroaniline in the presence of anilines may be:



It was shown in the previous section that chlorination in ortho position was favored by about one kilocalorie in carbon tetrachloride. In addition, the greater bulk of the silver complex may cause the anion to be much further away in the transition state for para substitution with the silver complex than it does with the protonated N-chloro-anilines (see figure 13). While in ortho substitutions the separation of charge for both chlorinating agents are of more similar magnitude.

It is interesting to point out that with hydrochloric acid and trichloroacetic acid o/p+2,4- ratios of ten and twelve were observed for the rearrangement of N-chloro-N-t-butylaniline in 0.40 M solutions in carbon tetrachloride (34). While the rearrangement under the similar conditions of temperature, solvent and concentration yielded an o/p+2,4- ratio of 7.0 in a water-washed glass vessel. These results suggest that the o/p+2,4- ratio may also depend on the type of acid by which the rearrangement is catalyzed and probably that the acid in water-washed vessels may not be protons but other acidic species on the walls of the vessel itself.

EXPERIMENTAL

1. Instruments

Chlorinated anilines in this study were separated for quantitative analyses on the Varian A 60-P and 600-D gas chromatographs. For preparative purposes, the Varian 1520 Autoprep was used. Infrared spectra were taken on the Perkin-Elmer 237, nmr spectra on the Varian A-60, and uv spectra on the Cary 14 spectrophotometer. Elemental analyses were done by the Schwarzkopf Microanalytical Laboratory.

2. Purification of Solvents

Benzene and hexane were treated with several portions of concentrated sulfuric acid until the addition of a fresh portion showed no color formation in the acid layer. Generally, one liter samples of the solvents required two 50 ml portions of the acid stirred for six hours each. The hydrocarbon was then washed with water, dried over sodium carbonate and distilled from sodium ribbon. Carbon tetrachloride was treated with acid as above, then one liter portions of it were refluxed with 50 ml of methanol and ten grams of potassium hydroxide for one hour.³⁸ These mixtures were extracted with equal quantities of water, dried over sodium carbonate, and distilled. Nitrobenzene was extracted with 6 M hydrochloric acid, then with 0.1 M sodium hydroxide, and finally with an equal volume of water. It was distilled after standing over calcium chloride for at least 24 hours.

3. Purification of Anilines

Commercially available anilines, e.g., N-methyl-, and N,N-dimethylaniline were obtained and were found to be better than 99% pure by gas chromatography. N-methylaniline, however, had an intense yellow color which became darker on exposure to light and oxygen. It was found that on distillation in nitrogen a lighter colored product was obtained. A much lighter, almost colorless product was obtained when the aniline was distilled from one per cent by weight of lithium aluminum hydride.

Synthesis of Anilines

4. p-Chloro-N-methylaniline

p-Chloroaniline (Eastman Yellow Label) was recrystallized from ether (mp 72-73°C). A 38.3 g (0.45 mole) of trimethyl-orthoformate, $\text{HC}(\text{OCH}_3)_3$, (Fischer Scientific, practical), and 1.2 g of concentrated sulfuric acid. The mixture was distilled to yield 42 g of p-chloro-N-formyl-N-methylaniline, bp 166-170°C (20 mm), lit.³⁹ bp 165-170°C (20 mm). The amide was hydrolyzed by refluxing for four hours with 120 ml of 3 M sulfuric acid. The reaction mixture was extracted with 200 ml of ether, and the aqueous layer was made basic and extracted with ether. The ether extract of the basic solution was dried over sodium carbonate and distilled to yield 22.2 g (53%) of p-chloro-N-methylaniline, bp 120°C (20 mm), lit.⁴ bp 120°C (20 mm); n_D^{20} 1.5816, lit.⁴ n_D^{25} 1.5779; nmr (CCl_4) τ 7.30 (s,3); 6.50 (s,1); 2.73-3.80 (symmetrical m, 4).

5. o-Chloro-N-methylaniline

A 38.3 g (0.30 mole) sample of o-chloroaniline (Eastman White Label) was refluxed for a half hour with 47.7 g of trimethylorthoformate, and 1.2 g of concentrated sulfuric acid. The mixture was dissolved in ether and extracted with two 50 ml portions of 1.0 M sulfuric acid. The ether layer was concentrated by evaporation and the residue was refluxed with 120 ml of 3.0 M sulfuric acid for four hours. After extracting the reaction mixture with ether, the aqueous layer was made basic with sodium hydroxide and extracted with ether. The ether extract was dried over sodium carbonate distilled to yield 32.0 g (76%) of o-chloro-N-methylaniline, bp 106°C (20 mm), lit.⁴ bp 106°C (20 mm); n_D^{24} 1.5784, lit.⁴ n_D^{25} 1.5780; nmr (CCl₄) tau 7.65 (s,3); 6.05 (s,1); 2.66-3.66 (m,4).

6. 2,4-Dichloro-N-methylaniline

A 4.05 g (0.025 mole) sample of 2,4-dichloroaniline (Eastman White Label) was refluxed for a half hour with 2.55 g (0.050 mole) of 90% formic acid. The mixture was dissolved in 50 ml of ether, stirred over five grams of sodium carbonate and filtered. The filtrate was evaporated to 15 ml and allowed to crystallize. This yielded 4.0 g (85%) of N-formyl-w,4-dichloroaniline, mp 159-160°C. This was dissolved in 50 ml of tetrahydrofuran and refluxed for four hours with 1.0 g of lithium aluminum hydride (Metal Hydrides Inc., 95%+ purity). The solvent was removed by evaporation, and the residue was dissolved in 6 N hydrochloric acid and extracted with 50 ml of ether. The aqueous layer was then made basic with sodium

hydroxide and extracted with two 50 ml portions of ether which were combined and dried over sodium carbonate. The dry solution was filtered and distilled to yield 2.4 g of product which on analysis by gas chromatography turned out to be a 1:5 mixture of p-chloro-N-methylaniline and 2,4-dichloro-N-methylaniline. A pure sample of the major product was obtained by preparative gas chromatography. n_D^{20} 1.5945; nmr (CCl_4) τ 7.20 (s, 3); 5.80 (s, 1); 2.20-3.70 (m, 3).

Anal. calcd. for $\text{C}_7\text{H}_7\text{Cl}_2\text{N}$: C, 47.74%; H, 4.01%.

Obsd: C, 47.74%; H, 4.12%.

Attempts to prepare o-chloro-N-methylaniline by the reduction of the formyl derivative in the manner described above gave N-methylaniline as the principal product. p-Chloro-N-methylaniline could be prepared by this method in very high yield.

7,8. o- and p-Chloro-N,N-dimethylaniline

A 61 g (0.50 mole) sample of N,N-dimethylaniline (Eastman) was refluxed with 67 g (0.50 mole) of N-chlorosuccinimide (Aldrich) in 500 ml of benzene for twelve hours to yield, as determined by gas chromatography, 6.0 g of unreacted N,N-dimethylaniline, 40.0 g (53%) of o-chloro-N,N-dimethylaniline, 20.0 g (27%) of p-chloro-N,N-dimethylaniline, and 9.0 g (10%) of 2,4-dichloro-N,N-dimethylaniline. Succinimide was removed from the reaction mixture by extraction with water, and the mixture of products in the benzene solution was dried over sodium carbonate, filtered, and distilled on a five-foot spinning band fractionating column.

o-Chloro-N,N-dimethylaniline was collected at 89°C (10 mm), lit.⁴ 102°C (22 mm); n^{24}_D 1.5513, lit.⁴ n^{24}_D 1.5510; nmr (CCl_4) tau 7.23 (s, 6); 2.60-3.33 (m, 4).

p-Chloro-N,N-dimethylaniline was collected at 112°C (10 mm), lit.⁴ bp 127°C (21 mm); n^{20}_D 1.5738; nmr (CCl_4) tau 7.30 (s, 6); 2.60-3.33 (symm. m, 4).

9. 2,4-Dichloro-N,N-dimethylaniline

In 15 ml of benzene was placed 1.55 g (0.01 mole) of p-chloro-N,N-dimethylaniline with 1.33 g (0.01 mole) of N-chlorosuccinimide (Aldrich, 98%+ purity) and the mixture was refluxed for twelve hours. Succinimide was removed by extraction with water, and 2,4-dichloro-N,N-dimethylaniline, better than 95% pure by gas chromatography, was further purified by preparative gas chromatography. n^{20}_D 1.5682; nmr (CCl_4) tau 7.24 (s, 6); 2.70-3.20 (m, 3).

Anal. calcd for $C_8H_9Cl_2N$: C, 50.56%; H, 4.77%; Cl, 37.31%; N, 7.37%. Obsd: C, 50.44%; H, 4.80%; Cl, 37.63%; N, 7.35%.

10. N-t-Butylaniline

t-Butylamine, 175 g (2.7 mole), (Eastman Yellow Label), was refluxed with 7.8 g (0.20 mole) of sodamide for 24 hours. To the refluxing mixture was added 32 g (0.22 mole) of bromobenzene and the sample was kept at reflux for another seventy-two hours. Unreacted t-butylamine was removed by distillation, and the residue dissolved in 100 ml of 6 N hydrochloric acid, was extracted with 200 ml of ether. The acid layer was made basic with sodium hydroxide and extracted

with ether. The extract of the basic solution was dried over sodium carbonate and distilled to yield 11.9 g (40%) of N-t-butylaniline, 105°C (22 mm); lit.⁴ bp 97°C (19 mm); $\bar{n}^{24}_D$ 1.5250, lit.⁴ $\bar{n}^{24}_D$ 1.5246; nmr (0.2 M, CCl₄) tau 8.78 (s, 9); 6.65 (s, 1); 2.80-3.66 (m, 5).

11, 12. o- and p-Chloro-N-t-butylaniline

A 2.98 g (20.0 m mole) sample of N-t-butylaniline was refluxed for one hour with 2.66 g (20.0 m mole) of N-chlorosuccinimide in 50 ml of benzene. The succinimide was removed by extraction with water, and the organic phase was dried over sodium carbonate. The sample was concentrated by evaporation to a volume of 5.0 ml and the products were collected by preparative gas chromatography. p-Chloro-N-t-butylaniline was obtained in a 1.2 g (32%) yield, $\bar{n}^{24}_D$ 1.5425, lit.⁴ $\bar{n}^{24}_D$ 1.5416; nmr (1.2 M, CCl₄) tau 8.70 (s, 9); 6.68 (s, 1); 3.22 (symm. m, 4).

o-Chloro-N-t-butylaniline was obtained in a 1.8 g (50%) yield $\bar{n}^{24}_D$ 1.5350, lit.⁴ $\bar{n}^{24}_D$ 1.5346; nmr (0.80 M, CCl₄) tau 8.66 (s, 9); 5.83 (s, 1); 2.80-3.70 (m, 4). Lit.⁴ nmr tau 8.63 (s, 9); 5.83 (s, 1); 2.70-3.60 (m, 4).

13. 2,4-Dichloro-N-t-butylaniline

In 50 ml of benzene, 0.92 g (5.0 m mole) of p-chloro-N-t-butylaniline was stirred with 5.0 g of calcium hypochlorite (Baker Purified Reagent) which had been premixed with 0.5 ml of water. Stirring was continued for a half hour at 25°C.

The mixture was filtered and to the filtrate was added 1.0 ml of 0.1 N trichloroacetic acid solution. The acidified filtrate was placed in a 43°C constant temperature bath for 48 hours. Benzene was removed by evaporation, and 2,4-dichloro-N-t-butylaniline, better than 98% pure by gas chromatography, was further purified by preparative gas chromatography.

n_D^{20} 1.5524; nmr (2.0 M, CCl_4) τ 8.60 (s, 9); 5.90 (s, 1); 2.72-3.33 (m, 3).

Anal. calcd for $\text{C}_{10}\text{H}_{13}\text{Cl}_2\text{N}$: C, 55.07%; H, 5.95%; Obsd: C, 55.36%; H, 6.05%.

14. m-Chloro-N-methylaniline

A 25.4 g (0.20 mole) sample of m-chloroaniline (Matheson) and 13.8 g (0.27 mole) of 90% formic acid were heated at reflux for a half hour. The condenser was removed, and the temperature was raised to 240°C and kept there for another hour. The product was cooled and dissolved in 100 ml of ether. The ether solution was extracted twice with 50 ml portions of 3 N hydrochloric acid, dried over calcium chloride, filtered, and distilled to yield 18.8 g (50%) of m-chloro-N-formylaniline, bp 155-158°C (2 mm). The distillate solidified to a crystalline solid mp 52-54°C. A 10.0 g portion of this solid (0.064 mole) was refluxed with 3.8 g of lithium aluminum hydride in 200 ml of tetrahydrofuran for 12 hours. The mixture was added slowly to water to destroy the excess hydride, and the aqueous mixture was extracted with 300 ml of pentane. The pentane solution was extracted with three 50 ml portions of 3 N hydrochloric acid which were combined, and made basic with sodium hydroxide. The basic solution was extracted with two 50 ml portions of ether which were combined, dried over sodium carbonate, filtered, and distilled to give 5.0 g (55%) of m-chloro-N-methylaniline, bp 117-120°C (22 mm), n_D^{25} 1.5812; nmr (CCl_4) τ 7.23 (s, 3); 6.45 (s, 1); 2.85-3.80 (m, 4).
Anal. calcd for $\text{C}_7\text{H}_8\text{ClN}$: C, 59.37%; H, 5.69%.
Obsd: C, 59.10; H, 5.63 .

15. Proof that m-Chloro-N-methylaniline Was Not a Product of the Chlorination of N-methylaniline.

m-Chloro-N-methylaniline had the same retention times as p-chloro-N-methylaniline on the following gas chromatographic columns:

10% poly-m-phenylether 5-ring on Chromosorb G

7% Versamid 900 on Chromosorb G

5% Apiezon N on Chromosorb G

5% Carbowax 20 M on Chromosorb G

20% SE 30 on Diatoport S

The infrared spectrum of the compound showed a sharp and intense band at 975 cm^{-1} which was not present in p-chloro-N-methylaniline. A synthetic mixture of 5% of m-chloro-N-methylaniline in p-chloro-N-methylaniline was prepared. In this mixture, the 985 cm^{-1} band of p-chloro-N-methylaniline had an absorption between 89 and 68 on the per cent transmittance scale, while the 975 cm^{-1} band of m-chloro-N-methylaniline absorbed between 89 and 77 on the same scale. Under those conditions an absorption going from 89 to 88 on the 975 cm^{-1} meta band could easily have been detected. Since the concentration is proportional to the log of the per cent transmittance

$$5\% \text{ meta in para} = k \log 89/77$$

$$= .0629 k$$

$$x\% \text{ meta in para} = k \log 89/88$$

$$= .0049 k$$

$$x = \frac{0.0049 \times 5\%}{0.0629} = 0.4\%$$

Therefore, 0.4% m-chloro-N-methylaniline could be detected in p-chloro-N-methylaniline when the absorbance of the 985 cm^{-1} band of p-chloro-N-methylaniline is at least as intense as $\log 89/68$. Since p-chloro-N-methylaniline is generally about 20% of the reaction product, 0.4% will be about 0.08% of the total reaction mixture. When spectra were taken on samples of p-chloro-N-methylaniline collected by gas chromatography from reaction mixtures in which the intensity of the para band at 985 cm^{-1} had an absorbance which was equal to or greater than $\log 89/68$. NO absorption at the 975 meta band was observed.

Analytic Methods

16. Gas Chromatography

The products obtained in the chlorinations of N-methyl-, N,N-dimethyl-, and N-t-butylaniline were separated under easily accessible conditions on commercially available gas chromatographs. The limiting factor in the separations was the choice of the column. It was observed that although a wide variety of liquid phases could be used to get satisfactory results, the choice of a solid phase was limited. When Chromosorb P (Varian), for example, was used as the solid support, poor resolution of the components were observed because of excessive "tailing" of the peaks. Good results were, however, obtained with Chromosorb G (Varian, acid washed, DMCS treated). The best results were obtained with a

solid support consisting of 33% by weight potassium hydroxide on Chromosorb P. The liquid phases which were used included Apiezon N, Carbowax 20 M, poly-m-phenylether 5-ring, Versamid 900, and SE 30 (all available from Varian Aerograph).

In a typical analysis, the products were first identified by their relative retention times. The quantitative determinations were made by use of an internal standard. The analyses were carried out in the following manner: A calibration mixture of known weights of 1,2,4-tribromobenzene and each of the anilines expected as a product of the reaction was prepared in a solution of approximately one molar in each component. The aniline to be chlorinated was weighed and a known weight of 1,2,4-tribromobenzene was placed into solution with it. At the end of the chlorination chromatograms were taken both of the calibration mixture and of the reaction mixture. The peak areas were measured with a planimeter (Keuffel and Esser #620015). The per cent yield of a given compound is obtained from the following formula:

$$\% \text{ Yield of compound X} = \frac{100 A_x a_s}{M A_s a_x}$$

where A_x is the area of the peak of compound X in the chromatogram of the product mixture.

A_s is the area of the internal standard peak in the chromatogram of the product mixture.

a_x is the area per millimole of compound X as determined from the calibration mixture.

Table XV

Relative Retention Times and Peak Widths* on the Analysis of
Anilines by Gas Chromatography

<u>Compound</u>	<u>Retention Time (minutes)</u>	<u>Peak Width (millimeters)</u>
p-dichlorobenzene ^a	1.00	2.5
aniline	1.53	3.5
N-methylaniline	1.76	4.5
o-chloro-N-methylaniline	2.68	5.5
o-chloroaniline	3.20	6.5
p-chloroaniline	5.87	11.5
p-chloro-N-methylaniline	6.28	12.0

* The peak width is the distance between its sides at half its height.

a) p-Dichlorobenzene was the internal standard in some runs.

Column: 12 ft x 0.25 in. aluminum packed with 7% Versamid 900 with 33% potassium hydroxide on Chromosorb P at 208°C and 60 ml of helium per minute.

Sample Size: 15 micro liters of approx. 0.5 M in each component

Instrument: Aerograph A 90-P.

Table XVI

Analytical Data Obtained in a Typical Analysis by Gas
Chromatography in the Chlorination of N-Methylaniline

a) The Calibration Mixture

<u>Compound</u>	<u>Weight of</u> <u>Sample (g)</u>	<u>m mole</u> <u>of</u> <u>Sample</u>	<u>Relative</u> <u>Areas</u>	<u>Relative</u> <u>Areas</u> <u>Per M Mole</u>
N-methylaniline	0.5365	0.501	2.10	4.15
o-chloro- N-methylaniline	0.7115	0.502	2.61	5.23
p-chloro- N-methylaniline	0.6995	0.494	2.36	4.77
2,4-dichloro- N-methylaniline	0.9180	0.521	2.78	5.33
TBB*	1.5800	0.502	2.90	5.78

b) The Reaction Mixture (23)

<u>Compound</u>	<u>Relative</u> <u>Areas</u>	<u>Relative</u> <u>Areas/m mole</u>	<u>m mole</u>	<u>Per Cent</u> <u>Yield</u>
N-methylaniline	54	4.15	13.0	9.9
o-chloro- N-methylaniline	413	5.23	79.4	60.7
p-chloro- N-methylaniline	94	4.77	19.7	15.1
2,4-dichloro- N-methylaniline	75	5.33	14.0	10.7
TBB	760	5.78	131	

* Internal standard 1,2,4-tribromobenzene.

a_s is the area per millimole of standard as determined from the calibration mixture.

M is the molar ratio of aniline to standard in the reaction mixture.

17. Product Analysis by NMR

Relative positions of the t-butyl resonance in various t-butylanilines were determined by taking spectra of mixtures of the compound at 50 or 100 cycles sweep width. The positions at which resonance was observed with reference to TMS was observed to be concentration dependent. But the relative positions of absorption of the components of a mixture showed only small variation in the same concentration range. Thus, when the concentration of a mixture of t-butylaniline was changed from 0.2 to 1.0 M in carbon tetrachloride at 43°C, the position of absorption of the t-butyl protons shifted downfield by (on the average) 5.0 cps from TMS. At the same time the relative positions of absorption of the components of the mixture changed by less than 1.0 cps. The relative positions of absorption of a number of t-butylanilines are listed in table XVII.

For quantitative analysis of reaction mixtures, the relative peak heights were used. This is a good measure of the area of the peaks only if all the peaks have the same width. If the peaks are assumed to be triangular, the peak width may be defined as the distance between the sides of the peak at half its height. This quantity when multiplied by the

height of the peak gives its area. The factor which governs the relative width of peaks in nmr is primarily the weak couplings with protons that are too far away to cause splitting of the signal.⁴⁰ In the case of t-butylanilines, the proton on the nitrogen does not couple if there are small quantities of acidic species present in the medium which speed up chemical exchange, and the ortho protons are too far away to cause significant broadening of the peaks. Therefore, the relative heights of peaks in this series of compounds are good measures of their relative areas. It was not quite clear that the same would hold for N-methyl-, and N,N-dimethylaniline. Table XVIII presents data on a number of alkyylanilines. The data were obtained from spectra of the anilines in 0.2 mole per cent of trichloroacetic acid in carbon tetrachloride solution. The areas of the peaks were determined by integration. In every spectrum, t-butylaniline was used as the standard in order to be sure that variations in the instrument did not affect the relative widths of the peaks.

<u>Mixture of Anilines</u>	<u>Alkyl Group</u>	<u>Relative Areas</u>	<u>Height in mm</u>	<u>Concentration</u>
N-t-butyl	t-butyl	71	158	0.5 M
N,N-dimethyl	dimethyl	88	200	---
N-t-butyl	t-butyl	103	147	0.8 M
o-chloro- N,N-dimethyl	dimethyl	91	132	---
N-t-butylaniline	t-butyl	101	189	1.0 M
N-methylaniline	methyl	66	125	---

Table XVIIRelative Positions of t-Butyl Resonance in t-Butylanilines

<u>Compound</u>	<u>Relative Position of Resonance (Cps)</u>
N,4-dichloro-N-t-butylaniline	-2.5
N-chloro-N-t-butylaniline	0.0*
p-chloro-N-t-butylaniline	1.5
N-t-butylaniline	4.0
2,4-dichloro-N-t-butylaniline	6.5
o-chloro-N-t-butylaniline	8.0

*This value moves between 70 and 75 cps downfield from TMS in carbon tetrachloride at 43°C as concentration varies from 0.2-1.0 in total aniline concentration.(Varian A60A).

Table XVIII
Ratio of Peak Widths of Some Anilines to Peak Width* of
N-t-Butylaniline in the nmr Spectra of Their Alkyl Groups

<u>Compound</u>	<u>Absorbing Group</u>	<u>Ratio</u>
N-t-butylaniline	t-butyl	1.00
N-methylaniline	methyl	0.98
N,N-dimethylaniline	dimethyl	0.98
o-chloro-N,N-dimethylaniline	dimethyl	0.98

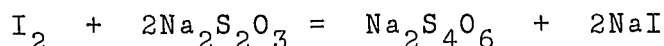
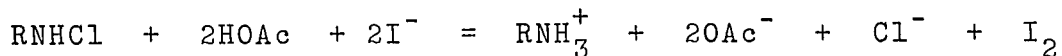
Spectra taken at 43°C in carbon tetrachloride with 2% of trichloroacetic acid.

* Distance between sides of peak at half its height on the assumption that peak is triangular.

18. Quantitative Analysis of N-Chloroanilines by Iodimetry

Several refinements were made on the standard method of iodimetry. First, in order to avoid repetitious preparations of starting materials, it was desirable to use as small a sample as possible. Secondly, since oxygen reacted with acidic solutions of potassium iodide, it was necessary to exclude it from the reaction mixture. Thirdly, an alternate end point detecting device was needed because starch did not give its intense blue color in this system, and many of the samples studied had intense blue or brown colors which made visual detection of the end point impossible. A satisfactory system which was developed involved the use of a "dead stop" titration technique with platinum electrodes for detecting the end point coulometrically.⁴¹ During the titration, the sample was maintained under an atmosphere of nitrogen. In a typical analysis, the cell containing the electrodes was charged with 20 ml of 50% aqueous acetic acid and 5 ml of 2 M potassium iodide. The mixture was stirred very rapidly with a magnetic stirrer, a ten millivolt potential was placed across the electrodes, and the current (1-5 micro amp) was recorded. A sample, 10.0 ml of 0.20 M N-chloro-N-methylaniline was added to the cell, the current jumped to 50 micro amp, and titration was carried out by adding 0.0101 N sodium thiosulfate until the current fell back to the recorded value. The titration curve of current versus time was exponential with the greatest drop taking place on the addition of the last few drops (about 1/30 ml each) of titrant. The stoichiometry of this titration

method was determined by the following equations:

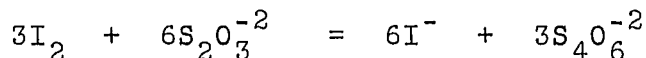
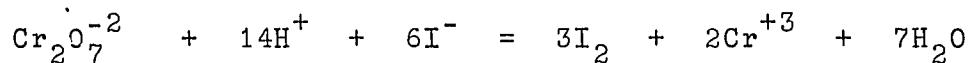


19. Standardization of Sodium Thiosulfate⁴²

Sodium thiosulfate (A.C.S. reagent grade $\text{Na}_2\text{S}_2\text{O}_3 \cdot 5\text{H}_2\text{O}$)

4.970 was dissolved in distilled water to which 0.1 g of sodium carbonate was added and the volume made up to one liter in a volumetric flask. Two samples of potassium dichromate (A.C.S. reagent Grade) were weighed and transferred into 200 ml stoppered Erlenmeyer flasks. Potassium iodide, 0.5 g and glacial acetic acid, 20 ml, were added to the flasks which were filled with nitrogen. They were stoppered and allowed to sit in the dark for a half hour, and then titrated with the thiosulfate solution until they were colorless.

<u>Weight of dichromate</u>	<u>m.equivs.</u>	<u>Volume Titrant</u>	<u>Normality of Titrant</u>
0.1000 g	1.020	100.7 ml	0.0101
0.0965 g	0.953	97.3 ml	0.0102



1.0 Equivalent = 98.08 g with respect of Cl^+

20. Preparation of N-Chloro-N-methylaniline

A 1.075 g (10.0 m mole) sample of N-methylaniline was dissolved in 500 ml of carbon tetrachloride and placed in an ice bath at 0°C. Calcium hypochlorite, 10.0 g (30m equivs. by our analysis) was mixed with 1.0 ml of water and added to the cold solution of N-methylaniline. The mixture was stirred for 15 minutes. It was then vacuum filtered very rapidly on a Buchner funnel with Genuine Whatman #1 filter paper and the volume was readjusted to 100 ml to give a 0.02 M solution of N-chloro-N-methylaniline. Titration of aliquots of the solution immediately after filtration showed a 99±1 % yield of N-chloro-N-methylaniline. Infrared spectra taken of the solution of the aniline before chlorination in a pair of 1.0 cm quartz cells showed an N-H stretching absorption at 3415 cm^{-1} with an intensity of 0.47 absorbance units. After chlorination, that peak had completely disappeared. N-ethylaniline and N-sec-butylaniline were also chlorinated by the method given above in benzene, carbon tetrachloride and pentane.

21. N-Chlorination and C-Chlorination of N-Methylaniline with N-Chlorobenzanilide

In a 500 ml flask equipped with a magnetic stirrer were placed 0.537 g (5.00 m mole) of N-methylaniline, 1.16 g (5.00 m mole) of N-chlorobenzanilide, 250 ml of carbon tetrachloride, and 0.268 g of 1,2,4-tribromobenzene. The solution was divided into two equal portions. One was stirred over 2.0 g of powdered sodium carbonate, and the other was left undisturbed.

Both were kept at 25°C. Soon after separating the solution into two portions, an aliquot of the sample which was not placed over sodium carbonate was titrated for positive chlorine, and it required 11.4 ml of a standard thiosulfate solution. Twenty-four hours later, another aliquot showed no evidence for the presence of positive chlorine. At the same time an aliquot of the sample which was stirred over sodium carbonate required 10.6 ml (93%) of the same thiosulfate solution for complete titration. The sodium carbonate mixture was filtered to give a pale yellow solution of N-chloro-N-methylaniline which was kept at 25°C. The residue was extracted with water, filtered and dried to give 0.48 g (96%) of benzanilide (mp 161-162°C). The N-chloro-N-methylaniline solution after standing at 25°C for four hours showed no further evidence for positive chlorine. Its products and that of the sample which was chlorinated directly were analyzed by gas chromatography.

<u>Products</u>	<u>Per Cent Yield from N-Chloroaniline Rearrangement</u>	<u>Per Cent Yield From Direct Chlorination</u>
N-methylaniline	5.7	4.9
o-chloro-N-methylaniline	62.5	66.8
p-chloro-N-methylaniline	11.2	12.2
2,4-dichloro-N-methylaniline	10.3	10.5

22. Kinetic Study of the Rearrangement of N-Chloro-N-methylaniline in Carbon Tetrachloride

Solutions of N-chloro-N-methylaniline in carbon tetrachloride, 0.02 to 0.10 M, gradually lost their ability to act as chlorinating agents on standing. Solutions of this compound at concentrations greater than 1.0 M were found to be quite unstable and could not be kept for any length of time without significant rearrangement. An example of the data obtained in a typical rearrangement is given below. These data were obtained by iodimetric titration of 5.00 ml aliquots of 0.020 M solution of N-chloro-N-methylaniline with 0.615 N sodium thiosulfate solution. The sample was kept in 0°C during the rearrangement.

<u>Time (minutes)</u>	<u>Titer (ml)</u>	<u>Per Cent of Initial Concentration</u>
0	14.98	100
40	14.78	99.0
75	14.54	97.0
140	14.32	95.5
195	14.04	94.0
255	13.64	90.5
315	12.54	83.5
375	12.30	82.0
435	6.92	46.0
495	1.70	11.3

23. Products of the Rearrangement of N-Chloro-N-methylaniline in Carbon Tetrachloride at 25°C

A 500 ml sample of an 0.02 M solution of N-chloro-N-methylaniline containing 3.148 g (10.0 m mole) of tribromobenzene was placed in a 25°C constant temperature bath and samples of it, 50 ml each, were removed at intervals for titration with standard sodium thiosulfate. The titrated samples were made basic with sodium hydroxide, the carbon tetrachloride layer was separated, and the aqueous layer was extracted twice with 50 ml of N-hexane. The hexane extracts were added to the carbon tetrachloride layer, and the mixture was dried over sodium carbonate. The dry solution was concentrated by evaporation to approximately 1.0 ml and the mixture was analyzed by gas chromatography. In the results given below, the samples are listed in the order in which they were removed for titration. A blue-green solid residue remained on the walls of the flask which on extraction with 1.0 ml of water gave a solution which was acidic to litmus, and gave a white precipitate with silver nitrate.

Products (N-methylanilines)	Per Cent of Products in Each Sample			
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
N-methyl	--	44.7	22.1	10.9
O-chloro-N-methyl-	25.8	41.3	56.5	66.4
p-chloro-N-methyl-	7.9	8.9	10.3	9.4
2,4-dichloro- N-methyl-	4.5	5.9	10.1	10.3

24. Variation of Products of Chlorination of N-Methylaniline with Extent of Chlorination by N-Chlorosuccinimide

A 0.696 g sample of N-chlorosuccinimide was dissolved in 400 ml of carbon tetrachloride to form a 0.013 M solution. N-Methylaniline, 0.537 g (5.00 m mole) was dissolved in 25 ml of carbon tetrachloride, and 0.604 g of 1,2,4-tribromobenzene was also dissolved in 25 ml of the same solvent. Mixture of the three solutions were prepared in the following order:

<u>Sample Number</u>	<u>Volume of Each Solution (ml)</u>		
	<u>N-Chloro-succinimide</u>	<u>N-Methylaniline</u>	<u>Tribromo-benzene</u>
1	60.0	5.0	5.0
2	70.0	5.0	5.0
3	80.0	5.0	5.0
4	90.0	5.0	5.0
5	100.0	5.0	5.0

The volume of each sample was adjusted to 110 ml by the addition of carbon tetrachloride, and the samples were kept in a 25°C constant temperature bath. At the end of 24 hours, addition of a 10.0 ml aliquot of each sample to potassium iodide in glacial acetic acid caused no measureable formation of iodine. The solutions were extracted with water, dried over sodium carbonate, and analyzed by gas chromatography. The products are listed on the next page.

Compound (Aniline)	Per Cent Yield of Products in Each Sample				
	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>5</u>
N-methyl-	27.0	13.7	---	---	---
o-chloro- N-methyl-	58.5	55.8	72.5	68.0	77.0
p-chloro- N-methyl-	12.7	13.7	15.3	14.6	7.6
- 2,4-dichloro- N-methyl-	---	3.4	7.2	12.4	19.6

25. Chlorination of N-Methylaniline with Chlorine

To 200 ml of an 0.02 M solution of N-methylaniline in carbon tetrachloride was added dropwise 30 ml of an 0.02 M solution of chlorine in carbon tetrachloride. The aniline solution was stirred very rapidly during the addition. The mixture was extracted with 50 ml of 1.0 N sodium hydroxide, and the organic phase was dried over sodium carbonate and analyzed by gas chromatography. The products observed were o-chloro-N-methylaniline, 17.2%; p-chloro-N-methylaniline, 8.5%; and 2,4-dichloro-N-methylaniline, 2.3% based on starting aniline.

26. Rearrangement of N-Chloro-N-methylaniline (0.02 M) with Added N-Methylaniline in Carbon Tetrachloride at 25°C

To 100 ml of a 0.02 M solution of N-chloro-N-methylaniline in carbon tetrachloride was added 100 ml of an 0.02 M solution of N-methylaniline in the same solvent. After standing at 25°C for two hours, an aliquot, 10.0 ml, of the solution was added to a mixture of potassium iodide in 50%

acetic acid. No measureable quantity of iodine was formed. Analysis of the products by gas chromatography gave N-methylaniline, 44.0%; o-chloro-N-methylaniline, 38.8%; and p-chloro-N-methylaniline, 9.9%.

A 100 ml sample of 0.02 M N-chloro-N-methylaniline in carbon tetrachloride was added to a 100 ml solution containing 2.150 g (20.0 m mole) of N-methylaniline. The chlorinated products obtained on analysis by gas chromatography, after standing for four hours at 25°C were in the following ratio: o-chloro-N-methylaniline 92%, p-chloro-N-methylaniline 8%.

27. Rearrangement of N-Chloro-N-methylaniline (0.01 M) with N-Methylaniline Hydrochloride at 25°C

To 100 ml of 0.02 M solution of N-chloro-N-methylaniline in carbon tetrachloride was added a mixture consisting of 100 ml of 0.02 M HCl in carbon tetrachloride, and 100 ml of 0.02 M solution of N-methylaniline in the same solvent. Ten minutes after mixing the solutions, a 10.0 ml sample of the mixture was removed and added to potassium iodide in 50% acetic acid. No formation of iodine was detected. The solution was extracted with 50 ml of 0.1 N sodium hydroxide, and the organic phase was dried over sodium carbonate and analyzed by gas chromatography. The products were N-methylaniline, 46.6%; o-chloro-N-methylaniline, 35.4%; p-chloro-N-methylaniline, 15.5%.

28. Rearrangement of N-Chloro-N-methylaniline (0.01 M) with N-Methylanilinium p-Toluenesulfonate at 25°C

To a 0.344 g (2.00 m mole) of N-methylaniline, and 100 ml carbon tetrachloride was added 0.214 g (2.00 m mole) of N-methylaniline in carbon tetrachloride. Ten minutes after mixing the solutions, a 10.0 ml sample of the mixture was removed and added to potassium iodide in 50% acetic acid. There was no detectable formation of iodine. The mixture was extracted with 0.10 N sodium hydroxide solution, and the carbon tetrachloride layer was dried over sodium carbonate and analyzed by gas chromatography. The products were: N-methylaniline, 44.2%; o-chloro-N-methylaniline, 34.5%; and p-chloro-N-methylaniline, 12.1%.

29. Rearrangement of N-Chloro-N-methylaniline (0.02 M) with Silver Salts and with N-Methylanilinium Salts at 25°C

A stock solution of 1500 ml of 0.040 M N-methylaniline in carbon tetrachloride was prepared, and a 700 ml sample of it was chlorinated with calcium hypochlorite. Samples of the chlorinated aniline, 100 ml each, were placed in the following mixtures:

- A) 100 ml of stock solution, 0.344 g (2.00 m mole) of p-toluene sulfonic acid, 0.558 g (2.00 m mole) of silver tosylate. Some of the acid and probably all of the silver salt was undissolved.
- B) 100 ml of stock solution, 0.344 g (2.00 m mole) of p-toluene sulfonic acid. Some of the acid remained undissolved.
- C) 100 ml of stock solution.

D 100 ml of stock solution, 1.554 g (2.00 m mole) of silver tosylate. The silver salt remained undissolved.

E 1.177 g (1.00 m mole) of silver tosylate. The silver salt remained undissolved.

F 100 ml of stock solution and 1.30 g (2.00 m mole) of trichloroacetic acid. This was a homogeneous solution.

G 100 ml of stock solution, 1.12 g (2.00 m mole) of silver tosylate, and 1.30 g (2.00 m mole) of trichloroacetic acid. The silver salt remained undissolved.

All of the mixtures were kept at 25°C for twelve hours. They were then extracted with 100 ml of 0.1 N ammonium hydroxide, the organic phase was dried over sodium carbonate and analyzed by gas chromatography. The results are presented in table XIX. In the samples containing trichloroacetic acid and toluene sulfonic acid rearrangement was complete within five minutes.

Table XIX

Products of Rearrangement of N-Chloro-N-methylaniline with N-Methylanilinium and Silver Salts

<u>Sample</u>	<u>Per Cent of N-Methylaniline and Chlorinated Products</u>			
	N-Methylaniline	o-Chloro-	p-Chloro-	2,4-Dichloro-
A	56.5	33.0	4.7	---
B	53.0	34.1	5.3	---
C	60.5	33.7	8.4	---
D	50.5	39.4	2.5	---
E	43.4	49.0	3.1	---
F	50.0	33.1	6.7	4.2
G	46.7	32.7	6.1	3.4

--- means that less than 1.0% was found.

30. Rearrangement of N-Chloro-N-methylaniline (0.02 M) with Sodium Carbonate at 25°C

A 200 ml sample of 0.02 M N-chloro-N-methylaniline solution in carbon tetrachloride was placed in a 500 ml flask and stirred very rapidly with 10 g of powdered sodium carbonate. Aliquots (10 ml) of the solution were removed at intervals and titrated for positive halogen with standard sodium thiosulfate solution (0.0099 N). An example of the data obtained in such a titration is given below.

<u>Time (hours)</u>	<u>Titer (ml)</u>	<u>Per Cent Rearranged</u>
0	19.85	0
17	18.02	9
38	16.40	17
65	14.90	25
95	13.40	32
115	12.15	38

After 115 hours, a 50 ml sample was transferred to a mixture of 10 ml of 1.0 M potassium iodide in 50 ml of 50% acetic acid, and the iodine was neutralized with sodium thiosulfate. The titrated mixture was made basic with sodium hydroxide, and the carbon tetrachloride layer was separated. The aqueous layer was then extracted twice with 50 ml portions of n-hexane. The hexane extracts were added to the carbon tetrachloride layer and the mixture was dried over sodium carbonate and analyzed by gas chromatography. The products were: Aniline, 6.2%; N-methylaniline, 60.4%; o-chloro-N-methylaniline, 12.9%;

p-chloro-N-methylaniline 3.6% and 2,4-dichloro-N-methylaniline, 1.2%.

31. Rearrangement of N-Chloro-N-methylaniline (0.02 M) with Sodium Carbonate and N-Methylaniline at 25°C

A stock solution of 0.02 M N-chloro-N-methylaniline was prepared in hexane by the method already described for the preparation of the compound in carbon tetrachloride. Three samples, 200 ml each, of the stock solution were stirred over 4.0 g of finely powdered sodium carbonate. To sample A was added 3.43 g (32.0 m mole) of N-methylaniline, and to sample B was added 6.86 g (64.0 m mole) of the same. Sample C contained only the N-chloro-N-methylaniline solution and sodium carbonate. Aliquots of 10.14 ml of A, B, and C were transferred to a solution of potassium iodide in 50% acetic acid and were titrated with standard sodium thiosulfate solution.

A

<u>Time (mins)</u>	<u>Titer (ml)</u>
0	18.85
95	17.40
255	15.45
1250	7.15

B

<u>Time (mins)</u>	<u>Titer (ml)</u>
0	19.58
120	16.92
230	14.60
1295	3.74

C

0	20.10
165	19.90
1155	19.82
2085	15.12
2115	15.00

32. Preparation of N-Chloro-N-t-butylaniline with Calcium Hypochlorite

To 1.49 g (10 m mole) N-t-butylaniline dissolved in 25 ml of carbon tetrachloride was added 10.0 g (30 m equivs. by our analysis) of calcium hypochlorite (Baker Purified Reagent) which had been premixed with 1.0 g of water immediately before use. The mixture was stirred vigorously at 25°C for 20 minutes. It was vacuum filtered very rapidly on a Buchner funnel with Genuine Whatman #1 filter paper. The volume of the filtrate was adjusted to 25 ml to give a 0.40 M solution of N-chloro-N-t-butylaniline.

Nmr (CCl_4) τ 8.80 (s, 9); 2.50-3.00 (m, 5); High resolution spectra showed that the t-butyl proton resonance

occurred 4-5 cps upfield from that of the N-t-butylaniline. Addition of 1.00 ml of this solution to a mixture of 5.0 ml of 1.0 M potassium iodide in 20 ml of 50% acetic acid gave iodine which required 4.16 ml of 0.096 N sodium thiosulfate for complete titration or 100.0% . A careful search of the region of the spectrum 15 cps downfield from the t-butyl signal at 8.80 tau showed no evidence for any ring chlorinated t-butylanilines nor for unreacted t-butylaniline. Under the conditions of the analysis, 0.5% of any of the chlorinated anilines or unreacted N-t-butylaniline could easily have been detected. The product was prepared by the same method in benzene and o-dichlorobenzene. N-Chloro-N-t-butylaniline was also prepared in a similar manner in benzene, o-dichlorobenzene and pentane. p,N-Dichloro-N-t-butylaniline was also prepared as above.

The N-chloro-N-t-butylaniline prepared above in carbon tetrachloride was kept in a polyethylene flask at 0°C over one month. During that time samples were removed for various experiments. Nmr spectra taken of the samples before use showed no evidence for any rearranged products (less than 0.5% rearrangement could have been detected).

33. Preparation of N-Chloro-N-t-butylaniline with N-Chloro-succinimide

To 1.362 g (10.0 m mole) N-chlorosuccinimide (Aldrich 98% + purity) was added 1.49 g of N-t-butylaniline (10 m mole) in 25 ml of carbon tetrachloride, and the mixture was stirred for

18 hours at 25°C with 2.0 g of powdered sodium carbonate in a 100 ml polyethylene flask. On filtering, a 0.40 M solution (as determined by titration with standard sodium thiosulfate) of N-chloro-N-t-butylaniline was obtained which had the same nmr spectrum as that obtained from the calcium hypochlorite chlorination of N-t-butylaniline.

34. Rearrangement of N-Chloro-N-t-butylaniline in Carbon Tetrachloride at 43°C

In similarly prepared glass Carius tubes, 1.00 ml aliquots of a 0.40 M solution of N-chloro-N-t-butylaniline in carbon tetrachloride (calcium hypochlorite preparation) were degassed by repeatedly freezing and thawing at 0.01 mm pressure. The tubes were sealed and placed in constant temperature baths at 43°C and 60°C. The tubes were prepared by standing in a chromic acid bath for one hour. Then they were washed with water and baked dry at 180°C for 12 hours. Samples were removed at intervals and titrated for positive halogen with standard thiosulfate.

<u>Time (Secs x 10⁻³)</u>	<u>Titer(ml)</u>
0.00	4.22
6.00	4.15
8.70	4.18
70.8	4.02
73.8	4.10
421.4	3.82
590.2	3.40

The products obtained by nmr analysis of the samples after all of the N-chloro-N-t-butylaniline had disappeared at 43°C were:

<u>Products</u>	<u>Water-washed Glass Vessels</u>	<u>HCl Catalyzed</u>	<u>Trichloro- acetic acid Catalyzed</u>
N-t-butylaniline	5.0	3.2	2.6
o-chloro-N-t-butylaniline	83.2	89.0	84.0
p-chloro-N-t-butylaniline	6.9	4.6	5.3
2,4-dichloro-N-t-butylaniline	5.0	2.8	3.1

Samples of 3.33 M N-chloro-N-t-butylaniline in carbon tetrachloride, 0.20 ml each, were placed in nmr sample tubes and to one tube was added 0.2 ml of 0.19 N HCl in carbon tetrachloride, to the other tube was added 0.2 ml of 0.019 N trichloroacetic acid in carbon tetrachloride. Spectra were run at intervals. From the peak heights obtained for the various chlorinated species, the concentration of N-chloroaniline was determined at various times in the rearrangement as explained in the section on nmr analysis. The log of concentration of N-chloro-N-t-butylaniline versus time was a straight line for both samples. Bimolecular rate constants calculated from the data were for the HCl catalyzed sample $k_1 = 1.94 \times 10^{-5} \text{ secs}^{-1}$ and for the trichloroacetic acid catalyzed samples $k_1 = 2.02 \times 10^{-5} \text{ secs}^{-1}$.

HCl catalyzed rearrangement of 1.66 M N-chloro-N-t-butylaniline in carbon tetrachloride at 43°C:

<u>Seconds x 10⁻³</u>	<u>Per Cent of Initial Concentration</u>
0.00	94.5
2.40	88.0
6.36	82.5
11.16	75.2
12.06	72.3
12.48	71.2
18.48	62.5
26.10	51.7
29.10	52.7

Trichloroacetic acid catalyzed rearrangement of 1.66 M N-chloro-N-t-butylaniline in carbon tetrachloride at 43°C:

<u>Seconds x 10⁻³</u>	<u>Per Cent of Initial Concentration</u>
0.00	93.5
2.58	87.0
6.72	78.5
12.78	70.5
18.96	60.6
24.30	51.5

35. Rearrangement of N-Chloro-N-t-butylaniline in Benzene, o-Dichlorobenzene and Nitrobenzene

In a similar manner as that described on page 105, 1.00 ml aliquots of 0.40 M N-chloro-N-t-butylaniline were degassed, sealed in Carius tubes and placed in constant temperature

baths at 43°C and 60°C. Some of the tubes were removed at intervals and titrated for positive halogen with standard sodium thiosulfate.

Rearrangement in Nitrobenzene at 60°C of N-Chloro-N-t-butyl-aniline

<u>Time (Secs x 10⁻³)</u>	<u>Titer (ml)</u>
0.00	3.80
4.80	3.70
10.80	1.20

Rearrangement in o-Dichlorobenzene at 60°C

<u>Time (Secs x 10⁻³)</u>	<u>Titer (ml)</u>
0.00	3.60
4.80	3.20
82.80	1.30
183.60	0.20

Rearrangements in Benzene at 60°C

<u>Time (Secs x 10⁻³)</u>	<u>Titer (ml)</u>
0.00	4.10
82.8	3.95
183.6	1.40

The products obtained from these rearrangements were determined by gas chromatography and are listed in the following table.

Table XX

Per Cent Yield of Products in the Rearrangement of N-Chloro-N-t-butylaniline
in Various Solvents and at Various Temperatures

<u>Solvent</u>	<u>Temp. °C</u>	<u>ØNHR</u>	<u>o-ClØNHR</u>	<u>p-ClØNHR</u>	<u>2,4-Cl₂ØNHR</u> *
Benzene	43	11.8	66.3	7.6	8.3
benzene	60	13.0	45.0	29.0	12.8
o-Dichlorobenzene	43	11.7	34.8	51.5	7.1
o-Dichlorobenzene	60	17.3	25.3	36.8	20.2
Nitrobenzene	43	8.5	33.4	49.5	8.5
Nitrobenzene	60	8.9	32.0	50.0	8.9

* R = t-butyl

36. Effect of Glass Surfaces on the Rate of Rearrangement of N-Chloro-N-t-butylaniline

Samples of 0.10 M N-chloro-N-t-butylaniline, 1.00 ml each, in carbon tetrachloride, were placed in glass tubes which were prepared in the following manner: Eight millimeter o.d. pyrex tubing was sealed off in six inch lengths and constricted four inches from the bottom. They were kept in a chromic acid bath for one hour, then washed exhaustively with water, and finally with a 5% sodium carbonate solution. Some of the tubes were washed with distilled water to remove all sodium carbonate. Both sets of tubes were then baked for 12 hours at 180°C. The 1.00 ml samples of N-chloro-N-t-butylaniline were then placed in the tubes and degassed by freezing and thawing four times at 0.01 mm pressure. They were sealed at the same pressure and placed in a 43°C constant temperature bath. Tubes were taken out at intervals, and their contents were transferred to a mixture of potassium iodide in 50% acetic acid, and titrated with standard sodium thiosulfate solution.

<u>Water-washed Tubes</u>		<u>Sodium Carbonate-washed Tubes</u>	
<u>Time (hours)</u>	<u>Titer (ml)</u>	<u>Time (hours)</u>	<u>Titer (ml)</u>
0.0	4.25	0.0	4.42
3.5	3.65	3.5	4.35
14.0	1.25	29.0	4.40
23.0	0.80	52.0	4.40

37. Effect of Oxygen on the Rate of Rearrangement of N-Chloro-N-t-butylaniline

Aliquots of a 0.40 M solution of N-chloro-N-t-butylaniline in carbon tetrachloride, 1.00 ml each, were placed in Carius tubes which had been cleaned with chromic acid, washed with water, and then with a 5% solution of sodium carbonate and baked dry at 180°C for twelve hours. Six tubes, filled with air, were stoppered, and placed in a 60°C bath from which they were removed at intervals, their contents placed in a mixture of 20 ml of 50% acetic acid and 5 ml of 1 M potassium iodide, and titrated with standard sodium thiosulfate.

<u>Time (mins)</u>	<u>Titer (ml)</u>
0	7.05
75	5.70
105	3.90
150	1.80

To six similarly prepared tubes, 0.2 g finely powdered sodium carbonate was added, and the tubes were shaken vigorously after standing in the 60°C bath for a half hour. They were also removed for titration at intervals.

<u>Time (mins)</u>	<u>Titer (ml)</u>
0	7.00
102	5.70
1740	6.15
2340	6.00

38. Rearrangement of N-Chloro-N-t-butylaniline With Added N-t-butylaniline

A stock solution containing 4.0 ml of 0.40 M N-chloro-N-t-butylaniline, and 40 micro liters of 0.2 M trichloroacetic acid was prepared. Samples of it 1.00 ml each, were added to specially prepared nmr sample tubes, and N-t-butylaniline was added to them in the following order: Tube A, none; tube B, 5.0 micro liter; tube C, 12.0 micro liter; tube D, 30.0 micro liter. The tubes were prepared in the following manner: They were washed with 20% nitric acid in sulfuric acid, then washed with water and finally with a dilute solution of sodium carbonate (ca. 0.2% solution). They were carefully drained to leave as small a residue of sodium carbonate as possible. Then they were baked for 12 hours at 180°C. The course of the rearrangement was followed by scanning the region of the spectrum between zero and 100 cps downfield from TMS.

The results of these observations are presented in tables XXI, XXII, XXIII, XXIV.

39. Rearrangement of N-Chloro-N-t-butylaniline With Added o-Chloro-N-t-butylaniline

o-Chloro-N-t-butylaniline, 0.0524 g (0.350 m mole) was added to 0.20 ml of 1.90 M N-chloro-N-t-butylaniline in carbon tetrachloride and the volume made up to 0.40 ml with carbon tetrachloride. The sample was placed in an nmr sample tube which had been washed with water and baked dry. It was kept in a constant temperature bath at 43°C and removed at intervals for nmr spectra to be taken. Resonance signals were observed

Table XXI

Rearrangement of N-Chloro-N-t-butylaniline with 1.0 Mole
Per Cent of Trichloroacetic Acid in Carbon Tetrachloride
at 42°C

<u>Time</u> (Sec x 10 ⁻³)	<u>Molar Ratio of Chlorinated Anilines</u>			
	<u>N-Cl</u>	<u>o-Cl</u>	<u>p-Cl</u>	<u>p-Cl,N-Cl</u>
0.00	1.00	0.00	0.00	0.00
1.44	0.97	0.03	0.00	0.00
3.84	0.95	0.05	0.00	0.00
8.94	0.90	0.09	0.00	0.00
13.08	0.82	0.18	0.00	0.00
16.74	0.82	0.18	0.00	0.00
20.82	0.77	0.17	0.03	0.01
24.24	0.74	0.18	0.04	0.02
33.60	0.67	0.25	0.04	0.02
78.60	0.43	0.49	0.04	0.02
(120 hours)	---	0.94	0.06	0.00

Table XXII

Rearrangement of N-Chloro-N-t-butylaniline with 10 Mole Per Cent of N-t-Butylaniline and 1.0 Mole Per Cent of Trichloroacetic Acid at 42°C

<u>Time</u> (Sec x 10 ⁻³)	<u>Molar Ratio of Chlorinated N-t-Butylanilines</u>			
	N-Cl	o-Cl	p-Cl	p-Cl,N-Cl
0.00	1.00	0.00	0.00	0.00
1.44	0.98	0.02	0.00	0.00
4.32	0.94	0.06	0.00	0.00
9.18	0.91	0.09	0.00	0.00
13.56	0.87	0.13	0.00	0.00
17.28	0.84	0.16	0.00	0.00
21.36	0.79	0.19	0.01	0.01
24.78	0.77	0.21	0.01	0.01
34.80	0.71	0.26	0.02	0.02
80.52	0.46	0.51	0.02	0.02
(120 hours)	----	0.94	0.06	0.00

Table XXIII

Rearrangement of N-Chloro-N-t-butylaniline with 25 Mole Per Cent of N-t-Butylaniline and 1.0 Mole Per Cent of Trichloroacetic Acid at 42°C

<u>Time</u> (Sec x 10 ⁻³)	<u>Molar Ratio of Chlorinated N-t-Butylaniline</u>		
	<u>N-Cl</u>	<u>o-Cl</u>	<u>p-Cl</u>
0.00	0.985	0.015	----
1.86	0.955	0.045	----
4.56	0.93	0.07	----
9.70	0.87	0.13	----
14.08	0.83	0.17	----
17.94	0.80	0.20	----
21.76	0.75	0.25	----
25.24	0.72	0.28	----
34.78	0.64	0.36	----
80.94	0.33	0.63	0.04
(120 hours)	----	0.93	0.07

Table XXIV

Rearrangement of N-Chloro-N-t-butylaniline with 148 Mole
Per Cent of N-t-Butylaniline and 1.0 Mole Per Cent of
Trichloroacetic Acid in Carbon Tetrachloride at 42°C

<u>Time</u> (Sec x 10 ⁻³)	<u>Molar Ratio of Chlorinated N-t-Butylanilines</u>		
	<u>N-Cl</u>	<u>o-Cl</u>	<u>p-Cl</u>
0.00	1.00	0.00	0.00
1.12	0.93	0.07	0.00
4.24	0.87	0.13	0.00
9.34	0.75	0.25	0.00
13.42	0.68	0.32	0.00
17.14	0.62	0.38	0.00
21.34	0.55	0.45	0.00
24.58	0.48	0.49	0.03
33.82	0.38	0.62	0.06
78.52	0.08	0.85	0.07
(120 hours)	----	0.93	0.07

for t-butyl protons at -1.6, 3.0, 5.0, 7.4 and 9.4 cps from that of the t-butyl resonance of N-chloro-N-t-butylaniline indicating the presence of these anilines, respectively: p,N-dichloro-N-t-butyl, p-chloro-N-t-butyl, N-t-butyl-, 2,4-dichloro-N-t-butyl-, and o-chloro-N-t-butyl-. There were no other peaks present which could be attributed to o,N-dichloro-N-t-butylaniline. After all positive chlorine had been used up the products observed on analysis by nmr were:

o-chloro-N-t-butylaniline	85.5%
p-chloro-N-t-butylaniline	6.3%
2,4-dichloro-N-t-butylaniline	4.0%
N-t-butylaniline	4.0%

Under the conditions of the analysis, an absorption corresponding to less than 0.5% of the total mixture could have been identified.

40. Reaction of N-Chloro-N-t-butylaniline with p-Chloro-N-t-butylaniline

N-Chloro-N-t-butylaniline, 0.20 ml of 1.90 M solution was added to 0.0447 g (0.244 m mole) of p-chloro-N-t-butylaniline and the volume was adjusted to 0.40 ml with carbon tetrachloride. The sample was placed in an nmr sample tube which had been washed with water and baked dry. It was then kept in a constant temperature bath at 43°C. The products were identified by the positions of the t-butyl resonance signal of the various anilines and were determined quantitatively by peak height analysis. Results are presented in table XXV.

Table XXV
Per Cent of Products and Reactants in Reaction of N-Chloro-N-t-butylaniline in

Time (Sec x 10 ⁻³)	Carbon Tetrachloride at 43°C				
	ϕ_{NHR}	$\phi\text{-Cl}\phi_{\text{NHR}}$	$\text{p-Cl}\phi_{\text{NClR}}$	$\text{p-Cl}\phi_{\text{NHR}}$	$2,4\text{-Cl}_2\phi_{\text{NHR}}$
1.20	6.3	4.2	7.0	29.6	0.6
1.38	5.6	4.6	7.4	29.3	0.6
2.34	14.4	7.3	13.3	22.7	1.7
2.70	15.3	10.8	13.1	22.1	1.4
3.30	16.0	12.1	12.9	21.2	1.6
4.50	17.9	14.1	13.6	14.7	2.3
8.40	18.8	21.3	13.8	19.8	3.0
15.60	17.7	30.2	10.3	20.4	7.1
(48 hours)	13.0	48.0	0	27.2	12.0

R = t-butyl

The same analytical method was used to study the following mixtures:

Mixture	N-Chloro-N-t-butylaniline	p-Chloro-N-t-butylaniline (micro liter)
H	0.04 ml, 0.40 M	12.0
K	0.04 ml, 0.40 M	4.0
M	0.04 ml, 0.40 M	120

Mixtures H, K, and M were run in tubes that were treated with sodium carbonate. Reaction did not take place until 20 micro liter of 0.2 M trichloroacetic acid was added to each tube. Data on these studies are presented in tables XXVI, XXVII and XXVIII.

41. Rearrangement of N-Chloro-N-t-butylaniline in High Concentrations of Trichloroacetic Acid

Samples of N-chloro-N-t-butylaniline, 3.0 ml of 0.33 M solution, were added to the following quantities of a 1.0 M solution of trichloroacetic acid and the volume of the mixture was adjusted to 4.0 ml with carbon tetrachloride.

- A) 0.05 ml
- B) 0.10 ml
- C) 0.20 ml
- D) 0.50 ml
- E) 1.00 ml

The samples were placed in a 60°C constant temperature bath

Table XXVI

Time (Sec x 10 ⁻³)	Mole Per Cent of Products and Reactants in Mixture H					
	ϕNClR	ϕNHR	$\text{o-Cl}\phi\text{NHR}$	$\text{p-Cl}\phi\text{NClR}$	$\text{p-Cl}\phi\text{NHR}$	$\text{2,4-Cl}_2\phi\text{NHR}$
0.00	74.0	0.0	1.0	0.0	24.0	0.0
1.74*	74.0	0.0	1.0	0.0	24.0	0.0
3.24	62.0	11.0	1.0	11.0	15.0	0.0
5.28	57.0	16.0	2.0	16.0	9.0	0.0
6.48	56.0	16.0	3.0	16.0	9.0	0.0
8.70	54.0	16.0	4.0	16.0	9.0	0.0
14.58	51.0	16.0	7.0	16.0	9.0	0.0
72.18	31.0	15.0	29.0	12.0	11.0	3.4
97.98	26.0	15.0	34.0	10.0	10.0	4.0
116.70	20.0	15.0	38.0	11.0	12.0	4.0
120.70	19.0	14.0	40.0	13.0	13.0	4.0
185.40	16.0	13.0	44.0	8.0	14.0	5.0

* Trichloroacetic acid added after this spectrum.

R = t-butyl

Table XXVII
Mole Per Cent of Reactants and Products in Mixture K

<u>Time</u> <u>(Sec x 10⁻³)</u>	<u>o-ClϕNHR</u>	<u>ϕNHR</u>	<u>ϕNClR</u>	<u>p-ClϕNHR</u>	<u>p-ClϕNClR</u>	<u>2,4-Cl₂ϕNHR</u>
0.00	1.0	0.0	90.5	8.7	0.0	0.0
3.12	1.0	0.0	90.5	8.7	0.0	0.0
5.46*	1.0	0.0	90.5	8.8	0.0	0.0
6.00	1.5	6.2	84.7	1.5	6.2	0.0
7.98	2.9	6.7	82.0	1.6	6.7	0.0
9.72	4.7	6.6	80.0	1.9	6.9	0.0
12.72	7.4	6.9	76.7	1.8	6.9	0.0
70.32	38.0	7.4	43.5	2.7	6.2	0.8
80.76	41.7	7.7	39.8	3.1	6.8	0.9
96.12	45.8	7.5	34.5	3.1	5.8	1.7
150.30	65.0	7.6	14.7	4.7	5.0	2.7
174.12	65.3	7.6	14.6	4.7	5.0	3.0

* Trichloroacetic acid was added after this spectrum was taken.

Table XXVIII
Mole Per Cent of Products and Reactants in Mixture M

<u>Time</u> <u>(Sec x 10⁻³)</u>	<u>ØNClR</u>	<u>ØNHR</u>	<u>o-ClØNHR</u>	<u>p-ClØNClR</u>	<u>p-ClØNHR</u>	<u>2,4-Cl₂ØNHR</u>
0.00*	7.4	15.5	0.5	15.9	60.5	0.0
1.86	6.8	15.5	1.4	14.7	61.3	0.5
2.46	7.0	14.7	1.4	14.4	62.0	0.5
3.18	6.9	14.9	2.4	13.8	61.1	0.9
10.08	6.2	14.9	3.0	13.3	60.5	1.5
13.68	6.1	14.4	3.2	13.0	62.0	1.3
25.32	5.0	14.7	4.1	12.7	61.5	2.1
69.32	2.6	12.2	8.4	7.8	64.7	4.3
118.92	1.2	11.6	9.4	6.1	66.0	5.8

* Trichloroacetic acid was added before the first spectrum was taken.

R = t-butyl

and left for 24 hours. They were then extracted with 2.0 ml of 1 M sodium hydroxide. The organic layer was dried over sodium carbonate, and concentrated to a volume of approximately 1.0 ml. The products observed on analysis by nmr are listed in table XXIX.

42. Protonation of 0.2 M solutions of N-Methylaniline and Chlorinated N-Methylanilines by Trichloroacetic Acid in Carbon Tetrachloride

N-Methylaniline, 0.4300 g (4.00 m mole), was dissolved in 10.0 ml of carbon tetrachloride. Aliquots of 1.00 ml of this solution were mixed with quantities of trichloroacetic acid and the volume adjusted to 2.00 ml in the following order:

<u>Tube #</u>	<u>Quantity of Trichloroacetic Acid</u>
1	1.00 ml of a 2.0 M solution
2	0.50 ml of a 2.0 M solution
3	0.20 ml of a 2.0 M solution
4	1.00 ml of a 0.2 M solution
5	0.40 ml of a 0.2 M solution
6	0.20 ml of a 0.2 M solution
7	0.10 ml of a 0.2 M solution

Next is listed the positions of nmr absorption of the various types of protons in the molecule.

Table XXIX

Mole Per Cent of Products and Unreacted N-chloroaniline in the Rearrangement of
0.25 M Solutions of N-Chloro-N-t-butylaniline With Varying Quantities of Tri-
chloroacetic Acid in Carbon Tetrachloride at 43°C

<u>Molar Ratio of Acid</u> <u>to N-Chloroaniline</u>	<u>ØNClR</u>	<u>ØNHR</u>	<u>o-ClØNHR</u>	<u>p-ClØNHR</u>	<u>2,4-Cl₂ØNHR</u>
0.20	0.9	3.9	86.5	3.9	3.9
0.40	1.1	4.9	82.5	5.3	6.1
0.80	1.0	14.2	65.5	5.7	14.2
2.00	0.0	37.3	20.8	8.4	33.6
4.00	0.0	42.4	10.5	13.4	33.6

R = t-butyl

<u>Tube #</u>	<u>(TCA)/(NH)^d</u>	<u>Positions of Absorption^a</u>		
		<u>NH</u>	<u>ArH^b</u>	<u>CH₃</u>
1	5.0	675	453 ^c	193
2	2.5	675	451 ^c	191
3	1.0	602	440	178
4	0.5	536	426	175
5	0.2	375	410	171
6	0.1	301	404	170
7	0.05	253	400	169

a) cps downfield from TMS

b) The center of the multiplet is given. Absorption is spread over 50 cps.

c) ArH is a singlet in these samples.

d) Molar ratio of trichloroacetic acid to N-methylaniline.

In a similar experiment 0.564 g (4.00 m mole) of o-chloro-N-methylaniline was dissolved in 10.0 ml of carbon tetrachloride and 1.00 ml of the solution was added to the trichloroacetic (TCA) acid and the volume adjusted to 2.00 ml.

<u>Tube #</u>	<u>Quantity of Trichloroacetic acid</u>
2	none
3	0.10 ml of a 0.2 M solution
4	0.20 ml of a 0.2 M solution
5	0.50 ml of a 0.2 M solution
6	1.00 ml of a 0.2 M solution
7	1.00 ml of a 0.4 M solution
8	0.50 ml of a 2.0 M solution
9	1.00 ml of a 2.0 M solution

The nmr absorptions of the various types of protons are listed below.

<u>Tube #</u>	<u>(TCA)/(NH)</u>	<u>Position of Absorptions</u>		
		<u>NH</u>	<u>ArH</u> ^b	<u>CH₃</u>
2	0.0	250	406	174
3	0.05	281	406	174
4	0.10	309	412	175
5	0.25	380	415	177
6	0.50	468	420	179
7	1.00	544	430	181
8	2.50	673	453	193
9	5.0	673	457	201

a) cps downfield from TMS

b) The center of the multiplet was chosen. The multiplet was spread over 50 cps.

c) doublet J = 5 cps

p-Chloro-N-methylaniline, 0.564 g (4.00 m mole), was dissolved in 10.0 ml of carbon tetrachloride. Aliquots of 1.00 ml of this solution were mixed with trichloroacetic acid and nmr spectra were taken of the mixtures. The concentration of p-chloro-N-methylaniline in these mixtures was 0.2 M.

<u>(TCA)/(NH)</u>	<u>Position of Absorption</u>		
	<u>NH</u>	<u>ArH</u>	<u>CH₃</u>
0.0	402	212	163
1.0	570	420	182
4.0	673	447	195
10.0	685	453	202

43. Reaction of N-Chloro-N-t-butylaniline with N,N-Dimethylaniline at 43°C

A 0.2 ml sample of a 2.0 M solution of N-chloro-N-t-butylaniline solution in carbon tetrachloride was mixed with 0.80 g (0.066 m mole) of N,N-dimethylaniline and the volume of the mixture was adjusted to 0.60 ml with the same solvent. The solution was placed in a nmr sample tube and spectra were taken at intervals. The products and reactants were identified by the positions of absorption of the various alkyl groups of the various anilines in the mixture, and the quantitative analysis of them was done by measurement of their peak heights.

<u>Compound</u>	<u>Alkyl Group</u>	<u>Position of Absorbance downfield from TMS (cps)</u>
N-chloro-N-t-butylaniline	t-butyl	74.0
p-chloro-N-t-butylaniline	t-butyl	76.0
N-t-butylaniline	t-butyl	78.4
o-chloro-N-t-butylaniline	t-butyl	80.8
N,N-dimethylaniline	di-methyl	172
p-chloro-N,N-dimethylaniline	di-methyl	170
o-chloro-N,N-dimethylaniline	di-methyl	165

As was shown earlier, N,N-dimethylaniline and o-chloro-N,N-dimethylaniline had peak widths that were 2% smaller than that of N-t-butylaniline. In addition, the t-butyl resonance is caused by nine protons per molecule while that of the N,N-dimethyl group is caused by only six. To adjust for these differences, the peak heights of the t-butylanilines were

divided by 10.0 and those of the dimethylanilines were divided by 6.83. The results were the relative number of moles of reactants and products in the reaction mixture at the time of the spectrum. In the experiment just described, spectra were taken at the times listed below and peak heights were measured for the species given.

Time Sec x 10 ⁻³	Peak Heights of N-t-Butylaniline (NH) and Chlorinated N-t-Butylanilines (mm)				Peak Heights of Dimethylaniline (NND) and Chlorinated Dimethylanilines (mm)		
	<u>NH</u>	<u>p- Chloro</u>	<u>o- Chloro</u>	<u>N- Chloro</u>	<u>NND</u>	<u>p- Chloro</u>	<u>o- Chloro</u>
0.0	65	0	27	160	217	15	32
2.2	98	18	58	122	225	23	54
12.3	112	42	122	0	198	33	76

When the peak heights of the t-butyranilines are divided by 10.0 and those of the dimethylanilines are divided by 6.83 in a given spectrum, the relative number of moles of each species in solution is obtained.

Time Sec x 10 ⁻³	Molar Ratio of N-t-Butylaniline (NH) and Chlorinated N-t-Butylanilines				Molar Ratio of N,N-Dimethylaniline (NND) and Chlorinated N,N-Dimethylanilines		
	<u>NH</u>	<u>p- Chloro</u>	<u>o- Chloro</u>	<u>N- Chloro</u>	<u>NND</u>	<u>p- Chloro</u>	<u>o- Chloro</u>
0.0	6.5	0.0	2.7	16.0	33.3	2.3	4.9
2.2	9.8	1.8	5.8	12.6	34.5	3.5	8.3
12.3	11.2	4.2	12.2	0	30.3	5.0	11.6

As can be seen, the sums of the relative number of moles in each row are not equal. This is so because the instrument had to be re-tuned between spectra. To normalize these values, therefore, the sum of the relative number of moles of all the t-butylnilines was taken in each row, and the molar ratio of each species in that row was divided by it. The result obtained is the change in the relative number of moles of products and reactants in the mixture with time.

Table XXX

Molar Ratio of Products and Reactants in the Chlorination of N,N-Dimethylaniline by N-Chloro-N-t-butylaniline

Time Sec x 10 ⁻³	Molar Ratio of N-t-Butylaniline (NH) and Chlorinated N-t-Butylanilines				Molar Ratio of N,N-Dimethylaniline (NND) and Chlorinated N,N-Dimethylanilines		
	NH	p- Chloro	o- Chloro	N- Chloro	NND	p- Chloro	o- Chloro
0.0	0.25	0.00	0.11	0.64	1.32	0.09	0.19
2.2	0.33	0.06	0.20	0.41	1.15	0.12	0.28
12.3	0.41	0.15	0.44	0.00	1.09	0.18	0.42

44. Reaction of N-Chloro-N-t-butylaniline with N,N-Dimethylaniline at 43°C Catalyzed by Trichloroacetic Acid

To two 1.0 ml samples of a 0.40 M solution of N-chloro-N-t-butylaniline in carbon tetrachloride was added separately 0.178 g (0.147 m mole), and 0.654 g (0.540 m mole) of N,N-dimethylaniline. The samples were placed in nmr sample

tubes which had been washed with a dilute (ca. 0.5%) solution of sodium carbonate and baked dry. To each sample tube was added 20 micro liters of 0.2 M trichloroacetic acid in carbon tetrachloride. Spectra of the mixtures were taken at intervals, and the relative molar ratio of products and reactants were calculated in the manner described (pp 127, 128). The results are recorded in Table XXXI and XXXII. In these studies, less than 2% of any of the para chlorinated species were formed.

Table XXXI

Molar Ratios of Products and Reactants at Intervals in the
Trichloroacetic Acid Catalyzed Reaction of N,N-Dimethylaniline
and N-Chloro-N-t-butylaniline

<u>Sec</u> <u>x 10⁻³</u>	<u>ØNHR'</u>	<u>o-ClØNHR'</u>	<u>ØNClR'</u>	<u>ØNR₂</u>	<u>o-ClØNR₂</u>
0.00	0.00	0.33	9.67	3.54	0.00
1.32	0.95	0.50	8.55	2.58	0.92
1.92	1.06	0.56	8.38	2.66	0.92
2.22	1.19	0.77	8.05	2.56	1.23
2.64	1.42	1.07	7.50	2.25	1.30
3.84	1.65	1.76	6.60	1.98	1.58
6.30	1.70	1.88	6.40	1.95	1.52
6.60	1.80	2.18	6.03	1.90	1.73
7.92	1.89	2.58	5.55	1.84	1.84
9.66	1.89	2.86	5.25	1.78	1.78
11.22	1.88	3.20	4.92	1.60	2.00
13.50	1.97	3.64	4.28	1.68	2.17
15.30	2.02	3.87	4.12	1.75	2.18
16.32	2.18	4.08	3.73	1.52	1.97
17.22	1.98	4.47	3.54	1.55	2.18
20.22	2.08	4.80	3.12	1.47	2.27
22.98	2.07	5.10	2.84	1.49	2.30
28.38	2.12	5.83	2.06	1.39	2.36
32.22	2.17	6.13	1.70	1.32	2.50
final	2.25	7.75	0	1.24	2.65
R = methyl			R' = t-butyl		

Table XXXII

Molar Ratios of Products and Reactants at Intervals in the
Trichloroacetic Acid Catalyzed Reaction of N,N-Dimethyl-
aniline and N-Chloro-N-t-butylaniline

$\frac{\text{Sec}}{\times 10^{-3}}$	$\phi\text{NHR}'$	$\text{o-Cl}\phi\text{NHR}'$	$\phi\text{NClR}'$	ϕNR_2	$\text{o-Cl}\phi\text{NR}_2$
0.00	0.63	0.44	8.89	12.1	0.45
0.30	0.89	0.48	8.63	14.2	0.89
1.02	1.17	0.67	8.10	12.9	1.23
1.38	1.17	0.68	8.15	12.5	1.24
1.98	1.34	0.77	7.88	12.5	1.34
2.82	1.64	0.93	7.50	12.4	1.67
3.54	1.67	0.92	7.45	12.1	1.64
4.98	1.79	1.00	7.13	11.7	1.75
5.76	1.94	1.14	6.92	11.8	1.90
8.52	2.22	1.38	6.40	11.4	2.14
10.08	2.28	1.53	6.20	11.0	2.24
11.04	2.35	1.65	6.00	11.2	2.35
12.84	2.62	1.85	5.51	10.6	2.53
15.90	2.86	2.16	4.97	10.6	2.74
18.12	3.06	2.41	4.50	10.4	2.86
21.96	3.22	2.83	3.87	10.2	3.05
25.68	3.46	3.20	3.32	10.4	3.36
28.62	3.58	3.54	2.88	9.9	3.40
Final	4.40	5.63	0	9.3	4.27

R = Methyl

R' = t-Butyl

CONCLUSION

This study has shown that N-chloroanilines can be prepared and studied in non-protic solvents such as carbon tetrachloride, hexane and introbenzene. It has demonstrated that N-chloroanilines are intermediates in the chlorination of anilines with calcium hypochlorite, N-chlorosuccinimide, and N-chlorobenzanilide. It has shown that the ortho/para ratio of products obtained from the rearrangement of the N-chloroanilines depends on a number of factors. These factors are:

1. Variations in solvent
2. Variations in temperature
3. Variations in the type of acid used as catalyst
4. The extent of chlorination when dichlorinated products are formed
5. The presence (in the case of N-methylaniline) of added anilines
6. The concentration of acid in the medium of the rearrangement.

Therefore, by proper choice of the chlorinating conditions, it is possible to obtain either the ortho or the para isomer as the major product of a chlorination and in high yield.

The theoretical implications of this study are somewhat subtle and demand careful consideration. If one studies the current literature on electrophilic aromatic substitution, one finds many convincing references to intramolecular rearrangements. As was shown in the Introduction, these references rely

heavily on the ability of the electrophile to form a stable compound by attaching itself to the substituent of the aromatic ring rather than substituting directly into the ring (as for example in the case of N-nitroanilines), or on the ability of the electrophile to form a complex with the substituent if it has an electron rich site but no bonding orbitals (as in the case of anisole). From either the stable compound or the complex, the electrophile then proceeds into the aromatic ring, and the total process could provide overall a lower energy pathway for introduction of the electrophile into the ring than the direct attack pathway. The pi complex transition state must therefore be of lower energy than the sigma complex which would be formed by direct attack of the electrophile on the aromatic ring. The coordination of an electrophile with the oxygen of anisole has been described by Kovacic as the basis of an explanation of certain differences in the ortho/para ratios observed when toluene and anisole undergo electrophilic aromatic substitution.⁴³

The interesting assumption which many authors make explicitly or implicitly is that the presence of high ortho/para ratios (i.e., greater than statistical in Neale's discussions⁴, and greater than expected from a substituent offering the same steric inhibition to attack but no electron rich site for complexing, in the explanations of Kovacic,⁴³) is evidence of intramolecular processes. Dewar specifically states:⁴⁴ "The rearrangement of PhNRX should therefore give a much higher proportion of ortho isomer than substitution of

the corresponding aniline derivative PhNHR by X^+ . This is an interesting conclusion since it suggests a possible method for distinguishing experimentally between inter and intramolecular rearrangements. To follow this rule would lead to the conclusion that in non-polar solvents the rearrangement of N-chloroanilines is an intramolecular process and in polar solvents it becomes an intermolecular process. It is interesting that in these non-polar solvents our results have shown that the process yielding high ortho/para ratios is the transfer of the chlorine from an N-chloroaniline to an aniline. One has therefore, to conclude that the rearrangement of N-chloroanilines does not follow the pattern described for N-nitroaniline, despite the fact that the electrophiles show similar reactivities and selectivities (see the Introduction). It would be interesting to determine the cause of this unexpected behavior.

It is critical to the existence of intramolecular rearrangements (a type of reaction that apparently only N-nitroanilines of all N-substituted anilines undergo)⁶ that the pi complex is really an intermediate in electrophilic aromatic substitutions. Much of the literature on the subject has been designed to prove its existence and there is little that can be found to contradict it. Yet it is disturbing to find that the rearrangement of N-chloroanilines does not follow the pattern and an obvious first step is an examination of the pi complex theory.

An interesting aspect of this theory is that a given product may be formed either by a pi complex rate-determining

process or by a sigma complex rate-determining process and the critical difference appears to be the state in which the electrophile appears. For example, chlorination of a series of aromatics varying in relative reactivities, from chloro-benzene to mesitylene, by a factor of 1.5×10^7 has been proposed to take place by sigma complex rate-determining processes when the electrophile is chlorine in acetic acid as solvent,⁴⁵ and the same series of compounds in nitromethane with the chlorinating agent $\text{FeCl}_3 \cdot \text{Cl}_2$ complex has been proposed to proceed by a pi complex rate-determining step. The only real difference seems to be in the nature of the electrophile. It appears that in all cases where pi complex formation is proposed to be the rate determining step, that the overall reaction is too fast to make absolute rate-determinations by conventional methods.⁴⁶

Olah has shown that for mixtures of benzene and toluene chlorinated with ferric chloride-chlorine complex in nitromethane, the reaction of the electrophile with the aromatic species is not a statistical process (see table XXXIII).

Table XXXIII

First Order Dependence in Aromatics in the Chlorination of Benzene and Toluene by $\text{FeCl}_3 \cdot \text{Cl}_2$ in Nitromethane at 25°C.⁴⁵

<u>Relative Ratio Toluene/Benzene</u>	<u>Observed Relative Rate</u>	<u>Ratio of Unimolecular Rate Constants k_t/k_b</u>
1/9	1.3	11.7
1/5	2.1	10.5
1	12.5	12.5
5	67.0	13.4
9	129.0	14.3

It should be noted that when chlorine is used as the chlorinating agent in acetic acid the ratio of rate constants is 344. The products observed from the $\text{Cl}_2 \cdot \text{FeCl}_3$ complex chlorination of toluene are ortho: 63.0%, meta: 2.2%, para: 34.8%. Those obtained from the chlorination with chlorine in acetic acid are ortho: 59.8%, meta: 0.5%, para: 39.7%.

In these examples, it appears that a meta position on toluene is approximately as reactive as a position on benzene both in the sigma and pi complex rate-determining processes. Thus when 100 units of toluene are chlorinated in the pi complex (FeCl_3 catalyzed) case, $100/12.5$ or 8 units of benzene should be chlorinated. Each position on benzene should therefore account for 1.3 units which is close to the 2.2% yield of m-chlorotoluene formed. In the sigma complex case, when 100 units of toluene is chlorinated, $100/344$ or approximately 0.3 units of benzene should be chlorinated. Each position on benzene should account for 0.05 units, and the yield of 0.5% m-chlorotoluene is five times as great as would be expected.

On the next page are listed some substrate selectivities, k_t/k_b , and some positional selectivities, 2/3 (o+p/m) calculated from reports by Olah^{45,46} on the competitive chlorination and bromination of toluene and benzene.

The data shows that in the Lewis-acid catalyzed reactions which are believed to proceed by pi complex rate-determining processes, positional selectivity is in the range of 2-15 times larger than substrate selectivity, and in the sigma

<u>Reagent</u>	<u>2/3 (o+p/m)</u>	<u>k_t/k_b</u>	<u>Solvent</u>
$\text{Br}_2 \cdot \text{FeCl}_3^a$	40	7.1	nitromethane
Br_2	220	605	acetic acid
Br_2	28	36.2	50% H_2O -dioxane
$\text{Br}_2 \cdot \text{FeCl}_3^b$	36	2.3	nitromethane
Cl_2	132	344	acetic acid
$\text{Cl}_2 \cdot \text{AlCl}_3$	28	13.5	nitromethane

a) Bromine added as a solution

b) Bromine added neat.

complex cases, that the substrate selectivity is about twice as great as the positional selectivity. Proponents of the pi complex intermediate would state that this difference indicates the presence of two different types of mechanisms. But one can see (above) that the method of introduction of the reagent has an effect on the substrate selectivity, and Olah has also shown that on dilution of his bromine-ferric chloride complex in nitromethane both the substrate selectivity and the positional selectivity changes. When the concentration of FeCl_3 is 3.0 M, and Br_2 is 1.5, the ratio of rate constants, toluene/benzene is 3.6 and the yield of m-bromotoluene is 1.8, when the concentration of this mixture is decreased by a factor of thirty, the relative rate constants change to 32 and approximately one per cent m-bromotoluene is formed.

Finally, it should be pointed out that Olah's argument that there is competition for the electrophile is not good grounds for the existence of the pi complex intermediate;

the lower substrate selectivity which he correlates to pi complex stability, may just be evidence for decreased selectivity as the reagents become more reactive. Selectivity would always be observed until the reaction became completely diffusion controlled. A comparison of substrate selectivities and positional selectivities shows that substrate selectivity is high whenever positional selectivity is high (although the relationship between changes in them is not linear). This non-linearity may simply be due to artifacts of measurements, or to as yet unexplored factors such as solvent effects and different entropies of the various transition states.

Our work has shown the following:

1) Synthesis of N-Chloroanilines

N-Chloroanilines can be prepared by the reaction of anilines with N-chlorosuccinimide, N-chlorobenzanilide or calcium hypochlorite. This seems to be a general reaction for all alkyl aniline. (See section 1 of the Discussion of Results and the Appendix). Although the products of the chlorination of N-methylaniline have been reported⁴ to be ring chlorinated anilines, we have shown that N-chlorosuccinimide chlorinates N-methylaniline and N-t-butylniline exclusively on the nitrogen to yield the respective N-chloroanilines.

2) Factors Affecting the Stability of N-Chloroanilines

Solutions of N-chloroanilines in carbon tetrachloride or hexane are stable and can be stored for months at 0°C if there is no acid present in solution or on the walls of the

container, and if there is no pathway available for generating acid in the medium. In section 2 of the Discussion of Results it was shown that there are two reactions that are primarily responsible for the decomposition of N-chloroanilines. They are an acid catalyzed rearrangement of the N-chloroaniline to give ring chlorinated products, and beta elimination of hydrogen chloride to give imines.

3) Effect of Catalytic Quantities of Acids on N-Chloroanilines

In section 3 of the Discussion of Results it was shown that N-chloroanilines rearrange to give ring chlorinated anilines with catalytic concentrations of acids. Addition of sodium carbonate reduces the rate of rearrangement of N-chloro-N-methylaniline and stops the rearrangement of N-chloro-N-t-butylaniline. In section 13 it was shown that silver ion, gave product ratios that were quite different from those obtained from the rearrangement with either hydrochloric acid or trichloroacetic acid, and these in turn gave product ratios that were different from those observed when the rearrangement was catalyzed by residual acids in a pyrex vessel that was washed with water and baked dry. Apparently the conjugate base of an acid does not affect the product ratios of the rearrangement because it was shown in section 12 of the Discussion of the Results that equal concentrations of hydrochloric acid and trichloroacetic acid gave similar product ratios and rate constants for the rearrangement of N-chloro-N-t-butylaniline under the same conditions of solvent and temperature.

4) Acid Catalyzed Exchange of Chlorine Between Anilines and N-Chloroanilines

N-Chloro-N-t-butylaniline in the presence of catalytic concentrations of acids exchanges chlorine with p-chloro-N-t-butylaniline. This exchange arrives at equilibrium in carbon tetrachloride at 43°C before one per cent of the rearranged product can be formed. A similar exchange has not been observed with o-chloro-N-t-butylaniline. It was shown in section 8 of the Discussion of Results, that this exchange makes it impossible to determine whether the rearrangement observed in the presence of p-chloro-N-t-butylaniline is an intramolecular, unimolecular process or an intermolecular one.

5) Rearrangement of N-Chloroanilines with Catalytic Quantities of Acids and Added Anilines

The rate of rearrangement of N-chloroanilines can be increased by the addition of samples of the aniline from which the N-chloroaniline was prepared. It was shown in section 6 of the Discussion of Results that such rate increases could only occur if there was an intermolecular ring chlorination of the added aniline by the protonated N-chloroaniline or of the protonated aniline by the neutral N-chloroaniline. This observation did not rule out the possibility of a competing intramolecular rearrangement, because variations in the acid strength as anilines are added could also account for the results. Later experiments, however, showed (item 7 of this summary) that an alternate explanation should be proposed.

It was also shown (section 7 of the Discussion of Results) that N,N-dimethylaniline was chlorinated when it was placed in a sample of N-chloro-N-t-butylaniline undergoing rearrangement. The data also showed that chlorination of dimethylaniline was the fastest process taking place in the system. i.e., intramolecular rearrangement of N-chloro-N-t-butylaniline if it did occur was a less favored process than intermolecular chlorination of t-butylaniline. It was therefore concluded that in the presence of added anilines, the intramolecular rearrangement, if it did exist might not be detectable.

Another piece of evidence which kept alive the possible existence of an intramolecular rearrangement was the observation that p-chloro-N-t-butylaniline forms an N-chloro derivative by exchange of chlorine with N-chloro-N-t-butylaniline and is chlorinated to yield 2,4-dichloro-N-t-butylaniline. On the other hand o-chloro-N-t-butylaniline which does not form an N-chloro derivative is not ring chlorinated. This suggested that in the rearrangement with catalytic concentrations of acids and no added anilines that ring chlorination might be proceeding to a large extent by intramolecular processes.

6) Protonation of Anilines by Trichloroacetic Acid in Carbon Tetrachloride Solution

NMR studies of mixtures of anilines and trichloroacetic acid in carbon tetrachloride have shown that the anilines are protonated. It was shown in section 9 of the Discussion of Results that with high acid to aniline concentration ratios

(5.0 and over) that better than 99% of N-methylaniline and its monochlorinated derivatives are protonated. Ionization constants in the range of 1-6 were calculated for these anilines.

7) Rearrangement of N-Chloroanilines in High Concentrations of Acids

N-Chloroanilines rearrange in high concentrations of acids to give mainly para and 2,4-dichloroanilines. It has been shown that these results would not be expected (see section 10 of the Discussion of Results) if the rearrangement with catalytic quantities of acid was to any significant extent an intramolecular rearrangement of the protonated N-chloroaniline. It may be added that these results also rule out the possibility that the rearrangement might be a chlorination of the protonated aniline by the neutral N-chloroaniline. No change in the nature of the products would have been expected as the acid concentration was increased.

8) Solvent and Temperature Effects on the Rearrangement of N-Chloroanilines

The products obtained from the rearrangement of N-chloroanilines are very highly dependent on the dielectric constant of the medium. In low dielectric solvents the major product obtained in the rearrangement with catalytic quantities of acid is the o-chloroaniline. As the dielectric constant of the medium is increased, increasingly larger yields of p-chloroaniline are formed. In solvents of low dielectric constants the product ratios are highly sensitive to the temperature at which the rearrangement is carried out. These results were

taken as evidence that with catalytic concentrations, the rearrangement involves at least two molecules, an aniline and a chloroaniline.

These observations (items 1-8) rule out the possibility that the rearrangement of N-chloroanilines is an intramolecular pi complex rate-determining process. The mechanism proposed for the rearrangement of N-chloroanilines with traces of acid is the transfer of a chloronium ion from a protonated N-chloroaniline to the ring of an aniline molecule. The variation in the ortho/para ratio in forming monosubstituted products is attributed principally to differences in charge separation in the transition states for ortho and para substitution, and to differences in the activation entropies for substitution in those positions. The high degree of ortho substitution observed under some conditions of the rearrangement cannot be attributed to the intervention of intramolecular processes.

APPENDIX: INITIAL WORK ON SOME NEW SYSTEMS1. Bromination of N-Methylaniline

A 10.7 g sample of N-methylaniline (100 m mole) was dissolved in 200 ml of carbon tetrachloride and to this solution was added 20 g of finely powdered anhydrous sodium carbonate. The mixture was stirred vigorously at 25°C, and a solution of 8.0 g of bromine (100 m mole) in 200 ml of carbon tetrachloride was added to it dropwise over a period of about four hours. There was no build up of color of bromine during the addition, and at the end, addition of a sample to a mixture of potassium iodide in glacial acetic acid showed no evidence for the formation of iodine.

Gas chromatographic analysis of the solution after filtering the mixture gave three peaks with retention times of 6.0, 14.0, and 37.0 minutes. The first peak was identified as N-methylaniline by injecting a known sample of compound and observing the retention time. The other two peaks are believed to be the o-bromo-, and p-bromo-N-methylanilines. A fourth peak was expected for 2,4-dibromo-N-methylaniline but it was not observed up to 88 minutes after the injection.

It is interesting to observe that under the conditions of the analysis that the monobromo-N-methylanilines can be cleanly separated from the monochloro-N-methylanilines.

<u>Compound</u>	<u>Retention Time (minutes)</u>
N-methylaniline	6.0
o-cchloro-N-methylaniline	9.0
o-bromo-N-methylaniline (peak II)	14.0
p-chloro-N-methylaniline	21.8
p-bromo-N-methylaniline (peak III)	37.0

Column used was 12 ft. x 0.25 in. aluminum packed with 7% Versamid 900 with 50% potassium hydroxide on Chromosorb P, at 180°C and 40 cc of helium per minute.

Attempts to collect samples of the bromo-N-methylanilines by preparative gas chromatography met with failure because under conditions in which the compounds could be vaporized, (injection port temperatures of 200°C and higher) extensive decomposition took place in the instrument causing it to go out of order.

2. Chlorination of N-sec-Butylaniline

A 2.98 g sample of N-sec-butylaniline (20 m mole, Aldrich) was dissolved in 500 ml of carbon tetrachloride and stirred vigorously with 20 g of calcium hypochlorite to which 2.0 g of water had been previously added. After stirring for 15 minutes at 25°C, the mixture was filtered on a Buchner funnel, and the solution after standing for 48 hours at 25°C was analyzed by gas chromatography. A mixture of four compounds was observed which had the following retention times:

<u>Suggested Compound</u>	<u>Retention Time (minutes)</u>	<u>Relative Areas</u>
N-sec butylaniline	3.30	10
o-chloro-N-sec- butylaniline	4.75	207
p-chloro-N-sec- butylaniline	8.80	15
2,4-dichloro-N-sec- butylaniline	10.60	13

The column used was a 12 ft. x 0.25 in. aluminum packed with 7% Versamid 900 with 50% potassium hydroxide in Chromosorb P, at 210°C with 40 cc of helium per minute.

3. Preparation of N-Chloro-N-n-butyylaniline

A sample of 1.49 g of N-n-butyylaniline (10.0 m mole, Aldrich) dissolved in 50 ml of hexane was stirred for 16 minutes at 0°C with 5.0 g of calcium hypochlorite to which 0.5 g of water was previously added. The mixture was filtered on a Buchner funnel, and the filtrate after standing for 24 hours at 25°C gave a mixture of four products which were analyzed by gas chromatography at 190°C and helium flow rate of 20 cc per minute. The column used was a 6.0 ft. x 0.25 in. aluminum packed with 5% Carbowax 20 M on Chromosorb G. The suggested products, retention times and relative areas of the chromatogram are given on the following page.

<u>Compound (aniline)</u>	<u>Retention Time (minutes)</u>	<u>Relative Areas</u>
N-n-butyl-	10.0	35
o-chloro-N-n-butyl-	14.6	252
p-chloro-N-n-butyl-	35.5	30
2,4-dichloro-N-n-butyl-	38.0	35

The o/p+2,4- ratio estimated on the assumption that the compounds had equal areas per mole in the chromatogram is 3.8 .

A 20 ml sample of N-chloro-N-n-butylaniline (the above preparation) was added to 0.486 g (4.0 m mole) of N-ethylaniline and the sample was kept at 25°C for 24 hours. The products were analyzed under the same conditions as above. The estimated o/p+2,4- ratio for N-ethylaniline was 10.5 and for N-n-butylaniline 7.3 .

<u>Compound (aniline)</u>	<u>Retention Time (minutes)</u>	<u>Relative Areas</u>
N-ethyl-	5.0	108
N-n-butyl-	10.0	104
o-chloro-N-ethyl-	7.0	160
o-chloro-N-n-butyl-	14.6	155
p-chloro-N-ethyl-	17.5	15
p-chloro-N-n-butyl-	35.5	21

4. Retention Times of Some Anilines on a Carbowax Column

<u>Compound</u>	<u>Retention Time (minutes)</u>
Aniline	2.0
o-chloroaniline	3.8
p-chloroaniline	7.7
2,4-dichloroaniline	11.0
N-methylaniline	2.0
o-chloro-N-methylaniline	2.6
p-chloro-N-methylaniline	6.8
N,N-dimethylaniline	1.1
N-isopropylaniline	1.5
N-sec-butyylaniline	2.0
N-ethylaniline	1.8
N-n-butyylaniline	3.4

Column: 6.0 ft. x 0.25 in. aluminum with 5% Carbowax 20 M on Chromosorb G, at 190°C and 30 cc of helium per minute.

5. Retention Times of N-t-Butylaniline on an SE 30 Column

<u>Compound</u>	<u>Retention Time (minutes)</u>
N-t-butyylaniline	2.7
o-chloro-N-t-butyylaniline	3.7
p-chloro-N-t-butyylaniline	5.0
2,4-dichloro-N-t-butyylaniline	7.5

Column: 6.0 ft. x 0.25 in. aluminum with 5% SE 30 on Chromosorb G, at 180°C with 30 cc of helium per minute.

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